Biomechanical studies of finger extension function

Analysis with a new force measuring device and ultrasound examination in rheumatoid arthritis and healthy muscles

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ABSTRACT

Aims

The overall aim of this thesis was to further our understanding of extensor muscles and their role for hand function. The aims of the studies were:

> ➢ To develop and evaluate a new device for finger extensor force measurements.

> ➢ To evaluate ultrasound as a tool for assessment of muscle architecture.

> ➢ To determine the correlation between extensor muscle force and hand function.

> ➢ To evaluate the degree of impaired finger extensor force in rheumatoid arthritis (RA) and the correlation to impaired hand function.

> ➢ To analyse the effect of hand exercise in RA patients and healthy subjects with ultrasound and finger extension force measurements.

Method

A new finger extension force measuring device was developed and an ultrasound based method was used to be able to objectively measure the finger extension force and analyze the static and dynamic extensor muscle architectures. Measurements were made of healthy volunteers (n=127) and RA patients (n=77) during uninfluenced and experimental conditions. A hand exercise program was performed and evaluated with hand force measurements, hand function test, patient relevant questionnaires (DASH and SF-36) and ultrasound measurements.

Results

The new finger extension force measurement device was developed and then validated with measurements of accuracy as well as test-retest reliability. The coefficient of variation was 1.8% of the applied load, and the test-retest reliability showed a coefficient of variation no more than 7.1% for healthy subjects. Ultrasound examination on m. extensor digitorum communis (EDC) showed significant differences between healthy men and healthy women as well as between healthy women and RA patients. The extension and flexion force improved in both groups after six weeks of hand exercise (p < 0.01). Hand function improved in both groups (p < 0.01). The

RA group showed improvement in the results of the DASH questionnaire ($p < 0.05$). The cross-sectional area of the EDC increased significantly in both groups.

Conclusions

A new finger extension force measuring device has been developed which provides objective and reliable data on the extension force capacity of normal and dysfunctional hands and is sufficiently sensitive to evaluate the effects of hand exercise. US provide useful information about muscle architecture. A significant improvement of hand strength and hand function in RA patients was seen after six weeks of hand training, the improvement was even more pronounced after 12 weeks. Hand exercise is thus an effective intervention for RA patients, providing better strength and function.

TABLE OF CONTENTS

Till Ola, Calle och Max

1 THE CONTENT OF THIS THESIS

In this thesis, studies of the forearm muscles and their biomechanical aspects have been analysed to further our understanding about force production in healthy compared to rheumatoid arthritis muscles. In order to achieve this, a new device has been designed to measure finger extension forces, an ultrasonic examination method was developed, and the hand function has been analysed using established evaluation methods (Figure 1).

Paper I, describes the development and evaluation of a new finger extension force measurement device (EX-it). Measurement accuracy and test-retest reliability were analysed and reference values for finger extension force were collected. EX-it provides objective and reliable data on the extension force capacity of healthy and rheumatoid hands.
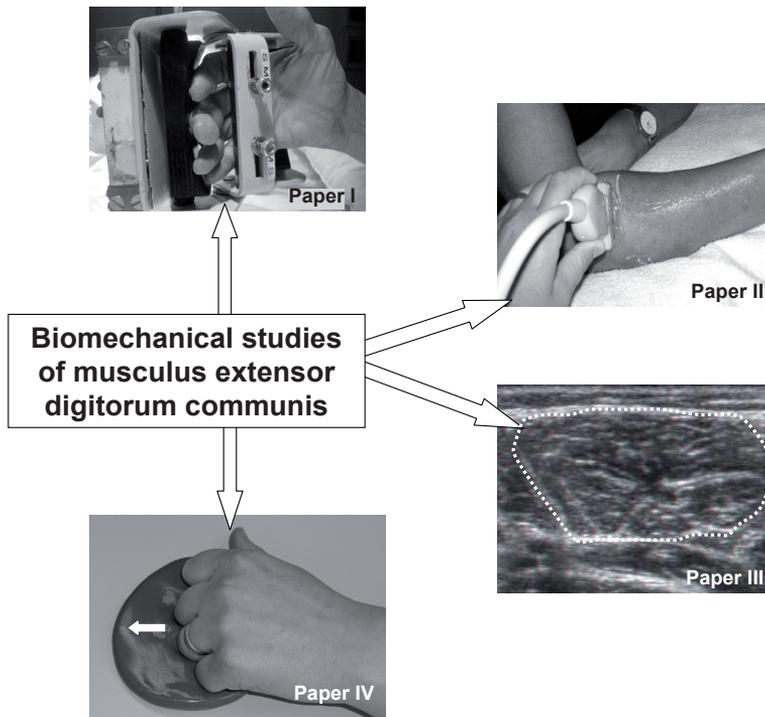
Figure 1. *Illustrations from the four studies in this thesis, (I) Finger extension force measurements on a patient with rheumatoid arthritis. (II) Ultrasound examination of m. extensor digitorum communis. (III) The dotted area is the cross-section area of m. extensor digitorum communis. (IV) One of the hand exercise movements performed with therapeutic training putty.*

Paper II, describes the usefulness of ultrasound as an examination tool for muscle architecture assessment. Muscle architectures/parameters that impact force development were identified and examined. These parameters were scrutinized and correlated to finger extension force capacity using EX-it.

Paper III, describes the differences found between healthy and rheumatoid arthritis (RA) patients in terms of the finger extension force capacity and muscle architecture for the m. extensor digitorum communis (EDC) using EX-it and US.

Paper IV, explores the usefulness of new examination techniques (ultrasound and finger extension force measurements) and established evaluation methods for evaluating hand exercise in RA patients and in healthy controls. Ultrasound and finger extension force measurements are sensitive enough to detect changes in force production and muscle function. These new methods can be used to evaluate the effects of hand exercise. A significant improvement of hand strength and hand function was seen already 6 weeks after the exercise program.

Some additional data, not previously presented, have been included in the results and discussion sections of this thesis.

1.1 List of papers

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I.   Brorsson S, Nilsdotter A, Sollerman C, Baerveldt A-J, Hilliges M. A new force measurement device for evaluating finger extension function in the healthy and rheumatoid arthritis hand. Technology and Health Care 2008; 16: 283-292.

II. Brorsson S, Nilsdotter A, Hilliges M, Sollerman C, Aurell Y. Ultrasound evaluation in combination with finger extension force measurements of the forearm musculus extensor digitorum communis in healthy subjects. BMC Medical Imaging 2008; 3: 8:6.

III. Brorsson S, Hilliges M, Sollerman C, Aurell Y, Nilsdotter A.. Extensor muscle force measurements and muscle architecture in rheumatoid arthritis patients. Submitted.

IV. Brorsson S, Hilliges M, Sollerman C, Nilsdotter A. A six weeks' hand exercise programme improves strength and hand function in rheumatoid arthritis patients. Accepted in Journal of Rehabilitation Medicine 2008.

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2 DEFINITIONS AND ABBREVIATIONS

Accuracy – the accuracy of a measurement device is composed of the repeatability and a deterministic error called bias. The bias can, in principle, be determined and corrected by careful calibration (Doebelin 1990).

Agonist – is considered to be the muscle that is primarily involved for producing joint motion or maintaining a posture (Smith 1996).

Antagonist – is a muscle that possesses the opposite anatomic action to the agonist (Smith 1996).

Biomechanical – the applications of mechanical knowledge about the human body's structure, functions and physics of movement. Biomechanics focuses on the effects of forces on the human body; especially concerning the muscles, and functioning of a particular body part, e.g. the extensor muscles in the forearm (Fung 1993).

Hand function – the ability to use the hand in daily activities. This term encompasses grip force, range of motion, sensation and motivation (Dellhag and Bjelle 1995).

Extremity specific indicators – health indicators (values) that are valid and reliable for the healthy and for patients with a variety of disorders. In this thesis, extremity specific indicators for the upper extremity were established (Atroshi, Gummesson et al. 2000).

Force – in this thesis force means the amount of power a muscle can produce and something that can be measured.

Generic indicators – General health indicators that are valid and reliable for patients with a variety of disorders, as well as for the general population (Sullivan, Karlsson et al. 1995).

Inter-observer agreement – measures variation occurring between several observers (Streiner and Norman 1995).

Intra-observer agreement – measures variation occurring from a single observer as a result of more than one exposure (Streiner and Norman 1995).

Micro-level – muscle architectural parameters that can not be seen without a microscope (Blazevich, Gill et al. 2007).

Macro-level – muscle architectural parameters that can be observed *in vivo* with the help of ultrasound or magnetic resonance imaging (Blazevich, Gill et al. 2007).

Non-invasive methods – Investigative methods that do not break the skin or enter an orifice of the body.

Reliability – the consistency of a measurement with a technique yielding the same results on repeated administrations (Streiner and Norman 1995).

Repeatability – the repeatability is the comparison of two or several measurements of the same individual under the same experimental setup (Doebelin 1990).

Test-retest reliability – a measure of consistency with which a technique yields the same results on repeated administrations (Hammer and Lindmark 2003).

Validity – the assertion that the measured parameter has bearing on the question under investigation (Streiner and Norman 1995).

ACR	AMERICAN COLLEGE OF RHEUMATOLOGY
ADL	ACTIVITIES OF DAILY LIVING
ASHT	AMERICAN SOCIETY OF HAND THERAPISTS
CSA	MUSCLE CROSS-SECTION AREA
CV	COEFFICIENT OF VARIATION
DASH	DISABILITY ARM SHOULDER HAND (EXTREMITY SPECIFIC QUESTIONNAIRE)
EDC	MUSCLE EXTENSOR DIGITORUM COMMUNIS
EX-IT	FINGER EXTENSION FORCE MEASUREMENT DEVICE
GAT	GRIP ABILITY TEST
MCP-JOINTS	METACARPOPHALANGEAL-JOINTS
MCT	MAXIMAL CONTRACTION TIME (FROM START TO FULL CONTRACTION)
RA	RHEUMATOID ARTHRITIS
ROM	RANGE OF MOTION
SD	STANDARD DEVIATION
SF-36	SHORT FORM 36-ITEM HEALTH SURVEY
US	ULTRASOUND
VAS	VISUAL ANALOGUE SCALE

3 BACKGROUND

Hand function requires interaction of muscles, tendons, bones, joints and nerves. The unique construction of the hand provides a wide range of important functions such as manipulation, sense of touch, communication and grip strength (Schieber and Santello 2004). The hand is used in many ways, and in many different situations in our daily lives; so injuries, diseases or deformities of the hand can affect our quality of life. Several of our most common diseases affect hand function. Therefore, it is very important to understand how healthy and diseased hands work in order to be able to design optimal rehabilitation strategies pursuant to hand injury or disease.

There are many different methods used today for evaluating hand and finger functions. One widely accepted method that provides an objective index of the hand and finger functions is hand force measurement (Balogun, Akomolafe et al. 1991; Innes 1999; Incel, Ceceli et al. 2002). The measurements used up to now, however, do not measure the entire range of aspects needed both for diagnostic and intervention evaluation purposes. There is also a potential for using modern non-invasive methods such as ultrasound and finger extension force measurements, but these have not been completely explored so far. In the present thesis, method development has been pursued in order to create a broader arsenal of assessment methods for hand function with special emphasis on the extensor muscles. An important factor in developing grip force is the synergy between the flexor and extensor muscles. The extensor muscles are active when opening the hand, which is necessary for managing daily activities (Fransson and Winkel 1991). Even though the extensor muscles are important for optimal hand function, surprisingly little attention has been focused on these muscles. It has, however, been difficult to evaluate hand extension force, since there is no commercially available measurement instrument for finger extension force. In addition, because of the lack of a device to assess extension force, there is limited basic knowledge concerning different injuries and how diseases affect the static and dynamic forearm muscle architecture or/and muscle interaction.

Impaired grip ability in certain diseases such as Rheumatoid Arthritis (RA) could be caused by dysfunctional extensor muscles leading to inability to open the hand (Neurath and Stofft 1993; Vliet Vlieland, van der Wijk et al. 1996; Bielefeld and Neumann 2005; Fischer, Stubblefield et

al. 2007). Deformities of the MCP-joints are common, and may lead to flexion contractures and ulnar drift of the fingers. Weak extensor muscles may play a role in the development of these hand deformities. Furthermore, knowledge concerning how the muscles are influenced by RA and the mechanism of muscle force impairments is not fully understood for RA patients. This group of patients would benefit from further hand/finger evaluation methods. We have therefore chosen to use this group of patients as a reference target group.

3.1 Biomechanics of the hand

It is important to understand the biomechanics of the hands and fingers as well as the muscle architecture and structure in order to develop new evaluation methods for finger extension force. The construction of the hand is quite complicated, including 29 joints, 27 bones and more than 30 muscles and tendons working together for range of motion (ROM), performing perception and force production (Figure 2).
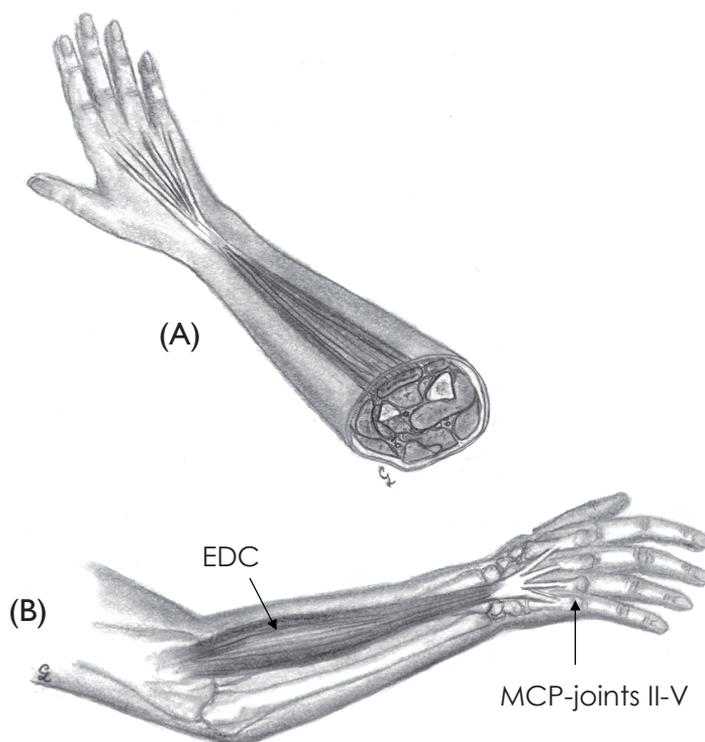
Figure 2. (A). Illustrates the cross-sectional view of the forearm. (B). This thesis placed a special focus on the extensor muscle EDC and the MCP-joints.

3.1.1 The construction of the hand

The metacarpophalangeal (MCP) joints II-V are condyloid joints that allow for movement in two planes, flexion/extension or adduction/abduction. The ROM in the joints is approximately 30–40 degrees extension, 70–95 degrees flexion and 20 degrees adduction/abduction. Ligaments connect the bones and provide stability of the joints; in the hand there are numerous ligaments that stabilize the joints. To provide stability to the metacarpal bones, there are ligaments working in conjunction with a thick tissue located in the palm (the palmar aponeurosis).

Muscles that control the hand and have their origin located near the elbow are called the extrinsic muscles. The tendons of these muscles cross the wrist and are attached to the bones of the hand. The large muscles that bend (flex) the fingers originate from the medial aspect of the elbow. The large muscles that straighten (extend) the fingers originate from the lateral aspect of the elbow. The extrinsic muscles are responsible for powerful grip ability.

In addition to these large muscles, there are smaller muscles in the hand, intrinsic muscles, that flex, extend, abduct (move outwards) and adduct (move inwards). The agonist for extension in fingers II–V is the muscle extensor digitorum communis (EDC) (Figure 3). This muscle originates at the lateral epicondyle of humerus; the muscle is connected to phalanges II–V by four tendons, which glide over the MCP-joints articulations. The tendons divide into three parts. The main part is attached to the extensor hood and two collateral ligaments are attached at the lateral and medial parts of the fingers. The extensor hood covers the whole phalange and is formed from the extensor digitorum tendon and fibrous tissue. The extension ability in the MCP-, proximal interphalangeal-, and distal interphalangeal-joints are produced by EDC, interossei and lumbricales muscles (Smith 1996; Marieb 1997).

Figure 3. *Illustrates finger extension that is primarily performed by the EDC.*

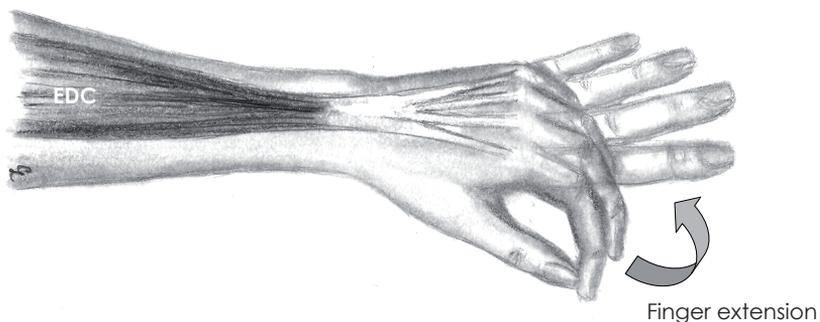Finger extension force is dependent on the wrist position. However, at the present time there is no consensus for the optimal wrist angle for finger extension force measurement. Researchers believe that a wrist position between 10-30 degrees is suitable for finger extension measurements (Li 2002).

3.1.2 Muscle force

The forces a muscle can produce depend on many factors such as the muscles' structure, muscle architecture, muscle-nerve interaction and physiological aspects. This thesis focuses mainly on how the muscle structure, at macro level, affects the forces produced. A brief overview of the micro architecture level and muscle control are described in this chapter.

The skeletal muscles have four behavioural properties, extensibility, elasticity, irritability and the ability to develop tension. Extensibility and elasticity provide muscles the ability to stretch or to increase in length and to return to normal length after stretching and these properties provide a smooth transmission of tension from muscle to the bones. The muscle's ability to respond to stimuli, irritability, provides the capability to develop tension. The tension that muscles provide has also been referred to as contraction, or the contractile component of muscle function. The tension that a muscle can develop affects the magnitude of the force generated, the speed, and length of time that the force is maintained; all these parameters are influenced by the muscle architecture and function of the particular muscle.

The manner in which the muscles are constructed and controlled contributes to muscle force production. The force that a muscle generates is also related to the velocity of muscle shortening, such as the force-velocity relationship, length-tension relationship, stretch-shortening cycle and electromechanical delay (Wickiewicz, Roy et al. 1984; Brand 1993; Fitts and Widrick 1996; Kanehisa, Ikegawa et al. 1997; Debicki, Gribble et al. 2004; Hopkins, Feland et al. 2007).

Macro-architecture

Muscle architecture has been studied by muscle-imaging techniques such as magnetic resonance imaging and ultrasound (US), and research has shown that there are numerous variations in the muscle architecture (i.e. fibre length, pennation angle, cross-sectional area (CSA), muscle volume etc.) within and between species. The architecture of a skeletal muscle is the macroscopic arrangement of the muscle fibres. These are considered relative to the axis of force generated (Otten 1988; Blazevich and Sharp 2005). The arrangements of muscle fibres affect the strength of muscular contraction and the ROM which a muscle group can move a body seg-

ment. It is important to understand the impact of muscle architecture parameters in order to design effective interventions for disease, injury rehabilitation, as well as for athletic training and exercise, especially considering the results of adaptation to physical training.

The pennation angle is the angle between the muscle fibre and the force generating axis (Figure 4). Early researchers have reported greater pennation angles in subjects that practice weight training compared to untrained subjects. It has been claimed that increase in pennation angle is biomechanically important since more tissue can attach to a given area of tendon, and slower rotation of the muscle fibre during contraction is possible through a greater displacement of the tendon, thus generating more force (Aagaard, Andersen et al. 2001; Kawakami, Akima et al. 2001). Fascicle length (muscle fibre) can be of importance for the biomechanics of the muscles, the change in fascicle length has been reported to have impact on high-speed force generation (Fukunaga, Ichinose et al. 1997). The fascicles containing a greater number of sarcomeres in series and generate force over
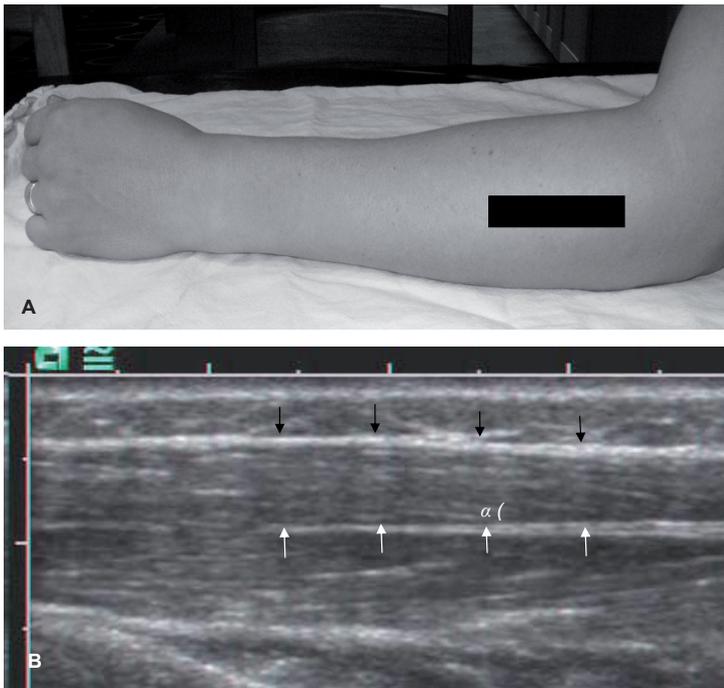
Figure 4. *(A) The black rectangle shows the position of the US probe during pennation angle measurements. (B) The longitudinal US image showing the superficial aponeurosis (black arrows), the deep aponeurosis (white arrows) and the pennation angle (α).*

longer ranges of motion and longer fibres also possess greater shortening speeds. The fascicle length can be estimated from the muscle thickness and the pennation angle (Figure 5), using equation (I);

(I) *Fascicle length = muscle thickness* $\times \alpha^{-1}$ (Ichinose, Kawakami et al. 2000).

From experimental studies, it has been claimed that the physiological cross-sectional area (PCSA) of a muscle is the only architectural parameter that is directly proportional to the maximum tetanic tension generated by the muscle. Powell etal (1984) used equation (II) for calculating the PCSA (Powell, Roy et al. 1984).

(II) $PCSA \ (mm^2) = \dfrac{muscle \ mass \ (g) \times \cos \ (\alpha)}{\delta \ (g/mm^3) \times fiber \ length \ (mm)}$, where α = pennation angle and

δ = muscle density (1.06).

Theoretically, the PCSA represents the sum of all CSA of the muscle fibres inside the muscle. The design of the muscles in terms of pennation angle,
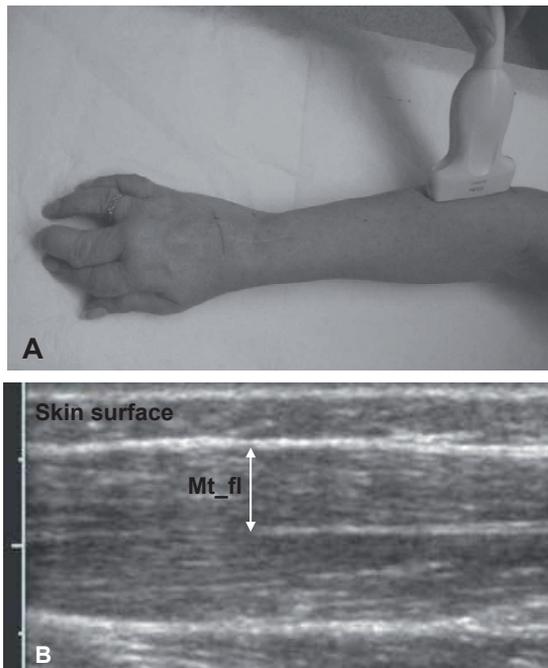
Figure 5. *(A) Position of the probe for ultrasound measurements of the EDC. (B) Longitudinal US image obtained at the measurement position. The fascicle length was estimated from the muscle thickness, defined as the distance between the subcutaneous tissue-muscle interface and the inter-muscle interface (Mt_fl) (indicated by the double-headed arrow) and the pennation angle.*

fibre length and PCSA reflects the muscles' capacity to develop force. Although each muscle is unique in architectural design, a number of generalizations have been made on the lower extremity muscles. For example quadriceps muscles are designed with high pennation angles, large PCSA and short muscle fibres, and this design is suitable for large force production. The same design pattern can be observed in the upper extremity, and the flexor muscles structure predicts that they generate almost twice the force as the extensor muscles (Lieber and Friden 2000).

To summarize: the research about muscle architecture and adaptation to speed and strength exercises shows that muscle architecture is plastic and can respond to exercise, although more research is required to fully understand the impact of varying methods of strength and speed training. To fully understand the adaptation of muscle architecture to all forms of interventions would require a formidable research effort. Surprisingly little research has described changes of muscle architecture when aging, despite that aging is associated with significant sarcopenia. Previous research has claimed that pennation angle and fascicle length were significantly smaller in older than younger individuals in some muscles such as m. soleus, m. gastrocnemius medialis and lateralis (Kubo, Kanehisa et al. 2003; Narici, Maganaris et al. 2003; Morse, Thom et al. 2005), but there were no age related changes in m. triceps brachii and m. gastrocnemius medialis concerning pennation angles for women (Kubo, Kanehisa et al. 2003). Furthermore, little research has been done concerning how muscle architecture adapts to disuse or diseased muscles, which is very important from a rehabilitation perspective. Kawakami et al. (2000) investigated changes in the muscle parameters fascicle length, pennation angle and CSA in m. triceps brachii and m. vastus lateralis after 20 days of bed rest. They found no significant changes in fascicle length and pennation angle even though there was a significant reduction of the CSA (Kawakami, Muraoka et al. 2000). Other researchers have reported decreased muscle size, muscle strength and decreased pennation angles after bed rest (Akima, Kuno et al. 1997; Narici and Cerretelli 1998; Kawakami, Akima et al. 2001). It has been claimed that one explanation for the different adaptations of muscle architecture in different disused muscles (due to bed rest) is that the changes depends on the individual muscle actions.

Micro-architecture

The skeletal muscles have a wide range of variations in size, shape, and arrangement of fibres. Skeletal muscles are composed of muscle fibres that are bundled together in fascicles, the fascicles are composed of about 200 muscle fibres.

Each muscle fibre is surrounded by the endomysium, which is connected to muscle fascia and tendons. The muscle fibres are formed by myofilaments, comprised of myofibrils. A contractile myofibril is composed of units, sarcomeres (Smith 1996; Marieb 1997). By using electron microscopy researchers have observed the muscle structure (ultra-structure) and structures such as sarcomeres, actin and myosin were analysed (Alberts 2002). These structures have become the basis of the theory of sliding filaments during muscle contraction and later to the Cross-bridge theory, which has become the accepted paradigm for muscle force production (Huxley 1954; Huxley 1957; Huxley and Simmons 1971).

Muscle control

Muscles allow us to move our joints, to apply force and to interact with our world through action. Muscles are important for us because they have the unique ability to shorten, and to do that with enough force to perform movements. Muscle fibres are arranged into functional groups; there, all fibres are innervated by one single motor neuron; these groups are called motor units. Movements that are precisely controlled such as the finger movements are produced by motor units with small numbers of fibres (Kandel, Schwartz et al. 1991).

When a muscle fibre is activated by a motor nerve impulse, the actin and myosin filaments in the sarcomere connect strongly to each other, pulling the filaments together. Sarcomeres are arranged in long chains that build up the muscle fibre, so when the sarcomeres contract, become shorter, the whole fibre becomes shorter. To be able to produce force the muscle must be innervated by a motor neuron, and the excitation-contraction coupling is along the whole fibre length simultaneously through the T-tubule system. This leads to rapid release of calcium ions from the sarcoplasmic reticulum. When the contraction signal ends, the calcium is driven back to the sarcoplasmic reticulum through ATP-driven calcium pumps (Kandel, Schwartz et al. 1991) .

Increase in neuromuscular function and muscle strength is attained when the load intensity exceeds that of the normal daily activity of the individual muscles (Hellebrandt and Houtz 1956; Karlsson, Komi et al. 1979). Increase in muscle performance at the beginning of strength training can be explained by physiological and neural adaptation, such as effective recruitment of motor units and reduction of inhibitory inputs of the alpha motor neurons (Hakkinen, Malkia et al. 1997). Several researchers have reported that muscle hypertrophy occurs after 6–8 weeks of strength training and that a certain level of muscle strength is needed to prevent a decline in functional capacity (Nygard,

Luopajarvi et al. 1988; Sale 1988; Kannus, Jozsa et al. 1992). Inactivity or decrease in physical activity leads to loss of muscle strength and a decrease in neuromuscular performance, this has been observed for patients with arthritis (Hakkinen, Hannonen et al. 1995). Some researcher claim that, during the early phase, muscle force production after exercise is more related to improved innervations than increased CSA (Blazevich, Gill et al. 2007).

3.2 Non-invasive evaluation methods

In this thesis, the effect of both the static and dynamic muscle architecture and the ability to produce force is studied in the extensor muscle EDC in healthy subjects and RA patients; either as physical performance or self-reported function (Figure 6). There are different evaluation methods available to evaluate muscle architecture, force production and hand function.

3.2.1 Grip force measurements

Hand force is an important factor for determining the efficiency of interventions such as physiotherapy and hand surgery. Hand force/grip strength is widely accepted as providing an objective measure of the hand function (Balogun, Akomolafe et al. 1991; Incel, Ceceli et al. 2002) and measurements of grip force have been used to evaluate patients with upper extremity dysfunction. However, measurements have mainly been made of the flexion force and pinch force. Even though flexion forces represent only 14 % and tripod pinch grip only 10 % of all daily hand grip activity (Adams, Burridge et al. 2004). Surprisingly little measurements have been made of the finger extension force, despite the fact that extension force is im-
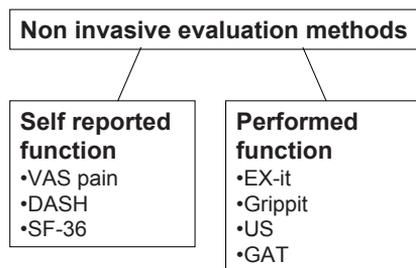
Figure 6. In this thesis non-invasive methods were used to evaluate hand function and hand force. Using self-reported function, the participants reported their pain level using the visual analogue pain scale (VAS pain) and filled in two patient-reported questionnaires, DASH and SF-36. The hand function was measured using two force measurement devices EX-it (finger extension force) and Grippit (flexion force), Ultrasound (US) was used for measuring the muscle architecture and the GAT was used for measuring the grip ability.

portant in developing grip force. Furthermore, it has been difficult to eva-luate hand extension force impairment, since no commercially available measurement instrument for finger extension force exists. Some research instruments have been designed. However they are complicated, with little clinical potential and do not have the ability to measure both whole hand extension force and single finger extension forces (Kilgore, Lauer et al. 1998; da Silva 2002; Li, Pfaeffle et al. 2003).

Hand grip measurements have been seen to be a responsive measure in relation to hand pain and correlate well with patients' overall opinion of their hand ability; these measurements provide a quick evaluation of patient's progress throughout treatment (Incel, Ceceli et al. 2002; Adams, Burridge et al. 2004). Grip force is influenced by many factors including fatigue, time of day, hand dominance, pain, sex, age and restricted mo-tion. Intrestingly, the synergistic action of flexor and extensor muscles is an important factor for grip force production (Richards, Olson et al. 1996; Incel, Ceceli et al. 2002). It is widely accepted that grip and pinch force measurements provide an objective index of the functional integrity of the upper extremity. Today there are devices for measuring some grips, such as Jamar™, Grippit™, MIE digital power and pinch grip analyser™ and Pin-chmeter™ (Nordenskiold and Grimby 1993; Lagerstrom and Nordgren 1998; Mitsionis, Pakos et al. 2008).

Severe weaknesses in RA patients' grip forces have been reported by several authors. Nordenskiöld et al. (1993), reported reduced flexion force for RA women compared to healthy controls using the Grippit device. Furthermore, Nordenskiöld (1997) reported a relationship between sig-nificant grip force and daily activities (Nordenskiold and Grimby 1993; Nordenskiold 1997). The activity limitations in relation to grip force and sex after 3 years of RA has been claimed to be lower for women than for men. The authors concluded that this result may be explained by reduced grip force rather than sex (Thyberg, Hass et al. 2005). Fraser et al. (1999) reported weakness in three different grip types using an MIE digital power and pinch grip analyser. They measured flexion force, pinch force and tri-pod force. They also measured forearm parameters which they expected to be relevant for producing forces, such as hand and forearm volume. They could however not find any significant differences between healthy and RA parameters (Fraser, Vallow et al. 1999). Buljina et al. (2001) reported the effectiveness of hand therapy for RA patients. They evaluated grip strength with the measuring device called Jamar 1113 (Sammons-Preston, Jackson, MI), then they analysed the tip-to-tip pinch, palmar pinch, key pinch, range of motions in the MCP-joints while pain in the hands was measured

by a visual analog scale (VAS). They reported the effectiveness of therapy and that the RA patients significantly increased their hand force (Buljina, Taljanovic et al. 2001). Jones et al. (1991) reported that RA patients hand force was 75 % lower than healthy subjects (Jones, Hanly et al. 1991). Even though hand exercises are used frequently for keeping and preventing loss of grip force for RA patients, only few studies have evaluated the result of grip improvement (Hoenig, Groff et al. 1993). Adams et al. (2004) reported flexion and tripod force recorded by an MIE digital grip analyser, hand function was evaluated with the Grip ability test (GAT) and the patient's questionnaire Disability Arm Shoulder Hand (DASH). They concluded that grip force was significantly correlated to self-reported assessment and hand function (Adams, Burridge et al. 2004).

3.2.2 Ultrasound examination

Ultrasound technology provides new and exciting possibilities to non-invasively access physiological mechanisms inside the living body, both at rest and during muscle contraction. Ultrasonic devices collect sound waves that are emitted by a probe after reflecting off the body's internal tissues; this provides detailed images of the body structures. The recent developments of the probes have enabled the use of US to examine the joint and surrounding soft tissues such as the muscles. The increasing interest for US among rheumatologists contributes to the understanding of the natural history of rheumatic diseases, and US is today important in the early diagnosis of RA (Kane, Balint et al. 2004; Grassi, Salaffi et al. 2005) .

US has been used in several studies to provide *in vivo* information about the muscle architecture of different muscles. Zheng et al. (2006) combined US with surface electromyography for evaluating changes in muscle architecture after using prosthetics (Zheng, Chan et al. 2006). US has also been used to study the differences between men and women regarding muscle parameters such as muscle pennation angles and muscle fascicle length (Kubo, Kanehisa et al. 2003)

US allows for dynamic studies of muscle architecture, Fukunaga et al. (1997) have developed a method to study the fascicle length during contraction (Fukunaga, Ichinose et al. 1997).

Furthermore, US has been used to analyse the muscle architecture's response to age, the authors concluded that some muscles in the lower extremities decreased in thickness with aging but the fascicle length did not decrees with aging (Kubo, Kanehisa et al. 2003). Loss of muscle mass with aging has been reported to be greater in the lower extremities than in the upper extremities. Decreases in CSA of the muscles have been reported to

be 25-33 % lower in young compared to elderly adults (Narici, Maganaris et al. 2003). However, several researchers have reported decreased muscle strength but not decreased CSA, so the force, expressed per unit of muscle CSA, has been reduced in older individuals (Young 1984; Macaluso, Nimmo et al. 2002; Narici, Maganaris et al. 2003). US has been applied to the rotator cuff muscles to analyse the dynamic contraction pattern of these muscles to confirm the neuromuscular intensity (Boehm, Kirschner et al. 2005). Fukunaga et al. (1997) used US to measure muscle architecture and function in human muscles. They pointed out that the use of cadavers for studies of architecture and modelling of muscle functions would result in inaccurate and, in some cases, misleading results (Fukunaga, Kawakami et al. 1997). Aagaard et al. (2001) used US to measure the response to strength training and the changes in muscle architecture. They concluded that the quadriceps muscle increased both its CSA and the pennation angle after heavy resistance training (Aagaard, Andersen et al. 2001). Rutherford and Jones (1992) did not find any increased pennation angles after resistance training, even though they reported increased CSA and muscle force in the quadriceps muscle (Rutherford and Jones 1992). US studies have also been performed on human skeletal muscles to explore the changes in muscle architecture that occur during dynamic contractions. The authors found that at a constant joint angle, the fascicle length and the pennation angles changed significantly during muscle contraction (Reeves and Narici 2003).

3.2.3 Function test evaluation

The Grip Ability Test (GAT) is designed for individuals with RA; it measures ADL ability. The test is based on three items chosen to represent different daily grip types. The test is performed following a standardized protocol consisted of three items: to put a "sleeve" (Flexigrip™ stocking) on their non-dominant hand, place a paper clip on an envelope and pour 200 ml into a cup from a 1 litre water jug. GAT is a reliable, valid and sensitive ADL test (Dellhag and Bjelle 1995). Hand function has been assessed by GAT for measuring grip ability and activity limitations in several studies. Dellhag et al. (1992) reported that RA patients have improved their hand function after just 4 weeks of hand exercise (Dellhag, Wollersjo et al. 1992). Bjork et al. (2007) showed significant differences in activity limitations between healthy controls and RA patients in there study using GAT (Bjork, Thyberg et al. 2007). The relationship between self-reported upper limb function and grip ability was studied in an early rheumatoid population by Adams et al. (2004). They reported correlation between GAT and the questioner DASH (Adams, Burridge et al. 2004). Dellhag et al. (2001) reported in

their study that patients with RA that have good hand function, low GAT score, displayed normal or increased safety margin during precision grip-lift compared to healthy controls (Dellhag, Hosseini et al. 2001).

3.2.4 Questionnaires

Self-administered questionnaires are recommended for evaluating functional disability from the patients' perspective (Guillemin 2000; Liang 2000). The hand function is affected early on in RA and can be evaluated with different methods. One widely used selfadministrated extremity-specific questionnaire is the Disability of the Arm, Shoulder and Hand (DASH) that is been reliable and validated for assessing upper limb functional ability in the RA population (Atroshi, Gummesson et al. 2000). DASH has been used for evaluating the effectiveness of patient-oriented hand rehabilitation programmes, and has shown significant differences between two rehabilitation programmes and surgery (Gummesson, Atroshi et al. 2003; Harth, Germann et al. 2008). Furthermore, DASH has been used by Solem et al. (2006) for evaluation of long-term results of arthrodesis (Solem, Berg et al. 2006). Adams et al. (2004) showed in their study that DASH was useful to evaluate the relationship between upper limb functional ability and structural hand impairment (Adams, Burridge et al. 2004).

Another commonly used generic questionnaire for evaluating functional disability in people is the Short Form 36-item Health Survey (SF-36), there a validated Swedish version has been developed (Sullivan, Karlsson et al. 1995). Generic healthy status measurements are commonly used for evaluation of RA patients. SF-36 has been used to detect the treatment effect in the study outcomes. Furthermore, use of SF-36 permits comparisons of physical and mental aspects in the RA population, as well as comparison between patients with RA, other patients groups and the general population (Tugwell, Idzerda et al. 2007). SF-36 has been used in several studies to evaluate the clinical outcome and quality of life after arthroplasty, and concluded the health status and the overall physical functions with significant improvements for RA patients (Angst, John et al. 2005; Ringen, Dagfinrud et al. 2008; Uhlig, Heiberg et al. 2008).

3.2.3 Perceived pain level

Visual analog scale (VAS) pain is a method frequently used to measure perceived pain level and the impact that high pain levels have on functional disability. Decreased functional ability in patients with RA has been reported correlated with on disease activity, disease duration, age, grip force and high pain level (Oken, Batur et al. 2008). Hand disabilities were detected in 81 % of RA patients and strongly correlated to pain level, grip force and

clinical and laboratory activity. Female RA patients have reported more pain and worse disability than men (Bodur, Yilmaz et al. 2006; Hakkinen, Kautiainen et al. 2006).

3.3 The hand in Rheumatoid Arthritis

RA is our most frequent autoimmune inflammatory disease, with a prevalence of nearly 1 %. RA is found throughout the world and affects all ethnic groups. It may strike at any age, but its prevalence increases with age; the peak incidence being between the fourth and sixth decades. The prevalence is about 2½ times higher in women than in men. The onset of symptoms usually involves symmetrical joints in hand and feet, but RA is a systemic disease and might affect any organ such as vessels, pleura or skin. There is often involvement of multiple joints and surrounding tissues. It's estimated that 80-90 % of the RA patients suffer from decreased hand function (Maini 1998; O'Brien, Jones et al. 2006). The hand in most patients may develop some typical pattern of deformity. These deformities are influenced by several factors, such as inflammation in the joint with distension of the joint capsule and ligament attenuation. Inflammation in and around tendons might distend tendon sheaths and cause tendon ruptures. The influence of disease by the characteristic MCP-joint deformity of ulnar drift (Figure 7), results of local joint forces (Smith and Kaplan 1967; McMaster 1972; Tan, Tanner et al. 2003; Bielefeld and Neumann 2005). Muscle involvement can lead to weakness and contractures. RA patients are frequently affected by pain, weakness and restricted mobility: the deformities of the hand, in various degrees, leads to limitation in ac-
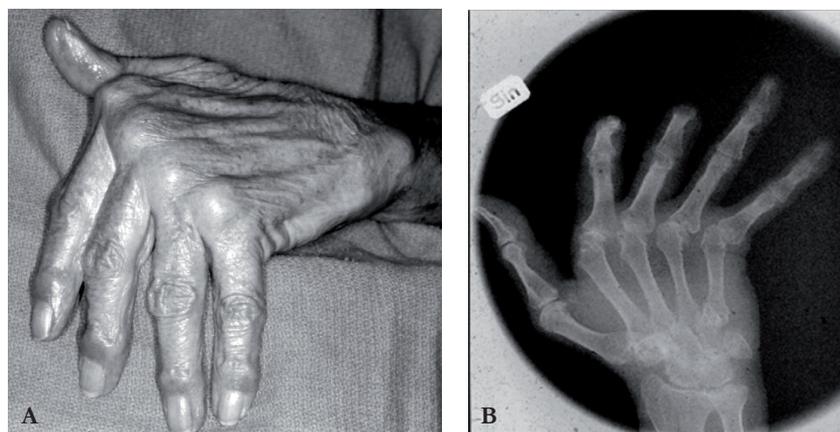
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Figure 7. The hand in most patients may develop some typical pattern of deformity; these images show the characteristic MCP-joint deformity of ulnar drift.

tivities of daily living (ADL) (Chung, Kotsis et al. 2004; Mengshoel and Slungaard 2005; Masiero, Boniolo et al. 2007).

The exact cause of RA is still unknown, however genetic, hormonal and environment factors have been reported to be involved in autoimmune diseases such as RA (Ollier and MacGregor 1995; Reckner Olsson, Skogh et al. 2001; Tengstrand, Ahlmen et al. 2004). Diagnosis of RA are based on ACR criteria which include; pain and swelling in at least three joint areas, symmetrical presentation, early morning joint stiffness for more than 1 hour, involvement of MCP joint or PIP joint or wrists, subcutaneous nodules, positive rheumatoid factor and radiological evidence of erosions. At least four of these signs or symptoms should be present for six weeks (Arnett, Edworthy et al. 1988). Pain and tenderness of the joints are well described and documented (Pearl and Hentz 1993), but there is less knowledge concerning how the muscles are influenced by the disease. The most common histological findings in RA are the pronounced muscle atrophy and nodular myositis. Magyar et al. (1973) observed changes in the muscles consistent with denervation using electron microscopy. These authors showed that the muscle changes might be due to a direct involvement of the neuromuscular system and that the pathological changes affect the contractile element in the muscles (Magyar, Talerman et al. 1973). An important part of hand function is based on the function of the muscles which are involved in finger and wrist motion and the ability to develop grip force. RA patients often report that they feel weakness, particularly when performing flexion force. There are several possible reasons for this weakness such as reduction in muscle fibre diameter, direct involvement of inflammatory processes in the muscle, joint deformity influencing muscle function and pain (Haslock, Wright et al. 1970; Leading 1984; Bruce, Newton et al. 1989). The muscle structure (ultra-structure) and changes in rheumatoid arthritis have been recognised pathologically and clinically. Although electron microscopy is valuable in investigating human skeletal muscle both in normal and RA muscles, only a few data sources document muscle ultra-structural alterations in RA patients (Haslock, Wright et al. 1970; Magyar, Talerman et al. 1973; Wollheim 2006). Furthermore, a non-invasive study on muscle architecture in RA patients appears to be poorly investigated.

3.3.1 Treatment of the Rheumatoid Arthritis hand

Treatment of RA is focused on reducing the inflammatory activity by medication, rehabilitation and surgery (Stenstrom and Minor 2003). New disease-modifying drugs for RA patients administered early after onset have made it

possible for people with this disease to stay more active and more fit than 10-20 years ago (Pincus, Ferraccioli et al. 2002).

Today's treatment options to increase hand function for RA patients include electrotherapy, injection therapy, manual therapy and traditional exercise prescription, but the evidence base for treatments remains weak, particularly when focusing on the hand (Weiss, Moore et al. 2004; Plasqui 2008). In 1974, Lee et al. reported in their study that immobilization and/or physical rest were beneficial in the treatment of RA, leading to a decrease in pain and joint swelling (Lee, Kennedy et al. 1974). Other groups have reported that the forces involved in using the hand lead to joint erosion and increased deformities (Ellison, Flatt et al. 1971; Kemble 1977).

Despite earlier fear of aggravating symptoms, there is now scientific evidence showing that various forms of exercise are both safe and beneficial (Stenstrom and Minor 2003). However, comparatively little research has evaluated the evidence for the benefits of hand exercise in RA (O'Brien, Jones et al. 2006). Recently reviewed effectiveness on hand exercise therapy in RA patients showed that only nine eligible studies have incorporated hand exercise therapy as part of the intervention (Chadwick 2004; Wessel 2004). Hoening et al. (1993) showed in their study that a home hand exercise program was effective for increasing the grip force in the RA hand (Hoenig, Groff et al. 1993). Intensive hand exercise has previously been reported to be effective for improving grip- and pinch force for RA patients (Ronningen and Kjeken 2008). Paper IV in this thesis shows that a regular home exercise programme for the RA hand is beneficial for grip (flexion and extension) force production. Furthermore, paper IV, shows that hand exercise improve the relation between flexion and extension forces as well as improved hand function.

Hand surgery has been regarded as beneficial for some patients with RA. Arthroplastic procedures of the wrist and fingers have been performed since 1960. An increasing number of patients with RA receive joint replacements in the MCP joints of the hand. The purpose of these operations is to improve the patients' extension ability, extension force, and hand function as well as reduce pain (Weiss, Moore et al. 2004). At present, when the outcome of surgery is evaluated, it is impossible to objectively test if the patients' finger extension force has been improved or not, since no force measurement device for finger extension force is commercially available. It is necessary to find methods to objectively measure hand function in order to be able to evaluate the functional impairment, as well as the results of therapeutic interventions i.e. surgery or physical therapy.

4 RATIONALE AND AIMS

The complicated biomechanical architecture of the hand poses challenges in the study and understanding of the control strategies that underlie fine coordination of finger movement and force capacity. A sometimes neglected but, important ability for obtaining good hand function is wrist and finger extension capacity. Grip force is widely accepted as providing an objective measure of the hand function (Balogun, Akomolafe et al. 1991; Incel, Ceceli et al. 2002), however, measurements have mainly been made of the flexion force despite the fact that the extension force is important in developing grip force. An important factor in developing grip force is the synergy between the flexor and extensor muscles (Fransson and Winkel 1991).

Many RA patients suffer from finger extension dysfunction with inability to open the hand (Bielefeld and Neumann 2005)(Vliet Vlieland, van der Wijk et al. 1996). Weak extensor muscles may play a role in the development of flexion contractures and ulnar drift. It would be of interest to analyse if this could depend on imbalance between flexion and extension force. Hand surgery is often performed in order to correct the extension system, flexion contractures and ulnar drift. It has until now been impossible to objectively test whether the patient's extension force has been improved by surgery since no force measurement device for finger extension force is commercially available.

There is also a need for further knowledge of the dynamic action of skeletal muscle and the relation between muscle morphology and muscle force. The force that can be generated is dependent on the muscle architecture; these architectural parameters can be studied non-invasively with US. By using US it is possible to obtain detailed, dynamic information on the muscle architecture. In order to assess how disease influences muscle morphology and function, it is necessary to establish baseline knowledge concerning normal forearm muscles.

The general aim of this thesis was to further our understanding of extensor muscles and their role for hand function in healthy compared to rheumatoid arthritis muscles. To achieve this, a new finger extension force measurment device, new assessment methods and established methods were used. More knowledge about the extensor muscles and the synergy between the flexor and extensor muscles can be important for designing rehabilitation strategies and for evaluating both functional impairment and the outcome of therapeutic interventions.

The specific aims of the studies were:

> ➤ To develop and evaluate new equipment for finger extension force measurements (paper I).

> ➤ To analyse the flexion and extension force in patients with RA compared to healthy controls (papers I, III and IV).

> ➤ To evaluate ultrasound as a tool for assessment of muscle architecture (paper II).

> ➤ To identify parameters describing the architecture of the EDC using ultrasound (papers II and III).

> ➤ To investigate the relationship between these muscle parameters and finger extension force in healthy controls and patients with RA (papers II and III).

> ➤ To evaluate the finger extension force in healthy controls and RA patients and the correlation to hand function (paper III).

> ➤ To determine the new developed finger extension force measuring device (and ultrsounds) ability to detect muscular changes after intervention (paper IV).

> ➤ To analyse the effect of hand exercise in RA patients (paper IV).

5 SUBJECTS AND METHODS

The four studies with focus on the extensor muscles and their biomechanical aspects are summarized in Figure 8. The studies were approved by the Ethics Committee of Lund University or local Ethics Committee at Halmstad University. The purpose of the study and the experimental procedures were explained to all the subjects before they gave their written consent to participate. All procedures complied with the Declaration of Helsinki.

5.1 Subjects

The m. extensor digitorum communis (EDC) was examined in healthy subjects and patients with RA according to the ACR criteria (Arnett, Edworthy et al. 1988). Individuals with inflammatory or muscle diseases, or previous hand or arm injuries were excluded. The inclusion criterion for the RA patients was disease duration time of at least one year and the

PAPER   DEVELOPMENT / DESIGN   APPLICATION

I — Development of a new finger extension force measurement device

II — Ultrasound method for examination on the EDC architechture

III — Healthy vs RA muscle extension force capacity and EDC architechture

IV — Healthy vs RA muscle respones to hand exercis
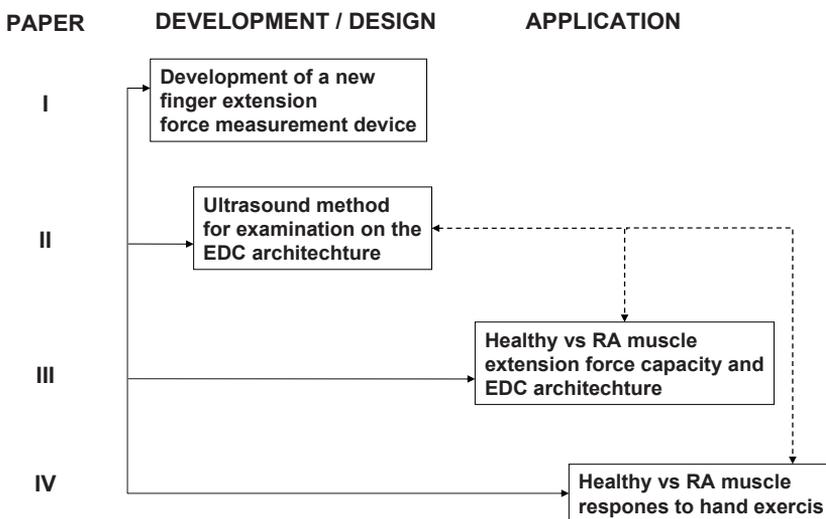
Figure 8. This thesis is comprised of four papers which focus on further understanding the force production of the extensor muscles and their role for hand function. To achieve this, two new methods were developed/designed. In paper I, a new finger extension force measurement device (EX-it) was developed. In paper II, an ultrasound based method was designed for measurements of the EDC. In paper III, these new methods were used in combination to study relationships between force and function. In paper IV, these new methods were used in combination with established methods to evaluate the effects of hand exercise.

TABLE 1. DETAILS OF THE SUBJECTS

PAPER	NUMBER OF HEALTHY VOLUNTEERS/PATIENTS	NUMBER OF FEMALE/MALE	AGE (RANGE)
I	87/57	105/39	(20-84)
II	40/0	20*/20	(37-73)
III	20/20	40*/0	(33-73)
IV	20/20	40*/0	(33-73)

* same subjects

subjects should be able to fully extend their fingers. For more information on the subjects involved in the different studies see Table 1.

In paper I, patients with RA (both in- and out patient clinic at Spenshult Rheumatic Hospital) and healthy controls were included. In paper II, both healthy men and women were matched for age and had similar occupations (office work). In paper III and IV, female patients with RA who visited the out patient clinic at Spenshult Rheumatic Hospital during one month were asked to participate in this study. A control group was selected to match the RA group for sex and age. In paper IV, four subjects, two controls and two RA patients withdrew from the study for reasons unrelated to the study; 36 subjects thus completed the study.

5.2 Study design

In paper I, a new device was developed to measure finger extension forces. In paper II, an ultrasonic examination method was developed. These methods were used together with established evaluation methods in paper III and IV (Table 2). In paper IV, the response to hand exercise in RA patients and healthy controls were evaluated. The total intervention period (hand exercise)

TABLE 2. EVALUATION METHODS

PAPER	EX-it	GRIPPIT	US	GAT	DASH	SF-36	VAS	HAND EXERCISE
I	x	x					x	
II	x		x					
III	x	x	x				x	
IV	x	x	x	x	x	x	x	x

The development/design of new methods used in the present thesis is for finger extension force measurements (EX-it). Modifications of methods used in the present study concern ultrasound (US) examination of the forearm muscle Extensor digitorum communis and a modification of hand exercise programs. Established methods used in the present thesis are Grippit™ (flexion force), grip ability test (GAT), the extremity specific questionnaire: Disability Arm Shoulder Hand (DASH) and the generic health questionnaire SF-36.
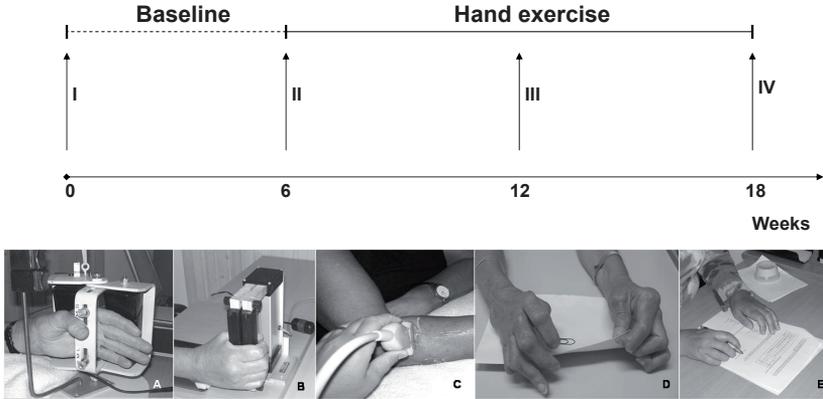
Figure 9. *In paper IV, the total study period was 18 weeks, divided into 6-week periods. Baseline values were determined on Occasions I and II. Thereafter, the hand exercise programme was started, and the effects were measured after 6 weeks (Occasion III) and 12 weeks (Occasion IV). Evaluation methods used: (A) finger extension force measurements (EX-it), (B) Flexion force measurements (Grippit™), (C) US examination of the EDC muscle, (D) grip ability test, and (E) questionnaires.*

was 18 weeks and evaluation measurements were made on four occasions, at 6-week intervals. On Occasions I and II baseline values were determined, and these values are presented in the text as Week 0. Data collected on Occasion III are presented as 6-week data and on Occasion IV as 12-week data (Figure 9).

5.3 Development of the finger extension force measuring device (EX-it) (paper I)

5.3.1 Design parameters

The repeatability and accuracy for a measuring device is very important. The major challenge here is to make sure that the repeatability on the same test subject is reliable. The repeatability is the comparison of two or more measurements of the same individual and is described. The accuracy of a measurement device is composed of the repeatability and of a deterministic error called bias. The bias can in principle be determined and corrected by careful calibration (Doebelin 1990). There are three main factors which contribute to the repeatability performance:

1) The validity of the measurement device itself, which can be tested separately by applying known loads on the device. Factors that cause variations between serial measurements are friction in the device and accuracy of the transducer used in the device. The choice of transducer and the design of the device do influence these parameters.

2) The repeatability of the measurement due to the interaction between the device and the user. One major factor is to place the hand and the fingers in exactly the same position in the device. The design of the device has a major influence on the ability to reproduce the same placement.

3) The repeatability of the user's ability to apply the maximum available force generated by the muscles. Factors that cause variations are the motivation and concentration of the user, tiredness of the muscles, and pain when maximum finger extension force is attempted. The functional design of the device does not influence these factors.

Factors 2 and 3 above have a great influence on the repeatability of measuring functional parameters in biological systems.

In order to evaluate finger extension ability without concomitant contribution from the wrist extensors, the device must isolate and measure the forces developed around the metacarpophalangeal joint (MCP). This approach allows measurements of the force exerted mainly by the EDC muscle. The forces are illustrated in Figure 10.

The repeatability is regarded as reliable if values remain within 10 % (due to user error), and are acceptable with values up to ± 15 % (Doebelin 1990; Hammer and Lindmark 2003). Hence the device itself does not require an extremely low repeatability error and the design criteria for the validity of the device was set to less than 2 % of the applied load. The functional design criteria of the device stipulated that it was to fit most hands irrespective of size and deformity, and it should fit both the right and left hand. It should be mobile, allow measurements of both single finger and whole hand extension exclusively on the MCP-joints. The device should also be able to measure small forces such as those expected in RA patient's single finger, as well as high forces in a healthy man's whole hand.
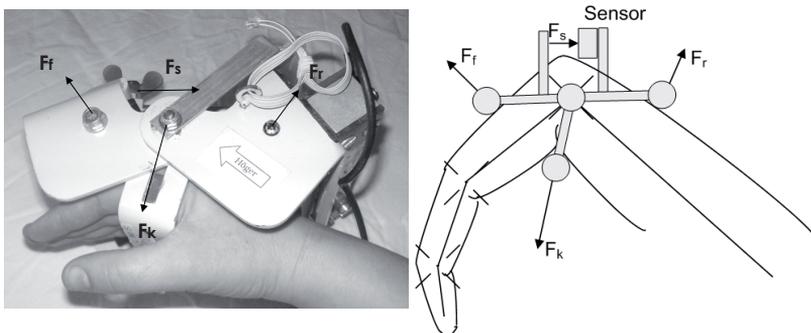

Figure 10. The forces F_k (force from the applied load), F_s (force on the sensor), F_f (force generated by the fingers under full extension), F_r (reaction force) are derived from MCP joint movement.

5.3.2 Design of EX-it

The method used to design the new device was dynamic product development (Ottosson 1999), in which the user interaction is important. EX-it was designed to measure finger extension force based on the biomechanics of the hand and provide data for all fingers together (excluding the thumb) as well as for single fingers. EX-it consists of three bars, one over the proximal phalanges (fingers), one on the volar, and one on the dorsal side of the hand. These three bars are attached to each other by means of rods on both sides. They are positioned in relation to the centre of rotation of the MCP joint so as to ensure equal forces in the device, which was suspended by a string during force measurements in order to eliminate reaction forces from the hand and wrist. The device is shown in Figure 11. EX-it is designed to ensure identical positioning of the hand for every measurement and to accommodate three different hand sizes (small, medium and large). The measurements can be made at different angles of the joint. The force measured is generated by the extension muscles located in the forearm.
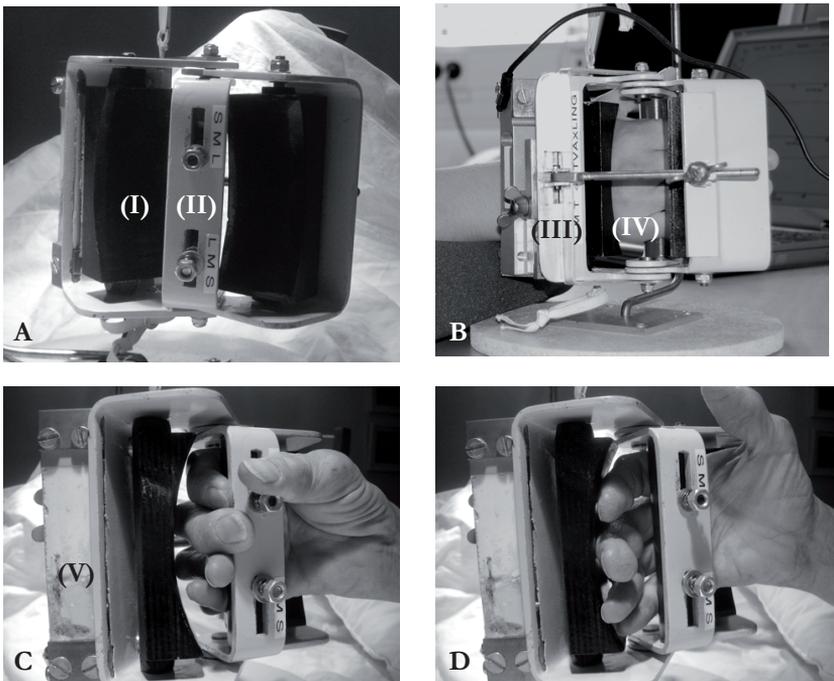

Figure 11. *(A) Front view of the extension force measuring device, showing the hand pad (I), and the size adjustment control for hand size (II). (B) The rear view of the extension device, showing the gear mechanism (III), and the position for the MCP-joints (IV). (C) illustrates the sensor (V) and an RA patient using EX-it. (D) illustrates finger force measurements on an RA patient.*

The device can adapt to different hands with three size adjustments, small, medium and large. The whole construction of the instrument is symmetric, allowing measurement of both right and left hand with the same unit. Measurements can be made in two load intervals with maintained resolution by using a simple gear mechanism. The first interval (low gear) is 0-95 N, which covers single finger measurements and whole hand measurement for patients with impaired strength (i.e. RA patients). The second interval (high gear) is 0-380 N and covers whole hand measurements in a healthy control group. A single point load cell (Tedea-Huntleigh, model 1022) is used as a sensor. The sensor capacity is 50 N and the total error in the applied load ± 0.03 %. An amplifier transmits the sensor signals to a computer board with a 12-bit analogue-to-digital converter that is connected to a hyper terminal on the computer. The measurements are evaluated in Matlab, in which a user interface has been developed (Figure 12). The measurement results are presented on the computer screen and can be presented in graphs showing the mean- and maximal force.
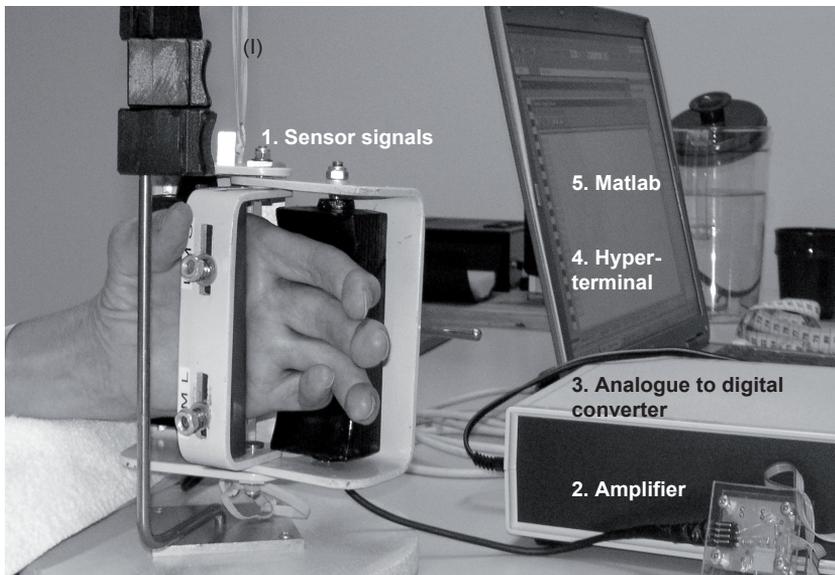
Figure 12. *This picture shows one of the RA patients using the new extension force measurement device. The sensor signals (1) are transmitted by an amplifier (2) to a computer board with an analogue-to-digital converter (3) which is connected to a hyper terminal (4) on the computer. The measurements are evaluated in Matlab™ (5). The device is suspended on a metal wire with a nylon thread (I) to eliminate reaction forces from the hand and wrist during the measurements.*

5.4 Evaluation procedures of EX-it

5.4.1 Calibration and measurement accuracy of EX-it

The device was calibrated and validated by applying known loads. A total of eleven different loads were applied and ten measurements were made for each load. The ability of the device to measure force over time was tested according to the methods described by Kilgore et al. (1998), by hanging loads on the bar, providing the force from applied load, F_k and observing the force output after 0, 30 and 60 minutes (Kilgore, Lauer et al. 1998).

The forces of interest for calibration are the force on the sensor (F_s = Force on the sensor) and the force resulting from the applied load (F_k = Force from applied load). The relationship between these forces is:

$F_k = C_g\, C_{m1}\, F_s$, where C_g is a constant equal to 0.5 for the low gear and 2 for the high gear, and the constant for this model (C_{m1}) is 3.8.

The transformation from sensor output values to force in N was achieved by least squares fitting of a straight line through the measured values. As an estimation of mean accuracy, the root mean square was used (equation III), defined as:

$$\text{(III)} \quad RMS = \sqrt{\left(\frac{1}{N} \sum_{k=1}^{N} \left(y_k - \hat{y}_k \right)^2 \right)} \quad y_k = \text{applied load,} \quad \hat{y}_k = \text{estimated applied load.}$$

The repeatability of all measurements x_i, $i = 1,2,....,N$ is expressed as coefficient of variation (CV)(equation IV).

$$\text{(IV)} \quad CV = \frac{std}{mean} \quad , \text{Where } mean = \bar{x} = \frac{1}{N} \sum_{k=1}^{N} xk \quad \text{and} \quad std = \sqrt{\left(\frac{1}{N-1} \sum_{k=1}^{N} \left(xk - \bar{x} \right)^2 \right)}$$

5.4.2 Test-retest reliability

To be able to evaluate the test-retest two test groups were selected, one test group performed measurements on finger II-V together and the other test group performed single finger measurements. The first group consisted of 20 (10 men and 10 women) healthy subjects (mean age 25 years (range 20-35 y)), and were used as a test group for whole hand measurements. The other group consisted of 10 (5 men and 5 women) healthy subjects (mean age 37 years (range 25-61 y)) and performed single finger extension force measurements.

A digital electronic device that provides data for flexion force (Grippit, Detektor AB, Göteborg, Sweden) was used for comparison (Nordenskiold and Grimby 1993).

The subjects were tested on three occasions during a single week, at the same time of day. Three consecutive measurements were performed per

hand on each occasion. The rest intervals between each measurement were at least 30 seconds for the extension measurements and at least 60 seconds for the flexion measurements (Lagerstrom and Nordgren 1998). The examination procedures are explained in chapter 5.7.

5.4.3 Functionality of EX-it

The design criteria for EX-it were that it should be suitable for most hands (irrespective of size and deformity), fit both right and left hands, and be able to measure small forces such as those in an RA patient's single finger, as well as the great forces of a healthy man's entire hand. A control group (12 men: mean age 60 years, and 45 women: mean age 55 years) and a group of RA patients (12 men: mean age 60 years, and 45 women: mean age 59 years) were used to evaluate the functionality of the EX-it device. All measurements were performed as described in chapter 5.7 and both hands were measured.

5.5 Ultrasound measurements (papers II, III and IV)

All ultrasound (US) examinations were performed with a Siemens Acuson Aspen system using a 7.5 MHz linear transducer (38 mm width). The dynamic image was recorded digitally as cine-loops. Ultrasound recordings were obtained during a change from a neutral relaxed position to maximal static contraction of the extensor muscles, maintaining a neutrally positioned wrist.

5.5.1 Muscle parameters measured with ultrasound

Limb lengths were measured using anatomical landmarks: underarm length, and the distances between the olecranon process of the ulna and the processus styloideus of the ulna. For measurement purposes, the live US images (cine-loops in the transverse and longitudinal planes) were reviewed and measurements were carried out on the still US image of the completely relaxed muscle, as well as the fully contracted muscle (live cine-loops). The optimal and standardized location for US measurements was a point distal from the origin of the EDC (the lateral epicondyle) corresponding to 15 % of the total ulnar length (Figure 13). This location exhibited the largest muscle area, which was clearly defined and thus easy to measure, and is referred to as the measuring point in the text.

The following parameters were measured: muscle thickness, muscle cross-sectional area (CSA), muscle volume, pennation angle, contraction pattern, and fascicle length. In addition, EDC distal muscle-tendon contraction was measured.

Anthropometry measurements of the length of the ulna, defined as the distance between the olecranon process of the ulna and the processus sty-
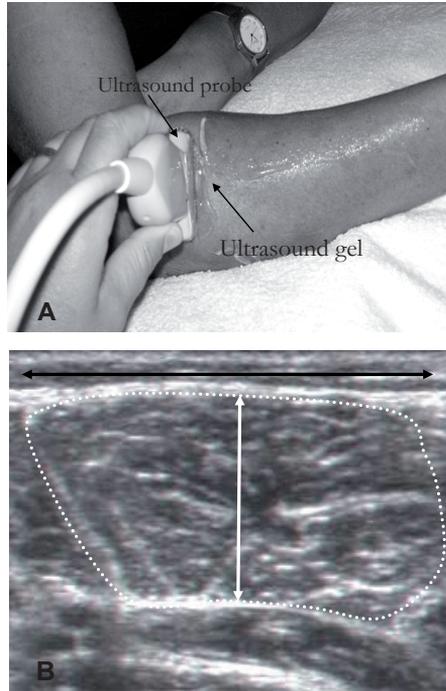
Figure 13. *(A) Position of the probe for ultrasound measurements of the EDC, 15 % distal from the EDC origin. (B) Transverse US image obtained at the measurement position. The CSA is the area within the dotted line and the muscle thickness is indicated by the double-headed white arrow, the muscle height is indicated by the black double-headed arrow.*

loideus of the ulna, were made carefully. The two landmarks were obtained with US and the ulna was then measured with a measuring tape. The muscle CSA and muscle thickness were measured on a still US image in the transverse plane at the measuring point. EDC volumes were calculated by summing the six cross-sectional areas, each of which was multiplied by the respective interslice distance. Measurements were made on saved images at different levels of the EDC. These cross-sectional areas were interspaced by a distance of 3 cm, starting at 15 % distal from EDC origin. Six measurements were made, at 15, 30, 45, 60, 75 and 90 % of the ulna length (Aagaard, Andersen et al. 2001).

Muscle fibre pennation angle

The pennation angle was defined as the angle created by the fascicles and the insertion into the deep aponeurosis (Figure 4). Longitudinal US images were recorded at 15 % distal from the muscle origin and was measured as the angle between the muscle fibres and the deep aponeurosis of

the insertion of the tendon when the fingers were extended (Rutherford and Jones 1992; Fukunaga, Kawakami et al. 1997).

Contraction pattern

The contraction pattern was defined by three descriptors: the change in the shape of the muscle CSA (defined as: the relation between muscle thickness (mt) and muscle length (ml) (mt/ml) in transverse direction) (Figure 13), movement of the deep aponeurosis and time from start to maximal contraction (MCT). Dynamic images were recorded at the measuring point in a transverse view to determine the change in muscle shape and the change in the position of the deep aponeurosis.

Fascicle length

The fascicle length was estimated from the muscle thickness and the pennation angle (α). The transducer was held parallel to the deep aponeurosis in the longitudinal plane in the position that best depicted the deep aponeurosis and was thus slightly oblique to the muscle fibres. The distance between the subcutaneous adipose tissue–muscle interface and the intermuscular interface in the cross-sectional image was defined as the muscle thickness (Figure 5) (Kubo, Kanehisa et al. 2003).

Range of motion in the distal tendon of the EDC

Three different approaches were taken to measure the distal insertion tendon position in the relaxed vs. the contracted muscle. Longitudinal and trans-sectional measurements at the level of the processus styloideus were evaluated.

5.6 Evaluation of ultrasound measurements (papers II, III)

All US images were interpreted blindly by two independent investigators (Observer I and Observer II) to establish the inter-observer agreement in the measurements. In order to estimate intra-observer agreement all the images were interpreted twice by one of the investigators (Observer I).

5.7 Standardized examination procedures (papers I, II, III, IV)

The procedure for the finger extension measurements was standardized in terms of sitting position, instructions and encouragement (Ashford, Nagelburg et al. 1996; Innes 1999). All measurements (force measurements and US) were conducted by the same investigator. The sitting position was that recommended by the American Society of Hand Therapists (Fess

1992). The subjects were seated in an upright position on a chair in front of the instrument, with their feet flat on the floor. Their forearm rested on a supporting pillow and their hand was placed in the extension measurement device, which was positioned on a table in front of them, with the other hand resting on the table. The wrist was not immobilized, and the joint angle was in a neutral position (0-30 degrees extension) during the measurements. The shoulder was adducted and neutrally rotated, while the elbow joint had approximately 90° flexion (Balogun, Akomolafe et al. 1991; Li 2002). The examiner first demonstrated the extension/flexion grip procedure, and the subjects were allowed to familiarise themselves with the device and practice sub-maximally. The subjects were then instructed to extend and press their fingers as hard as possible against the resistance of the bar (hand pad) in the extension device, and squeeze their fingers against the resistance bar in the Grippit device. The verbal instructions for the extension measurements were: "I want you to open your hand like this, and press as hard as you can for three seconds". The instructions for the Grippit device were: "I want you to press against the resistance bar as hard as you can for ten seconds". No verbal or other form of encouragement was given during the measurements. The subject was given the signal, "Three, two, one and begin". All extension force measurements were conducted with the same joint angle at the MCP joint and the same hand position in the device. Data (extension and flexion force in N) were collected and saved for further analysis.

Before and after the measurement, the subjects were asked to report the level of pain in the fingers/wrist, based a visual analogue scale, ranging from 0 to 10 (0 = no pain, 10 = highest pain tolerance limit, (Berntson and Svensson 2001)).

Before the US measurements, the subject's forearm was measured, and six points were marked on the arm. The subjects were seated as described above, US images of the hand were recorded in the relaxed position and while performing the finger extension force measurements. Ultrasound transmission gel (AQUASONIC® 100) was used for US imaging. Ultrasound images were obtained from each subject once/occasion.

5.8 Hand exercise (paper IV)

5.8.1 Hand exercise programme

The exercise programme was designed according to Flatt (Flatt 1974) and included four different tasks focused on finger flexion and extension

movements. The exercise was performed five times a week for 12 weeks. Each task was repeated 10 times and the position of maximal effort was held for 3–5 seconds with a 20-second rest between (Figure 14). The exercise sessions were separated by at least one day. The exercise programme took about 10 minutes to complete and the participants used therapeutic putty (THERAPEUTIC PUTTY, 85 g) for finger resistance. The participants were free to choose soft, medium or firm putty. The participants kept diaries during this training period in which all hand exercise occasions were noted.

5.8.2 Evaluation methods

The following evaluations were carried out on all participants: hand/finger force measurements, US evaluation of muscle architecture in the EDC, a grip ability test and questionnaires (Figure 9).

Two devices were used to measure muscle force, the EX-it, for measuring finger extension force and the Grippit, for measuring finger flexion force (Nordenskiold and Grimby 1993; Brorsson, Nilsdotter et al. 2008a). The force measurements and US examination of the EDC were performed according to methods described in chapter 5.7.

Ultrasound examination of the EDC muscle was performed according to description in chapter 5.7. The measurements produced data on CSA, muscle thickness, pennation angle and contraction pattern (change in shape of the muscle and time from start to maximal contraction (MCT)).

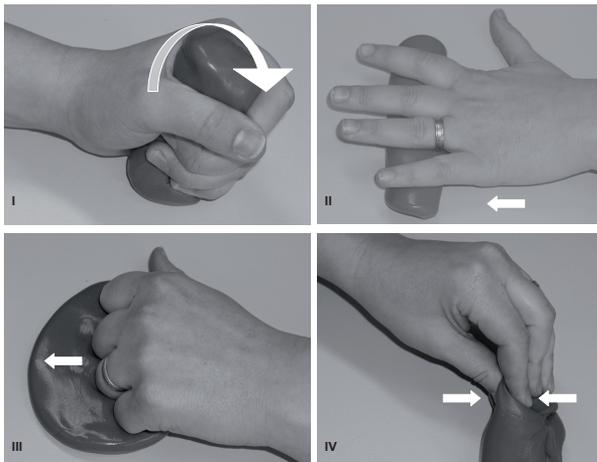*Figure 14.* The arrows illustrate the movement directions. (I). The hand squeezes the putty. (II). The putty is rolled between the wrist proper and the fingertips. (III). The wrist of the clenched fist is placed in the putty, and the fingers extended (movement in the MCP-joint) in the putty. The fingertips are flexed during the motion. (IV). The thumb and the index finger (middle-, ring- and little finger) pinch the putty.

Hand function was evaluated with the grip ability test (GAT), which measures the degree of limitation of ADL and is designed for patients with RA (Sollerman and Sperling 1978; Dellhag and Bjelle 1995; Sollerman and Ejeskar 1995). It comprises three items chosen to provide optimal representation of different daily grip types. When performing the GAT the subject was seated at a table and asked to perform the following tasks; (A) put a flexi-grip stocking on their non-dominant hand, (B) put a paper clip on an envelope, and (C) pour 200 ml from a 1-litre water jug into a cup. The activities were timed in seconds and a correction factor of 1.8 for items (A) and (C) are used before calculating the summary score. Maximum score is 276, and score below 20 is defined as no hand function.

Two patient questionnaires were used, the Disabilities of Arm, Shoulder and Hand (DASH) questionnaire (extremity specific) and the Short-Form health survey containing 36 questions (SF-36) (generic). The subjects were asked to rate the amount of difficulty they have in carrying out activities of ADL over the past week on a 5-point scale. DASH consists of 30 questions concerning the patient's health; (21 items) difficulties performing different physical activities because of arm, shoulder or hand problems, (5 items) severity of each of the symptoms of pain, activity-related pain, tingling, weakness and stiffness and (4 items) social activities, work, sleep and self-image affected by the disease. DASH also has a section about sport/hobbies and a section about work performance. In this study only the ADL disability section was used. The scores of DASH range from 0-100; were a higher score indicating a worse disability. In this study, the Swedish version of DASH was used (Atroshi, Gummesson et al. 2000). The SF-36 measures physical and mental health. Changes in health can be seen over time with repeated measurements. The questionnaire is designed to measure the generic health in the general population but also for different patient groups. The SF-36 is divided into eight domains; PF (physical function), RP (role physical), BP (bodily pain), GH (general health), VT (vitality), SF (social functioning), RE (role emotional) and MH (mental health). All dimensions are independent of each other. The SF-36 scores are between 0-100, a higher score indicate worse disability. In this study the Acute Swedish version of SF-36 was used (Sullivan, Karlsson et al. 1995).

5.9 Statistics (papers I, II, III, IV)

Descriptive data included either median or quartiles or means ± SD values. In paper I coefficient of variation (CV) is presented as SD/mean. In paper IV, the mean value of the baseline measurement was used in the analyses. The Mann-Whitney U-test was used for group comparisons of indepen-

dent samples and the Wilcoxon test was used for comparisons in groups. To assess the correlations between the measured variables, Spearman's rank (rs) correlation test was applied. A p-value of less than 0.05 (two-tailed test) was considered to be significant. Repeatability and agreement of the continuous variables were assessed using the graphic technique described by Bland and Altman (Bland and Altman 1986). Cohen's kappa was used for discrete variables in evaluating intra- and inter-observer agreement. Interpretation of the kappa value was based on the guidelines proposed by Landis & Koch (Landis and Koch 1977). SPSS version 15.0 for Windows XP and MedCalc 5.0 were used for the statistical analysis.

6 RESULTS

6.1 Evaluation of EX-it (papers I, II, III)

The functionality of EX-it was evaluated from data acquired from 144 test subjects. All test subjects were able to use the EX-it device and to position their hand in it with the exception of two subjects with large and/or deformed hands, these experienced difficulties placing their hand in the instrument due to the relatively narrow space between the adjustment bar and the hand pad. The hand sizes of the 144 test subjects were determined and the distribution was found to be: 35 % small, 40 % medium and 25 % large. The instrument allowed the measurement of forces in a wide range (1–170 N).

The calibration and measurement accuracy of EX-it is expressed as the root mean square. It was 0.87 N for the low interval and 1.59 N for the high interval. At most, the CV was 1.8 % of the load. The results are presented in Figure 15. The force output was stable and did not change over time (Figure 16).

The test-retest reliability of EX-it and comparison to Grippit is expressed as the CV. The mean CV of the EX-it was 5.7 % (range 3.2–8.9) for men and 7.1 % (range 3.6–10.0) for women (dominant hand). The CV of the Grippit device was 5.4 % (range 2.9–9.6) for men and 5.8 % (range 2.9–9.5) for women (dominant hand). All measurements are summarised in Table 3.

The reliability in single finger measurements for men was 13.5 % (range 11.2–14.7) and for women 11.2 % (range 8.6–13.1). The mean values for single fingers are shown in Table 4.
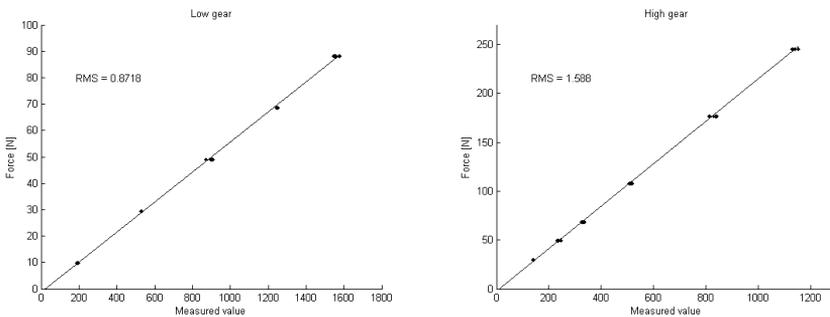

Figure 15. *Validation of the low force interval, 0–95 N, left (RMS = 0.87 N), and the high force interval 0–385 N, right (RMS = 1.59N) the vertical axis shows applied load and the horizontal axis shows the digital value from the sensor.*
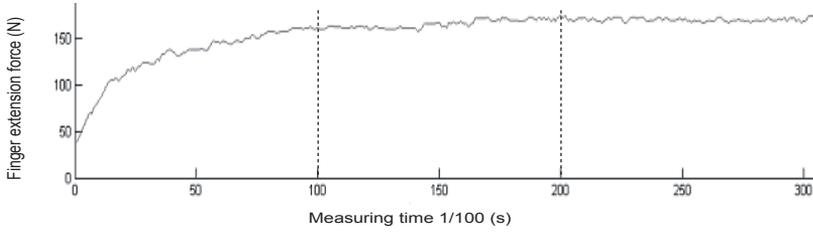
Figure 16. *Force plot from whole hand measurement. The x-axis shows the time, in 1/100 second increments. The mean value between 100 and 200 is taken as the measured force value. The measurement results can be presented in graphs, on a computer screen or printed on paper, showing the mean, maximal forces and continuous force over the measured time.*

TABLE 3. TEST-RETEST FINGER EXTENSION FORCE

	DOM				DOM	
	MEAN ± SD	CV (%)			MEAN ±S D	CV (%)
MEN				WOMEN		
M1	100.5 ± 3.2	3.2		W1	42.7 ± 3.2	7.4
M2	108.7 ± 5.6	5.2		W2	55.1 ± 4.2	7.6
M3	108.4 ± 5.5	5.1		W3	60.8 ± 6.1	10.0
M4	112.0 ± 7.9	7.0		W4	59.9 ± 5.3	8.8
M5	95.1 ± 4.8	5.0		W5	61.3 ± 4.3	7.0
M6	119.9 ± 8.3	6.7		W6	65.5 ± 3.2	5.0
M7	108.4 ± 6.6	6.1		W7	67.9 ± 2.6	3.8
M8	126.4 ± 4.6	3.6		W8	81.5 ± 7.3	8.9
M9	113.4 ± 7.3	6.4		W9	64.4 ± 6.0	9.3
M10	80.3 ± 7.2	8.9		W10	47.7 ± 1.7	3.6

Maximal mean extension force of ten measurements at dominant (dom) hand.
Mean ± SD (Dom), measured force presented in N. Men (M#), Women (W#),
coefficient of variation (CV).

TABLE 4. EXTENSION FORCE IN SINGEL FINGERS

	MEAN ± SD	CV (%)		MEAN ± SD	CV (%)
MEN (n=5) Finger			WOMEN (n=5) Finger		
II	40.6 ± 2.9	11.2	II	17.2 ± 1.6	8.6
III	64.7 ± 6.0	14.4	III	18.6 ± 2.3	11.4
IV	62.1 ± 5.3	14.7	IV	15.0 ± 1.8	11.8
V	41.4 ± 2.6	13.7	V	11.3 ± 1.4	13.1

Single finger extension force expressed as mean maximal extension force ± standard deviation
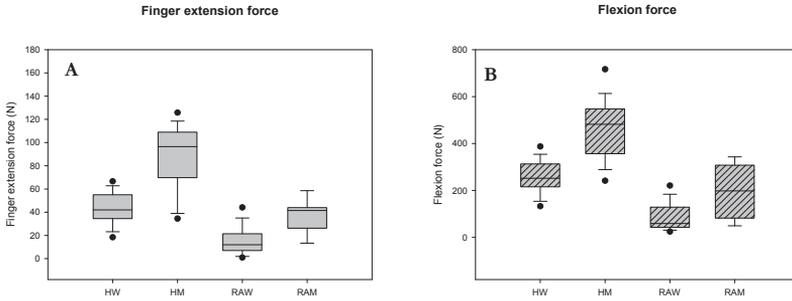(N). Coefficient of variation (CV) %, number of subjects (n). Values are from fingers II-V.

Figure 17. *(A) Finger extension force in dominant-hand. (B) Flexion force in dominant-hand. The box-plots represents healthy women (HW), healthy men (HM), women with RA (RAW) and men with RA (RAM). The results are from participants in all papers (n=80 HW, n=47 HM, n=65 RAW and n=12 RAM).*

6.2 Finger extension and flexion force (papers I, II, III, IV)

The mean maximal finger extension force and flexion force in the dominant hand for healthy subjects and RA patients are presented in Figure 17. The mean maximal finger extension force in the non-dominant hand for healthy men was 89.7 ± 29.9 (13–162) N, healthy women 44.5 ± 12.3 (22–72) N, male RA patients 42.8 ± 16.6 (11–65) N and for female RA patients 17.5 ± 10.4 (1–44) N.

In papers I and III, the extension force was significantly reduced in the RA group (men, $p < 0.05$, and women $p < 0.001$) compared to the control group. In paper II, there was a significant difference reported between the finger extension force for men and for women ($p < 0.001$).

In paper I and III, the relation between flexion and extension force was analysed. There was a significant relation between flexion and extension forces for healthy men ($p < 0.01$), healthy women ($p < 0.01$), and for men with RA ($p < 0.05$), but there was no significant relation for RA women ($p = 0.50$). However, in paper IV, the relation between flexion and extension force for RA women become significant ($p < 0.05$) after 12 weeks of hand exercise.

6.3 Muscle architecture parameters in the EDC measured with US (papers II, III)

There was a significant difference between the muscle anatomy of men and women. The results of the US measurements and the differences in muscle architecture parameters between healthy men and women, and healthy women and RA women are summarised in Table 5. The overall shape changes in muscle CSA during contraction were more pronounced for men than for women, ($p < 0.01$). Furthermore, the overall shape changes

TABLE 5. MUSCLE ARCHITECHTURE OF EDC

MUSCLE PARAMETERS	HEALTHY MEN (n=20)	HEALTHY WOMEN (n=20)	RA WOMEN (n=20)
Thickness (cm)	1.2 (1.0-1.6)**	1.0 (0.7-1.2)*	0.8 (0.6-1.2)
CSA (cm^2)	2.5 (1.6-3.3)**	1.8 (1.0-2.6)*	1.7 (0.4-2.5)
Fascicle length (cm)	6.6 (3.8-9.5)**	4.8 (3.9-7.0)*	4.4 (2.4-6.7)
Pennation angle (degree)	6.7 (3.3-8.5)*	5.3 (4.0-8.5)	5.6 (3.8-6.5)
Volume (cm^3)	27.5 (18.6-43.1)**	16.7 (9.7-28.9)**	12.5 (3.1-23.5)

Muscle paramters are presented as median (range). * $p < 0.05$, ** $p < 0.01$ (significant differences between healthy men – healthy women and between healthy women – RA women).

of the muscle architecture and the contraction times were more pronounced in the control group than in the RA group ($p < 0.01$).

6.4 Muscle architecture parameters in relation to force (papers II, III)

The extension force showed a strong correlation to some muscle architecture parameters, the results are summarised in Table 6.

When the data from paper II (men and women) and paper III (healthy women and RA women) were analysed together, finger extension force was strongly correlated to muscle volume, muscle thickness, muscle CSA and change in muscle shape. No correlations were found between extension force and pennation angles or extension force and fascicle length.

6.5 Evaluation of US measurements (papers II, III)

To be able to evaluate the inter- and intra-observer agreement, the interpretation of the dynamic images were assessed regarding CSA, pennation

TABLE 6. CORRELATION OF MUSCLE ARCHITECTURE TO EXTENSION FORCE

MUSCLE PARAMETERS	FINGER EXTENSION FORCE		
	HEALTHY MEN (n=20)	HEALTHY WOMEN (n=20)	RA WOMEN (n=20)
Thickness (cm)	0.38	0.47*	0.48*
CSA (cm^2)	0.48*	0.35	0.15
Volume (cm^3)	0.58**	0.70	0.40
Pennation length (degrees)	0.38	0.49	0.07
Fascicle angle (cm)	0.60	0.65	0.99
Shape change	0.79	0.30	0.50*

* $p < 0.05$, ** $p < 0.01$

angle and muscle thickness. The intra-observer agreements are expressed as the mean kappa value for the two repeated measurements, and the inter-observer agreements as the mean kappa value for the two investigators (Table 7). The mean inter-observer difference in CSA was 0.22±0.2 cm² for men, 0.08±0.2 cm² for healthy women and -0.05±0.3 cm² for RA women. The difference in the mean value of the pennation angle was -0.20±0.7° for men, -0.30±0.9° for healthy women and -0.05±0.8° for RA women. The mean inter-observer difference in muscle thickness was 0.03±0.07 for men, 0.05±0.08 for healthy women and 0.06±0.1 cm² for RA women.

The distributions of the differences and limits of agreement for 95 % of the cases obtained from the inter-observer assessment of the three parameters are presented for healthy men and women in Figure 18 and for healthy women and RA women in Figure 19. The mean intra-observer difference for CSA was 0.10±0.1cm² for men, -0.04±0.1 cm² for healthy women and -0.02±0.1 cm² for RA women. The difference in the mean value of the pennation angle was -0.4±0.5° for men, -0.33±0.8° for healthy women and 0.18±1.2° for RA women. The mean intra-observer difference for muscle thickness for men was -0.05±0.1 cm, for healthy women 0.03±0.0 cm and for RA women 0.02±0.0 cm.

In US imaging it is necessary to have well defined anatomic landmarks in order to establish reliable reference points for measurements. No major difficulties were encountered in assessing the muscle CSA, muscle thickness or pennation angles. However, no reliable landmark was obtained for measurements of the range of motion in the EDC distal tendon during muscle contraction, and because of this, consistent results could not be obtained with the equipment and method used. Rotation of the muscle was observed at the deep aponeurosis during contraction, but could not been measured with the methods used.

TABLE 7. INTRA- AND INTER OBSERVER AGREEMENT, EXPRESSED AS KAPPA VALUES

MUSCLE PARAMETERS	CSA (cm²)	MUSCLE THICKNESS (cm)	PENNATION ANGLE (degrees)
Intra-observer agreement (m)	0.90	0.89	0.80
Inter-observer agreement (m)	0.8l	0.86	0.84
Intra-observer agreement (w)	0.92	0.85	0.81
Inter-observer agreement (w)	0.83	0.75	0.84
Intra-observer agreement (raw)	0.92	0.92	0.76
Inter-observer agreement (raw)	0.83	0.89	0.74

HEALTHY MEN (m), HEALTHY WOMEN (w), WOMEN WITH RA (raw). NUMBER OF SUBJECTS IN EACH GROUP = 20.

Figure 18. *Inter-observer assessments concerning muscle CSA, muscle thickness and muscle pennation angles. Each dot represents a subject, filled dots are men and unfilled dots are women.*
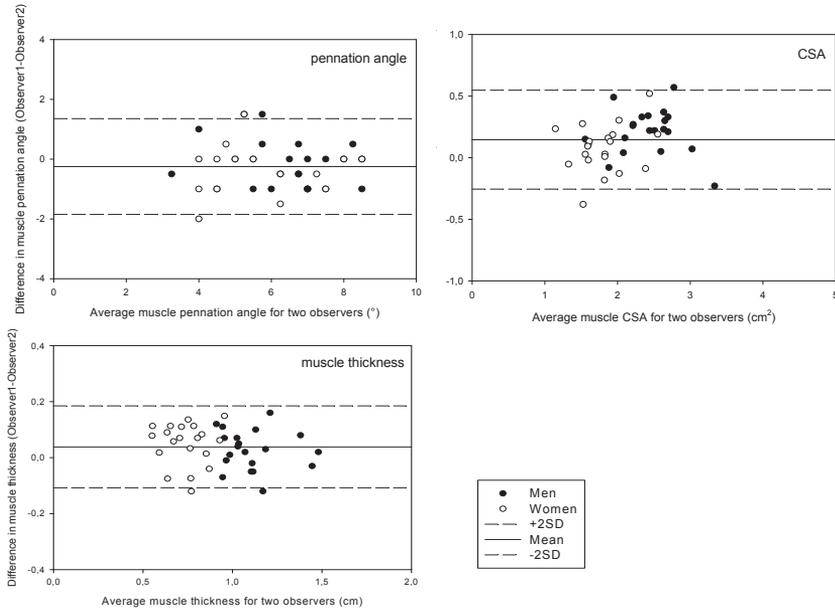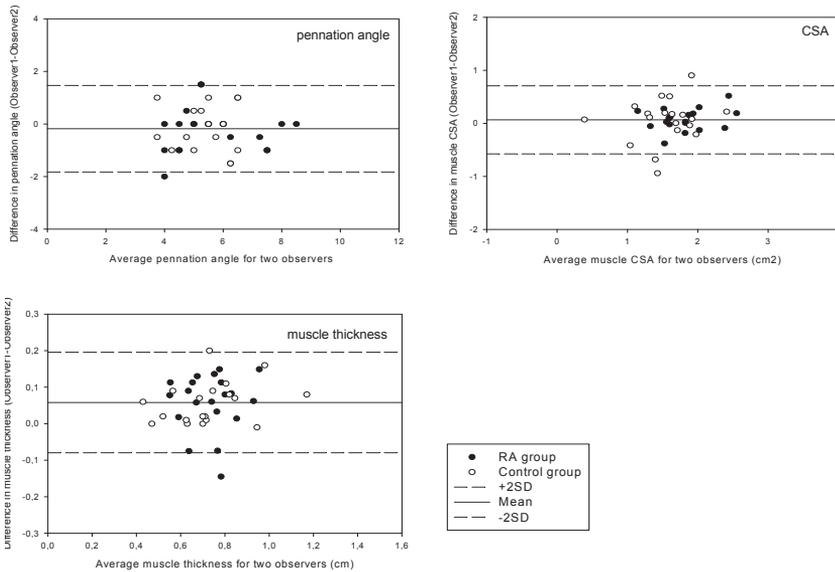

Figure 19. *Inter-observer assessments concerning muscle CSA, muscle thickness and muscle pennation angles. Each dot represents a subject, unfilled dots are healthy women and filled dots are women with RA.*
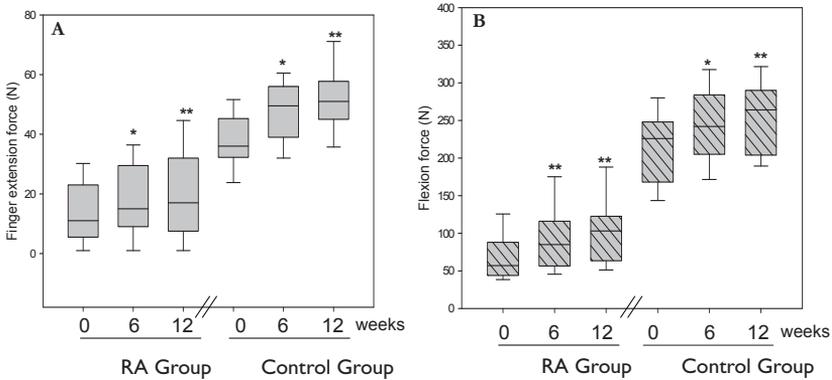
Figure 20. *Illustrates the finger extension force (A) and flexion force (B) in the two groups of participants in paper IV after 6 and 12 weeks of hand exercise. Both groups show significant improvement after 6 and 12 weeks (* p < 0.05, **p < 0.01).*

6.6 Hand exercise evaluated with non-invasive methods

6.6.1 Force measurements

Both extension force (RA group, $p < 0.05$, control group, $p < 0.05$) and flexion force (RA group, $p < 0.01$, control group, $p < 0.05$) increased significantly after 6 weeks of hand exercise therapy. The strength increased further in both groups after 12 weeks of hand exercise (Figure 20).

6.6.2 Ultrasound measurements

The results of the US measurements are summarised in Table 8. After 6 weeks of hand exercise therapy, the CSA of the EDC muscle in the RA group increased significantly, and after 12 weeks of hand exercise the CSA showed additional significant increase in both groups. The pennation angles did not significantly increase after hand exercise therapy in any of the groups and no increase was seen in muscle thickness in the RA group. However, the muscle thickness increased significantly in the control group after hand exercise therapy.

No improvement was observed in the MCT in the RA group after 6 weeks of hand exercise, while it increased in the control group. After 12 weeks of hand exercise the MCT in both groups demonstrated significant improvement. The change in muscle shape increased significantly after hand exercise.

6.6.3 Hand function and perceived pain level

Both the RA group and the control group showed significant improvement in the GAT after 6 weeks as well as after 12 weeks. The results are summarised in Table 9.

TABLE 8. MUSCLE ARCHITECTURE EVALUATED WITH ULTRASOUND BEFORE AND AFTER HAND EXERCISE

Values of architecture parameters are given before training (0 weeks) and after 6 and 12 weeks of training. The median and range for EDC muscle cross-sectional area (CSA), pennation angle, muscle thickness, time from start to full contraction (MCT) and shape change.

Muscle parameter	Week	RA GROUP (n=18)		CONTROL GROUP (n=18)	
		Median	Range	Median	Range
CSA (cm²)	0	1.7	0.9–2.5	1.8	1.4 –2.6
	6	1.9	1.0–2.5**	2.0	1.4–2.4
	12	1.9	0.9–2.5**	2.1	1.8–2.4**
Pennation angle (degrees)	0	5.8	3.8–6.5	5.4	4.0–8.5
	6	5.6	3.5–7.5	7.0	4.0–9.0
	12	5.5	3.5–8.0	6.3	4.0–9.0
Thickness (cm)	0	0.8	0.5–1.2	1.0	0.7–1.2
	6	0.9	0.5–1.1	1.1	0.8–1.3*
	12	0.9	0.6–1.1	1.1	0.8–1.3**
MCT (s)	0	1.6	1.2 –2.3	1.2	0.7–1.7
	6	1.6	1.1–2.0	1.0	0.6–1.5**
	12	1.4	1.0 –2.3*	1.1	0.6–1.5*
Muscle shape change	0	0.3	0.3–0.5	0.4	0.3–0.5
	6	0.4	0.3–0.5*	0.5	0.4–0.6**
	12	0.4	0.3–0.6**	0.5	0.3–0.6*

$* p < 0.05 ** p < 0.01$

TABLE 9. HAND FUNCTION EVALUATIONS BEFORE AND AFTER HAND EXERCISE

Median values of hand function tests before (week 0) and after 6 and 12 weeks of hand exercise. Median and range are given for the grip ability test (GAT), disability, of arm shoulder and hand questionnaire (DASH) and reported pain level (VAS). Number of subjects (n #).

	Week	RA GROUP (n=18)		CONTROL GROUP (n=18)	
		Median	Range	Median	Range
GAT	0	19.8	16.5–51.6	13.4	8.9–16.9
	6	16.8	14.4–40.0**	11.5	6.9–15.8**
	12	16.1	12.1–30.2**	10.3	7.7–14.5**
DASH	0	37.3	8.8–62.5	2.5	0.0–16.3
	6	37.5	5.8–75.0	2.1	0.0–17.5
	12	39.2	6.7–47.5*	5.0	0.0–15.0
VAS	0	1.5	0.0–6.0	0.0	0.0–2.0
	6	2.5	0.0–7.0	0.0	0.0–2.0
	12	2.0	0.0–7.0	0.0	0.0–2.0

$* p < 0.05 ** p < 0.01$

Neither the RA group nor the controls showed any significant improvement in DASH score after 6 weeks of hand exercise therapy. However, after 12 weeks of hand exercise the RA group showed a significant improvement in the DASH score, while there was still no improvement in the control group. Neither group showed any significant improvement in the SF-36 score after the hand exercises (Figure 21). However, some of the RA patients reported "tiredness" in there hands after the exercise.

The exercises caused no significant change in the pain level (Table 9).

6.6.4 Effects of hand exercise on rheumatoid and healthy hands

At baseline there was a difference between the RA patients and the healthy controls concerning extension and flexion force ($p < 0.001$), DASH ($p < 0.001$), GAT ($p < 0.001$), VAS ($p < 0.001$), muscle thickness ($p < 0.01$) and duration of maximal contraction ($p < 0.01$). The hand exercise did not affect these differences between the two groups.

The pennation angle did not differ significantly between the groups and did not change during the period of hand exercise. The CSA of the EDC muscle showed a significant difference between the two groups before the period of hand exercise ($p < 0.05$), but after 6 weeks no significant difference
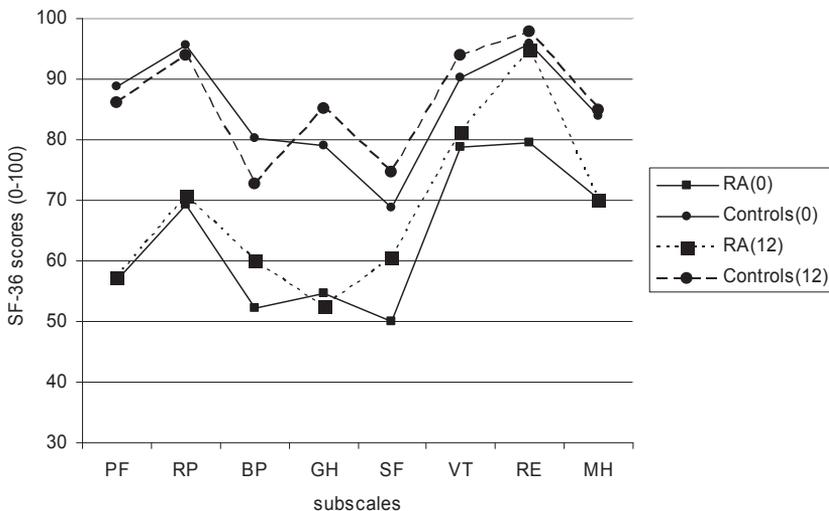

Figure 21. *Results of the SF-36 questionnaire, before (0) and after 12 weeks (12), of hand exercises. The scale is 0–100, from worst to best. The questionnaire is designed for measuring the generic health in the general population but is also useful for different patient groups. SF-36 is divided into eight health profiles scales; physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). All dimensions are independent of each other.*

was observed between the groups (p = 0.4). No further changes in the CSA were observed after 12 weeks of hand exercise (p = 0.09). The change in muscle shape showed significant differences between the two groups before and after 6 weeks of hand exercise (p < 0.01), but after 12-weeks of hand exercise no significant differences were seen between the groups (p = 0.26).

The SF-36 showed significant differences between the two groups regarding PF and GH (p < 0.05) before and after hand exercise. Differences in BP and SF in the two groups were significant before hand training (p < 0.001 and p < 0.01, respectively), but after 12 weeks of hand exercise these parameters were not significant.

6.7 Relation between hand force and hand function

The relation between hand force and hand function was analysed for healthy women and RA women (participating in study III and IV). In the RA group, there was a correlation between GAT and Grippit before hand exercise (p < 0.05) but not after 12 weeks of exercise (p = 0.18). In the control group no significant correlation was shown between GAT – Grippit, however Grippit was correlated to DASH both before (p < 0.05) and after hand exercise (p < 0.01). In the RA group there was no correlation between Grippit and DASH.

The relation between flexion and extension force was significant between healthy men (p < 0.05) and women (p < 0.05) as well for RA men (p < 0.05) but not for RA women (p = 0.18) (in paper I). When this analysis was done on participants in paper IV, the flexion and extension force in the RA group was not significant before hand exercise (p = 0.24), however, after 12 weeks of hand exercise there was a significant relation between flexion and extension force in the RA group (p < 0.05).

In paper I, a strong correlation was found between the extension force and the perceived pain level (p < 0.01) for patients with RA. The pain levels reported by the women with RA were 3.7 ± 2.8 (range 0–9) before and 4.0 ± 2.9 (range 0-9) after the measurements, and by men with RA 1.9 ± 2.2 (range 0–6) before and 2.1 ± 2.4 (range 0–7) after the measurements. There was a significant difference between perceived pain levels reported by RA men and RA women (p < 0.05). Furthermore, there was a correlation between force capacity and age in the RA group (p < 0.05), but not in the control group. No one reported any pain in the control group. In paper III, the RA group had a median pain level of 2.0 (range 0–7) and the control group had a median pain level of 0.05 (range 0–1). No significant correlation was found between pain level and extension force capacity (in papers III and IV) or extension force and age.

7 GENERAL DISCUSSION

To further our understanding of hand function, and specifically the extensor muscles' function and ability to produce force, this thesis describes the development and results of new non-invasive methods, a new finger extension force measurement device, EX-it, and an ultrasound imaging method. These new methods can be used in combination to dynamically study functionally important muscle parameters. Furthermore, the results of this thesis show that finger extension force measurements and ultrasound are effective methods for evaluating improvement after hand exercise. The effect of hand exercise on the extensor muscles could be objectively evaluated with EX-it and ultrasonic imaging. The study also demonstrates the usefulness of short-term hand exercise for patients with RA and that a home exercise programme can enhance hand function.

7.1 Methodological considerations

The new finger extension force measuring device, EX-it, was found to be reliable in healthy individuals through test-retest procedures (7.1 %) (Brorsson, Nilsdotter et al. 2008a). However, the reliability of the new device has not been tested on the rheumatoid hand. Test-retest measurements have been carried out on patients with RA with the Grippit device, showing a CV of 27 % (Hammer and Lindmark 2003). However, the results in the present study, showing significant improvements of 36-40 % in hand strength after 12 weeks of exercise, can be regarded as reliable.

The use of US to assess *in vivo* muscle architecture has been shown to be reliable both in healthy subjects and patients with RA (Brorsson, Nilsdotter et al. 2008b). In the present study every effort was made to maintain standard measuring methodologies, including measurement sites for the ultrasound transducer and a standardized procedure with the metacarpophalangeal (MCP) - joint in a fixed position during the extension force measurements.

7.1.1 Reliability in force measurements

The results concerning the variation in flexion force are in the same range as previously presented results for healthy subjects (Lagerstrom and Nordgren 1998). Hammer and Lindmark (2003) presented in their study a variation of 10 % between measurements. They performed flexion force measurements on patients with stroke, and concluded that this result could be regarded as good

(Hammer and Lindmark 2003). However, the CV of the test subjects are affected by many factors for example the number of repeated measurements and cognitive status. There appears to be no standard regarding the number of measurements per day. In previous studies, two or three measurements have been made per day, and it was stated that the mean values of these measurements should be used as maximum values (Innes 1999). Another factor that influences the force is the subject's posture during measurements. In the present study we took special care in positioning the test subjects and followed the American Society of Hand Therapists' recommendations. The repeatability of the measurements also depends on the interaction between the device and the subject. It is thus important to place the hand and fingers in exactly the same position for each measurement. The subject's ability to apply maximum force is determined by neuromuscular factors. These can be influenced by motivation, concentration and learning, as well as muscle fatigue and pain, causing variation in the measurements (Incel, Ceceli et al. 2002).

7.1.2 Ultrasound to assess *in vivo* muscle architechture

Various methods can be used to study muscle architecture, including ultrasound, magnetic resonance imaging (Juul-Kristensen, Bojsen-Moller et al. 2000; Aagaard, Andersen et al. 2001) and laser diffraction. Laser diffraction is an invasive technique, while magnetic resonance imaging is only suitable for static measurements. Ultrasound, on the other hand, is non-invasive and clearly shows the movement of the muscle (Fukunaga, Ichinose et al. 1997). It is also harmless, can be repeated and offers the possibility of dynamic examinations. The limitations with US are the quality of the examinations, which are dependent on the investigator's ability to reproduce the imaging conditions (measurements), to find correct landmarks in both transverse and longitudinal direction and standardise the procedures.

Ultrasound has been shown to be a highly valuable tool to assess *in vivo* muscle architecture for studying muscle function and relationships between muscle force and muscle size (Maughan, Watson et al. 1984; Hakkinen and Keskinen 1989; Kawakami, Abe et al. 1993; Fukunaga, Kawakami et al. 1997).

7.1.3 Statistics

Non-parametric tests were used (paper II, III and IV) due to rather few participants, simplicity and the robustness in the methods. The Bonferroni method is not necessary to use on this material since not many enough correlated parameters were used. Bland and Altman's graphical method was used to study the agreement between Observer I and II (Bland and Altman 1986). The graphs show the differences between each pair of measurements plotted

against their mean, with one line showing the mean of the differences, and two more lines representing two SD above and below the mean. The graphs must be interpreted in relation to the clinical situation, and the acceptable difference in measurements. Intra- and inter-observer kappa values for the muscle parameters were good to excellent. Our results regarding kappa analysis are in the same range as previous studies (Boehm, Kirschner et al. 2005; Qvistgaard, Torp-Pedersen et al. 2006). In order to make a complete evaluation of the repeatability of the ultrasound method, the whole ultrasound investigation ought to be repeated by another examiner. However, this was not possible within the frame of this project.

7.2 Ethical considerations

The Ethics committee at Lund University approved the studies. Written informed consent was obtained for all participating subjects and they were informed that they could withdraw from the study at any time. From another perspective, the number of subjects participating in study IV can apprehend as small. Presently there is a general agreement for RA patients regarding the necessity for rest during an acute flare. Furthermore, there is a wide variation in the activities recommended for the non-acute rheumatoid hand. This wide variation in hand exercise may be due to the few objective studies regarding the effect of hand exercise on the rheumatoid hand. The numbers of participants are in the same range as in previous studies.

7.3 Limitations

In order to generalize the results of the present study, a larger group of RA patients should be investigated. However, the size of the study groups is comparable to those in previous studies involving hand exercise in RA patients (O'Brien, Jones et al. 2006). The effects of medication and other concomitant treatment on the study results are unknown. Detailed information about the hand deformities in the RA patients was not measured, but all patients in the study were able to extend their fingers. The range of disease duration in the RA group was wide (2-40 years) and may also have influenced the results. Hakkinen et al. (1997) reported that the loss of muscle strength and functional capacity in patients with RA may be prevented by performing physical exercise with sufficient intensity on a regular basis (Hakkinen, Malkia et al. 1997).

7.3.1 Extension force measurements

According to previous research, a coefficient of variation (CV) of less than 2 % of the applied load can be regarded as good (Doebelin 1990). The CV

of the instrument's accuracy was 1.8 % of the applied load. A measurement error of 1.8 % is somewhat high, although it is within the range of previously reported force measuring devices (Chadwick and Nicol 2001). However, these measurements were made using a prototype and some of the technical solutions can be improved in the final device.

The results from paper I, show an acceptable accuracy and reproducibility in the clinical setting, but the design could be improved. A more intuitive and attractive instrument, will facilitate the way it is used and reduce the need for instructions and supervision. The technical construction could be improved too, for example with a smaller sensor. Data acquired from the present study showed that the measuring range of the sensor used was smaller than expected. A future instrument could perhaps be designed to measure both flexion and extension force at the same rotation centre making two different instruments for flexion and extension force measurements unnecessary. A dynamic measuring capacity would increase the instrument's usability as a training and feedback instrument in rehabilitation.

7.3.2 Standardization of landmarks for ultrasound examination

The range of motion in the distal tendon and the rotation in the EDC could not be measured. However, such measurements would be very interesting, since it is likely that these parameters are important in developing force. Kawakami et al. (1998) showed in their study (on the m. medial gastrocnemius, lateral gastrocnemius and m. soleus) how the muscle parameters changed during contraction, and suggested that the changes could reflect the muscles' ability to produce force (Kawakami, Ichinose et al. 1998).

7.4 Gender perspectives on muscle architectures and force production

7.4.1 Force production

In paper I, the results showed that women with RA had a lower grip force (both flexion and extension) than men with RA. These results are in agreement with previous research concerning sex and flexion grip force (Nordenskiold and Grimby 1993; Hakkinen, Kautiainen et al. 2006). The present study also demonstrated a decrease in extension force capacity in RA patients compared with healthy subjects. One interesting result is that women with RA showed approximately the same amount of weakness in extension force as in flexion force, relative to healthy controls (60 %), while men with RA exhibited a 40 % lower finger extension force and a 60 % lower flexion force

than healthy men. The decrease in force in the RA patients could be the direct effect of the disease on muscle function, but could also be due to the fact that the RA group experienced more pain than the control group, which could influence their maximal muscle exertion. The present study does not contradict the theory that pain level affects gripping force. Previous studies have reported that loss of hand gripping strength can result from pain, or fear of pain, or mechanical malfunction (Thyberg, Hass et al. 2005).

7.4.2 Muscle architecture

In paper II ultrasound examinations revealed significant differences between the muscle architecture in men and women. The men had a larger muscle volume, muscle CSA, muscle thickness, longer fascicles and larger pennation angles. Furthermore, this paper presents differences in the correlations between muscle architecture and extension force between men and women. These could be due to the experimental set-up or methodological problems, although a great effort was made to standardize the procedures and we have demonstrated good validity and reproducibility of the methods used in this thesis. Another explanation could be that the study population was too small to detect correlations. However, this is not very likely since there is not even a statistical tendency towards significance. Yet another possibility could be that there is a breakpoint, in other words, the muscle has to have a specific size before any correlation is seen between muscle volume and force, and muscle CSA and force. This would explain why the men in this study showed a correlation between force and muscle volume and CSA, but not the women. It must also be noted that muscle properties are not the sole factor in determining muscle function, the neural-muscle interaction also influences the movement pattern and force production of the muscles (Blazevich, Gill et al. 2007).

7.4.3 Muscle architecture and force generation

Architectural differences between muscles are claimed to be the best predictors of force generation (Lieber and Friden 2000). Several muscle architectural parameters are theoretically related to force, and decreases in muscle volume, muscle CSA, muscle pennation angle and muscle fascicle length are regarded as being important causes of declining strength (Ichinose, Kanehisa et al. 1998; Kubo, Kanehisa et al. 2003). However, in this thesis no correlation was found between finger extension force and fascicle length. One reason for this could be the geometric method used to calculate the fascicle length. The method is based on several assumptions, for example, that the fascicles are straight. It is generally accepted that a close relation exists

between the CSA of a muscle and its ability to generate force (Maughan, Watson et al. 1984; Young 1984). Paper II revealed a correlation between muscle CSA and finger extension force for men but not for women. These results are partly in agreement with previous studies. Fukunaga et al. (2001) found a relationship between isometric arm flexion force and the CSA of the arm flexor muscle, and their conclusion was that arm force is proportional to the CSA (Fukunaga, Miyatani et al. 2001). The present findings in this thesis suggest that muscle strength is related to muscle volume for men but not for women. However, a correlation was found between muscle volume and finger extension force in the present study when the data from the two groups were pooled together (rs = 0.85, p < 0.01). Previous research groups used magnet resonance imaging to study the relationship between muscle volume and force. They found correlations between muscle volume and muscle force in both the upper and lower extremities. However, their study groups were small (n=18 and n=10) and the data from men and women were not analysed separately (Trappe, Trappe et al. 2001; Holzbaur, Delp et al. 2007; Holzbaur, Murray et al. 2007).

In an experimentally impressive study, Zuurbier and Huijing measured the muscle pennation angles (in the medial gastrocnemius in rat) using small wire markers on the muscle surface, which were filmed during contraction. The results of their study showed that the pennation angle varied considerably in the muscle (Zuurbier and Huijing 1993). Two other research groups have made significant contributions in the area of fibre rotation during muscle shortening. Rotation allows muscle fibres to maintain a higher level of force than if they are constrained to maintain a constant pennation angle (Fukunaga, Ichinose et al. 1997; Kawakami, Ichinose et al. 1998). The results of the present thesis support previous findings concerning muscle rotation during contraction. The finding that the pennation angle appears to be free to rotate during contraction has a number of implications that make the equation proposed by Powell et al (Powell, Roy et al. 1984):

$$PCSA \ (mm^2) = \frac{muscle \ mass \ (g) \times \cos \ (\alpha)}{\delta \ (g/mm^3) \times fiber \ length \ (mm)}$$, unreliable in predicting force in certain

muscles. This is one potential explanation for the results in paper II and III where we found a correlation between the change in shape of the muscle and the extension force, but no correlation between pennation angle and finger extension force.

7.5 Disease perspectives on muscle architectures and force production

In rheumatoid arthritis, impaired finger extension is a common symptom, in this thesis differences in extension muscle force capacity as well as in muscle architectural parameters, between normal and RA muscles are reported.

The relation between flexion and extension forces were reported from paper I, III and IV. The RA group did not have any significant relation between flexion and extension force before hand exercise, but after 12 weeks of hand exercise there was a significant relation between flexion and extension force. In papers I, III and IV, a pronounced decrease (as compared to the control group) in finger extension force was found in the RA group. Earlier studies have reported that RA patients also have weaker grip, pinch and tripod force than healthy controls, and it has been suggested that force assessment could be used as an accurate indicator of upper limb ability and that grip force (i.e. flexion and pinch force) should be included in the evaluation and follow-up of the patients with RA in hand rehabilitation units (Helliwell and Jackson 1994; Fraser, Vallow et al. 1999; Adams, Burridge et al. 2004; Bodur, Yilmaz et al. 2006). The decrease in force capacity could be explained by a direct effect of the disease on muscle function, disuse or impaired neuromuscular transmission, or different medications, but the decrease could also be due to the fact that the RA patients experienced more pain than the healthy subjects, a situation which could influence their maximal muscle exertion. Loss of hand grip force has been shown to result from pain, or fear of pain, or mechanical malfunction (Fraser, Vallow et al. 1999). Data obtained in this thesis show a significant correlation between finger extension force and pain level (paper I).

7.5.1 Muscle architecture and force

Paper III showed a strong correlation between finger extension force and muscle thickness (contracted muscle) this result is in line with previous studies on other muscle systems. A correlation has been established between quadriceps muscle thickness and knee extension force as well as muscle thickness in the masseter and temporals and bite force (Freilich, Kirsner et al. 1995; Pereira, Gaviao et al. 2007). Paper III, demonstrated a strong correlation between finger extension force and muscle thickness (in both the RA group and the control group), and this may provide a clinically useful measure for evaluating the outcome of hand surgery and hand rehabilitation.

Furthermore, paper III presents significant differences in muscle architecture between the two groups concerning all muscle parameters examined, except pennation angle, being significantly decreased in the RA group. The shape change of the RA group's muscles was significantly decreased compared to the healthy group's muscles and the contraction time was also longer. One muscle parameter, muscle thickness was significantly correlated to finger extension force in the RA and the control group. Furthermore, the RA group showed a correlation between the shape change of the muscle and finger extension force. The present study could not support some expected correlations such as correlation between finger extension force and muscle CSA. Helliwell and Jackson (1994) reported a correlation between CSA and grip strength both for RA patients and healthy controls. However, they had measured and correlated the flexion force with an estimated CSA (using an equation based on forearm circumference, area from radius and ulna (antropometric data) and skin thickness) (Helliwell and Jackson 1994).

One explanation for the lack of correlations between finger extension force and CSA can be that it is also possible that a muscle designed for precision tasks and grip control rather than force exertion is constructed differently from the large force-generating muscles in the lower limbs. It may also be due to methodological problems, although we have shown good validity and reproducibility of our methods in papers II and III.

7.6 Benefits from hand exercise

7.6.1 Effects after 6 weeks of hand exercise
Hand strength, both flexion and extension finger force, increased significantly in both groups after hand exercises. The finger extension force improved by 36 % in the RA group and by 25 % in the control group. The flexion force was improved by 40 % in the RA group and by 14 % in the control group. Previous studies on flexion force support our results on the hand strength of RA patients (Buljina, Taljanovic et al. 2001; Stenstrom and Minor 2003). Although hand strength improved in the RA group, there is still a significant difference in muscle strength between RA patients and healthy controls (p < 0.01). The present study shows improved hand function in both groups (p < 0.01), which is in agreement with the findings of Björk et al. (2007), who reported that increased hand function was seen in early RA (Bjork, Thyberg et al. 2007), and Dellhag et al.(1992) who reported improved hand function after 4 weeks of hand exercise (Dellhag, Wollersjo et al. 1992).

The hand exercises significantly increased the EDC muscle CSA in the

RA group, but not in the control group. There was a significant difference between muscle CSA in the two groups before the exercise period, but after 6 weeks no significant difference was observed between the groups. One explanation of the greater response in the RA group could be that the intensity of the training programme and the resistance of the therapeutic putty were adequate for this group. Stenstrom and Minor (2003) reported in their study that the load for strength exercises for RA patients should be 50–80 % of a maximal voluntary contraction, and should be performed 2–3 times per week (Stenstrom and Minor 2003). Previous research has shown that a significant increase in fascicle angle occurs with increased muscle CSA or thickness in response to prolonged periods of heavy weight training (> 14 weeks) (Aagaard, Andersen et al. 2001). Our findings do not support these results, as there was no significant increase in pennation angle in either group, although muscle CSA was increased in the RA group and muscle thickness increased in the control group.

Our study showed significant improvements in both groups concerning change in muscle shape, and the MCT increased significantly in the control group. In previous studies it has been suggested that an early increase in strength is accompanied by an increase in muscle contractility (Blazevich, Gill et al. 2007). The present study showed rapid adaptation in both RA patients and those with healthy muscles.

7.6.2 Effects after 12 weeks of hand exercise

After 12 weeks of hand exercise, hand strength further increased in both groups. The extension force in the RA group increased by 52 % and the flexion force by 56 %, compared with the baseline values, while in the control group, the extension force improved by 35 % and the flexion force by 19 % compared with the baseline values. The reason why the RA group responded so positively to this hand exercise programme could be that the RA patients had been reluctant to use their hands because of fear of pain and/or fatigue, but once they started the training programme they experienced encouraging results.

After 12 weeks of hand exercise the EDC muscle CSA showed significant improvement also in the control group. Muscle parameters such as CSA and muscle shape change improved further in the RA group and after the exercise period there was no significant difference between the two groups concerning these two muscle parameters. One explanation of this could be muscle hypertrophy and adaptive changes in the neuromuscular system (Hakkinen, Malkia et al. 1997). The MCT in the RA group increased significantly after 12 weeks, while it increased after only 6 weeks in the control group. This could be explained by the fact that muscles in RA

patients are weaker at baseline and the muscle function is reduced, which can present itself as loss of functional balance and coordination (Ekdahl and Andersson 1989).

In the present study the ADL improved significantly in the RA group after 12 weeks, measured with the DASH questionnaire. Positive effects of hand exercise on ADL have not previously been reported using DASH. It is notable that there was a difference concerning pain, reported by SF-36 at baseline, between patients and controls, which disappeared after 12 weeks of exercise. However, there was still a difference in physical function between the two groups. The explanation could be that it is possible to influence the pain reported by the patients more than their physical function with exercise.

7.7 Clinical implications

Ultrasound is a non-invasive and harmless method that can be used to visualise functionally important muscle parameters dynamically. Finger extension control is one of the most difficult motions to regain after disease/injury and is also very important for prehensile activities (Cauraugh, Light et al. 2000). Since both EX-it and US in the present thesis have been shown to be sensitive in their evaluation of hand exercise, it can be expected that these methods can be used to evaluate other interventions, such as surgical procedures, physiotherapy and/or pharmacological treatment. With these new methods, arthroplastic interventions in the MCP-joints of the fingers can objectively be evaluated. In a longer perspective it may be possible to establish more efficient rehabilitation programmes for RA patients.

Furthermore, force measurements are a quick and easy measure of hand impairment and function, and are useful when evaluating hand status. EX-it in combination with other non-invasive evaluation methods (i.e. grip ability tests and health assessment questionnaires) will provide more information on hand function. The values of finger extension force obtained in this thesis may serve as a reference for assessing the results of MCP joint arthroplasty, tendon transfers or other surgical interventions.

Patients with rheumatoid arthritis suffer from a variety of functional deficiencies, of which impaired muscle function is a serious one. There is a recent trend towards the use of non-invasive methods in studying disease-specific changes, such as magnetic resonance imaging and ultrasound. Increased knowledge concerning muscle morphology and function in RA will allow better diagnosis and evaluation of interventions, such as surgical procedures, physiotherapy and/or pharmacological treatment. In a longer perspective it may be possible to establish a more efficient rehabilitation programme for

RA patients. If combined with functional and clinical measures of disability, information on muscle architecture could then be used as an objective tool in the assessment of hand function after physical therapy and hand surgery. In this thesis no negative effects of EX-it, US or the exercise programme on self reported pain level were reported in the RA group.

It is possible that RA patients need continuous exercise to prevent loss of muscle strength and to improve the performance of activities of daily living (Stenstrom 1994; Hakkinen, Malkia et al. 1997; O'Brien, Jones et al. 2006; Masiero, Boniolo et al. 2007). However, the response to exercise from RA patients must be further evaluated to find out if longer exercise period can obliterate the differences between healthy and rheumatoid arthritis muscle strength and function; or to find out if these differences depend on a disease-specific effect on the rheumatoid arthritis muscles. Furthermore, the relation between the extension and flexion force become significant increased after hand exercise and the hand function was also increased. Therefore hand exercise deserves consideration for routinely inclusion in the treatment of RA patients.

8 CONCLUSIONS

The general aim of this thesis was to further our understanding of extensor muscles and their role for hand function in healthy compared to rheumatoid arthritis muscles. To achieve this, both new assessment methods were developed and established methods were used. The following specific conclusions were drawn from the present studies:

- ➢ A new finger extension force measuring device has been developed. This device provides objective and reliable data on the extension force capacity of normal and dysfunctional hands.

- ➢ An ultrasound based method was designed for measuring muscle architecture parameters in EDC. Important muscle architectural parameters regarding force development were identified. US is a useful tool in order to obtain detailed, dynamic and static information on muscle architecture.

- ➢ Our results indicate that rheumatoid arthritis affects skeletal muscle. The results showed differences in extension and flexion force capacity, muscle architectural parameters and/or functionality, i.e. duration of contraction, between healthy subjects and RA patients.

- ➢ EX-it and US was sufficiently sensitive to evaluate muscular changes after hand exercise.

- ➢ A significant improvement of hand force and hand function in RA patients was seen after six weeks of hand training, the improvement was even more pronounced after 12 weeks. Hand exercise is thus an effective intervention for RA patients, providing better strength and function.

Based on the results above it thus be concluded that the new non-invasive methods that we have combined provides new and detailed information concerning finger extension force capacity and the EDC architecture.

Muscle architecture is a primary determinant of muscle function and further understanding of structure-function relationship is of great clinical importance. Not only to elucidate the physiological basis of force production and movement, but also to provide a scientific rationale for surgical

treatment that may involve arthroplasties and tendon-transfer procedures. Furthermore, this thesis shows that regular hand exercise help to increase the hand function and hand force in RA. Hand exercise deserves consideration for routinely inclusion in the treatment of RA patients.

9 FUTURE IMPLICATIONS

Several questions have arisen during the study and require further research. It would be of interest to analyse how EDC responds during contraction at different locations of the muscle. In paper II , III and IV, the movement pattern in the muscle was observed, but we were unable to measure it with the methods used for this thesis. Further knowledge about *in vivo* muscle pattern could provide information about the muscle as well as the elastic characteristics of the aponeurosis and tendon.

> ➤ Is it possible that the EDC, a muscle designed for precision tasks and grip control rather than force exertion, is constructed differently from the large force-generating muscles?
>
> ➤ Can US be used as a diagnostic tool for analysing muscle disease?
>
> ➤ Are muscle movement patterns related to force production?
>
> ➤ Does this muscle movement appear in other muscle groups?

RA patients significantly increased their hand force and hand function after exercise. However, the response to exercise from RA patients must be further evaluated. It would be interesting to combine invasive and non-invasive methods to be able to answer the following questions:

> ➤ Would longer periods of hand exercise obliterate the differences between healthy and rheumatoid arthritis muscle force and function?
>
> ➤ Do the muscle's architecture, force production and decreased function depend on disease specific effects on the rheumatoid arthritis muscles?

It would be of great interest to investigate the possibility to objectively evaluate interventions, such as surgical procedures, physiotherapy and/or pharmacological treatment with the help of EX it and US.

> ➤ In a longer perspective, can it be possible to establish more efficient rehabilitation programmes for RA patients through further knowledge about the muscle biomechanics?

SAMMANFATTNING

Bakgrund

Den mänskliga handen kan ses som ett sinnesorgan eller hjärnans förläng-ning mot yttervärlden. Handen har också en central roll i kroppspråket och i varje människas kommunikation med omvärlden. Därför kan olika typer av handskador skapa stora problem för den drabbade såväl i yrkes-livet som på fritiden.

En grupp som ofta drabbas av nedsatt handfunktion är patienter med Rheumatoid Arthritis (RA). Patientgruppen har ofta försämrad handfunk-tion på grund av värk och nedsatt greppfunktion. För patienten kan detta medföra dagliga problem med vardagliga sysslor som till exempel att kamma håret, öppna mjölkkartonger eller att hålla fast ett glas när man dricker.

I detta arbete studeras underarmsmuskulaturen och dess biomekanik för att bättre förstå kraftutveckling hos friska jämfört med patienter med RA. För att uppnå detta har vi utvecklat ett nytt kraftmätningsinstrument, desig-nat en ultraljudsmetod samt utvärderat handfunktion med redan etablerade utvärderingsinstrument.

Syfte

Det övergripande syftet med avhandlingen var att öka förståelsen för extensor-muskulaturens roll vid handfunktion. Syftet med delarbetena var:

➢ Att konstruera och utvärdera ett nytt mätinstrument för finger-extensionskraft (paper I)

➢ Att studera muskelarkitekturen i extensor digitorum communis med hjälp av ultraljudsundersökningar (paper II)

➢ Att beskriva muskelarkitektur (statiskt och dynamiskt) och dess relation till kraftutveckling (paper II & III)

➢ Att undersöka eventuella skillnader i muskelarkitekturen i frisk jämfört med reumatisk muskel (paper III)

➢ Att utvärdera effekten av handträning hos reumatiker jämfört med friska kontroller (paper IV)

Metoder

Ny apparatur och nya metoder utvecklades för att möjliggöra studier på ex-tensormuskulaturen. I den första studien konstruerades ett nytt mätinstrument som mäter extensionskraften i fingrarna (EX-it). Instrument kalibrerades och validerades av 144 personer. I den andra studien designades en ultraljudsme-

tod för att utvärdera muskelarkitekturen som styr fingrarnas extensionsrörelser. Inter- och intra-observationsstudier genomfördes och referensmaterial på 40 friska män och kvinnor togs fram. I den tredje studien användes EX-it i kombination med ultraljud för att studera muskelarkitekturen statiskt och dynamiskt. Undersökningarna är gjorda på 20 kvinnor med Rheumatoid Artrits och 20 friska åldersmatchade kontroller. I studie fyra användes ovanstående metod i kombination med redan etablerade utvärderingsinstrument för att undersöka effekten av handträning för patienter med RA (n=20) jämfört med friska (n=20).

Resultat

Ett nytt instrument för fingerextensionskraft, EX-it, har utvecklats. EX-it är kalibrerat (varians i instrumentet, 1.8 %) och validerat. Variansen för friska personer var 7.1 %. Vi har även visat att EX-it kan användas för både friska och deformerade händer.

Ultraljudsundersökningarna visade signifikanta skillnader i muskelarkitektur mellan friska män och kvinnor, och mellan friska kvinnor och kvinnor med RA. Det kan också konstateras att handträning är en effektiv metod för att förbättra styrka och funktion i handen. Redan efter sex veckors träning hade handstyrkan (p < 0.01) och handfunktionen (p < 0.01) ökat signifikant. Muskelarkitekturen utvärderades med ultraljud och visade en signifikant ökning i muskelns tvärsnittsarea.

Slutsats

Nya metoder för objektiv bedömning av extensormuskelaturens kraft och funktion har utvecklats och utvärderats. Resultaten visar att EX-it är tillförlitligt och kan användas för att detektera förändring i extensionskraft efter handspecifik träning. Vidare vissar denna avhandling att RA-patienter är signifikant svagare i sin extensorkraft och att det finns muskulära skillnader mellan frisk och reumatisk muskulatur. Det kliniska resultatet, att sex veckors träning bidrar till signifikant ökning av handstyrka och handfunktion hos reumatikerpatienter, visar att handträning är effektivt för denna patientgrupp. En kort sammanfattning av forskningsresultaten har visats i Vetenskapslandet på Kunskapskanalen. Det går att se inslaget via www.hh.se/vetenskapslandet >Inslag 2007.

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FOOTNOTE

Since many references have several authors, only the two first authors are mentioned (in alphabetical order) in this thesis.