2010

International Symposium on Dupuytren’s Disease

Saturday, May 22, 2010
Sunday, May 23, 2010
### Saturday, May 22, 2010

#### 7:00am - 8:00am
Registration & Breakfast, *Sevilla Room*

#### 8:00am - 10:00am
**Session 1: Introductory Comments and Concepts**

- **8:00am - 8:15am**
  - Charles Eaton MD: Welcoming remarks.
- **8:15am - 8:45am**
  - Wolfgang Wach PhD: The Development of the Dupuytren Society.
  - Lee Osterman MD: Cline's contracture: Dupuytren was a thief. A history of surgery for Dupuytren's contracture.
  - Ghazi Rayan MD: Dupuytren's disease: anatomy, pathology, presentation.
- **9:00am - 9:15am**
  - Ardeshir Bayat MD PhD: Use of genetic analysis tools to study Dupuytren's.
- **9:15am - 9:45am**
  - Albrecht Meinel MD: The palmar fibromatosis, the loss of flexibility of the palmar finger tissue. A new insight into the disease process of Dupuytren's contracture based on clinical and anatomical findings.
  - Hanno Millesi MD: Changes of the visco-elastic properties of the palmar fascia as pathogenetic basis of Dupuytren's Disease.
- **9:45am - 10:00am**
  - Sandip Hindocha MD: Frequency of primary and incidence of recurrent Dupuytren's disease significantly impacts on the cost to the health service.

#### 10:00am - 10:15am
Break

#### 10:15am - 12:15pm
**Session 2: The Myofibroblast**

- **10:15am - 10:30am**
  - Paul Werker MD PhD: Management of soft tissue contractures: a surgical perspective.
- **10:30am - 10:45am**
  - Paul Zidel MD MS: Dupuytren's versus burn scar contracture.
- **10:45am - 11:00am**
  - Boris Hinz PhD: Fundamental aspects of myofibroblast contraction.
- **11:00am - 11:15am**
  - Sem Phan PhD MD: Mechanisms of myofibroblast differentiation.
- **11:15am - 11:30am**
  - Véronique Moulin PhD: Tissue engineering and the myofibroblasts.
- **11:30am - 11:45am**
- **11:45am - 12:00pm**
  - Heinrich Seegenschmiedt MD PhD: Review Of Radiotherapy For Morbus Dupuytren &Ledderhose.
- **12:00pm - 12:15pm**
  - Open Discussion: The Myofibroblast

#### 12:15pm - 1:00pm
Lunch, *Indigo Restaurant*

#### 1:00pm - 3:00pm
**Session 3: Demographics and Genetics**

- **1:00pm - 1:15pm**
  - Sandip Hindocha MD: Familial pattern and inheritance of Dupuytren's Disease: a comparison of populations and pedigrees in the UK and Iceland.
- **1:15pm - 1:30pm**
  - Guido Dolmans MD: A clinical genetic study of familial Dupuytren's Disease in the Netherlands.
- **1:30pm - 1:45pm**
  - Vilhjalmur Finsen PhD: The epidemiology of Dupuytren's disease in Bosnia.
- **1:45pm - 2:00pm**
  - Hans Hennies PhD: Characterization of the epidemiology and genetic basis for Dupuytren Contracture.
- **2:00pm - 2:15pm**
  - Guido Dolmans MD: A first genome-wide association study in Dupuytren's disease.
- **2:15pm - 2:30pm**
  - Sandeep Kathju MD PhD: Establishing an animal model of Dupuytren's contracture by profiling genes associated with fibrosis.
- **2:30pm - 2:45pm**
  - Sandra Kraljevic Pavelic PhD: Microarray expression analysis of Dupuytren's contracture.
- **2:45pm - 3:00pm**
  - Guido Dolmans MD: Linkage analysis in six Dutch families with Dupuytren's disease.

#### 3:00pm - 3:15pm
Break

#### 3:15pm - 5:15pm
**Session 4: Collagen and Cell Biology**

- **3:15pm - 3:30pm**
  - Susan Emeigh Hart VMD PhD: A primer of collagen biology; synthesis, degradation, subtypes and role in Dupuytren's contracture.
- **3:30pm - 3:45pm**
  - Janine Morris PhD: Collagen degradation and the expression of proteases involved in collagen metabolism in the contraction of collagen gels by Dupuytren's disease-derived fibroblasts.
- **3:45pm - 4:00pm**
  - Martin Robson MD: Using laboratory models to develop molecular mechanistic treatments for Dupuytren's disease.
- **4:00pm - 4:15pm**
  - David O’Gorman PhD: Primary Dupuytren's Disease cell interactions with the extra-cellular environment: a link to disease progression?
- **4:15pm - 4:30pm**
  - Christina Raykha MSc: Insulin-like Growth Factor Binding Protein (IGFBP)-6: A mediator of myofibroblast differentiation in Dupuytren’s Disease?
- **4:30pm - 4:45pm**
  - Sandip Hindocha MD: Annexin’s role in Dupuytren’s disease - identification of a novel biomarker involved in the apoptotic pathway.
- **4:45pm - 5:00pm**
  - Sandip Hindocha MD: Dupuytren’s disease shows profound hematopoietic and mesenchymal stem cell abnormalities involving palmar fat and skin in addition to fascia: Novel implications for pathogenesis and therapy.
- **5:00pm - 5:15pm**
  - Open Discussion: Collagen and Cell Biology

#### 6:15pm - 7:00pm
Cocktail Reception, *Chopin Ballroom*

#### 7:00pm - 9:00pm
Dinner Reception and Presentation, *Chopin Ballroom*

- **7:00pm - 9:00pm**
  - Paul Wylock MD: A Working Day of Guillaume Dupuytren
7:00am - 8:00am  Breakfast  
Sevilla Room

8:00am - 10:00am  Session 5: Surgical Treatments  
8:00am - 8:15am  Lynn Ketchum MD: Dermofasciectomies and full-thickness skin grafts in the treatment of Dupuytren’s contracture: a thirty-six year study.  
8:30am - 8:45am  Andrey Zhigalo MD: The features of surgical tactic in treatment of patients with severe stages Dupuytren contracture.  
8:45am - 9:00am  Ilse Degroef PhD MD: Surgical outcome of Dupuytren’s disease. No higher self-reported recurrence after segmental fasciectomy.  
9:00am - 9:15am  Michael Papalozos MD: Minimizing cutaneous necrosis and delayed healing after surgical treatment for Dupuytren’s contracture: the mini-chevrons incision.  
9:15am - 9:30am  Bernhard Lukas MD: Treatment of severe Dupuytren contracture by homodigital flaps.  
9:30am - 9:45am  Massimiliano Tripoli MD: The “Jacobsen flap” for the treatment of stage III-IV Dupuytren’s disease at the little finger: our review of 123 cases.  
9:45am - 10:00am  Paul Smith MD: A Logical Approach to the PIP Joint in Dupuytren’s.

10:00am - 10:15am  Break

10:15am - 12:15pm  Session 6: Needle Release and Manual Therapy  
10:15am - 10:30am  Holger Erne MD: Percutaneous needle fasciotomy a serious alternative?  
10:30am - 10:45am  Annet Van Rijssen MD: 5-year results of first-ever randomised clinical trial on treatment in Dupuytren’s disease: percutaneous needle fasciotomy versus limited fasciectomy.  
10:45am - 11:00am  Roger Khouri MD: Extensive Percutaneous Aponeurotomy and Lipografting: A new treatment alternative for Dupuytren’s disease.  
11:00am - 11:15am  Bing Siang Gan PhD MD: Needle aponeurotomy for Dupuytren’s contracture, the HULC experience.  
11:15am - 11:30am  John Agee MD: Growing the PIP straight with the Digit Widget.  
11:30am - 11:45am  Terri Skirven OTR/L CHT: Hand therapy for Dupuytren’s: Concepts, practical tips and problems.  
11:45am - 12:00pm  Albrecht Meinel MD: The role of static night splinting after contracture release for Dupuytren’s disease. A preliminary recommendation based on clinical cases.  
12:00pm - 12:15pm  Deborah Larson BScOT, MSc: Splinting after contracture release for Dupuytren’s disease (SCoRD) - a pragmatic, multi-centre, randomized controlled trial.

12:15pm - 1:00pm  Lunch  
Indigo Restaurant

1:00pm - 3:15pm  Session 7: Biologic Intervention: Dupuytren’s and Related Conditions  
1:00pm - 1:15pm  Marie Badalamente PhD: Injectable collagenase clostridium histolyticum for Dupuytren’s contracture: results of the cord 1 study.  
1:15pm - 1:30pm  Anne Ouellette MD MBA: Outcomes of Apligraf use in Dupuytren’s surgery using the McCash incision improves long term outcome.  
1:30pm - 1:45pm  Ilse Degroef PhD MD: Cellular implant improves surgical outcome in Dupuytren’s disease.  
1:45pm - 2:00pm  Heinrich Seegenschmidt MD PhD: Radiotherapy For Primary Or Recurrent Morbus Ledderhose: 12 Year Long-Term Outcome Of A Prospective Phase 2 Trial.  
2:00pm - 2:15pm  Wayne Hellstrom MD: Medical Management of Peyronie’s Disease.  
2:15pm - 2:30pm  Terry Spiikens DPM: Cryotherapy for Plantar Fibromas.  
2:30pm - 2:45pm  Chriishan Samuel PhD: Relaxin: an emerging therapy for fibroproliferative disorders.  
2:45pm - 3:00pm  Davor Jurisic PhD MD: Screening of potential prodrugs on cells derived from Dupuytren’s disease patients.  
3:00pm - 3:15pm  Ilse Degroef PhD MD: Highly-dosed neo-adjuvant tamoxifen improves surgical outcome in segmental fasciectomy in high risk patients with Dupuytren’s disease.

3:15pm - 3:30pm  Break

3:30pm - 5:15pm  Session 8: The Future  
3:30pm - 5:10pm  Panel Discussions: Global collaboration for Dupuytren's and related conditions.  
5:10pm - 5:15pm  Charles Eaton MD: Closing remarks.
Session 1: Introductory Comments and Concepts
Welcome to the 2010 International Symposium on Dupuytren’s Disease. I am a hand surgeon and here’s my story. Larry Hurst and Marie Badalamente worked for years developing collagenase treatment for Dupuytren’s. Their industry partner hosted a Dupuytren’s patient on line discussion forum. A patient read about needle release on that forum and asked me to visit Paris and learn it there from Dr. Lermusiaux. I did. Three things happened. First, I became very busy treating Dupuytren’s with this new procedure. I have now treated about 8000 Dupuytren hands. Second, I realized that I am very lucky, and wanted to give back to the community that gave me this opportunity, starting with this symposium. Third, I don’t have the answer for Dupuytren’s, and it’s driving me crazy. It’s a problem which faces all of us. We are not all that different. There’s a good chance that genetic testing would show that you and I share a common ancestor, and if we had better information on chromosome number 6, we might find that our common ancestor carried the gene for Dupuytren’s. Any of us could have Dupuytren’s.

The quest to find the best way to treat this has challenged the most talented people in the world for hundreds of years. In 1974, Marc Iselin posed a number of questions in a piece titled “Mysterious aspects of Dupuytren’s contracture”. If it’s not a tumor or infection, why does it act like one? Why is it so unpredictable? How does it form cords in areas where there really isn’t a defined fascia? Why does it blow up unpredictably after surgery? Forty years later, we only have more questions. Could it be a congenital viral infection? How can we turn it off? When is therapy not enough or too much? If it’s genetic, why is it so variable, both individually and in large groups of affected people? What is the deal with blue eyes? This list goes on forever, but really there is just one question: What do we have to ask, what do we have to know, what do we have to do to find a cure? Well, we start with meetings like this.

This is the sixth, possibly seventh international meeting on Dupuytren’s. The first that I could find was organized in 1966 in Paris by Gossett, Tubiana and Hueston, then one in Torino, Italy in 1981. Professor Millesi chaired the 1983 Vienna meeting, McFarlane the 1985 London, Ontario congress. The 1991 Hannover symposium was led by Berger, Delbrück, Brenner and Hinzman. Nearly twenty 20 years later Hurst and Badalamente had a symposium in Stony Brook. Now, we meet in Miami. These conferences have had three main topics: science, surgery and disease modification. In books on Dupuytren’s, if you count the pages, you’ll find that the great majority of writing has been split between science and surgery. But disease modification - that’s what we really need, because Dupuytren’s is not a surgical disease: it’s a medical condition for which there is not yet a medicine. We need to work together with this goal in mind. My hope is to spur efforts to make progress with disease modifying treatments. We’ll always need surgery, but we won’t always need much.

Dupuytren’s hands are all different, like snowflakes: one process, infinite variety. Most people who have surgery for Dupuytren’s do pretty well, but a significant number do very poorly. They don’t come back for another surgery. They say things such as “If I had known what I was getting in to, I never would have had that surgery”. You don’t hear that from people who have had surgery for other hand problems. Those of you who don’t offer alternative treatments for Dupuytren’s have no idea, really no idea at all, how many people there are who want to be treated but do not want and will not have surgery for Dupuytren’s.

The more you look at Dupuytren’s, from any angle, the more impossible it seems. It seems simple, but it’s not. How do you solve an impossible problem? Question convention. Examine failure. Engage outsiders. We are all outsiders. None of us truly understands Dupuytren’s, but we each have the gift of a unique perspective to contribute. We need to communicate. Blocked by different languages, different professional environments, and by the constraints of publishers, we are a Zen koan: If a tree falls in the woods, and someone sees it and writes a book about it, but doesn’t write clearly, and the book goes out of print, and time passes, did someone discover a falling tree? The answer? No. We can not work in isolation. We have to share what we know. Discover, simplify, communicate.

Dupuytren’s is genetic, it’s mechanical and it’s biological: it’s all of these; you can’t separate these and understand Dupuytren’s. The gap between the laboratory model and the real thing can be just as big a hurdle as the gap between the clinical plan and its execution. We have to cross these obstacles. And we can, because we have two strengths. First, we are explorers – every one of us. We have a need to discover. We are comfortable with difficult challenges, each in our own way, and in our lives we each have witnessed things that few other people have seen. We all know that if we don’t reach for the unknown, we will never know what lies within our grasp. Second is that we are all lifetime students. We are academics. We see the beauty of science in the universe, appreciate mathematics in everyday things, and enjoy learning new perspectives.

It’s a tough problem, but not impossible. There are three very interested groups who can and must work together: patients, researchers and clinicians. To this end, I established the Dupuytren Foundation, a charitable organization with a mission to promote efforts to find better treatment options for Dupuytren’s and related conditions. Dr. Wolfgang Wach created the Dupuytren Society, a patient oriented
internet based association. The Foundation and the Society are the hosts of this symposium. The ultimate goal of this symposium is to create an academic international Dupuytren’s task force to develop and carry out large scale collaborative multicenter research and clinical studies to develop better treatment options for Dupuytren’s – to work for a cure.

Up to this point, international symposia on Dupuytren’s have been about current concepts, state of the art. This symposium is about the future. Inroads into Dupuytren’s disease modification have potential impact on the treatment of other fibrotic conditions including pulmonary fibrosis, renal interstitial fibrosis, cirrhosis, scleroderma and other life altering conditions. We all stand on a great threshold. Welcome to the 2010 International Symposium on Dupuytren's Disease. Here is your chance to make a difference.
8:15am-8:30am  Wolfgang Wach PhD: Dupuytren Society: Joining forces in fighting Dupuytren’s disease

Dupuytren Society was founded in 2003 in Germany. Goals are spreading knowledge of therapeutical options to treat Morbus Dupuytren and Ledderhose, support of patients and patient groups, supporting research, and – last not least – bringing medical doctors and patients together. Dupuytren Society considers itself a joint interest group of patients and doctors. Because Dupuytren’s disease is not confined by borders Dupuytren Society has been acting internationally from the very beginning.

Today Dupuytren Society manages English and German web sites and runs two forums with close to 1,500 registered users from all over the world. Many more unregistered users are accessing our forum, typically 500 – 700 per day. We have been supporting several research projects, including this conference.
8:30am-8:45am  Lee Osterman MD:  Cline’s contracture: Dupuytren was a thief

Though he captured the eponym, Baron von Dupuytren plagiarized most of his thoughts from Sir Henry Cline and his pupil Astley Cooper. Henry Cline first dissected a hand with Dupuytren’s contracture in 1777 and defined the abnormality of the palmar fascia and ten years later described its treatment by palmar fasciotomy. Cooper later wrote in 1822 “When the Theca is Contracted, Nothing Should be Attempted for the Patient’s Relief, as no Operation or Other Means Will Succeed; but When the Aponeurosis is the Cause of the Contraction, and the Contracted Band is Narrow, it May be with Advantage Divided by a Pointed Bistoury, Introduced Through a Very Small Wound in the Integument. The Finger is then Extended and a Splint is Applied to Preserve it in the Straight Position”. Cooper’s description is more akin to Needle aponeurotomy. Dupuytren visited Cooper at Guy’s hospital in 1826 and did not perform his first surgery until June 12, 1831. He also described a wider transverse incision, leaving the wound open as later echoed by the McCash technique.

Another contribution by Dupuytren was his stress on postoperative extension splinting to prevent recurrence thus influencing the postoperative therapy for the next 175 years. He, like Cooper, emphasized an occupational predisposition.

Jean Goyrand (1803-1866) presented his thesis on retraction of the fingers to the Royal Academy in 1834-5 and contrary to Dupuytren he argued for fasciectomy. As anesthesia and wound management advanced the limited incisions of the 19th century became more complex and the fasciectomy more radical. Recurrence rates drove surgeons to more and more radical fasciectomies as epitomized by Skoog. Complications and stiff hands led Hueston and others to advocate limited fasciectomies. Results seemed to vary more in relation to patient disease and motivation than to the specific type of surgery performed.

Hueston noted the lack of recurrence beneath and skin graft and thus championed the technique of Dermofasciectomy and skin grafting in 1962. He reserved its use for recurrent surgery and high diathesis patients. Protracted recovery and residual PIPJ contracture remained the rule.

The wheel continues to turn and in this upcoming era a return to minimalist fasciotomy techniques, whether by needle or collagenase brings us full circle back to the limited fasciotomy of Cline and Cooper.
Anatomy

Palmar fascial Complex (5 components)

- Radial aponeurosis
  Pretendinous band (PTB) to thumb: Very small
  Distal commissural ligament (DCL): Extension of natatory ligament (NT)
  Proximal commissural ligament (PCL): Extension of transverse ligament of the palmar aponeurosis (TLPA)

- Ulnar aponeurosis
  Abductor digiti minimi (ADM): soft tissue coalescence

- Central aponeurosis
  Three dimensional fiber orientation
  Longitudinal
    PTB: split distally. Split PTB terminates into 3 layers (McGruther)
    - Superficial layer: Attaches in dermis
    - Middle layer: 1) Free in digit and 2) Continue as spiral band
    - Deep layer: Flexor and extensor mechanism
  Transverse
    NL: Continuous proximal border and U shape distal border.
    Contributes to formation of lateral digital sheet (LDS)
    TLPA: Deep to PTB, gives origin to septa of Legueu Juvara

- Palmodigital fascia
  Spiral band (SB) of Gosset: Along with soft tissue coalescence
  Contributes to the formation of LDS

- Digital fascia (neurovascular bundle surrounded by 4 ligaments)
  1. Gosset lateral digital sheet
  2. Grayson’s ligament
  3. Thomine retrovascular fibers
  4. Cleland’s ligaments
  Landsmeure retinacular ligaments (transverse and oblique)

Pathology

Nodules: Palmar or digital
Cords: Palmar, palmo-digital or digital
Normal bands form pathologic cords
Cords cause tissue or joint contracture

- Dermopathology
  Grapow fibres / Micro-cords / Skin thickening
  1st layer of split PTB / Dermal cord / Skin pit

- Radial aponeurosis
  PTB / Pretendinous Cord / MP joint flexion contracture
  DCL / Distal commissural ligament cord / First web space contracture
  PCL / Proximal commissural ligament cord / First web space contracture

- Ulnar aponeurosis
  ADM coalescence / Isolated digital cord / PIP joint contracture
  Isolated digital cord components are similar to spiral cord without PTB

- Central aponeurosis
  PTB / PT Cord / MCP joint flexion contracture
  Septa L&J / Vertical cord / Stenosing tenosynovitis
- **Palmodigital fascia**
  - NL / Natatory Cord / Web space contracture
  - SB / Spiral Cord / PIP and MCP joint flexion contracture
  - Spiral Cord components = PTB + SB + LDS + Grayson's ligament (McFarlane)

- **Digital fascia**
  - 2nd layer of split PTB / Central Cord / PIP joint flexion contracture
  - LDS / Lateral Cord / PIP joint flexion contracture
  - Retrovascular fibers / Retrovascular Cord / PIP joint flexion contracture

**Clinical Types**

1. **Typical Dupuytren’s disease**
   Caucasian male, northern European, 57 years of age, has bilateral progressive disease, and more than one digit involved. Family history is often present and genetic factors are important in the pathogenesis. Treatment is often surgical.

2. **Non-Dupuytren’s disease**
   Ethnic diversity, no gender predilection, lack of family history, non-ectopic, non-progressive or regressive, unilateral, confined to the palm and in line with a single digit. Factors contributing to pathogenesis are: trauma, previous surgery and diabetes. Treatment is non-surgical.

The vast discrepancies in the disease prevalence (2-42%) and treatment outcome ie recurrence (0-71%) are probably related to lack of differentiation between these types. Future epidemiologic and outcome studies should take into account the types of palmar fascial contracture, typical DD and atypical DC. Rayan G. OKO chapter on Dupuytren’s Disease, AAOS web site www.aaos.org.

**Dupuytren’s Disease Textbooks**

DD is a nodular palmar fibromatosis of unknown cause, commonly affecting the hands. DD is often a familial condition that has been reported in twins and is extremely common in individuals of North European extraction. Genetic studies have yet to identify the genes involved in DD formation. It was Dupuytren’s assistant Goyrand in 1834 who first noted the link between DD and its familial predisposition. Since then, several reports have suggested the presence of familial tendency in DD. Average figures for family incidence have been reported to vary from 10 to 30%, however, studies with specific enquiries and clinical examination of relatives of DD cases have shown the presence of a family history in patients with rates as high as 44% to 68%. Ling in 1963 interviewed 50 DD cases and reported a 16% positive family history but after examination of the hands of 832 relatives of those 50 DD cases he showed that the incidence of family history had risen to 68%. Several case reports have indicated the presence of DD in twins. Observations in twin studies and family studies suggest genetic heredity for DD. Early case reports documented four pairs of monozygotic twins both presenting the disease. Familial prevalence in DD has been documented and individuals with a strong family history of DD may develop more severe forms of the disease at a younger age. We determined a sibling recurrence-risk ratio of 2.9 in north-western England population. Studies characterising racial population prevalence and DD phenotype also suggested a geographic variation that may be consistent with genetic predisposition. DD inheritance mode has been shown to be autosomal dominant mode with variable penetrance; however, it is currently unclear if DD is a complex oligogenic or a simple monogenic mendelian disorder. Hu et al. have established a 6cM region on chromosome 16q (between marker D16S419 and D16S3032) in a five-generation Swedish family, with a maximal two-point logarithm of odds score of 3.18 at D16S415. In addition, a possible role for transforming growth factor (TGF)-β in DD has been suggested. Case-control studies have been carried out to assess the association between DD susceptibility and single nucleotide polymorphisms (SNP) in the TGF-β pathway. These studies have focused on TGF-β1, TGF-β2, TGF-β receptor one (TGF-βRI), TGF-βRII, and TGF-βRIII. Although there is a lack of association between DD and these SNPs, it is possible that other un-investigated regions of the genes may still contain DD causative polymorphisms or mutations. Increased activation or expression of TGF-β1 can be induced by Zf9 transcription factors or mitochondrial alterations (partial mitochondrial depletion or treatment with mitochondrial inhibitor). Positive association has been determined between DD susceptibility and the presence of a G allele versus an A allele SNP at position 1140 of Zf9 transcription factor. In addition, we reported a positive association between DD susceptibility and a heteroplasmic mutation located within the mitochondrial 16s rRNA region. Previous cytogenetic studies have shown acquired structural and numerical chromosomal abnormalities in cells grown from DD tissue samples compared to normal palmar fascia. These studies demonstrated a variable number of abnormalities in affected tissue, compared to normal palmar fascia. All studies showed cells grown from DD tissue to be trisomic for chromosome 8 with a few being trisomic for 7 and Y chromosome abnormalities. However, the transverse fascial tissue used as control showed similar chromosomal aberrations as the DD nodular tissue. Evidence for chromosome trisomy 8 is also found in other benign tumours. However, another study looking at 40 DD tissue samples from 36 DD cases did not reveal any consistent chromosomal structural changes. The HLA-antigen status of Dupuytren’s patients has been recorded and at least one possible pattern of association has emerged. There is a gradation in expression of certain genes in DD tissue phenotypes (cords and nodules) compared to external control fascia. Transcriptome (mRNA transcripts present in a cell at a given time) profiling is not only predictive of disease but of disease phenotype. These results indicate a number of significant candidate genes associated with DD formation. Genetic studies may provide clues for molecular mechanisms involved in DD pathogenesis and may help further development of strategies for diagnosis, therapy and prophylaxis of DD.
9:15am-9:30am  Albrecht Meinel MD: The palmar fibromatosis or the loss of flexibility of the palmar finger tissue: A new insight into the disease process of Dupuytren’s contracture based on clinical and anatomical findings

Today it is generally accepted that Dupuytren’s disease starts as a nodule somewhere within the palmar soft tissue of the hand – the fibro-fatty-layer between the skin on one side and the aponeurosis and the fibrous tendon sheaths, respectively, on the other side. Nevertheless, the traditional view of the disease process is still using the picture of a contraction of pre-existing fibrous bands. Yet the key to a consistent pathogenesis can only be found if the structural and functional mix of tissue is taken into account that the fibromatosis creates in the subcutaneous tissue. Already more than 50 years ago Vernon Luck had focused on the interaction between the proliferating nodule and the fibrous bands, and he developed a concept of the pathogenesis that in its fundamental view is still valid today. The concept presented in this paper is based on Luck’s concept.

The basic biomechanical processes in the living hand are instrumental in understanding the disease process. The soft palmar tissue above the aponeurosis and the fibrous tendon sheaths consists of skin anchoring fibers, enclosed fat and skin. When fingers are moved this area is subject to very significant changes in length. Stationary tissue areas only exist in the mid palm and in the fingertips. The interposed soft tissue above the finger skeleton is compressed and folded up when the fingers are flexed and unfolded when the fingers are extended. This requires a complex structure of the skin anchoring fibers to allow for tension free tissue movements. When being used and in their relaxed position fingers are more or less flexed and thus the compressed, folded tissue is the dominant tissue formation. The proliferating nodule of fibromatosis now occupies the subcutaneous tissue predominantly in its flexion formation, and effect that so far has not sufficiently been taken into account. So there is no need for implicating a contracting tissue process. The fibromatosis occupies the shortened, compressed tissue. The fat is being displaced and a conglomerate develops that consists of proliferating tissue, enclosed skin anchoring fibers in their flexion position, and attached structures of deeper tissue, like the aponeurosis or the vertical septa. When the fingers are extended this complex becomes subject to tension which has an effect on morphogenesis and histogenesis of the Dupuytren tissue. The fibromatosis “freezes” the flexion formation of the palmar tissue and the flexed fingers cannot be extended freely anymore, thus creating the well known extension deficit. The since 400 years postulated and never ultimately proven concept of contraction digitorum thus becomes redundant. The pulling tension acting on Dupuytren tissue can explain the transformation of fibroblasts into myofibroblasts, the tendiniform alignment of the tissue conglomerate and the reactive hypertrophy of the attached fiber structures. And the structural remodeling of the subcutaneous fibers can interpret the frequently observed displacement of the finger nerves. These typical findings are illustrated in detail using clinical and anatomical in situ pictures. And the therapeutic consequences of this contraction free concept are discussed and include a minimized resection at fasciectomy and a long-term use of static night splinting.
9:30am-9:45am  Hanno Millesi MD: Changes of the visco-elastic properties of the palmar fascia as pathogenetic basis of Dupuytren`s disease.

Hypothesis:
Due to the most popular thesis of the pathogenesis of Dupuytren`s disease (DD) the pathology starts with the occurrence of cellular nodules. In contrast other authors (Millesi 1965) believe that DD is a systemic disease which occurs also in the plantar aponeurosis at the penis as induratio penis plastica and that changes of the properties of the collagen fiber bundles of dense connective tissue also outside of the actual aponeurosis proceed the cellular proliferation. To collect informations about this question the visco-elastic properties were studied.

Method:
We studied the residual elongation (1), which is a quantitative description of the viscous component of a visco-elastic tissue, and the so called recovery time (2). A second stress-strain test does not follow the same pattern as the first one. It takes some time until the tissue recovers to the original state in a way that another stress-strain provides the same pattern as the first one. We have studied: 1) The residual elongation of the following tissues after elongation of 2.5%, 5% and 10%.
   1. Normal palmar aponeurosis of patients without DD.
   2. Normal palmaraponeurosis of patients with DD at another location.
   3. Thickened fiber bundles from patients with DD without occurrence of nodules or contracture bands in the area.
   4. Contracture bands
   5. Advanced contracture bands.
2) The recovery time of specimens of the same 5 groups.

Results:
Residual elongation:
After 10% elongation the residual elongation in apparently normal tissue of the palmar aponeurosis of patients with DD without any macroscopic or microscopic sign of DD was significantly increased over the control. Thickened fiber bundles without cellular proliferation had a significant increase in all three categories. The same was observed in group 4 and 5.
Mechanical recovery:
The mechanical recovery time of normal palmar aponeurosis of patients without DD was about 10 minutes. This value did not differ significantly in group 2 and 3. There was however an enormous increase in group 4 and 5.

Conclusion:
From this study the conclusion can be drawn that the occurrence of cellular proliferation is preceeded by changes of the visco-elastic properties of the fiber bundles of the palmar aponeurosis. The development of bands and the occurrence of contracture are accompanied by an enormous increase of the recovery time.
9:45am-10:00am  Sandip Hindocha MD:
Frequency of primary and incidence of recurrent Dupuytren’s disease significantly impacts on the cost to the health service

Hindocha S, Hearndon A, Stanley JK, McGrouther DA, Bayat A

Introduction:
Dupuytren’s Disease (DD) is a disease of the palmar fascia with unknown aetiology. Surgical resection of diseased tissue is the primary mode of treatment. Unfortunately DD is recurrent following surgical management which can be debilitating for the patient. There have been many attempts to conduct epidemiological studies to calculate the incidence or prevalence of DD. We aim to conduct an epidemiological study to calculate the prevalence of DD operative activity in five major Hand units in the North West of England.

Methods:
Surgical codes for DD operations were identified including operative procedures for revision or recurrent cases between April 2001 and March 2003. The average cost of a DD procedure is estimated at £2,200. The total number of primary procedures and revision procedures was calculated in a 24 month period. Cost during this period was also calculated.

Results:
A total of 494 primary DD operations were conducted and 148 (30%) revision procedures, equating to an estimated cost of £1,412,400 in 2 years for 5 trusts or £282,480 for an individual trust.

Conclusion:
It is evident from this study that DD bears a significant financial burden on the health service. It is crucial to perform primary DD surgery at the correct time and to also carry out the most beneficial procedure to minimise recurrence. Guidelines are suggested to improve the exact timing and type of surgical management in order to optimise patient treatment and operative cost.
Session 2: The Myofibroblast
Any injury to soft tissue and skin will initiate a cascade of events, ultimately resulting in the formation of a scar. The type of scar that is formed and its behaviour in time depends on a great number of variables such as the general condition of the patient (nutritional state and underlying diseases), the age of the patient (young versus old), type of injury (crush versus clean cut), amount of contamination with dirt and bacteria, condition of the soft tissues (healthy versus damaged by radiotherapy, chemotherapy, systemic medication), location of the scar on the body, its position relative to skin tension lines (parallel versus perpendicular), the skin type (Fitzgerald’s skin types), the amount of tension on the wound, wound management etc., etc.

A surgically inflicted scar, planned and placed respecting the above in a healthy patient, usually remains within the borders of the original wound and may end as a fine line, which is hardly visible. Nevertheless, it may also become atrophic or hypertrophic or even grow beyond the borders of the original wound and give rise to the formation of a keloid. Besides, any scar has a tendency to contract which in itself may cause functional or aesthetic problems, necessitating further action.

There are various treatment modalities available for scars in the skin. Their application is dictated by the appearance of the scar, but usually consists of topical application of silicone gel sheeting, steroid injection and pressure, and 585-nm pulse dye laser, if erythema persists for more than 1 month. Whenever the primary wound conditions have been unfavourable, re-excision can be done. Widespread burn hypertrophic scars can best be treated at burn centres with the earlier mentioned treatments combined with custom made pressure garments, massage and ultrasound. Ultimately skin transpositions and transplantation might be unavoidable.

The treatment of keloid is even more difficult and should take place in specialized centres. Minor, immature keloids can be treated with intra-lesional steroid injections combined with silicone sheeting. More mature keloids usually do not respond to this treatment and need excision combined with low-dose radiotherapy on the fresh scar to reduce the rate of recurrence.

In plastic surgery we are not only faced with a great variety of skin scars. Scars may also form around tendons or joint and thereby limit function, or form in response to the implantation of a foreign body such as a breast implant and cause capsular contraction, or at the adaptation site of vessels or nerves hampering the passage of blood or the outgrowth of axons. Last but not least, it may form in diseases such as Dupuytren’s, Ledderhosen’s or Peyronie’s for unknown reasons.

The aim of this presentation is to summarize what is we know about scar formation and explain how plastic surgeons try to manage this process and modulate it if necessary in all these circumstances.
10:30am-10:45am  Paul Zidel M.D., M.S.: Dupuytren’s versus Burn Scar Contractures

Scal formation and resultant contracture can be considered the body's response to an untoward event. The purpose of this presentation is to review the intersection of burn scar contractures and Dupuytren's contractures.

Hypothesis:
Burn scar contractures and Dupuytren’s contractures have significant similarities, which can allow cross-referencing of literature and treatment modalities to affect eventual outcomes. Although the underlying mechanisms, time frames and phases may vary, common methods may alter outcomes in both.

Methods:
Extensive literature search is being conducted for overlapping knowledge base basic information and treatment considerations. All aspects are being explored, both on the cellular and DNA level as well as macro and physical modalities.

Results:
Desmouliere and Gabbiani have written on the role of the myofibroblast in wound healing and fibrocontractive diseases with hypertrophic scar containing significant amounts of myofibroblasts. The progressive depth of the burn or wound injury alters the subset of fibroblasts. Fibroblastic formation has been modulated by cytokines such as TGF-beta, IGF-1, Interferons and possible T-lymphocytes. The “physical stretch model” has been reviewed. The common thread throughout multiple studies suggests that there are significant similarities of scar and contracture formation by burns and Dupuytren’s to warrant further investigation and application.

Summary:
The mechanisms of injury are different between burns and Dupuytren's. The burn insult is usually a single inciting external event causing superficial to deep progression. Dupuytren's is an internal insidious progression. The end result in a subset of patients though is quite similar. It is the identification of these patients and their response to intervention which successfully alters the deteriorating cascade that is exciting. The hypertrophic burn scar contracture and the Dupuytren's contracture have significant commonality and overlap to warrant further combined data sharing to alter long-term effects.
10:45am-11:00am  Boris Hinz PhD:  Fundamental aspects of myofibroblast contraction

The high contractile force generated by myofibroblasts is beneficial for physiological repair but detrimental for organ function when it becomes excessive such as in the dramatic contractures characterizing Dupuytren’s diseases. I will present a new model of how myofibroblast contraction leads to irreversible tissue contractures. We support this model with recent findings combining Ca2+ fluorescence imaging with atomic force microscopy, culture on compliant substrates, and microbead tracking using myofibroblasts in cell culture. We show that Rho/ROCK signaling promotes strong isometric cell contraction that can locally relax fibrils within a stressed matrix. This is analogous to creating slack by binding off regions of tension in a stretched rubber band. Unrestrained matrix is then free to be remodeled by weak and short-ranged microcontractions. Microcontractions occur periodically and are regulated by spontaneous cytoplasmic Ca2+ oscillations. This is the first time that two functionally and regulatory independent modes of contraction are shown to collaborate in the same cell to promote overall matrix contracture. We want to exploit our knowledge to therapeutically interfering with myofibroblast contraction to suppress connective tissue contractures.
A distinct subpopulation of fibroblasts in fibrotic tissue is characterized by expression of \(-\) smooth muscle actin (\(-\)SMA) and consequently referred to as myofibroblasts. These cells express high levels of extracellular matrix and exhibit contractile properties that may be significant in pathological alteration of mechanical properties of affected fibrotic tissues. Moreover they express high levels profibrogenic cytokines such as transforming growth factor \((\text{TGF})\). These are key properties of tissues undergoing fibrosis, thus insights into the genesis of these cells should advance understanding of the pathogenesis of fibrotic diseases. There is compelling evidence, especially in vitro that myofibroblasts are derived from appropriately stimulated (e.g. with TGF\()\) resident tissue fibroblasts, which normally do not express \(-\)SMA. Recent studies also implicate epithelial and endothelial cells as potential additional sources through a process referred to as epithelial or endothelial-mesenchymal transition (EMT). An additional potential source is the circulating “fibrocyte”. The relative contributions by these mechanisms to the overall myofibroblast population remain uncertain, especially in vivo. The mechanisms involved in myofibroblast differentiation from these diverse cell types are likely to have different components, although there may be similarities with respect to downstream TGF\(_\beta\) signaling, since this is a common agent found to be effective in inducing differentiation in all these cell types.

Give that \(-\)SMA is a key marker of myofibroblast differentiation, an obvious focus for studies into this process is directed at regulation of expression of this gene. Since TGF\(_\beta\) is a potent inducer of differentiation, most studies have focused on how it affects \(-\)SMA gene expression. Aside from involvement of the canonical Smad signaling pathway, there is evidence that MAP kinase signaling may also be involved. Studies in smooth muscle cells have implicated CArG elements, E-boxes and a purine rich motif in regulating gene expression. The corresponding transcription factors such as serum response factor (SRF) and transcription enhancer factor-1 (TEF-1) have been identified. Additionally a Smad binding element (SBE), a TGF hypersensitivity region (THR), and a TGF control element (TCE) are present in the \(-\)SMA promoter and found to be essential for induction of \(-\)SMA expression in response to TGF\(_\beta\) treatment. Additional transcription factors, such as p53, Krüppel-like factors, C/EBP, Sp1 and Sp3 have been found to be important transcriptional regulators of \(-\)SMA gene expression, although their specific importance in myofibroblast differentiation may not be identical to that in smooth muscle cells. There is evidence that some of these factors may interact with each other to affect their binding to DNA and/or activity on gene expression. The involvement of additional factors has not been ruled out. Certain repressive factors, such as gut Krüppel-like factor (GKLF), Nkx2.5, YB-1, NF B, PPAR and the liver-enriched inhibitory protein (LIP) isoform of C/EBP suggest that differentiation may be due, at least in part, to a de-repression phenomenon. Finally additional factors have been shown to have regulatory effects on myofibroblast differentiation in both fibroblasts and non-fibroblastic cell types, such as in EMT. These include the Notch signaling pathway, which appears to be important in EMT. The role of epigenetic regulation in myofibroblast differentiation adds another layer of complexity to this process. The importance of histone acetylation and DNA methylation in regulating myofibroblast differentiation is increasingly being recognized. In summary the mechanisms underlying myofibroblast differentiation are multifactorial and complex.
11:15am-11:30am  Veronique Moulin PhD: Tissue Engineering and the Myofibroblasts

Myofibroblasts are cells that are present during wound healing and numerous fibrous pathologies. They are known to contract and secrete new extracellular matrix but the complete role of these cells as well as their interactions with other cells are still not well understood. The use of a tissue engineering approach allows placing cells in a very similar context found in vivo with the presence of major elements as fibroblasts (Fb), myofibroblasts (Myo), keratinocytes (K), microvascular endothelial cells (MVEC) and/or matrix. Various methods of tissue engineering reconstruction have been performed, the method of E. Bell being the most famous where cells were seeded in a collagen gel. In our lab, we have developed a new method allowing to reconstruct tissue very similar than original one, stimulating the cells to create their own matrix similarly than they do in vivo.

Dermal cells (with or without MVEC) were allowed to grow in the presence of ascorbate. These cells formed manipulatable sheets that were then superimposed and left to adhere. Human K can then be seeded before elevating the tissue construct to the air-liquid interface to form a fully differentiated epidermis.

Thickness of the mesenchymal tissue is a good reflection of the balance of the production and degradation of the matrix and has allowed us to understand some of the phenomena involved during formation of the hypertrophic scars (Hscar). The thickness of dermis was increased when K isolated from Hsc were used in comparison with K from normal biopsies. Collagen, MMP and cell growth variation can explain the fibrotic response of Fb depending on K origin. We thus can conclude on a possible role of K during Hsc formation, secreting factors enhancing fibrosis. Capillary formation has been analyzed depending on Fb origin. When MVEC were seeded with Fb, they organized in a capillary-like network that was morphologically different depending on Fb origin. When mesenchymal cells were isolated from normal wound or Hsc, a significant increase in capillary-like structure number and length was observed in comparison with network organized in presence of Fb from normal skin. We hypothesize that Fb from wounds and Hsc could play a more important role on neovascularization than expected.

The interaction of keratinocytes, endothelial cells and fibroblasts are vital during the development of normal and pathological scars. The use of a tissue engineering approach can help to understand pathogenesis of Hsc and other fibrosis.
11:30am-11:45am Giulio Gabbiani PhD MD:
The N-terminal peptide of α-smooth muscle actin Ac-EEED inhibits myofibroblast contraction: therapeutic implications

It is well accepted that connective tissue remodeling during wound healing, fibromatoses and fibrotic diseases depends on myofibroblast contractile activity. Myofibroblasts are characterized by the neo-expression of α-smooth muscle (SM) actin (SMA), the actin isoform typical of vascular SMCs. Experimental work has shown that α-SMA expression is responsible for tension production by myofibroblasts. Our laboratory has produced a specific antibody for α-SMA whose epitope is the N-terminal sequence Ac-EEED unique for this protein. This sequence, microinjected in myofibroblasts or administered to cultured myofibroblasts by means of a cell penetrating peptidic sequence, displaces α-SMA from stress fibers and reduces myofibroblast contractility. We have also tested the action of Ac-EEED in vivo using a model of splinted wound. When the peptide is administered once a day from the 8th to the 10th day after producing a 2 by 2 cm splinted wound on the dorsal region of rats it results on a significant reduction of wound contraction 24 hours after removal of the splinting frame. These results show that Ac-EEED can influence myofibroblast contraction in vitro and wound contraction in vivo and suggest that this peptide represents a new candidate for the treatment of inappropriate connective tissue remodeling in several pathological situations, including Dupuytren’s disease.
Purpose:
This paper will review the radiobiological basis and the historical development of the use of radiotherapy in treating Morbus Dupuytren and Morbus Ledderhose. It will demonstrate how initial phase 1 – 2 studies slowly developed into phase 3 clinical trials and today’s treatment concept, and it will also explore areas still to be researched.

Material:
First clinical proposals to treat Morbus Dupuytren with ionizing radiation started in the 40es of the last century. Initially large fractions of 8 – 10Gy applied every month over a period of several months were used either with Radium sources or with low-energy X-ray equipment; thus, total doses similar to those used in cancer treatment, i.e. 40 - 60 Gy were applied. In the initial clinical studies no selection criteria were applied to indicate radiotherapy. No radiobiological research and rationale was defined. Thus, in some cases positive effects of radiotherapy were observed, while in other cases effects were only marginal or not existing. Typically for these initial study concepts and results were inconsistent selection criteria, and different stages of MD as well as different dose concepts and low numbers of patients treated. From a modern viewpoint the clinical outcome was insufficient with regard to statistics and long term follow-up.

An important step forward was the radiobiological discovery that RT is efficient in the early stage of MD, which is characterized by mitotic proliferation of fibroblasts and myofibroblasts. Clinical studies focusing on these early stages of MD including stages with nodules and cords and minor function deficit showed in long-term follow-up, that with each step of clinical progress radiotherapy becomes less and less efficient.

Results:
The final proof for the effectiveness of RT has been a long term controlled phase 3 study including a control group and two radiotherapy groups (21 and 30 Gy). Design, conduct and results of this study will be discussed in detail. Finally, detailed biological mechanisms have been discovered which help to understand long-term stabilisation achieved by radiotherapy. In addition to Morbus Dupuytren, similar effective clinical trials have been performed for Morbus Ledderhose.

Despite concerns regarding acute and chronic side effects of radiotherapy, no severe effects have been observed and salvage operation was possible without increased perioperative toxicity. Mild effects, like skin dryness, have been seen, but no damage of blood vessels, or changes in the radiated tissue that might render later surgery impossible. Moreover, no secondary cancer has been observed or reported. All other concerns will be addressed.

Conclusion:
A global standard of treatment sequence and its documentation is required. A proposal will be made to standardize clinical examination and findings for better comparison of clinical data. Further research is necessary to create an interdisciplinary research and clinical database.
12:00pm-12:15pm  Questions and Answers: Morning Sessions
Session 3:
Demographics and Genetics
1:00pm-1:15pm  Sandip Hindocha MD: Familial pattern and inheritance of Dupuytren’s disease: a comparison of populations and pedigrees in the UK and Iceland

Hindocha S, Gudmundsson K, Arngrimson R, Jonsson T, McGrouther DA, Bayat

Introduction:
Dupuytren’s disease (DD) is familial disorder of unknown aetiology. Understanding the exact inheritance pattern in DD is of relevance for better understanding and clinical management of the disease. A variety of inheritance patterns with a variable penetrance have been reported to date. The aim of this study was to compare the inheritance patterns of DD in two different populations which are commonly affected with DD.

Method:
Patients diagnosed with DD (n = 135) were randomly selected from two hospitals in Manchester, and Wrightington in the UK as well as in Reykjavik, Iceland. Family pedigrees were drawn for each patient with a positive family history and analysed demographic details, environmental risks, and the severity of disease were assessed. The variant penetrance in the UK DD cohort was estimated by calculating the population attributable risk.

Results & Conclusion:
The presence of DD in 979 relatives was obtained from 60 (44%) patients with a positive family history. Patients with a family history had a greater severity of disease than those who did not (p<0.05). An autosomal dominant pattern of inheritance with full penetrance was identified in 38 (63%) cases. The level of penetrance in the whole DD cohort was estimated at 35%. The population attributable risk was calculated at 22%. A unique Icelandic family with 22 affected members in a family of 45 members showed autosomal dominance with complete penetrance. We have identified a pattern of inheritance in familial DD which can be used to calculate the relative risk of this condition. This can be used in clinical practice to counsel patients on the likelihood of their family members developing DD in addition to planning the correct surgical treatment. Those with a stronger family history and therefore more severe disease may benefit from dermofasciectomy as a primary treatment.
**Hypothesis:**
In order to elucidate the genetics of Dupuytren’s disease, we investigate the mode of inheritance of familial Dupuytren’s disease in the Netherlands.

**Method:**
Patients with Dupuytren’s disease with two or more affected first-degree relatives were asked to participate in the study together with their family. In five families, all members were clinically examined. In the six other families, the diagnosis of Dupuytren’s disease was based on information provided by the proband. All participants completed an extensive questionnaire.

**Results:**
Eleven pedigrees, consisting of 475 family members and including 66 subjects diagnosed with Dupuytren disease, were studied. Of the affected family members, 67% were male and 33% female. Paternal transmission was observed in 45% of cases and maternal transmission in 55% of cases. Fifty-two percent of the offspring of the affected individuals also have Dupuytren’s disease.

**Summary:**
Our data suggest an autosomal dominant mode of inheritance for familial Dupuytren’s disease, but with a reduced penetrance. This confirms previous studies.
Vihjalmur Finsen PhD: The epidemiology of Dupuytren’s disease in Bosnia

Vilhjalmur Finsen, Dragan Zerajic

Background:
It is generally held that Dupuytren’s disease is more common in northern than in southern Europe, but there are very few studies from southern European countries.

Methods:
We examined the hands of a random sample of 1207 men and women over the age of 50 years in Bosnia.

Results:
The prevalence of Dupuytren’s disease was highly age dependent, ranging from 17 % for men between 50-59 years to 60 % in the oldest men. The prevalence among women was lower. The great majority only had palmar changes without contracture of the digit. The prevalence was significantly lower among Bosnian Muslim men than among Bosnian Croat and Serbian men and significantly increased among diabetics. No association could be detected between Dupuytren’s disease and smoking, alcohol consumption or living in rural or urban areas.

Conclusion:
We conclude that, contrary to previous opinion, Dupuytren’s disease is common in Bosnia.
1:45pm-2:00pm  Hans Hennies PhD: Characterization of the epidemiology and genetic basis for Dupuytren contracture

Kerstin Becker, Sigrid Tinschert, Katja-Martina Eckl, Serena Torres, The Dupuytren Study Group, Peter Nürnberg, Hans Christian Hennies

Hypothesis:
Dupuytren disease is a multifactorial fibromatosis that causes progressive and permanent contracture of the palmar fascia with subsequent flexion contracture of the fingers. A strong genetic predisposition exists but few is known about the epidemiology and the molecular etiology and pathogenesis of the disease.

Methods:
We have embarked on a comprehensive study to unravel the genetic factors involved in Dupuytren contracture. Clinical and epidemiological data were collected using a standardized questionnaire. DNA was extracted from blood samples, and RNA and fibroblasts were isolated from fresh tissue samples. Cultured cells were analyzed for the expression of myofibroblast markers such as smooth muscle actin before and after stimulation with transforming growth factor. Association analysis and expression profiling are done using Affymetrix SNP and gene arrays.

Results:
To date we have collected tissue and blood samples from 440 German and Swiss patients. 77 (18%) of the patients were females. 176 patients (40%) had a positive family background. In cases with positive family history both hands were affected in 64% as compared to 45% with no known family history. The mean age at first surgical treatment was 58 ± 13 years of age and ranged from 22-86 years. It was 58 ± 13 years in male and 60 ± 13 years in female patients. 32 patients also had knuckle pads and 27 patients showed plantar fibromatosis. 12% of the patients also had diabetes, 3% rheumatoid arthritis, and 1% epilepsy. We did not observe a clear risk factor, since about one third of the patients were (former) smokers and an association with alcohol abuse was not seen.

Summary:
A first whole genome association study is under way and further large scale genetic and cell biological analyses will be performed in order to gain insight into the genetics and pathogenesis of Dupuytren contracture. Our findings will also contribute to the understanding of stress-induced and age-dependent changes in myofibroblasts.
Guido Dolmans MD: A first genome-wide association study in Dupuytren’s disease

G.H.C.G. Dolmans, C. Wijmenga, R.A. Ophoff, P. van der Vlies, B.H.R. Wolffenbuttel, P.M.N. Werker

Hypothesis:
In order to understand the origin of Dupuytren’s disease, a genome-wide association study (GWAS) will be performed to search for genes contributing to this disease.

Methods:
In a large multicenter study in the Netherlands blood was collected for DNA isolation from approx. 1000 Dupuytren patients who visited the outpatient clinics of these hospitals. Patients are diagnosed by a qualified Plastic Surgeon. Genotyping of the samples will be conducted using Illumina CytoSNP-12 arrays. The genotyping data of 2000 individuals participating in a large population-based biobank (‘Lifelines’) will be used as controls. Cases and controls are of Caucasian origin.

Results:
We are currently in the process of genotyping 1000 Dupuytren’s disease cases. Control data has already been generated. Data analysis is expected to be completed by May 2010.

Summary:
The first GWAS on Dupuytren’s disease is currently ongoing. In order to confirm found genetic associations, replication is crucial. We are currently building a second cohort for replication studies.
Introduction:
Dupuytren’s contracture (DC) is characterized by the progressive development of a scar-like collagen-rich cord within the palmar fascia of the hand that results in permanent finger contracture. Currently, DC is incurable and is most commonly treated by surgical resection of the diseased tissue. To date no successful animal model has been described in which to evaluate potential non-surgical treatments for Dupuytren’s contracture.

Hypothesis:
In the present study, we hypothesize that establishing an animal model will ultimately serve as platform to compare variety of treatments for DC.

Methods:
Fibroblasts derived from carpal tunnel release (CTR) and DC patients were reconstituted in 0.1% low melting point agarose in Hank’s Balanced Salt Solution and tagged with Lipophilic Tracer DiR cell-labeling solution; these cells were injected into the forepaw of nude rats. The injected cells were frequently tracked in the forepaw by placing the animal into a Xenogen Ivis Spectrum imaging system for 4 - 8 weeks. At the end of 4 - 8 weeks palmar fascia tissues were harvested from both control (CT –derived fibroblasts) and experimental (DC-derived fibroblasts) animals to perform quantitative real time RT-PCR (qRT-PCR) for candidate genes of interest.

Results:
Our initial studies showed that fibroblast-derived from palmar fascia of carpal tunnel (CT) and DC patients persisted successfully in the forepaws of nude rats. Initial studies with qRT-PCR using RNA derived from four week tissues showed that mRNA levels of alpha-smooth muscle actin and type I collagen were significantly elevated in the forepaws of rats injected with DC-derived fibroblasts but not in the forepaws of rats that received CT-derived fibroblasts. The increase in α-SMA suggests fibroblast to myofibroblast transformation that ultimately may result in scar formation and contracture.

Summary:
Since DC in humans is a slow progressive disease often times requiring years to progress, in order to obtain a successful animal model which recapitulates the actual contractures typical of DC it may be necessary to inject DC-derived fibroblasts into the forepaws of nude rats periodically over months. Future studies will include injecting DC-derived fibroblasts into the forepaws of the rats once every fifteen days for a period of six months to determine if this would result in to the gross phenotypic changes observed in DC. Tissues harvested from these animals at set intervals will be utilized to perform histology, immunohistochemistry, western blot and qRT-PCR analyses to determine the changes in ECM composition and on specific genes of interest associated with fibrosis in treated vs. control animals.
Introduction:
Dupuytren’s disease (DD) is a connective tissue disorder characterized as nodular palmar fibromatosis that causes permanent contraction of one or more fingers. It has a well understood pathology but its etiology remains elusive. Surgical treatment remains the only gold standard for the disease treatment. However, it does not eliminate processes that lead to the disease symptoms appearance, and therefore, about 10% of patients have recurrence and require a new surgery. Some of the risk factors connected with DD are trauma, diabetes, alcoholism, epilepsy and liver disease. In addition, men are 10 times more likely to develop the contracture and more than 25% of older population will become affected by DD as well. We employed a high-throughput technology, the DNA microarray, to screen the entire genome for the changes in gene expression in diseased tissue as to characterize DD at a molecular level and find those genes that might be involved in of disease pathogenesis. We analyzed the obtained transcriptomics results in a biological context of protein changes revealed by our previous proteomic profiling of DD tissue samples. Important signaling molecules and signaling pathways arose from our analysis that might be central to the DD pathogenesis.

Material & Methods:
Primary cell cultures were established from surgically removed affected and patient-matched unaffected DD fascia. Total RNA was isolated by RNeasy mini kit (Qiagen) and further used for microarray expression analysis (HG-U133A array, Affymetrix). Data was analyzed by the software MAS5, GeneSpring and GENEMAPP that gave a list of 18 differentially expressed genes among the cells grown from affected and unaffected samples. Selected genes were further analyzed by a TaqMan probe based real-time PCR and the results were processed with geNorm, rest-384-beta and comparative CT method for relative quantification. For the protein status study, Western blot analyzes of cells grown from affected and unaffected tissue samples were performed.

Results & Discussion:
A total of 10 out of 18 differentially expressed genes that had the same expression pattern as obtained by microarray analyzes were confirmed by real-time PCR. RT-PCR data showed variability in the expression among patients which is expected in working with clinical samples. Gene was considered to be confirmed if in 10 or more patients his expression was the same as on the array. Proteins encoded by confirmed genes are directly involved in:
- interaction with actin and smooth muscle contracture
- remodulation of extracellular matrix
- proliferating and anti-apoptotic signals
Guido Dolmans MD: Linkage analysis in six Dutch families with Dupuytren’s disease

G.H.C.G. Dolmans, K.R. van Eijk, R.A. Ophoff, C. Wijmenga, P.M.N. Werker

Hypothesis:
Mapping genes in Dupuytren’s disease using pedigree-based linkage analysis will provide insight into the location of causal genes.

Methods:
Six Dutch families, in which Dupuytren’s disease is inherited in an autosomal dominant pattern, were ascertained by a trained clinician. Blood was drawn from 32 participating family members, of which 30 affected and 2 unaffected. A genome wide linkage analysis with 10,000 SNPs was performed.

Results:
Parametric linkage revealed a region on chromosome 14 with a LOD score of 1.9. Also in a non-parametric linkage this region has a LOD score of 1.8. More families and family members are ascertained at this moment to improve the power of the study.

Summary:
The first attempts of discovering genetic linkage in six Dutch families are made.
Session 4:
Collagen and Cell Biology
Collagen is the primary structural protein of the extracellular matrix. To date, 28 structurally distinct subtypes of collagen have been identified which serve not only as structural components of the interstitial matrix but also function as adhesive and occlusive components of basement membranes, as anchoring fibrils between cells and the interstitium, and as integrative transmembrane proteins. In addition to their structural functions, collagens have a number of physiologically important roles as well. Collagen can serve as an extracellular “sink” for a number of growth factors and cytokines that are released in active form during the process of collagen degradation; additionally, the degradation products of collagen have a number of physiologic activities that are important to the process of wound healing.

The extracellular matrix collagens are not static but are constantly being remodeled in response to the local environment. Collagen remodeling is tightly regulated in vivo, resulting in a balance between synthesis and degradation which allows the quantity and quality of the extracellular matrix to be adapted precisely to physiologic need. Disregulation of the balance between these two processes has been shown to have a role in the pathogenesis of a number of fibrotic conditions, notably in Dupuytren’s contracture.

Despite their broad structural and functional diversity, all collagens have some features in common. They are the only proteins which contain hydroxyproline as well as an unusually high content of the amino acids glycine and proline. Furthermore, all collagen subtypes contain within their structure at least one domain composed of a cross-linked triple-helical motif. The triple helical structure renders collagen impervious to enzymatic degradation by most proteases as long as it is intact; only a few proteases (known as collagenases) have the ability to recognize and digest this triple helical motif. In mammals, interstitial collagens are primarily degraded by several members of the matrix metalloproteases (MMPs), with lesser contributions from the cysteine proteases cathepsins L and K. In contrast, a number of enzymes isolated from a variety of bacteria and marine organisms have been shown to have potent collagenolytic activity; the best characterized of these are the collagenases secreted by Clostridium histolyticum. These were discovered over fifty years ago and have had broad application as research tolls for cell culture, tissue transplantation and disease modeling, and are currently being investigated in therapeutic applications (most recently in the non-surgical management of Dupuytren’s contracture and similar pathologic fibrotic conditions).
Hypothesis:
An imbalance of collagen deposition and degradation contributes to Dupuytren’s disease pathology. The major collagen-degrading enzymes at neutral pH are from the matrix metalloproteinase (MMP) family, whilst related enzymes from the ADAMTS (a disintegrin and metalloproteinase domain with thrombospondin motifs) are procollagen propeptidases involved in collagen synthesis. Our hypothesis was therefore that these enzymes (MMP-1, -8, -13 and -14 and ADAMTS-2, -3 and -14) would contribute to contraction of the collagen-rich matrix which underlies disease pathology.

Methods:
Fixed fibroblast populated collagen lattice (FPCL) assays were established using fibroblasts derived from the palmar fascia of Dupuytren’s disease patients undergoing fasciectomy. Collagen lattices were allowed to develop tension over 48 hours prior to release and their subsequent contraction was followed over 24 hours using Image J software. Gels were harvested under tension at 24 and 48 hours, then at 3 hours and 24 hours after release by immediate immersion in Trizol. RNA was extracted, reverse transcribed and qRT-PCR was used to quantify gene expression. Taqman Low Density Arrays were employed to measure expression of MMPs, ADAMTSs and also the tissue inhibitors of metalloproteinases (TIMPs. In parallel, a hydroxyproline assay was performed on the lattice conditioned media to quantify collagen degradation. Statistical analysis utilised one way ANOVA with Tukey’s multiple comparison test.

Results:
Collagen lattices from six Dupuytren’s fibroblast lines contracted similarly after release. Hydroxyproline assay clearly demonstrated that collagen break down occurs concomitant with gel contraction. MMP1 and MMP13 expression increased in collagen gels compared to monolayer culture and this expression further increased as tension developed and then decreased with release. MMP14 expression was minimally altered by tension, but increased upon release of the lattice. MMP8 was not significantly expressed. ADAMTS2, ADAMTS3 and ADAMTS14 were also regulated across this model with ADAMTS3 particularly increasing in expression under tension. It should also be noted that TIMP1 expression was high in these cells and increased with tension.

Summary:
The expression of a number of proteases involved in collagen metabolism is regulated during the process of collagen gel contraction and release. Collagen degradation takes place despite apparent high expression of inhibitors in a similar manner to we previously described in the Dupuytren’s palmar fascia itself (Johnston et al. 2007). We are currently using an siRNA approach to dissect the function of individual enzymes in this model of cell-mediated collagen contraction.

Hypothesis:
Transforming growth factor beta (TGF-B) has been implicated in the pathobiology of progressive fibrotic disorders. Modern laboratory models can demonstrate the role of TGF-B in Dupuytren’s Disease and molecular mechanistic treatments proposed.

Methods:
An in vitro model, the fibroblast-populated collagen lattice (FPCL), and an in vivo model, Dupuytren’s affected palmar fascia explanted onto an athymic “nude” rat, were used to evaluate the hypothesis. Collagen lattices were populated with fibroblasts harvested from Dupuytren’s affected palmar fascia or with normal palmar fascia fibroblasts. Gel contraction was measured daily for five days. The supernatant obtained from the culture medium was analyzed by human TGF-B2 immunoassay. Identical FPCLs were established and had tamoxifen 8umol/ml added.

Specimens of Dupuytren’s affected palmar fascia were explanted onto the “nude” rats and perfused with either TGF-B2, TGF-B2 antibody, or saline as a control. Biopsies were harvested from the explanted tissues at 30 and 60 days. Part of the biopsies were used for immunohistochemistry and part placed in tissue culture for cell kinetics. Histology, trichrome staining, and immunohistochemistry for TGF-B2, collagen I, and collagen III were performed on the biopsy sections. Total protein, DNA synthesis, and cell counts were evaluated from the cell cultures.

The numerical data between the groups in the various experiments were compared using a one-way analysis of variance. An all pairwise comparison procedure (Tukey’s test) was performed for statistically significant differences identified by ANOVA. Significant differences were determined to have a P value <0.05.

Results:
FPCLs populated with fibroblasts from Dupuytren’s affected palmar fascia contracted significantly more than FPCLs populated with normal palmar fascia fibroblasts (P<0.001). In tamoxifen-spiked FPCLs, lattice contraction was less than in untreated FPCLs (P<0.05). The amounts of TGF-B2 measured in the FPCL supernatants were also less when fibroblasts were exposed to tamoxifen (P<0.05).

Perfusion of explanted Dupuytren’s tissue by TGF-B2 upregulated collagen I and collagen III from the explants when compared to vehicle control (P<0.001). Perfusion with antibody prevented this upregulation when compared to vehicle control (P<0.001). Cell cultures derived from fibroblasts obtained from the explants perfused with TGF-B2 increased DNA synthesis, protein production, and fibroblast kinetics. Apoptotic protein assessment suggested that TGF-B2 decreases apoptosis, allowing a decrease in programmed cell death.

Summary:
- Etiology of Dupuytren’s Disease is unclear.
- Dupuytren’s Disease is pathobiologically related to other progressive fibrosing disorders.
- TGF-B plays a role in the pathogenesis of Dupuytren’s Disease.
- Agents that abrogate or neutralize TGF-B may provide novel treatment for Dupuytren’s Disease.
Hypothesis: Dupuytren's Disease cells modify their extra-cellular environment to promote a disease-like phenotype in adjacent fibroblasts, promoting disease progression.

Methods: Primary cells derived from Dupuytren's Disease (DD) cord tissue or phenotypically normal palmar fascia from DD patients (PF) are being assessed in novel collagen-based culture systems to assess the ability of DD cells to condition their extra-cellular matrix (ECM). In our sequential collagen culture system, we use transwells to determine whether DD cells, grown on a 0.4µM pore size membrane embedded in a type-I collagen matrix attached to the insert well, can secrete factors that affect the protein expression of PF cells subsequently cultured on conditioned collagen. In our co-culture system, DD cells are seeded onto type I collagen-coated transwell inserts with 0.4µM pores to avoid escape of cells but allowing diffusion of growth factors and other molecules. The insert well is also coated in type I collagen and seeded with PF cells. The co-cultures are maintained for 7 days during which both cell populations can be either left untreated or subjected to exogenous addition of growth factors and cytokines. The gene expression of the cell cultures assessed by Real Time PCR. T tests and ANOVA analyses are performed using SPSS.

Results: Preliminary data from our sequential collagen culture indicate that collagen conditioned by DD cells induces -catenin accumulation in patient-matched PF cells. Collagen conditioned by PF cells does not result in detectable accumulation of cytoplasmic -catenin. Co-cultures are currently underway to determine if DD cells can induce changes in the expression of TGFB1 (encoding TGF-1), TGFB2 (encoding TGF-2) and POSTN (encoding periostin) in PF cells.

Conclusions: We have previously demonstrated that TGF -1-induced -catenin accumulation in DD cells is modified by Type-I collagen substrate interactions. Our recent data indicate that DD cells can also condition their collagen substrate with factor(s), yet to be identified, that induce PF cells to increase their cytoplasmic -catenin levels. Increased -catenin accumulation in PF cells may be indicative of a proliferative response. DD and PF co-culture results are pending. These novel collagen-based culture systems are designed to detect DD cell interactions with the ECM and adjacent PF cells and may allow us to identify that may promote disease progression.
Hypothesis:
Down-regulation of IGFBP6, encoding Insulin-like growth factor binding protein-6, leads to decreased IGFBP-6 levels, in turn increasing IGF-II availability in DD, to promote differentiation of myofibroblasts and the deposition of collagen into the ECM.

Methods:
Primary cells derived from Dupuytren’s Disease (DD) cord tissue or phenotypically normal palmar fascia from DD patients (PF) are being assessed for proliferation (WST-1 assays) and myofibroblast differentiation and contractility (Stressed Fibroblast Populated Collagen Lattice assay, sFPCL) with or without the addition of exogenous recombinant IGFBP-6 alone or in combination with transforming growth factor (TGF)-β -smooth muscle actin levels are assessed by immunoblotting to confirm myofibroblast differentiation. Chromatin Immunoprecipitation (ChiP) assays are used to assess TGF-β-induced β-catenin /TCF/LEF transcription complex binding to the IGFBP6 promoter. T tests and ANOVA analyses are performed using SPSS.

Results:
Microarray analyses indicate a decrease in IGFBP6 mRNA expression in DD cord tissue relative to patient-matched palmar fascia. TGF-β treatment of primary DD cells induced an increase in cytoplasmic β-catenin levels and repression of IGFBP6 mRNA levels. PF cells were less sensitive than patient-matched DD cells to TGF-β-induced repression of IGFBP6 transcription. ChiP assays to confirm TGF-β-induced β-catenin /TCF/LEF transcription complex binding to the IGFBP6 promoter are underway. Preliminary data indicate that exogenous IGFBP-6 treatment has no discernable effect on DD or PF cell proliferation, however exogenous addition of IGFBP-6 inhibits TGF-β-induced contractility of DD and PF cells in sFPCLs. The effects of exogenous IGFBP-6 on DD and PF cell COLIA1 and IGF2 mRNA expression are currently being assessed using Real Time PCR.

Conclusions:
TGF-β induces β-catenin accumulation in DD and PF cells and induces the repression of IGFBP6 expression, potentially through β-catenin /TCF/LEF transcription complex interactions with the IGFBP6 promoter. As the primary function of IGFBP-6 is to sequester IGF-II, repression of IGFBP-6 may increase IGF-II availability in DD. As combinatorial interactions between TGF-β and IGF-II have been shown to result in myofibroblast differentiation and increased collagen production in other systems, it is plausible that decreased IGFBP6 expression is specifically targeted to DD to facilitate myofibroblast differentiation and collagen deposition in this disease.
Introduction:
Dupuytren's disease (DD) is a benign fibro-proliferative disease albeit with tumour like properties. DD is thought to be an imbalance between apoptosis and proliferation of myofibroblasts implicated in its pathogenesis. Annexin’s are part of a family of calcium dependent phospholipid binding proteins involved in the apoptotic process and have been shown to be over expressed in certain cancers. We hypothesise that profiling DD apoptotic cells will aid in the understanding of disease pathogenesis and recurrence.

Materials & Methods:
DD in patients (n=5) with significant fixed flexion deformity were enrolled in this study. Biopsies were taken from the diseased cord, nodule, perinodular fat and skin overlying the nodule. Immunohistochemistry and QRT-PCR with Annexin 2, 5 and 11 were conducted. Tunnel assay was also carried out. Results were compared with external and internal controls.

Results:
Annexin 2 and 11 were over expressed in DD cases in comparison to controls (RQ = 0.8 to 1). Annexin 5 was under expressed in diseased skin, fat, cord and nodule of diseased patients. The apoptosis profiling carried out showed a reduction in apoptosis in DD tissue compared to carpal tunnel control.

Conclusion:
This study identifies a potentially significant biomarker profile in the development of DD which may help further understanding of the apoptotic pathway involved in DD aetiology. Further work will enable a better understanding of the cellular mechanisms involved in DD allowing developments of non-surgical therapy which may used as an adjunct to surgery to reduce disease recurrence.
4:45pm-5:00pm  Sandip Hindoha MD: Dupuytren’s disease shows profound hematopoietic and mesenchymal stem cell abnormalities involving palmar fat and skin in addition to fascia: Novel implications for pathogenesis and therapy

Hindocha S, Iqbal SA, Farhathullah S, McGrouther DA, Paus R, Bayat A

Background:
DD is a common fibroproliferative disease affecting the hand. Myofibroblasts found in the DD palmar fascia are responsible for digital contracture. However, their exact source is unknown. Palmar skin and fat-derived cells as a potential origin of abnormal cells remains underexplored.

Objective:
To characterise hematopoietic and mesenchymal stem cells in Dupuytren’s disease (DD) fascia, fat and skin compared to carpal tunnel control.

Methods:
Nine DD patients with digital fixed flexion deformity were enrolled, and biopsies taken from the diseased cord, nodule, peri-nodular fat, distant palmar fat and the skin overlying the nodule. Fluorescence Activated Cell Sorting (FACS), immunohistochemistry and quantitative real time polymerase chain reaction (QRT-PCR) were used to identify expression of five mesenchymal (CD’s 13, 29, 44, 90, 166) and two hematopoietic (CD’s 34, 117) stem cell markers.

Results:
There was a significantly higher expression of CD13 in all examined DD tissue sites compared to controls (p=0.02). In addition CD44 was significantly over expressed in the cord and nodule (p=0.02), while CD34 was over expressed in the skin overlying DD nodules (p=0.008). The mean number of positive cells expressing all stem cell markers were significantly greater in the DD cord compared to carpal tunnel fascia (p= 0.003).

Conclusions:
This study provides the first detailed characterization of mesenchymal stem cells in DD which are predominantly located in the cord. DD appears to represent a benign tumor that may potentially result from abnormal mesenchymal progenitor cell expansion than a primary inflammatory disorder. If confirmed, adipodermofasciectomy may be a potentially important primary therapy.
5:00-5:15pm  Questions and Answers:  Afternoon Sessions
Dinner Reception and Presentation
A Working Day of Guillaume Dupuytren

At the time of Dupuytren's birth in 1777, France was still governed by an absolute monarch Louis XVI. When Dupuytren died in 1835, he had lived through two revolutions (1789 and 1830), a republic, a ‘Directoire’, a consulate, an empire under Napoleon and another two royal restorations under Louis XVIII and Charles X.

Dupuytren was always closely involved in these historic events as he was in direct contact with the leading figures from the different periods, both privately and professionally. He played an important role in the organisation and reorganisation of medical surgical education. As the “head surgeon” of the Hôtel-Dieu hospital, the largest hospital in France, he treated not only a large and highly varied number of surgical patients but also the victims of riots, insurrection, revolutions and wars, as well as victims of the cholera epidemic of 1832.

His role in the development of modern surgery and surgical pathology was so overwhelming that the period during which he was “head surgeon” is called the Dupuytren age in the history of surgery in France. The centre of his life was the operating room at the Hôtel-Dieu hospital in Paris which also served as a lecture room, consultation room and dissection room during his life.

Surgery was not only a profession but a life to be experienced

The name Dupuytren became immortal. Not only in the contracture of the palm, which he described extremely precisely, but also in a specific fracture of the fibula. His name also survives in road names, in the “Musée Dupuytren”, the museum of pathological anatomy in the medical faculty in Paris, in the new university centre in Limoges, which is named after him and in an amphitheatre in the Parisian Hôtel-Dieu hospital. The anniversary of his birth and death are also still remembered in Pierre-Buffière where he was born and in Paris where he studied, worked, lived and died. A statue of him has been erected in the inner courtyard of the Hôtel-Dieu hospital in Paris and a memorial has been built in his place of birth.

Let us walk through a working day of this famous surgeon.
Session 5:
Surgical Treatment
8:00am-8:15am  Lynn Ketchum MD: Update: Dermofasciectomy and full-thickness grafts in the treatment of Dupuytren’s contracture: A thirty-six year study

Purpose:
Dupuytren’s disease frequently results in crippling deformities of the hands and has a high incidence of recurrence after limited fasciectomy. We report a 36 year experience with full-thickness grafts to resurface defects created by releasing Dupuytren’s contractures with dermofasciectomy.

Methods:
Dermofasciectomy and full-thickness skin grafts were used in 153 patients on 204 hands with Dupuytren’s contractures from 1970 to 2005.

Results:
Our first study followed 36 hands in 24 patients for an average of 3.9 years post-operatively between 1970-1985. There was no recurrent disease in the palms or digits covered by the full-thickness grafts. The incidence of extension outside the grafts was 8.3%. The study was continued from 1985-2005. An additional 168 hands in 129 patients were treated with the same procedure and followed an average of 2.8 years post-operatively. Again, there was no recurrent disease in the palms or digits covered by the grafts and the extension rate was comparable at 9.5%.

Conclusions:
This 36 year study of 204 hands demonstrates the validity of using dermofasciectomy and full-thickness grafts in the treatment of patients with Dupuytren’s contracture who are likely to develop recurrent disease.
Hypothesis:
We hypothesized that palmar cutaneous branches of the digital nerves (observed intra-operatively, diverging from the proper digital nerves towards the midline) are a constant anatomical feature (not previously described), and aimed to map the location of these nerve branches, in order to predict their position as an aid to surgery.

Methods:
10 fresh frozen cadaveric hands were examined. The A1 pulley and common digital nerves to each finger were identified. The proper digital nerves were traced distally, carefully noting any branches deviating towards the midline over the palmar aspect of the proximal phalanx. The distance from the midpoint of the proximal extent of the A1 pulley to the origin of the 1st palmar cutaneous branch of the digital nerve was measured. The length of each finger from the proximal midpoint of the A1 pulley was measured, allowing a ratio of the distance from the pulley to the 1st nerve branch to be calculated for each finger.

Results:
Palmar cutaneous branches of the digital nerves over the proximal phalanx were found as a constant anatomical feature in all 40 fingers investigated. Each pair of palmar cutaneous branches converged to form a “chevron shape”, and appeared to serve a dense concentration of Pacinian corpuscles. Distally, each proper digital nerve was found to have multiple smaller palmar cutaneous branches deviating towards the midline of the finger. The index finger radial border was found to have the greatest numbers of these. The mean distance from the A1 pulley base to the origin of the 1st palmar cutaneous nerve branch was 15.59mm (range: 15.21 – 16.12mm). The mean ratio of the 1st palmar cutaneous nerve branch origin to finger length was 1:5.25 (range 1:4.7 – 5.6) or as a mean percentage of finger length 19.1% (range 17.8 – 21.1).

Summary:
During surgical dissection for Dupuytren’s disease the proper digital nerves must be identified and protected. In our experience, the 1st palmar cutaneous nerve branches we identified can be mistaken for the proper digital nerve, especially when they are a similar calibre. This could lead to an inadvertent injury of the proper digital nerve. A previous study established the surface landmarks for the proximal edge of the A1 pulley 1. These landmarks and our data can predict the position of the potentially misleading 1st palmar cutaneous nerve branches of the digital nerves facilitating safer surgical dissection.

Purpose of research:
Development of the optimal method and technique of severe stages Dupuytren contracture surgical treatment based on clinical and anatomical investigations for optimizing the treatment outcomes.

Materials and methods:
The research consisted of two parts, clinical and anatomical. The anatomical part included 2 trials which were executed on 17 upper limbs of nonfixed cadavers. In the first anatomical trial, intra-arterial injections of black latex were given and arterial anatomy was documented macroscopically and microscopically using optical devices, hand size measurements, vessel measurements (rated diameter and length), and photography. In the second anatomical trial, red ink injections were performed, which enabled the combination of preparation with evaluating the stained areas of palm surface restricted by the dermal arterial perfusion regions. In the clinical part we estimated the treatment results of 100 patients (107 operations). Control group (the first group) consisted of 45 patients (45 operations) who were operated by general methods (partial fasciectomy) without using optical devices. The second group consisted of 55 patients (62 operations) who were operated after evaluating palmary skin arterial perfusion by high frequency dopplerography (total aponeurectomy). The latest outcomes were estimated in concordance with DASH scale and by using the integral index introduced by professor A.E. Belousov.

Results:
Investigation of skin perfusion maintained by anatomically invariable nutrition arteries ranged from 0.2 to 0.6 mm in diameter and from 4.0 to 6.0 by length. These vessels perforated palmary aponeurosis and after that branched to subcutaneous fatty tissue. Two types of branching were revealed: trunk and multibranch. The trunk type was observed in the middle and in distal third of palm and multibranch type was more typical for proximal third.

The quantity of dermal nutrition arteries was significantly more in proximal third of palmar surface than in the middle and distal third (p>0.05). Thus there were 47-59 nutrition arteries in proximal third, 10-14 in the middle and only 5-9 vertical arteries which stayed permanent.

Discussion:
The peculiarities of vessel architectonics detected in experiment show the high risk of iatrogenic damage in their distal part. This fact allows the separating of two areas-proximal and distal. It is exposed that each artery supplies a certain round from skin area. Analysis of treatment results shows that in the second group the complication rate is 26% compared to 57.8% in the control group. Using microsurgical technique and doplerography reduced the incidence of arterial and nerve damage frequency from 28.9% to 5.1%, and reduced postoperative hematoma formation from 17.8% (control group) to 10.2% (main group). The recurrence rates in the main group were 6 times less than in the control group (5.1% and 42.2%, respectively). The functional outcomes in the main group were significantly better than in the control group that were illustrated in diagram.
Diagram 1. Functional outcomes

The average DASH-score in first group was 3.85 (range 0-45.4).

**Summary:**
In conclusion we can say that application of microsurgery technique and taking into consideration the peculiarities of palmar surface perfusion allows significant reduction of complication rates and greatly improves the functional results of surgical treatment of severe stage Dupuytren contracture. We suggest that total aponeurectomy is a promising alternative to partial fasciectomy with a low risk for a recurrence.
8:45am-9:00am Ilse Degreef PhD:
Surgical outcome of Dupuytren's disease. No higher self-reported recurrence after segmental fasciectomy

Degreef I, MD, PhD & De Smet L, MD, PhD

Hypothesis:
Incomplete strand resection leads to higher recurrent contractures after surgery for Dupuytren's disease, contrasting with more invasive surgery. What is the long term influence of surgical technique on disease recurrence?

Methods:
A retrospective analysis of 216 surgically treated patients with a minimum 2 year follow-up was conducted with a postal questionnaire.

Results:
Reported recurrence rates were somewhat lower in segmental fasciectomy (43%), which was performed in 39% of the patients, compared to an overall reported recurrence rate of 54% in all surgical procedures. In total fasciectomy with skin resection and grafting, patients reported a surprisingly high recurrence rate of 63%.

Summary:
No higher recurrence risk in segmental fasciectomy was noticed and total fasciectomy with or without skin resection did not appear to guarantee indefinite results. At this point, surgical treatment in Dupuytren's disease is confined to correcting contractures, without curing the patients. Therefore, unless segmental fasciectomy is unfeasible due to the severity of the contractures, we suggest to always consider minimal invasive surgery as a surgical option in the treatment of Dupuytren's disease.

Figure 1: Overview of the different surgical techniques with patients' reported recurrent and non-recurrent subgroups (Z=z-plasty; MM=segmental fasciectomy; Br=Brunners' incisions; FTG=total fasciectomy with full thickness grafting)

Figure 2: Illustration of the significant difference (p = 0.0006) in postoperatively improved visual analogue scale for satisfaction of tamoxifen patients (group 2), but not in the placebo group (p = 0.3) (group 1)
9:00am-9:15am Michael Papaloizos MD: Minimizing cutaneous necrosis and delayed healing after surgical treatment for Dupuytren’s contracture: The mini-chevrons incision

Author: Michael Papaloizos, MD

Hypothesis:
Open fasciectomy requires adequate exposure of the diseased tissue. Longitudinal incisions with Z-plasties or zigzag designs are most commonly used for this purpose. Elevation of large skin flaps may lead to secondary necrosis and delayed healing, the most common complications of surgical treatment. Our hypothesis was that raising flaps in a zigzag fashion but with very short arms could be an advantage regarding primary skin healing.

Patients and Methods:
Continuous prospective series of all patients presenting with and operated for Dupuytren’s contracture between November 2007 and November 2009. 54 patients (10 F/44 M, mean age 63 years, 47-94, three with recurrent disease) were operated using the mini-chevrons incision and followed by the same surgeon at regular intervals (mean FU 7 weeks, 4-16). Fasciectomy was otherwise performed according to standard rules. Severity of the disease was graded according to the number of affected rays, digital extension and Tubiana’s stages (1 to 4). Skin healing was graded from 0 (no necrosis) to 3 (multiple points, extended or deep necrosis), at day 5 (first dressing), 12 (stitches removal) and 30. Other complications were recorded.

Results:
Number of affected rays 1 : 22, 2 : 16, 3 : 9, 4 : 5, 5 : 2. Digital extension up to PIP: 34, up to DIP :12. Tubiana’s stage I :14, II : 27, III-III+ :12, IV :1. The common approach was: one ray, one incision, implying multiple separate incisions, sometimes even on both sides of the same finger. Suction drainage was applied in three cases. No skin resection nor graft was performed. Skin outcome (see figure for examples): 7 superficial localized necroses at day 5; 13 superficial localized necrosis and 4 lightly more extended necroses at day 12; 3 minimal residual necroses requiring no dressing at day 30. Four hematomas with spontaneous resolution. The second week was the most critical. More severe disease was associated with more healing problems. All together, no serious skin necrosis and a high degree of satisfaction for the surgeon and the patients in this series.

Summary:
The mini-chevrons incision has many advantages. For the surgeon: simple design, easy to learn and easy to teach, it is versatile, ubiquitous, easy to combine with other local flaps (V-Y) or incisions. For the patient: primary skin healing and, hence, immediate postoperative quality of life are promoted.

3 patients postoperatively:
1a: at 5 days; 1b: same at 5 weeks; 2: at 12 days; 3a : at 12 days; 3b: detail (same case)
9:15am-9:30am  Bernhard Lukas MD: Treatment of severe Dupuytren’s contracture by homodigital flaps

B Lukas, A Elgammal, H Erne

Introduction:
Management of Dupuytren’s disease with severe contracture of the proximal interphalangeal joint is always a challenge for hand surgeons due to the soft tissue defect created by full release to the PIP joint. There are 2 methods to cover this defect, either by Z-plasty or by using homodigital skin flap.

Purpose:
The purpose of this study is to evaluate the results of the homodigital skin flap in covering the defects after release of severe contracture of the PIP joint. The technique of the operation, the failure rate, the recurrence rate and the final results were evaluated 1-4 years after the operation.

Patient and methods:
In 40 cases the dorsoulnar skin flap from the proximal phalanx was used to cover the defect after release of PIP joint. The average PIP joint contracture was 73° using Tubiana’s classification. The donor site was closed by a full thickness skin graft taken from the ipsilateral forearm.

Results:
In 80% of the cases in this study, it was possible to reach full extension of the PIP joint; in half of these patients, open arthrolysis was necessary to reach full extension. In the other 20%, there was 15° loss of extension in average.

Conclusion:
The mid term results of the use of dorsoulnar skin flap to cover the defects following release of severe PIP joint contracture in Dupuytren’s disease showed superior results in our hand. It is an easy technique, it has a minimal complication rate and allow full extension of the PIP joint in most of the cases.
9:30am-9:45am  Massimiliano Tripoli MD: The “Jacobsen flap” for the treatment of stage III-IV Dupuytren’s disease at little finger: our review of 123 cases

Massimiliano Tripoli M.D., Francesco Moschella M.D, Michel Merle M.D.

The surgery for advanced stages of Dupuytren’s disease of the little finger is controversial: in literature several techniques have been described with variable reported results and postoperative complications. Percutaneous needle fasciotomy, “McCash technique” and dermofasciectomy are often performed for surgical treatment but they present significant complications and limits. This paper reviews our experience using the “Jacobsen flap technique”, a modification of the McCash procedure. 123 patients with Dupuytren’s disease at stage III and IV at little finger underwent surgery with the “Jacobsen flap technique” between 2001 and 2009 at the Department of Plastic and Reconstructive Surgery of Palermo. None had undergone previous Jacobsen flap surgery. Follow-up ranged from 4 months to 3 years. No hematomas, infections, necrosis of the skin flap occurred postoperatively. The 49% of all the patients were at stage 0 after mean 18 months by the surgery, and they considered “excellent” the result obtained. We found that “Jacobsen flap” technique, for the significant correction of the contracture, the low rate of complications, and the relatively simple surgical approach is an excellent alternative to percutaneous needle fasciotomy, dermofasciectomy or amputation.
This presentation presents a logical approach to correction of PIP joint contractures in Dupuytren’s contracture. It is based on an analysis of 78 patients with PIP joint contractures. Once a contracture has reached 60° there is an 80% chance that the central slip will have become attenuated. Central slip attenuation requires a different post operative splintage regime. Digital fasciectomy may be affected in releasing PIP contracture. On the other hand, after fasciectomy there may be residual contracture which requires release of flexor tendon sheath or the palmar plate. Complete correction may be achieved but may leave an unstable finger which moves into extension or flexion but is unstable in the middle range due to tightness of the accessory collateral ligaments. The value of gentle passive manipulation versus surgical release of the PIP joint will be discussed.
Session 6:
Needle Release and Manual Therapy
Introduction:
The treatment of Dupuytren's contracture is a subject of controversial debates since a long time. The conventional aponeurectomy represents a time consuming procedure regarding the operation as well as the period of recovery. Additionally one has the risk of serious complications like infections, nerve lesions, diminished blood flow of the finger, intolerance for cold temperatures and reduced range of motion. The present study reconsiders if the less invasive procedure "Percutaneous Needle Fasciotomy" could be a serious alternative, less time consuming and less risky?

Material and Method:
In 2008 and 2009, 63 rays in 47 patients with Dupuytren`s contracture were treated using the technique of the "Percutaneous Needle Fasciotomy". With the Classification of Tubiana 34 rays stage I, 21 stage II, 7 rays stage III and 1 stage IV were categorized. Under local anesthesia the percutaneous needle fasciotomy in a fan-shaped fashion at several levels (on average 2) were performed. Immediately after the procedure a splint was adjusted in full extension of the fingers to wear during night for 3 months.

Results:
Within the retrospective study 43 patients (58 rays) were reviewed with a mean follow up of 11.1 months. The mean age of the patients was 60.3 years (29 men, 14 women). 39 patients with 52 rays had a totally free extension after the operation. 4 patients (6 rays) retained a mild residual flexion contracture between 5 – 10°. There was neither infection nor injury of nerve, vessel or tendon. No second operation was needed. The mean total gain was 59°. 6 patients had measurable reoccurrence of a mild flexion contracture. 98% would undergo the procedure again if necessary.

Conclusion:
The technique of "Percutaneous Needle Fasciotomy" is reliable and relatively simple to perform, when compared to the open aponeurectomy. The rate of complications is low. The time of operation and period of recovery is obviously shorter than for the conventional technique. Therefore the "Percutaneous Needle Fasciotomy" could be seen a serious alternative.
10:30am-10:45am  Annet Van Rijssen MD:  5-year results of first-ever randomised clinical trial on treatment in Dupuytren's disease: percutaneous needle fasciotomy versus limited fasciectomy

A.L. Van Rijssen, H. ter Linden, P.M.N. Werker

PURPOSE: To compare the long term outcome of percutaneous needle fasciotomy (PNF) and limited fasciectomy (LF) as treatment modalities for Dupuytren’s disease in a randomised controlled fashion with 5-year follow-up. Short-term results of PNF and LF had been comparable (Van Rijssen et al J Hand Surg Am. 2006 May-Jun;31(5):717-25)

Methods:
In between 2002 and 2004, patients with a mimimal contracture of 30o in any joint were randomly assigned to the treatment arms. All patients were invited at 6 months, 1 year and then yearly untill 5 years postoperatively. We recorded the total passive extension deficit (TPED), patient satisfaction, hand-function recovery, and complication rate until recurrence or extension of the contracture were found (primary endpoints defined as a worsening of TPED of at least 30o compared to the postoperative measurement) or until they were 5 years post treatment.

Results:
Recently the last patients reached the 5 years mark. 108 patients with 112 hands had reached the primary endpoint or stayed in for 5 years; 60 of these had undergone PNF, 52 LF. In the PNF group, six patients (10%) were lost for follow-up or deceased. In the LF group, 10 patients (19.2%) were lost for follow-up or deceased.

The recurrence rate in the PNF group was 85%. Recurrence occurred after a mean of 2.3yrs. None had an extension at that time. Of the recurrences 9 were treated by LF, 25 again by PNF and 12 patients chose not to undergo secondary treatment. The recurrence rate in the LF group was 23.8%. Recurrences occurred after a mean of 3.7 years. One patient had extension of the disease (2.4%). Of the recurrences 4 were treated by PNF, and the rest (6 patients) chose not to undergo secondary treatment.

The recurrence rate of PNF was statistically higher than of LF(p = 0.00). The mean time to recurrence of PNF was much shorter than that of LF and this was also statistically significant (p = 0.01).

Conclusion:
Recurrences are far more frequent and occur sooner after PNF. Most patients that had undergone PNF were nevertheless still satisfied with the result and chose it again as treatment modality.
10:45am-11:00am  Roger Khouri MD: Extensive Percutaneous Aponeurotomy & Lipografting: A Novel Treatment for Dupuytren’s Disease

Steven E. R. Hovius, MD, PhD, Hester J. Kan, Xander Smit, MD, PhD, Ruud W. Selles, PhD, Roger K. Khouri, MD

Background:
Surgical resection of Dupuytren contracture remains the standard for treatment but is fraught with morbidity and prolonged recovery. The purpose of this paper is to introduce a new minimally invasive treatment alternative for Dupuytren’s Disease (DD) and to evaluate its safety and efficacy.

Methods:
a-Technique: Using steady extension force, a meticulous subdermal dissection of the cord is performed through multiple superficial nicks along the entire contracture band. This technique disintegrates the cord and separates it from the dermis. The resulting space is grafted with a loose lipoaspirate and the hand splinted in extension. One week postoperatively, patients were allowed to use the hand. Splinting continues for 6 months at night. b-Patients: Over the past three years we performed the procedure on 67 hands in 52 patients. We treated the complete spectrum of Dupuytren’s disease including recurrences.

Results:
Overall patients were very satisfied, having full recovery in 2-4 weeks. Maximum follow up was 3 years. All patients who were treated for recurrent disease (n=13) favoured the new technique over their previous open surgery. Four out of 52 patients were not satisfied, 1 had clear recurrence (severe diathesis) and 3 had dystrophies (of which 2 had dystrophies before in the other hand after open surgery). No tendon injuries were encountered and we had 1 nerve injury after treating a recurrence. At one year follow up MP joint recurrence was none, PIP joints were straight in 50%, and a mean reduction of 35 degrees in the other 50%. None of the PIP’s was same or worse one year postoperatively.

Conclusion:
We describe a new, safe and minimally invasive approach to the treatment of Dupuytren’s contracture. This technique differs from standard percutaneous release in two major points: (1) full dermal separation and disintegration of the cord along its entire span, and (2) subdermal fat grafting to provide padding and to prevent scarring and recurrence. The most striking was the fast postoperative recovery and the softness of skin in the operated area. Fat grafting percutaneous fasciotomy seems to change the biology of the disease, to restore the missing subdermal fat and to rejuvenate the hand.
11:00am-11:15am Bing Siang Gan PhD MD: Needle aponeurotomy for Dupuytren’s contracture, the HULC experience

Bing Siang Gan, David O’Gorman

Patients with Dupuytren’s disease (DD) have increasing access to internet information regarding needle aponeurotomy (NA) as a minimally invasive treatment for Dupuytren’s contracture. It is likely that patients will request this treatment modality in increasing numbers. To investigate the indications and safety profile of this treatment method, we reviewed the experience at the Hand and Upper Limb Centre in the use of this treatment modality.

Methods:
Consecutive patients treated with NA since Jan 2008 were reviewed and analysis is still ongoing.

Results:
NA is a safe and effective modality for MP joint contractures with a precentral cord NA is less useful in the treatment of PIPJ contractures with diffuse proximal phalangeal disease NA is useful to relieve a sense of tightness in patients with mild disease without joint contractures

Conclusions:
NA may be a rapid and useful adjunct in the treatment of DD, in particular for mild disease and disease affecting the MPJ only.
11:15am-11:30am John Agee MD: Growing the PIP straight with the Digit Widget

All PIP contractures are secondary to force imbalance. There is either too much flexor torque or not enough extensor torque or a combination of the two. In Dupuytren’s disease, at least initially, all PIP contractures are secondary to increased flexor torque. In advanced and long standing contractures, especially those with previous surgery, decreased extensor torque serves to frustrate the surgeon’s best efforts at restoring joint extension.

As Dupuytren’s progressively limits PIP extension, all tissues palmar to the joint’s axis of rotation contract thereby creating additional short, but otherwise normal collagen to join the disease itself as a mechanical constraint to active and passive extension.

Each angular degree of PIP contracture produces a secondary force imbalance for its MP joint and thereby creates a torque imbalance that favor’s MP hyperextension. Ironically, the contracture Dupuytren’s creates at the PIP is easier to treat if there is a concomitant MP contracture...ideally one just adequate to prevent MP hyperextension. Such constraints to MP hyperextension assure maximal transmission of intrinsic and extrinsic muscle forces to extend its interphalangeal joints.

External splints and casts are impotent to reverse PIP contractures; their potential to reverse contractures are limited by their interface pressures that create ischemic skin: 30 grams/square cm is about all the precious dorsal skin can take.

Skeletal extension torque reverses PIP contractures by “growing” the contracted tissues back toward normal length. By transmitting forces to the joint via skeletal pins, extension torque creates a selective growth of short tissues. Extension torque causes skin and joint capsule on the extensor side of the PIP to exhibit the opposite phenomenon by contracting. Most importantly, extension torque avoids the soft tissue tearing and hemorrhage that accompanies joint manipulation into extension.

Simple mechanical analysis of finger contractures is of value in approaching all finger contractures.
11:30am-11:45am Terri Skirven OTR/L CHT: Hand Therapy for Dupuytren’s Contracture:

Value of Preoperative Therapy
Record sensibility, ROM, functional limits
Screen CT, patient expectations
Education regarding PO course

Postoperative Management
Need for Therapy?
-Postoperative swelling
-Wound healing
-Scar formation
-Restricted finger motion
-Compromised function with activities of daily living (ADL)

Postoperative Complications
Initial Therapy Assessment
-P/AROM
-Pain
-Edema
-Sensation
-Wound/graft assessment

Relevant Considerations
-Degree of contracture and duration (especially PIP)
-Full extension achieved in surgery?

Post-Op: Preferred Treatment
No Tension, Early Referral
-24 hours PO
-Wound care
-Edema control
-Dorsal block splint
-Gentle motion day 3
-Written precautions

Rationale for No Tension Technique
-Mechanical stress on digital vessel and nerve may contribute to local hypoxia and inflammation
-Tissue anoxia may contribute to free radical release and adverse cellular response
-Hypertrophic scar will form in lines of tension

Post op Management Day 3-7
-Dorsal block splint
-Gentle composite flexion exercise
-Limited extension
-Soap and water, light dressing
-Edema control, coban

Postoperative Splinting
-After 3 weeks wean splint to night time wear
-Redevelop if loss of digit extension is noted
-May need to continue night extension splinting for 6+ months as a retainer

“No pain no gain” (not!)
-Over aggressive exercise can incite an exaggerated and prolonged inflammatory response
-Recommended: Consistent active exercise within a comfort range
Post-Op Exercises
Frequency modified according to patient response and the presence of severe edema, large hematoma, incision splitting or signs of a flare reaction

- Exercise Frequency
  - Hourly
  - 3-4x daily
  - 5-6x daily

Physical Agents
- Heat
- Cold
- Ultrasound
- Electrical stimulation

Scar Management
No tension to incision scar through the use of protective splint and exercise technique

Scar Management
- Light massage
- Topical lotion/cream
- Pressure
- Putty elastomer
- Silicon gel sheets

Problems
- Residual limitations in motion
- Continue exercises
  - Corrective splints, straps, serial casts

Return to functional activity
- Work activities
  - Depends on the nature of the work
  - Sedentary vs. manual labor

Recreational
- Golf
- Other sports
  - Use of gloves and padded handles
Albrecht Meinel MD: The role of static night splinting after contracture release for Dupuytren’s disease. A preliminary recommendation based on clinical cases

Albrecht Meinel

Recommendations for using a static night splint after surgery are as old as the literature on Dupuytren’s. The coachman, M. Demarteau, who was treated with fasciotomy by Dupuytren in his famous lecture of December 1831, afterwards wore a night splint „for another month and an excellent result was achieved“ (D. Elliot, 1990). Yet firm data on the effectiveness of static or dynamic splinting is still missing. Results of the multicenter study initiated 2008 at Massachusetts General Hospital are pending, but for the sake of our patients we should consider what information we already have today. And indeed, a review of available individual cases reveals remarkable results.

We have been using exclusively static night splints, no dynamic splints. The splints aim at maintaining in the long term the extension position that was achieved by fasciotomy. As compliance is probably the most critical factor affecting the results of splinting it is of utmost importance that the splint is easy to apply and comfortable to wear. We are using two types of static splints: In cases where the extension deficit was fully or nearly fully removed, excellent compliance and results have been achieved with FixxGlove, a golf glove like splint that was developed in cooperation with Inocare Austria and Inocare International. In cases with a remaining extension deficit, an individual, adapted splint is used that provides a comfortable silicon bed for the finger. Splints are worn for a period of 6 months after treatment and exclusively at night. Splinting is re-established whenever the fibromatosis is becoming active again. In most cases the patient himself decides whether this is the case.

We believe that this splinting can reduce the risk of contracture recurrence. Cases without recurrence for two or more years have been observed. This is more or less to be expected but much more impressive is the fact that remaining extension deficits measurably improve with splinting. The same applies to nodules and cords which clearly reduce in size and soften when a splint is worn. This is demonstrated on a variety of our patients.

Our experience demonstrates that a comfortable static night splint can support and improve the effectiveness and sustainability of fasciotomy. Splinting seems to enhance the effect of modified biomechanical conditions achieved by fasciotomy. The concept of pathogenesis that understands the disease as fixation of the flexed fingers may also suggest that splinting in extension position might even be prophylactically efficient in avoiding contracture and become a non-surgical therapy.
12:00pm-12:15pm  Deborah Larson BScOT, MSc:  Splinting after contracture release for Dupuytren’s disease (SCoRD) – a pragmatic, multi-centre, randomized controlled trial

Jerosch-Herold, C; Shepstone, L; Chojnowski, A and Larson, D

Hypothesis:
The use of a static night splint in addition to post-operative hand therapy after fasciectomy or dermofasciectomy will result in better self-reported hand function, improved finger range of motion and higher patient satisfaction at one year after surgery.

Methods:
The evidence for post-operative splinting is equivocal and of poor quality reporting both positive and negative findings. A large, multi-centre, pragmatic, randomised controlled trial was designed with Research and Ethics committee approval. Patients presenting to a surgeon with a Dupuytren’s contracture affecting one or more digits of the hand and requiring fasciectomy or dermofasciectomy were eligible and invited to partake in the study. Patients were randomised to one of 2 groups after undergoing surgery: i) splint group receiving a static night splint at approximately 10 days after surgery to be worn for 6 months as well as hand therapy; or ii) non-splint group receiving hand therapy only. Patients in the splint group were asked to complete weekly splint diaries to monitor adherence. The primary outcome was self-reported hand function and disability assessed through DASH (Disabilities of Arm, Shoulder and Hand) questionnaire. Secondary outcome measures were total range of finger movement and patient satisfaction. Data was collected prior to surgery, at 3 months, 6 months and 1 year after release. In order to detect a minimally clinically important difference of 15 points on the DASH with a power of 90% a minimum of 51 patients were required in each group. The main analysis will use an intention-to-treat approach.

Results:
218 patients were invited to join the study of whom 172 (79%) consented. 18 patients were subsequently excluded due to a variety of reasons e.g. death/delayed or cancelled surgery. A total of 154 patients with a mean age of 67 years (range 36 to 89) were randomised to a splint (77 patients) or non splint (77 patients) group. 78% were male and the most common contracture involved the little then ring finger. 76% of operations were for single digit disease. Five patients have been lost to follow up and final data collection will be completed in January 2010 with the full results available in April 2010.

Summary:
This definitive pragmatic randomised controlled trial will provide much needed high quality evidence regarding the clinical effectiveness of night-time splinting for patients undergoing fasciectomy/dermofasciectomy.
Session 7: Biologic Intervention: Dupuytren’s and Released Conditions
**Summary**

- This study demonstrates the efficacy and safety of injectable collagenase as a novel non-surgical treatment in patients with Dupuytren’s contracture.
- Injectable collagenase was significantly superior to placebo in reducing contractures and improving range of motion in affected joints.
- Collagenase injection(s) were generally well tolerated.

---

**Hypothesis:**

Dupuytren’s contracture limits hand function, diminishes quality of life, and may ultimately disable the hand. The purpose of this study was to conduct a Phase 3, FDA regulated, controlled, multicenter clinical trial to test the safety and efficacy of injectable collagenase clostridium histolyticum as a novel nonsurgical treatment for contractures caused by Dupuytren’s contracture.

**Methods:**

A total of 308 patients with joint contractures of >20° were randomized in this double blind, placebo-controlled, prospective study at 16 different sites in the U.S. There were 245 males and 63 females with a mean age 62.7±9.5 years. The patient’s metacarpophalangeal or proximal interphalangeal joint contractures were randomized to receive, if needed, up to three collagenase (clostridium histolyticum) injections (0.58 mg per injection) or placebo into the affected cord at 30 day intervals. One day post injection, the treated joints were then manipulated up to three times with the use of a standardized procedure (finger extension) in an effort to rupture the cords. The primary endpoint was a reduction in primary joint contracture to 0° to 5° of full extension 30 days after the last injection. Primary efficacy analysis was done using the Cochran-Mantel-Haenszel test. Twenty-six secondary endpoints were evaluated, and adverse events were collected.

**Results:**

Efficacy results on n=306 patients demonstrated that the proportion of joints that met the primary endpoint of 0° to 5° of full extension was significantly higher when injected with collagenase (clostridium histolyticum) as compared to placebo (64.0% vs. 6.8%, P<0.001) (Figure 1A and 1B). This was also true for all 26 secondary endpoints (P≤0.002). Overall, joint range of motion was significantly improved after collagenase treatment (43.9° to 80.7°) compared with placebo treatment (45.3° to 49.5°)( p<0.001). Most commonly reported adverse events were localized edema, pain, swelling, bruising, pruritus, and transient regional lymph node swelling and pain, which resolved without treatment in a median10 days. Three treatment-related serious adverse events were reported: two tendon ruptures and one complex regional pain syndrome. No significant changes in flexion or grip strength, no systemic allergic reactions, and no arterial or nerve injuries were observed.

---

**Figure 1A.** Left hand of a 66 year old patient with a 75 degree contracture of the MP joint, little finger and 20 degree contracture of the MP joint, ring finger, pre injection showing full correction of contractures.

**Figure 1B.** Same patient as in Figure 1A, 30 days post one collagenase injection showing full correction of contractures.
Anne Ouellette MD MBA: Outcomes of Living, bi-layered skin substitute use in Dupuytren’s surgery using the McCash incision improves long term outcome

E. Anne Ouellette, MD., MBA, Melissa Diamond, Anna-Lena Makowski, HTL

Hypothesis:
Living, bi-layered skin substitute coverage of wounds after Dupuytren’s surgery using the McCash incision improves long term outcome.

Methods:
Chart review of 137 patients (153 hands) patients undergoing surgery to release Dupuytren’s contracture between 1999 and 2007 was conducted. Patients who had McCash incisions followed by application of living, bi-layered skin substitute skin graft during this time period was contacted for follow-up evaluation. The patients filled out an Upper Extremity Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire collecting information on pain level, range of motion and activities of daily living. The patients also submitted pictures of their palmar scar. Descriptive statistics was used to present DASH scores. Students T-test (2-tailed) was used to evaluate the difference in time from surgery to skin healing between patients receiving living, bi-layered skin substitute coverage with patient that did not.

Results:
36 patients had the living, bi-layered skin substitute skin graft applied to their surgical wounds, of these 9 have submitted their outcome information to date. Average follow-up time was 76 months (range 30-129 months). Average DASH score for this group was 8. Dash score distribution was n=7 (DASH 0-10), n=1 (11-20), n=0 (21-30), n=1 (31-40), n=0 (41-100). (Table 1). Wounds covered with Living, bi-layered skin substitute(n=10) took longer to heal than wounds not covered (n=17), 40 days vs 27 days (p<0.05). The scars healed well for all patients. (Figure 1).

Summary:

- Statistically significant different time to skin healing; wounds took longer to heal after coverage with Living, bi-layered skin substitute
- DASH scores received to date is predominantly in the lower range (0-10) indicating a good outcome. This data compares to average DASH scores of 3.85 and 32 post long term surgical follow-up reported in the literature not using a skin graft.
- Palmar scars healed well in all subjects based on long term follow-up photos.

Table 1: Distribution of DASH scores. No scores were over 40.

Figure 1. Patient 60 months post McCash incision covered with living, bi-layered skin substitute. DASH score 3.3.
Hypothesis:
Are we able to improve the surgical outcome of strand interruptions in Dupuytren’s disease by creating an augmented ‘firebreak’ effect with an absorbable cellulose implant, a known absorbable adhesion barrier?

Methods:
In a case control prospective study, we included 33 operations in 29 patients with a high probability for recurrent disease. The cellulose was implanted in the first 15 patients. Intraindividual control was done in 4 patients. Goniometric evolution was monitored on digital photography and satisfaction was measured on a visual analogue scale (VAS) with a preliminary 1 year follow-up.

Results:
With the implant, the postoperative range of motion improved significantly by 36% and remained unchanged after 3 months with a 1 year follow-up. Likewise, the VAS for satisfaction improved more.

Summary:
We conclude that cellulose implants may improve the surgical outcome of segmental fasciectomy in Dupuytren’s disease by achieving a better finger extension and a high patients’ satisfaction.

Figure 1: Schematic illustration of the surgical technique in the fifth digit: after segmental strand resection resulting in full finger extension the absorbable cellulose is implanted to mechanically interrupt the fibroproliferative strands.

Figure 2: Goniometric evolution of the total extension lack in metacarpophalangeal and inproximal interphalangeal joints in both groups (preop = before the surgery; intraop = during surgery; m = months after)
1:45pm-2:00pm Heinrich Seegenschmiedt MD PhD: RADIOTHERAPY FOR PRIMARY OR RECURRENT MORBUS LEDDERHOSE: 12 YEAR LONG-TERM OUTCOME OF A PROSPECTIVE PHASE 2 TRIAL.

M. Heinrich Seegenschmiedt, Etienne Hanslian, Mark Wielpütz

**Purpose:**
Long-term outcome analysis of a prospective phase 2 study to analyze the use of radiotherapy (RT) for Morbus Ledderhose (ML) to prevent disease progression.

**Methods:**
From 1997 to 2009 over 143 patients with ML have been referred to our clinic with symptomatic and progressive ML to receive RT for prevention of disease progression. As of 12/2009, 138 pts (71 M; 67 F) have been evaluated for at least 1 year follow-up (FU; median: 6 years). 54 patients had one foot (28 R, 26 L) affected and 84 had bilateral affliction; thus, a total of 222 feet were afflicted and additional 54 feet were uninvolved and observed in long-term FU. While 47 (34%) patients (94 feet) with 67 affected feet, but only minimal symptoms served as control without RT, 91 (66%) patients and 126 feet received RT for primary (n = 66) or recurrent ML. Of the 138 pts, 68 had Morbus Dupuytren (MD) or knuckle pads (n = 8), keloids (n = 11), diabetes mellitus (n = 12), epilepsy (n = 2), liver disorders (n = 7), foot trauma (n = 13), and 39 patients reported nicotine abuse. Time from first observation to first consultation was 12 months. RT was applied with 10 x 3Gy in two RT series of 5 x 3Gy separated by 8 weeks and delivered using 125 to 150 kV photons, lead rubber shielding and superflab bolus for individual set-up. ML was classified in 4 grades; the clinical evaluation (toxicity, efficacy) was performed at 3 months and 1 year after RT and every year thereafter.

**Results:**
Acute and late side-effects were minimal: 26 and 6 feet developed CTC grade 1 and 2 skin changes; chronic side-effects (mostly dry skin within the RT portal) were observed in 20 feet. At last FU, clinical disease progression was observed in 11 of 126 (9%) feet; 56 (44%) had stable disease and 59 (47%) showed objective remission of disease. 24 of 62 feet with cords. Moreover, total relief or reduction of symptoms was also pronounced in the RT group: 18 of 22 feet with itching, 48 of 62 with tension sensation, 74 / 100 with pressure sensation, 71 / 86 with pain during walking and 32 / 47 with pain at rest. In contrast, in the control group without RT, 23 of 67 (34%) feet progressed and required treatment, 34 (61%) remained stable and 10 (15%) had a spontaneous remission or reduction of symptoms without treatment.

**Conclusion:**
External beam RT is effective and improves long-term outcome for progressive ML; RT is well tolerated and reduces or avoids otherwise necessary surgical procedures. As no primary treatment is available sofar, RT appears to be the treatment of choice when symptoms progress and affect daily quality of life and invasive procedures are to be avoided.
Peyronie’s disease (PD) is a wound-healing disorder in which a fibrotic plaque forms in the tunica albuginea layer of the penis. It clinically presents as any combination of penile pain, angulation, and erectile dysfunction. Recent studies indicate that PD has a prevalence of 3%–9% in adult men. Although the exact etiology has not been established, PD likely results from a predisposing genetic susceptibility combined with an inciting event such as microtrauma during intercourse. During the initial acute phase (6–18 months), the condition may progress, stabilize, or regress. For this reason authorities recommend a more conservative treatment approach, with a trial of oral and/or intralesional pharmacotherapy, before surgical reconstruction is considered. Oral therapies most commonly employed include tocopherol (vitamin E) and paraaminobenzoate (Potaba), with colchicine, tamoxifen, propoleum, and acetyl-L-carnitine being used less often. There are a limited number of long-term placebo-controlled studies with these oral agents, and for the most part, studies have failed to show a consistent beneficial effect. Intraleisonal injection therapy for PD is more commonly used as a first-line therapy. The current approach includes injection with interferon-a-2b, verapamil, or collagenase (Xiaflex, Auxilium, Philadelphia, PA). Other available therapies that have not consistently shown efficacy in placebo-controlled studies include corticosteroids, orgotein, radiation, and extracorporeal shockwave therapy. Surgery is considered when men with PD do not respond to conservative or medical therapy for approximately 1 year and cannot perform satisfactory sexual intercourse. Ongoing basic research in PD will likely identify future targets for medical exploitation.
This presentation will describe the usage of cryotherapy for plantar fibromas, Dupuytren’s contracture of the plantar surface of the foot. We will cover the benefits of using this procedure. A review of the usage of cryoanalgesia in allopathic medicine will be discussed along with some research articles. The mechanism of action, physiological principles and basic principles of this surgical technique will be discussed. A step by step presentation of a case study of a cryosurgical procedure will be shown for a patient with a plantar fibroma. The presentation will conclude with some practice pearls to highlight the usage of cryotherapy.
Originally described for its ability to remodel the birth canal during pregnancy, the hormone relaxin is emerging as both an endogenous inhibitor of collagen turnover and a potential therapy for the progressive fibrosis that occurs during tissue repair and end-stage organ disease. Relaxin has now been shown to potently and rapidly inhibit fibrogenesis in diverse experimental models of dermal, cardiovascular, renal (glomerular and tubulointerstitial), pulmonary/airway and hepatic disease. In several of these models, short-term continuous infusion of relaxin is also able to reverse established fibrosis. Importantly, relaxin only inhibits pro-fibrotic cytokine (TGF-ß, angiotensin II, interleukin-1) stimulated collagen and fibronectin deposition in primary fibroblast culture models in vitro and animal models of injury/disease in vivo without affecting basal matrix turnover; suggesting that it is a safe therapeutic. Consistent with this, relaxin has been evaluated in a number of clinical trials and has demonstrated an excellent safety profile in humans with minimal side-effects. The anti-fibrotic actions of the hormone have been found to primarily involve the down-regulation of Smad2 phosphorylation as a means of interfering with TGF-ß signaling and hence, the ability of TGF-ß to promote myofibroblast differentiation and collagen production. Additionally, relaxin has been found to antagonize TGF-ß stimulated collagen I lattice contraction, while promoting matrix metalloproteinase expression and activity, and inhibiting the actions of the tissue inhibitors of metalloproteinases to induce collagen breakdown. These combined actions along with its ability to promote vasodilation, angiogenesis and wound healing highlight its potential as a therapy for fibroproliferative disorders; which will be discussed.
Dupuytren’s disease is a fibroproliferative disorder, the cure for which is still limited to surgical excision of the affected fascia, often leading to high recurrence rates. Due to this fact, non-surgical treatments are being investigated, among them those targeting molecular processes of proliferation and differentiation in Dupuytren’s cell cultures. Drugs with antiproliferative action may be valuable in D.D. treatment. Through characterization of changes on D.D. specific cells, we therefore, decided to test the therapeutic potential of new cytostatic drugs for D.D. treatment and/or for reduction of post-operative recurrence rates. The N-sulphonylpyrimidine derivate, amidino-substituted benzimidazol(1,2-a)quinoline, and amidino dihydrothienothienyl(2,3-c)quinolone hydrochloride, known to affect proliferation process, were tested for their antiproliferative activity on primary fibroblasts/myofibroblasts cell cultures derived from the palmar fascia of patients with D.D. Only amidino dihydrothienothienyl(2,3-c)quinolone hydrochloride acted in a highly specific manner on cells derived from diseased fascia of D.D. patients and exhibited a low cytotoxic effect. This result might be a consequence of its specific activity on cytoskeleton changes occurring in differentiating cells. A similar short term differential antiproliferative effect was observed by the N-sulphonylpyrimidine derivate that was, however, completely lost after 6-and 14-day treatments. The amidino-substituted benzimidazol(1,2-a)quinoline exerted a strong nonspecific, dose related antiproliferative activity on cell types.
3:00pm-3:15pm Ilse Degreif PhD MD: Highly-dosed neo-adjuvant tamoxifen improves surgical outcome in segmental fasciectomy in high risk patients with Dupuytren’s disease

Degreif I, MD, PhD & De Smet L, MD, PhD

Hypothesis:
Are we able to improve the surgical outcome of strand interruptions in Dupuytren’s disease by adding highly dosed neo-adjuvant tamoxifen?

Methods:
Prospective randomized double-blind study, protocol according to the CONSORT standards, to investigate the possible adjuvant effect of tamoxifen on subtotal fasciectomy in patients with Dupuytren’s disease, who show a high risk for recurrence (Abe grade 4 or more). Goniometric evolution was monitored on digital photography and satisfaction was measured on a visual analogue scale (VAS) with a preliminary 1 year follow-up.

Results:
With the implant, the postoperative range of motion improved significantly by 32% and remained unchanged after 3 months with a 1 year follow-up. Likewise, the VAS for satisfaction improved significantly more.

Summary:
We conclude that highly dosed neo-adjuvant tamoxifen improves the surgical outcome by segmental fasciectomy in Dupuytren’s disease by achieving a better finger extension and a high patients’ satisfaction.

Figure 1: Comparison of the Tubiana relative correction coefficient in both groups. A significant difference (p = 0.001) is seen in total correction, where the placebo group showed a total correction of the MCP and PIP joints of 61% (SD 26.8) (group 1) compared to 93% (SD 13.2) in the tamoxifen group. Looking at the isolated PIP joint, which is most difficult to correct, the difference is also statistically significant (P = 0.007) from 49% in group 1 towards 89% in group 2.

Figure 2: Illustration of the significant difference (p = 0.0006) in postoperatively improved visual analogue scale for satisfaction in the tamoxifen patients (group 2), but not in the placebo group (p = 0.3) (group 1).
Session 8:
The Future
3:30pm-5:15pm

Panel and Open Discussions:
Global collaboration for Dupuytren’s and related conditions
Presentation Questions and Answers
Future Plans

Charles Eaton MD: Closing remarks.
Biographies
John Agee MD
Hand Surgeon
Hand Biomechanics Lab, Inc., Sacramento, CA, US

Dr. Agee is a hand surgeon in private practice in Sacramento, California. He created and runs the Hand Biomechanics Lab, Inc, which is focused on patient care, the study of hand biomechanics, and research and development of surgical devices. He is involved in original research in a variety of hand related investigations, including stability of the tendons in the carpal tunnel, carpal tunnel pressures as a function of grasp and pinch, biomechanics of 1st CMC joint, biomechanics of the extensor tendons and their juncture in dynamic stability of the MP joints, multiplanar ligamentotaxis for reduction of distal radius fractures, and other topics. His surgical device research and development inventions include external skeletal fixators to treat PIP fracture dislocations (TurnKey) Force Couple Splint, distal radius fractures (WristJack), Reverse PIP flexion contractures (Digit Widget); endoscopic release of the carpal tunnel: HBL/3M (Inside Job); MP joint prostheses.

He lists the privilege of patient care and daily fellowship with bioengineers and medical personnel as his career highlights. His interests include designing and building “machines” from those that fly to those that treat patients. Future plans include developing biomechanical models to investigate the etiology of carpal tunnel syndrome, osteoarthritis of finger IP joints and the thumb carpometacarpal joint and attracting next generation hand surgeons with common interests to join in his pursuits.

Marie A. Badalamente, PhD
Professor, Department of Orthopaedics
State University of New York at Stony Brook, NY, US

Dr. Badalamente received her PhD in Cell Biology from Fordham University, Bronx, NY. She was a faculty member at the State University of New York, Downstate Medical Center, Department of Anatomy for a short time before joining the faculty of the Department of Orthopaedics, SUNY Stony Brook when the University Hospital/Medical Center at Stony Brook opened. Her research program in Orthopaedics has involved numerous medical students, Orthopaedic residents and Fellows.

Her research interests have included basic science and clinical research studies/trials in Dupuytren’s disease. She was awarded the 2009 Orthopaedic Research and Education Foundation/American Academy of Orthopaedic Surgeons outstanding clinical research award, along with her colleagues, Lawrence C. Hurst, MD and Edward D. Wang, MD for their work “Injectable Clostridial Collagenase: Striving Toward Nonoperative Treatment Options for Fibroproliferative Disorders”. This body of work described the use of injectable collagenase for the treatment of Dupuytren’s disease and adhesive capsulitis.

In 2010, the US Food and Drug Administration approved injectable collagenase for the treatment of Dupuytren’s disease. Future plans include clinical development of collagenase for multiple Orthopaedic and non-Orthopaedic indications/disorders.

Ardeshir Bayat MD PhD
Clinician Scientist
University of Manchester, Manchester, GB

“My initial exposure to research was a project on the process of wound healing as a first year medical student at University College London, UK. This small study encouraged me to do a one year project on the same topic as part of an intercalated BSc. Following the completion of my basic surgical training, I had the opportunity to continue with basic scientific research. Having completed a one year research fellowship from the Royal College of Surgeons of England in understanding the molecular basis of wound healing, I subsequently gained an MRC clinical training fellowship. This award led to a successful PhD in molecular genetics of wound healing at the University of Manchester. I then began my specialist training in Plastic Surgery with an interest in Hand surgery. Following completion of my PhD, I was successful in achieving an NIHR clinician scientist award in 2006. I am now a principal investigator and group leader in plastic & reconstructive surgery research at the Manchester interdisciplinary biocentre at the University of Manchester, England, UK. The focus of my research is in wound repair and regeneration.

Currently, my group (www. prsr. org) comprises of several post docs, experimental officers, PhDs, MSc, and MRes students. Additionally, I often supervise project and elective medical students. My laboratory has a full independent capacity in carrying out molecular, cellular, and histological research in tissue biology utilizing state of the art equipment in addition to access to our own in vitro organotypic and organ culture models of tissue repair.

My lab is based at the MIB (Manchester Interdisciplinary Biocentre) (www. mib. ac. uk) at the University of Manchester. Examples of my current active international academic collaborators in the field of repair and wound healing include collaborators in Europe (University of Lubeck, Lubeck, Germany and Linköpings University, Linköping, Sweden) as well as in the USA (Harvard University, Boston, Massachusetts). “

Dr. Bayat has authored over over 75 publications in peer reviewed journals.
Robert Choa MD  
**Nuffield Orthopaedic Centre**  
Oxford Deanery, UK

Robert Choa, Nuffield Orthopaedic Centre, Oxford Deanery, UK. Member of the Royal College of Surgeons of Edinburgh: “As a junior surgical trainee in the UK system I have found myself drawn towards hand surgery, and have been fortunate to have worked with a highly respected team of hand surgeons in Oxford. Patients with Dupuytren’s disease form a significant portion of the workload which we encounter. One of my senior colleagues remarked on the nerve branches which we have researched during a fasciectomy, this prompted our cadaveric study. Not only has this project significantly improved my understanding of the disease, but it has also encouraged me to disseminate our results and also to further my knowledge by coming to Miami!”

Ilse Degreef MD PhD  
**University Hospitals Leuven**  
Pellenberg, BE

Dr. Degreef was born in Leuven and is married with 3 children. She is a full time staff member at the Orthopaedic Department at the University Hospitals Leuven in Belgium, Europe. There, she now is responsible for the surgical treatment of upper limb pathology, more specifically for hand or wrist disorders, elbow pathology and neurological disorders in the upper limb at the Orthopaedic Department of the University Hospitals Leuven.

The last 4 years, she has dedicated her academic carrier towards developing new insights and introducing new strategies for the treatment of Dupuytren’s disease in cooperation with Prof Dr L De Smet and Prof Dr S Tejpar. She received a clinical grant from the University Hospitals Leuven for 3 years and the Biomet Research Award for her project on developing new treatment methods in therapy-resisting Dupuytren’s disease. She finished her PhD on new treatment strategies in therapy-resisting Dupuytren’s disease.

Guido H. C. G. Dolmans MD  
**University Medical Center Groningen**  
Groningen, NL

Dr. Dolmans is a resident in Plastic, Reconstructive and Hand surgery at University Medical Center Groningen, the Netherlands. After completing medical school with honors he worked for two years at the department of Plastic and Hand Surgery of Catharina Hospital Eindhoven, where he developed a special interest in Hand Surgery.

Guido is currently working on a PhD thesis regarding the genetics of Dupuytren’s disease. Under supervision of Professor Paul Werker, he has set up a multicenter study in the Netherlands. His ambition is to extend the project internationally.

Charles Eaton MD  
**Hand Surgeon**  
The Hand Center, Jupiter, FL, US

Born in West Palm Beach, Florida, Dr. Eaton received a BS in physics at Emory University and graduated medical school at Washington University in St. Louis. He completed general surgery residency at Boston University, plastic surgery residency at New York University, hand fellowship at New York University with Drs. Beasley, Melone and Chiu, and a fellowship at the Microsurgery Research Centre in Melbourne, Australia with Mr. O’Brien and Mr. Morrison. He spent several years as an assistant professor of plastic surgery at the University of Utah with Dr. Lister before moving back south Florida where he works as a private practice hand surgeon. He has a particular interest in Dupuytren’s disease and has performed needle aponeurotomy on over 8000 hands. He is the author and webmaster of e-hand.com and other web sites, has published numerous articles and book chapters in the field of hand surgery, and has lectured internationally on hand related topics. He is active with national and international hand surgery organizations. Dr. Eaton created the Dupuytren Foundation, a public charity intended to promote research, education and global collaboration to develop better treatment options for Dupuytren’s disease and related conditions. He is the primary organizer of the 2010 International Symposium on Dupuytren’s Disease.

Dr. Eaton has seven children and five grandchildren. He is fascinated by music, photography, mathematics, history, computer technology, nature, and by opportunities to do good work for future generations.

Susan Emeigh Hart VDM, PhD, DACVP, DABT, ERT  
Sr. Director, Drug Safety & Metabolism  
**Auxilium Pharmaceuticals, Inc.** , Malvern, PA, US

Dr. Emeigh Hart is a board certified veterinary pathologist (both Veterinary Anatomic Pathology and Veterinary Clinical Pathology) through the American College of Veterinary Pathology. She is also certified in General Toxicology through the American Board of Toxicology (ABT), and is a peer recognized expert toxicologist (Eurotox Registered Toxicologist), certified by the UK Register of Toxicologists. Her nineteen year career in industry has provided her with broad-based experience in all aspects of preclinical drug development for both small molecule pharmaceutical agents and biotechnology products (including novel agents such as naturally derived peptides, aminosterols and non-antibody, non-recombinant proteins). Her areas of expertise include renal, hematologic and ocular pathology and physiology, biomarker identification and development, pathology of commonly used laboratory animals, mechanistic toxicology, mitochondria’ pathology, interstitial matrix biology, and cell-matrix interactions.

Dr. Emeigh Hart received her undergraduate degree from the Pennsylvania State University and her veterinary medical degree from the University of Pennsylvania School of Veterinary Medicine. After a brief tenure in mixed veterinary practice she enrolled in a combined veterinary pathology residency and Ph. D. program in the Department of Pathobiology at the University of Connecticut, where she also concurrently held an NIEHS-sponsored postdoctoral fellowship through the School of Pharmacy, Section of Toxicology. She started her career at Ciba-Geigy in Farmington, Connecticut as a Staff Pathologist in the Crop Protection division. She then joined Pfizer, Inc. as a Senior Pathologist in Drug Safety
Evaluation (DSE). While at Pfizer, she was involved in the initiation of the Center of Excellence in Ocular Toxicology, received two DSE Achievement Awards in Science, and was Exploratory Candidate Management Team Member of the Year. She then joined the DuPont Pharmaceuticals Company as a Principal Research Scientist in Safety Assessment and from there joined AstraZeneca Pharmaceuticals as a Preclinical Project Director. It was while working at AstraZeneca that Dr. Emeigh Hart attained her certification in clinical pathology, and following this she was reassigned to Safety Assessment as Associate Director (Clinical Pathologist). From there, she went to Genera Corporation in Plymouth Meeting, PA, to serve as the Director (later Senior Director) of Safety Assessment, where in addition to her responsibilities for oversight of the company's preclinical toxicology programs she also contributed to a number of drug discovery research programs, both internal and resulting from external collaborations.

Currently, Dr. Emeigh Hart is the Senior Director of Non-Clinical Development at Auxilium Pharmaceuticals, where she is responsible for the execution of all non-clinical drug discovery, development and regulatory programs in support of compound registration. This has included an active role in the non-clinical development, regulatory activities and recent FDA approval of collagenase clostridium histolyticum as well as participation in a number of external research collaborative projects with this product.

Dr. Emeigh Hart has an extensive bibliography which includes book chapters, peer-reviewed publications and published abstracts. She is an active member of a number of professional organizations (ABT, ACVP, ASVCP, BioSafe, STR SOT). She has held several offices, served on committees, and has been invited to present on a variety of topics at local, national and international meetings.

Dr. med. Holger C. Erne
Oberarzt, Center of Hand Surgery, Microsurgery, Plastic Surgery Orthopädische Klinik München-Harlaching, München, DE

Dr. Erne received his Doctor’s Degree at Albert-Einstein-Universität Ulm, and completed residencies at Klinik für Unfall- und Wiederherstellungschirurgie / Klinik für Viszeral- und Gefäßchirurgie Schorndorf and Klinik für Allgemeinchirurgie und Zentrum für Schilddrüsenchirurgie Neu-Ulm. He qualified as a general surgeon and received a Diploma of Mountain Medicine from the Universität Heidelberg. He completed a fellowship in at the Klinik für Handchirurgie und Ellenbogenchirurgie Bad Neustadt / Saale under Professors Lanz, Prommersberger and Schoonhoven and also the Robert E. Carroll Fellowship at Columbia University Presbyterian Medical Center in New York under professors Carroll, Rosenwasser and Strauch. He is now Oberarzt at the Center of Handsurgery, Microsurgery, Plastic Surgery, Orthopädische Klinik München-Harlaching.

Dr. Erne has authored multiple publications covering a variety of upper extremity topics. His current interests include Dupuytren’s disease, aseptic osteonecrosis, scapholunate ligament lesions, sports related injuries and reconstructive surgery. He is a member of the Deutsche Gesellschaft für Handchirurgie (DGH), Deutschsprachige Arbeitsgemeinschaft für Handchirurgie (DAH), Bundesverband der Deutschen Chirurgen (BDC) and Robert E. Carroll Hand Club.

Vilhjalmur Finsen PhD
Professor
St. Olav’s University Hospital, Trondheim, NO

Dr. Finsen was born in Oslo. After medical school at the Royal college of Surgeons in Ireland, Dublin, he became a licensed specialist in general surgery and orthopedic surgery. He is head of the hand surgery service at St. Olav’s University Hospital, Trondheim, Norway and professor of orthopedic surgery at the Norwegian University of Science and Technology. He has authored about 75 scientific papers, approximately one third of which deal with aspects of hand surgery.

Giulio Gabbiani MD PhD
Professor
University of Geneva, Geneva, CH

Dr. Gabbiani earned an MD degree at the University of Pavia (Italy) and a PhD degree at the University of Montreal (Canada). He has been Assistant Professor at the Institute of Experimental Medicine and Surgery, University of Montreal, Research Associate at the Department of Pathology of Harvard Medical School, Assistant Professor at the Department of Pathology and Immunology of the University of Geneva (Switzerland) and then Professor in the same Department, where he is now Emeritus Professor.

The scientific interests of Dr. Gabbiani include soft tissue remodeling during development and pathological situations, such as wound healing and organ fibrosis as well as arterial smooth muscle adaptation during development and diseases, e. g. atheroma formation and restenosis. Cell modulation during these phenomena has been studied using cytoskeletal markers, in particular actin isofrom expression. Dr. Gabbiani was the first to describe the myofibroblast, a cell intermediate between the fibroblast and the smooth muscle cell that has been shown by several laboratories to be responsible of connective tissue remodeling in developmental and pathological settings.

Dr. Gabbiani has been Secretary and President of the European Cytoskeleton Forum, Secretary and Chairman of the European Vascular Biology Association, Secretary of the European Tissue Repair Society. He is in the Editorial Board of the American Journal of Pathology and of Arteriosclerosis Thrombosis and Vascular Biology. He has received several distinctions including a degree of Doctor Honoris Causa from the University of Gothenburg (Sweden) and from the University of Limoges (France).

Bing Siang Gan MD PhD
Associate Professor
Hand and Upper Limb Centre, London, Ontario, CA

Dr. Gan graduated from the Medical Faculty at Erasmus University in Rotterdam, The Netherlands in 1988. He then went on to earn a PhD in Medical Sciences (Subspecialty Pharmacology and Experimental Therapeutics) from the University of Calgary. After a rotating internship at the Regina General Hospital in Regina, Saskatchewan, a residency in Plastic Surgery was completed at the University of Western Ontario.
Teaching Hospitals. This clinical training was followed by post-residency Fellowships in Microsurgical Reconstruction (Toronto General Hospital, University of Toronto) and Hand and Microsurgery (Massachusetts General Hospital, Harvard University), as well as a research post-doctoral fellowship (Department of Cell Biology, Hospital for Sick Children, University of Toronto).

Dr. Gan has been with the Hand and Upper Limb Centre at St. Joseph’s Health centre since 1998 and has an academic practice focused on hand and wrist surgery, microsurgical reconstruction and complex wound reconstruction. In conjunction with Dr. David O’Gorman, he directs the HULC Cell and Molecular Biology Laboratory located in the Lawson Health Research Institute. Dr. Gan has a particular research interest in Dupuytren’s contracture and other fibrosing conditions, like hypertrophic scarring. His research program has been funded by a number of external agencies, including the American Society of Plastic Surgeons, Canadian Society for Surgery of the Hand, American Association for Hand Surgery, the National Science and Engineering Research Council and since 2002, the Canadian Institutes of Health Research.

Dr. Gan is currently the Secretary of the Ontario Society of Plastic Surgeons and Secretary of the OMA Section of Plastic Surgery. He is a member of the Board of Directors of the Canadian Society of Plastic Surgeons, serves on the Regional Advisory Committee of the Royal College of Physicians and Surgeons of Canada. Dr. Gan is also a member of the Royal College Examination Board in Plastic Surgery. He is the President of the Canadian Society for Clinical Investigation for 2009-2011.

**Wayne J G Hellstrom MD**  
*Professor*  
*Tulane University School of Medicine, Tulane, LA, US*

Dr. Hellstrom is professor of urology and chief of andrology (male infertility and sexual dysfunction) at Tulane University School of Medicine in New Orleans, where he has been a faculty member since 1988. His practice is specialized in the diagnosis and treatment of male sexual dysfunction including Peyronie’s disease, surgical and vascular reconstruction, prosthetic surgery, male infertility (both surgical and medical therapies), male hypogonadism, premature ejaculation, BPH, and urethral stricture disease.

A clinician, author, and lecturer, Dr. Hellstrom has published over 300 peer-reviewed articles in professional publications and has authored numerous chapters in textbooks. He also is the editor of “Male Infertility and Sexual Dysfunction” and “The Handbook of Sexual Dysfunction.”

Dr. Hellstrom earned his undergraduate and medical degrees at McGill University in Montreal and completed his urology residency at the University of California at San Francisco and his fellowship at the University of California at Davis. Dr. Hellstrom has been awarded many honors in the field of urology, male infertility, and erectile dysfunction, and is currently the Secretary General of the International Society of Sexual Medicine (ISSM), and president-elect of Society for Urologic Prosthetic Surgery and past president of the Sexual Medical Society of North America and the American Society of Andrology. In addition, he is associate editor of The Journal of Sexual Medicine, International Journal of Andrology, Asian Journal of Andrology, Current Sexual Health Reports and specialty editor for the Journal of Urology.

**Hans C Hennies PhD**  
*Division Head, Dermatogenetics*  
*Cologne Center for Genomics, University of Cologne, Köln, DE*

Dr. Hennies received a master’s degree in biochemistry for his work on human microsatellite DNA at Freie Universität Berlin. His PhD thesis was the Molecular characterization of palmoplantar keratodermas at the Institutes for Human Genetics, Humboldt-Universität zu Berlin, and Biochemistry, Freie Universität Berlin. He received postdoctoral training in human genetics and experimental dermatology in Berlin and London. He is a scientist at the Max Delbrück Center for Molecular Medicine in Berlin, group leader in molecular genetics. He is the head of the Division of Dermatogenetics at the Cologne Center for Genomics, Universität zu Köln and principal investigator at the Center for Molecular Medicine Cologne and the Cologne Cluster of Excellence on Cellular Stress Responses in Aging-Associated Diseases. His major research interests in genetic skin, hair, and connective tissue diseases, studies in genomics and human molecular genetics into the identification and characterization of genes involved in monogenic and multifactorial disorders, mutation spectra, gene and protein function in development and disease. He is also involved in translational research in genetic disorders using new disease models and gene based and substitution therapy.

**Sandip Hindocha MD**  
*University of Manchester*  
*Wigan, GB*

Dr. Hindocha is a specialty registrar and research fellow in plastic Surgery; Liverpool & Manchester, UK. His research interest is identification of biomarkers and genetics of Dupuytren’s Disease. He has published papers and presented nationally and internationally in scientific and clinical meetings. His comments are: “It is apparent from UK Clinical Research Collaboration and modernising medical careers that there is a shortage of academic surgeons. It is important that every effort is geared towards enhancing academic research in modern surgery and I am fully committed to furthering this cause. I aim to pursue a career in academic plastic surgery. I also intend to continue with further enhancement of my own knowledge and involvement with future projects. I am positive that this pursuit would continue throughout and subsequent to completion of my specialty training in plastic surgery.”

**Boris Hinz PhD**  
*Associate Professor*  
*University of Toronto, Toronto, Ontario, CA*

Boris Hinz is Associate Professor at the Matrix Dynamics Group, Faculty of Dentistry, University of Toronto, Canada. He is cross-appointed Professor with the Faculty of Medicine, Department of Surgery and the Institute of Biomaterials and Biomedical Engineering at the University of Toronto. Dr. Hinz holds a PhD degree in Cell Biology and Theoretical Biology from the University of Bonn, Germany. He was postdoctoral fellow of Dr. Giulio Gabbiani, Department of Experimental Pathology, Centre Medical Universitaire, University of Geneva, Switzerland. Dr. Hinz then moved on to lead a research group at the Ecole Polytechnique Fédérale
Sandee p Kathju, MD PhD  
**Assistant Professor**  
**Drexel University College of Medicine, Pittsburgh, PA, US**

Dr. Kathju is a Board-certified plastic surgeon whose interests extend to multiple aspects of fibrotic and scirrhous pathologies. He is a part of the Armed Forces Institute of Regenerative Medicine, where his work focuses on developing new technologies to engineer scarless wound healing in adults, and to reduce the inflammatory and cicatricial consequences of burn injury. Clinically he maintains an active practice with a special interest in reconstructive surgery for scar-related morbidities. His interest in the molecular and cellular basis of Dupuytren contracture is another extension of these researches.

Dr. Kathju is an Assistant Professor of Microbiology and Immunology at Drexel University College of Medicine, an attending surgeon in the Division of Plastic Surgery of the West Penn Allegheny Health System, and Director of the Wound Healing Program, Center for Genomic Sciences at the Allegheny-Singer Research Institute.

---

**Lynn Ketchum MD**  
**Hand Surgeon**  
**Leawood, KS, US**

Dr. Ketchum grew up in New Orleans, LA., attended Tulane Medical School, and after completing residencies in General Surgery at the Ochsner Clinic and Plastic Surgery at the U of Kansas Medical Center, he spent two years in the Navy during the Vietnam war, then was a full-time Plastic Surgery faculty member at the U of Kansas Medical Center for eleven years. He received the first place award in the annual Plastic Surgery Educational Foundation Essay contest for his work on “The Effect of Triamcinolone on Tendon Healing” which allowed him to visit many of the top hand surgeons in Europe. He was awarded a patent on the first Continuous Passive Motion machine. Dr. Ketchum spent a six-month sabbatical doing biomechanical research with Dr. Paul Brand at the Leprosy Hospital in Carville, LA.

Dr. Ketchum has been in private practice for over thirty years in Overland Park, KS, where he established a Hand Surgery Fellowship program and trained twenty hand fellows. He has remained intimately associated with the KU Plastic Surgery program by training two Plastic surgery residents in hand surgery each year for three months each, and during that period has remained clinical professor of Plastic surgery in that department. His main interest in medicine is the study and treatment of Dupuytren’s disease. Outside of medicine, his main interests are traveling and golf. Lynn has been happily married to his wife Carly for almost eighteen years; he has two children and several grandchildren.

---

**Davor Jurisic MD PhD**  
**Department for Plastic and Reconstructive Surgery**  
**University Hospital Center Rijeka, HR**

In medical school, Dr. Jurisic was named “best student in generation”. He undertook postgraduate study Biomedicine and Surgery, trained in general surgery, plastic surgery, and passed European exam of Plastic surgery under the EBOPRAS.

Dr. Jurisic has a broad scope of clinical practice, including breast reconstruction and aesthetic breast surgery, Zgreb bariatric surgery team participation, hand surgery and aesthetic surgery in Slovenia. He has published academic papers on a variety of topics, including both clinical and molecular biology aspects of Dupuytren’s disease. His future plans include further investigation of the molecular mechanism and possible therapeutic targets in Dupuytren’s disease, pursuing both private practice and further developing his Department. He is in the process of becoming assistant professor.

---

**Sandra Kraljevic Pavelic PhD**  
**Assistant Professor, Head of Laboratory for Systems Biomedicine**  
**Department of Biotechnology, University of Rijeka, HR**

Dr. Kraljevic Pavelic is assistant professor at University of Rijeka, Croatia and head of Laboratory for Systems Biomedicine. Her main scientific interests include tumour gene therapy and chemotherapy, study of molecular mechanisms underlying Dupuytren’s disease, proteomics and transcriptomics.

She is a member of Croatian’s Academy of Science and Arts Board for Genomics and Proteomics in Oncology, Croatian Society for Oncology, and Croatian Medical association. She received the award for excellence in science of the Ministry for Science, Education and Sport of Croatia.

Debbie Larson BScOT, MSc  
Accredited Hand Therapist  
Norfolk and Norwich University Hospital, NHS, UK

Ms. Larson trained in occupational therapy at the University of Alberta, Canada and completed an MSc in Hand Therapy in the UK. She is married to Adrian Chojnowski, a hand surgeon, and together they have built a strong clinical practice at the Norfolk and Norwich Hospital.

They have joined with researchers from the University of East Anglia (Norwich) to form the Norwich Dupuytren’s Group. UEA members include: Christina Jerosch-Herold, reader in occupational therapy; Lee Shepstone, professor in medical statistics; and Ian Clark, professor of biological sciences. Publications include matrix metalloproteinase expression in Dupuytren’s disease and relationship to clinical outcome. Debbie will present the effectiveness of splinting following Dupuytren’s surgery. Future research of the group includes measurement of MMP’s to predict disease aggression and investigating outcome measures.

Bernhard Lukas Dr med  
Orthopädische Klinik München-Harlaching Zentrum für Handchirurgie, München, DE

Dr. Lukas studied at the Ludwig-Maximilian-Universität München (Munich). After passing examination and approbation, he received promotion and then an apprenticeship to medical specialist of Surgery and Plastic Surgery at Chirurgischen Klinik Innenstadt der LMU München. He is the Assistant medical director of department Plastic Surgery and hand surgery at Chirurgischen Klinik Innenstadt der LMU München, the Chief physician of hand surgery, microsurgery and plastic surgery at Orthopädischen Klinik München-Harlaching, and the Chief physician of hand surgery at Behandlungszentrum Vogtareuth. He has authored a number of hand and microsurgery academic publications.

Dr. Lukas is a member of the: Deutsche Gesellschaft für Handchirurgie (DGH); Deutschsprachige Arbeitsgemeinschaft für Handchirurgie (DAH); Deutsche Gesellschaft der Plastischen, Rekonstruktiven und Ästhetischen Chirurgen (DGPRÄC); Gesellschaft für Orthopädische Traumatologie und Sportmedizin (GOTS); and Deutschsprachige Arbeitsgemeinschaft für Mikrochirurgie (DAM).

Albrecht Meinel MD  
Hand Surgeon  
Tauberbischofsheim, DE

Dr. Meinel completed his medical studies at the Ludwig-Maximilians-University München and had further training and work as visceral and orthopaedic surgeon at the Ruprecht-Karls-University Heidelberg. His postdoctoral thesis was: Morbus Dupuytren – Streckhemmung statt Fingerkontraktion. Formalgenese und Pathomechanik der Palmarfibromatose (MD – extension blockage instead of contraction. Pathogenesis and pathomechanic of the palmar fibromatosis).

Dr. Meinel was chief of staff of surgery in Tauberbischofsheim Hospital / Germany for over twenty years and more recently has practiced Dupuytren out-patient surgery in Würzburg.

Dr. Meinel: “My studies and work, now in and former times, are focused on the history of Dupuytren research as well as the anatomy, pathogenesis and surgical treatment of Dupuytren’s Contracture. For the last seven years I have been especially concerned with percutaneous needle fasciotomy and splinting in Dupuytren therapy. These themes will also form the basis of my work in future. I’m married to Katja. We have two grown-up children and now, to our great pleasure, a little granddaughter in Berlin. My free time I enjoy with photography and drawing, and sometimes on the golf course.”

Hanno Millesi MD  
Professor  
Millesi Center Vienna, Vienna, AT

Dr. Millesi was born in Villach, Austria, graduated as medical doctor at the University of Innsbruck, and trained in General and Plastic Surgery. He has served in a series of prestigious academic positions: Head of the unit of Plastic and Reconstructive Surgery of the 1st Surgical University Clinic, Medical Faculty, University of Vienna; Professor and Head of the Department of Plastic and Reconstructive Surgery at the 1st Surgical University Clinic, Medical Faculty, University of Vienna; Head of the Ludwig Boltzmann Institute of Experimental Plastic Surgery; Full Professor of Plastic Surgery, Medical Faculty, University of Vienna; Professor emeritus; Medical Director of the Vienna Privat Clinic, and most recently Foundation of Millesi Center of Peripheral Nerve Surgery.

His scientific interests include: Dupuytren’s Contracture; Scar Contracture; Skin Tension at rest and during movements; Significance of visco-elastic properties of tissue; Healing and regeneration of nerves; Development of a reliable technique of nerve grafting; Comprehensive treatment of lesions of peripheral nerves and brachial plexus lesions; Significance of fascias for Plastic and Reconstructive Surgery.

Dr. Millesi has practiced medicine for sixty years, and in his remarkable career has published many important scientific contributions relating to these scientific interests. He continues to provide both research and clinical contributions to the fields of plastic surgery, nerve surgery and hand surgery.

Janine Morris PhD  
Senior Research Associate, Biomedical Research Centre  
University of East Anglia, Norwich, Norfolk, GB

Dr. Morris: “I am a Senior Research Associate who has been working in Prof. Ian Clark’s laboratory for just over for 13 months. The group as a whole has interests in the proteolysis of the extracellular matrix in connective tissue diseases such as arthritis and specifically for me, in Dupuytren’s disease. My research focuses on the role of specific matrix metalloproteinases (MMPs) in Dupuytren’s disease and this is carried out with human tissue samples via collaboration with Mr. Adrian Chojnowski from the Norfolk and Norwich University Hospital.”
My accomplishments so far include detailed gene profiling of the MMP enzymes from human Dupuytren fibroblasts and attributing certain gene expression patterns to their contractile activity. I hope to take this further by using siRNA techniques to gain greater understanding of which MMPs are contributing to the pathology behind Dupuytren’s disease. I am also interested in the effect that sulphoraphane has on the contractile potential of Dupuytren’s fibroblasts. I work closely with our local hospital and have met many patients with Dupuytren’s disease. This gives me the motivation to move my research forwards towards a clinical application that will improve the lives of people suffering with this disease."

Veronique Moulin PhD
Professor
LOEX-Université Laval, Hopital Saint Sacrement, Quebec, CA

Dr. Moulin is professor at the surgery department of the faculty of medicine at Laval University, Canada. She is researcher at the LOEX at the Centre hospitalier affilié universitaire de Québec. Her work is dedicated to the comprehension of wound healing and fibrosis phenomena using several study models such as tissue engineered skins and animal models. Her most recent achievements comprise the production using tissue engineering techniques of a reconstructed skin model for wound healing studies, functional studies of wound dermal cells, the myofibroblasts and evidence of the importance of interactions between keratinocytes, the epithelial cells of the skin, and dermal cells during fibrosis.

David O’Gorman PhD
Assistant Professor, Hand and Upper Limb Centre
Lawson Health Research Institute, London, Ontario, CA

David B. O’Gorman co-directs (with Dr Bing Siang Gan) research in the Cell and Molecular Biology Laboratory of the Hand and Upper Limb Centre, St Joseph’s Hospital, in London, Ontario, Canada. He is a research scientist at the Lawson Health Research Institute and Assistant Professor in the Departments of Surgery and Biochemistry at the University of Western Ontario (UWO). Dr O’Gorman competed his doctoral degree in the Department of Molecular Medicine, Faculty of Medicine at the University of Sydney, Australia and his postdoctoral training at UWO. His current research interests represent a coalescence of his background as a pathology technician, graduate and postdoctoral training in clinical biochemistry and cancer cell biology, and postdoctoral research into growth factor-mediated proliferation and differentiation during development. Dupuytren’s Disease and wound healing have become his primary research foci as they incorporate the regulation of many of the growth factors that affect tumour growth through processes that are often recapitulations of development. He considers the potential to understand the biochemical interactions in these processes, and thereby assist in the development of novel therapies, a challenge and a privilege. Dr O’Gorman’s laboratory focuses on extra-cellular matrix (ECM) interactions in Dupuytren’s Disease and abnormal wound healing, including the identification and characterization of disease-associated ECM molecules and modeling their interactions with primary cells in vitro.

A Lee Osterman MD
Professor of Hand/Orthopedic Surgery
Thomas Jefferson University Philadelphia, PA, US

Dr. Osterman grew up in Wheeling, West Virginia before attending Yale College where he majored in photography. After graduation, he traveled on a Guggenheim fellowship photographing original stained glass in Europe. Subsequent to that, he traveled to Tanzania where he photographed doctors working with the Wagogos and the Masai on an UNESCO project that eventually became a book, Jungle Doctor Panorama. That experience, combined with a family medical background, set him on a course to medical school.

He spent the next 10 years of training at the University of Pennsylvania where he did his medical school, orthopaedic residency and hand fellowship with Dr. F. William Bora. It was in his first few weeks in the anatomy lab that his realized his future passion. “The most human part of a cadaver is its hand.” The only time away was an internship at Mt. Sinai Medical School in New York City where he met his future wife, Elissa Topol, and a microvascular fellowship with Dr. Jim Urbania at Duke University.

He returned to Penn where he became a tenured Associate Professor and where he practiced and taught until 1993. Then the two Philadelphia hand groups from Penn and Thomas Jefferson merged to form The Philadelphia Hand Center, a practice that encompasses the full gamut of shoulder to hand problems, including congenital reconstruction, microsurgery, trauma and adult reconstruction. PHC has a teaching complement of 6 ACGME hand fellows, multiple orthopedic and plastic residents, the Evelyn Mackin hand therapy fellowship and international fellows. He divides his time between teaching (not only locally but around the world), writing (he has edited one of the most popular hand surgery texts, Rehabilitation of the Hand, as well as authored numerous articles), and an active clinical practice. He is a Full Professor of Hand and Orthopedic Surgery at Thomas Jefferson University and President of the Philadelphia Hand Center.

He has served in many leadership positions in both the American Society for Surgery of the Hand and the American Association for Hand Surgery. He is currently President of the AAHS and Chairman of the Hand Fellowship Directors. He is Past President of the Eastern Orthopedic Association.

He finds enjoyment in the mountains of Colorado where he skis in the winter and spends part of the summer biking, hiking, and absorbing good music in the natural beauty of the area. His oldest daughter, Meredith, is an orthopedic surgery resident. His middle daughter, Alexis, lives in Denver where she is getting her doctorate in psychology. His youngest daughter, Zoe, is a junior at Colorado College.
Anne Ouellette MD MBA
Professor
Miami International Hand Surgical Services, Miami, FL, US

Dr. Anne Ouellette has more than 25 years of experience as a hand surgeon in Miami, Florida. She spent 23 years with the University of Miami where she achieved the rank of Professor. She serves as Chief of Hand Surgery and Director of the Hand fellowship Program at Jackson Memorial Hospital. Dr. Ouellette started Miami International Hand Surgical Services, LLC, an affiliate of Jackson Health System and retired from the University of Miami. Dr. Ouellette is an accomplished researcher and innovator, always striving to better patient outcomes and healthcare in general. Her main focus and interest is always the patient's wellbeing. Dr. Ouellette enjoys teaching medical students, residents, fellows, and colleagues from a variety of backgrounds and encourages their success as academic clinicians as well.

Academically, her research interest in hand and upper extremity encompasses a wide range of areas, including biomechanics of wrist instability, repair of injured nerves, and skin coverage and psychological intervention for upper extremity trauma patients. Her research efforts have resulted in 13 book chapters, more than 24 peer reviewed articles and numerous presentations at academic meetings all over the world. Clinically, Dr. Ouellette incorporates innovative procedures in her patient care. More than 16 years ago Dr. Ouellette developed an in situ “sling” for the treatment of wrist instability with excellent patient satisfaction. Another innovative application of advanced technology Dr. Ouellette uses is to apply engineered skin substitute on surgical wounds after Dupuytren's release to improve outcome. Limited wrist fusion is another example of a special technique Dr. Ouellette performs. This technique is predominantly used in Rheumatoid Arthritis patients and relieves pain while some wrist function is preserved. Furthermore, Dr. Ouellette is pursuing projects addressing the need for improved patient involvement in their own treatment and outcomes by implementing new technologies in patient education and outcome research at the Miami International Hand Surgical Services, LLC.

Michael Y Papaloïzos MD
Associate Professor, Plastic and Reconstructive Surgery
Lausanne University Hospital, Lausanne, CH

Dr. Papaloïzos was born in Switzerland, and received his medical education at Lausanne University School of Medicine, Lausanne, Switzerland. He trained in general and orthopedic surgery in Lausanne, peripheral nerve and plexus surgery at the Longeraie Clinic with Professor A. Narakas. He completed a fellowship in plastic, reconstructive and hand surgery at Zurich University Hospital with Professors V. E. Meyer and M. Frey and then a one year research fellowship at Lund University with Professor G. Lundborg. He completed his Doctoral Thesis at Lausanne University School of Medicine. He served as Consultant, Hand Surgery Unit, Geneva University Hospital and then founded the Center for Hand Surgery and Therapy in Geneva, Switzerland with associates André Chamay and Philippe Cuénod. He is currently Consultant and associate professor, Plastic and Reconstructive Surgery, Lausanne University Hospital.

Dr. Papaloïzos has authored twenty five peer-reviewed publications and given 80 presentations at national and international meetings. He was awarded the 2001 Koch Award of the American Society for Surgery of the Hand for the paper with the greatest future clinical application to the practice of hand surgery. His main interests are in peripheral nerve, wrist, arthritis and Dupuytren’s surgery, both clinical and experimental. He is a member of the Swiss Society for Hand Surgery, Swiss Society for Plastic and Reconstructive Surgery, Swiss Society for Neuroscience, German speaking Society for Microsurgery (DAM) and ASSH.

Sem Phan PhD MD
Professor
Department of Pathology, University of Michigan, MI, US

Dr. Phan earned both a PhD in Biological Chemistry and an MD at Indiana University. After Anatomic Pathology residency and Immunology Fellowship, he progressed to become Professor and Director of the Graduate Program in Molecular & Cellular Pathology, University of Michigan Medical School. He has held chair and member positions on a number of NIH program projects as well as other research committees and councils, served as associate editor of the American Journal of Pathology and received numerous academic awards and honors.

Dr Phan’s research is directed at understanding the cellular and molecular mechanisms of tissue repair and fibrosis. His current projects are directed at 5 major interrelated directions: the contribution by bone marrow progenitor cells to fibrosis; the mechanism of telomerase reverse transcriptase (TERT) induction, growth factor ligands and transcriptional regulation of the TERT gene in the role of the bone marrow in fibrotic lung disease; development of the FIZZ1 knockout mouse and attempts at identification of the FIZZ1 receptor; analysis of the transcriptional and epigenetic regulation of the mechanisms of myofibroblast differentiation and the role of nitric oxide in induction of myofibroblast apoptosis; studies of the role of the eosinophil and epithelial-mesenchymal crosstalk in pulmonary fibrosis. Future plans include continuation of work on relevant signaling pathways directing regulation of the α-smooth muscle actin gene in myofibroblast differentiation. New pathways involving epigenetic regulation via histone modifications and DNA methylation will be explored, and mechanisms involving miRNA will be identified and elucidated. The roles of telomerase induction and the FIZZ or resistin-like family of molecules are also of continued interest. These will eventually be put in the context of potential novel therapeutic approaches that will exploit discovery of these new pathways and mechanisms.

2010 International Symposium on Dupuytren's Disease
Ghazi Rayan MD  
Program Director, Hand/Orthopaedic Surgery  
INTEGRIS Baptist Medical Center, Oklahoma City, OK, US

Dr. Rayan graduated with honors from Alexandria University Medical School, Alexandria Egypt. He completed Orthopedic Surgery residency at the Union Memorial-Johns Hopkins Hospital Baltimore, MD and the Hand and Microsurgery Fellowship at the Raymond Curtis Hand Center. He has served on and chaired 54 committees, local, domestic and international. Dr. Rayan has served on the American Society for Surgery of the Hand as Council Member and on 8 Task Forces, given 224 scientific presentations, published 156 scientific articles, 27 book chapters and has been the editor of 6 books. He is currently Clinical Professor of Orthopedic Surgery Oklahoma University, Adjunct Professor, Department of Anatomy /Cell Biology, Director Oklahoma Hand Fellowship Program, and is Chair Division of Hand Surgery, INTEGRIS Baptist Medical Center.

Martin C Robson MD  
Emeritus Professor, Division of Plastic Surgery  
University of South Florida, Tampa, FL, US

Dr. Robson received his MD from the Johns Hopkins University. He completed his general surgery residency at the Brooklyn Army Medical Center and his plastic surgery residency at Yale. He has served as Chief of Plastic Surgery at the University of Chicago, Wayne State University, and the University of Texas Medical Branch. He is presently an Emeritus Professor at the University of South Florida. He is a Fellow of the American College of Surgeons and holds Honorary Fellowships from the Royal College of Surgeons of England and the Royal Australasian College of Surgeons. He has served as President of the American Burn Association and received its Distinguished Service Award. He has been President of the Wound Healing Society and is a recipient of its Lifetime Scientific Achievement Award. He has also received Lifetime Scientific Achievement Awards from the Association of Advanced Wound Care and the World Union of Wound Healing Societies. He has been Chairman of the American Board of Plastic Surgery, Chairman of the Residency Review Committee for Plastic Surgery, Chairman of the Plastic Surgery Research Council, and President of the Association of Academic Chairmen of Plastic Surgery. He has authored over 600 publications mostly devoted to wound healing, wound infection, burns, and proliferative scarring.

Chrishan S Samuel PhD  
Senior Research Fellow  
Howard Florey Institute, University of Melbourne, Victoria, AU

Dr Samuel is a Senior Research Fellow and Head of the Relaxin-Fibrosis Laboratory at the Howard Florey Institute, Melbourne, Australia. He is also an Honorary Senior Research Fellow in the Department of Biochemistry and Molecular Biology, The University of Melbourne, Australia. His research interests are associated with establishing therapeutic strategies for organ fibrosis, with a particular focus on determining the anti-fibrotic and protective actions of the hormone, relaxin. He has over 80 career publications and his work is supported by the National Health & Medical Research Council of Australia, the National Heart Foundation of Australia, other Australian funding bodies as well as a number of commercial and philanthropic sources.

M Heinrich Seegenschmiedt MD PhD  
Professor  
Radiation Center Hamburg, Hamburg, DE

Professor Seegenschmiedt comes from Erlangen, Bavaria; He is married and has five children. He received his Degree in Medicine and PhD summa cum laude from the University of Würzburg. He trained in pathology, internal medicine, Hematology / oncology, diagnostic radiology and Radiotherapy at the City Hospital Nürnberg and universities of Würzburg and Erlangen-Nuremberg.

He received a research grant from the German Cancer Aid Association the Department of Radiation Oncology, Hahnemann University in Philadelphia (USA) under Prof. Luther Brady. He then worked as physician specialist in radiation therapy, University of Erlangen-Nuremberg. He received his post-doctoral qualification in Radiation Oncology at the University of Erlangen-Nuremberg with the subject “Interstitial hyperthermia and radiation therapy in ENT-tumors”, and for that he was given first prize of the renowned Wilhem Conrad Röntgen-Prize of the German Society of Radiology.

Professor Seegenschmiedt was Medical Director, Department of Radiation Oncology & Radiotherapy, Alfried-Krupp Hospital in Essen. He currently is professor at the Radiation Center Hamburg. Professor Seegeenschmiedt is first and co-editor of several German and English international textbooks, primary and co-author of over 180 book chapters and 120 Medline listed papers.

He is involved with a number of international associations, particularly on issues of organization, quality management and of training. He has headed the commission, "Radiotherapy of the Medical Association of North Rhine. He is also a member of numerous national and international professional societies: DEGRO, ARO, ESTRO, ASTRO, RSNA, German Cancer Society and a member of Review and Editorial Boards of numerous journals.

Terri Skirven OTR/L CHT  
Director, Hand Therapy  
Philadelphia Hand Center, Philadelphia, PA, US

Ms. Skirven has been teaching in the Hand and Upper Quarter Programs since 2000. Her primary teaching interests include management of wrist conditions. She earned her BS in Occupational Therapy at the University of Pennsylvania, and became qualified as a Certified Hand Therapist. She is the Director of Hand Therapy of the Philadelphia Hand Center, Board Member and Director, Hand Rehabilitation Foundation, Philadelphia, Co-chair of the Philadelphia Hand Meeting, Board Member of the American Hand Therapy Foundation, Guest editor, Journal of Hand Therapy, 2005, special issue on Tendon and Nerve and Co-editor for the 6th edition of Hunter-Mackin-Callahan: Rehabilitation of the Hand and Upper Extremity. She serves on the Editorial Board of the Journal of Hand Therapy.
Speaker Biographies

Paul Smith MD
Consultant in Plastic and Reconstructive Surgery
Bishopswood Hospital, Northwood, Middlesex, GB

Mr. Smith trained in Glasgow, London and the United States. In Glasgow he was involved in research with Cannesburn the Centre for Plastic Surgery and at that time was involved in developing the anatomical basis of the groin flap and undertaking research into axial pattern flaps in general. He was clinical instructor in Plastic Surgery at Duke University, North Carolina, and a Christine Kleinert Fellow in hand surgery at Louisville, Kentucky. He was awarded 1st prize in the Resident Competition in the United States and the Pulvertaft prize for hand surgery. After completing his training at Mount Vernon Hospital where he was appointed consultant, he was appointed consultant at Great Ormond Street. He has been an invited Visiting Professor in Plastic Surgery in Australia, South Africa, Canada and the US.

Mr. Smith was a founding member of RAFT (Reconstruction of Appearance and Function Trust) based at Mount Vernon. This postgraduate institution funds research into plastic surgery. RAFT has been responsible for training 15% of the current plastic surgeons in the UK and has included 6 Hunterian Professorships.

Mr. Smith has been in Consultant Practice at Mount Vernon Hospital Regional Plastic Surgery Centre and at the Hospital for Sick Children Great Ormond Street and has been responsible for running the Hand Surgery service in both institutions. He has published extensively in the Hand Surgery literature, including editing Lister’s The Hand.

Massimiliano Tripoli MD
Department of Plastic and Reconstructive Surgery
University of Palermo, Palermo, IT

Dr. Tripoli was born in Palermo. He earned his Medical Doctor Degree Magna cum laude at the University of Palermo with the thesis “Aspetti biomolecolari nella eziopatogenesi della malattia di Dupuytren”. He continued there as a resident and earned a Postgraduate degree in Plastic, Reconstructive and Aesthetic Surgery with the thesis “Artroplastica digitale con protesi; nuovi materiali e nuove vie di approccio all’impianto “. He was a Fondation André Bouriez fellow in Hand Surgery and Microsurgery at Nancy-France (Médipole Saint-Jacques Gentilly) and Luxembourg (Hôpital central Kirchberg) with Professor Merle. He earned a research doctorate in Traumatology at the University of Catania. He is currently a research doctor the Department of Plastic and Reconstructive Surgery, University of Palermo.

Dr. Tripoli’s research activities have included investigation of wound healing in patients undergoing vacuum therapy, efficacy of brevity TGF-beta3 for improvement of disfiguring scars, video microsurgery, anatomy of cervical artery vascular territory and investigation of pharmacological thrombolysis for the resolution of venous thrombosis in revascularized free flaps. He has given a number of academic presentations and has published articles in peer-reviewed journals on a variety of plastic and hand surgery topics, including basic science research and clinical aspects of Dupuytren’s disease. His surgical interests include hand trauma, head and neck surgery, laser surgery and skin cancer. His other personal interests include Story of Shoah, drawing, oil painting and photography.

Terry L Spilken DPM
Foot Care of Livingston
Livingston, NJ, US

Dr. Spilken graduated from the New York College of Podiatric Medicine in 1979. He is the former Dean of Student Services and was also the Dean of Graduate Medical Education at the New York College of Podiatric Medicine. He currently holds the rank of Adjunct Associate Professor in the Department of Medical Sciences. Dr. Spilken is the author of two books, “The Dancer’s Foot Book” and “Paddings and Strappings of the Foot”. He is also the editor of “Podiatry Board Certification Review Notes” and “Podiatry Practice Examination and Study Guide”. His most recent edited book is entitled “Podiatric Pearls II: Helpful Hints for the Podiatrist” which follows the publication of the first edition.

Dr. Spilken was the podiatric consultant for more than 15 professional dance companies and the podiatrist for the NY Islander hockey team. He has appeared on many radio and television shows discussing podiatry and has been quoted in numerous magazines and journals. He has lectured internationally on such topics as cryosurgery, sports medicine and dance medicine. He has a private podiatry practice in Livingston and Edison, New Jersey. He has hospital privileges at St. Barnabas Medical Center in Livingston, New Jersey. He previously had privileges at the Lincoln Medical and Mental Health Center in the Bronx, New York, where he was Chairman of the Department of Podiatry as well as an attending to the hospital’s Department of Surgery/Podiatry.

Annet Van Rijssen MD
Resident Plastic Surgery
Groningen University Medical Center Groningen, NL

Dr. Rijssen studied Medicine at the University of Groningen, and started as a Surgery resident in the Isala Clinics, Zwolle, The Netherlands. She is a Senior Resident in Plastic Surgery at the department for Plastic and Reconstructive Surgery of the Isala Clinics, Zwolle. She is currently working on her thesis on the treatment of Dupuytren’s disease under the supervision of Professor P. M. N. Werker at the University Medical Hospital Groningen. She authored the first published comparison of needle aponeurotomy versus fasciectomy for Dupuytren’s contracture.

Wolfgang Wach PhD
Dupuytren e. V / Dupuytren Society
Westerbuchberg, DE

Dr. Wach received his PhD in Solid State Physics at the University of Munich, Germany. After six years of research in ion implantation he worked in electronic design at Siemens and as General Manager at AT&T Microelectronics Europe. He started his own software company CAL in 1995 and Dupuytren Society in 2003. Dupuytren Society is an internationally acting organization of patients and medical doctors. He is currently one of the chairmen of Dupuytren Society.
Paul MN Werker MD PhD
Professor and Head of the Department of Plastic Surgery
Groningen University Medical Center Groningen, NL

Dr. Werker completed his Medical school in Utrecht (NL), Aberdeen (UK) and London (UK), and his specialty training to become a plastic surgeon in Utrecht too, which he finished at the end of 1995. In London he started a PhD project on free flap preservation in 1987, which he completed in 1992. Following a microsurgery fellowship together with Dr. Joe Banis in Louisville, KY, he returned to Utrecht to become an attending at the University Medical Centre. In between 1999 and 2006 he worked as a consultant plastic surgeon at the Isala Clinics in Zwolle, one of the major training hospitals in NL. In 2006 he became Professor and Chief at the Department of Plastic Surgery at the University Medical Centre in Groningen-NL.

His main scientific interest is in Dupuytren’s Disease, Facial Palsy Reconstruction and Breast Reconstruction. He is (co-)author of 50 peer reviewed papers and 5 book chapters and has presented at more that 130 national and international meetings.

In Dupuytren’s Disease, Dr. Werker’s research focuses on genetics, anatomy and clinical trials.

Andrey Zhigalo MD
Military Medical Academy, Clinic of Military Traumatology and Orthopedy, St. Petersburg, RU

Dr. Zhigalo was born in Brest, Belarus. He finished secondary school № 5 in Murmansk with a silver medal in 1999, graduated from the Military Medical Academy in 2005. In 2006 - 2007 years he served the training center for combat medics in the rank of commander of medical school - an instructor. Now he is an adjunct at the clinic of Military Traumatology and Orthopedics. He has written 36 published works, including 11 rationalizational proposals and 1 monograph (“Fundamentals of microvascular techniques and Reconstructive Surgery”) and designed the patent for application.

The theme of dissertation: “Characteristics of surgical tactics in treatment of patients with severe Dupuytren's disease”.

He is captain of the Medical corps adjunct the Department of Military Traumatology and Orthopaedics, the Military Medical Academy.

His future plans are to write a monograph on the issue of treatment of Dupuytren’s disease and introduce the needle aponeurotomy in the Commonwealth of Independent States.

Paul Wylock MD
Professor and Head of the Department of Plastic Surgery
University Hospital Brussels, BE

Dr. Werker was born in Ghent, Belgium. He earned his M. D. at the University of Ghent, worked Military Service as a general practitioner in Germany, trained in General Surgery at St Joseph Hospital in Venlo, Holland, affiliated with the Radboud University Nijmegen, and then trained in Plastic Surgery at the University Hospital of Ghent. He practiced as a Plastic Surgeon, and started of the Unit of Plastic Surgery at the new University Hospital of the Free University Brussels (from scratch!). He received the National Award of the Belgian Hand Group in 1982 with a study of Dupuytren’s disease. He has been Teacher in plastic surgery and Teacher of hand surgery in the “Collegium Chirurgicum Plasticum”.

Dr. Wylock is currently Head of the Unit and Professor, University Hospital Brussels. He is Chairman of the national teaching courses of the Collegium Chirurgicum Plasticum. He has been an invited guest professor in Congo, Vietnam, Myanmar, Saudi Arabia and Madagascar. He is a Member of the Belgian Society of Plastic, Reconstructive and Aesthetic Surgery, National Secretary of the Belgian Society, Past President of the Royal Belgian Society of Plastic Surgery, Past President of the Belgian Hand Group, Historian of the Belgian Hand Group and of the Royal Belgian Society of Plastic Surgery, Member of the Alpine Workshop, the IPRAS, the ISAPS and the EURAPS.

Dr. Wylock has 3 children and 6 grandchildren. His leisure activities include history of medicine lecture, gardening, hiking, and travelling (discovery of other cultures). He has recently published the biography “The Life and Times of Guillaume Dupuytren 1777-1835”.

Paul Zidel MD MS
Chief, Hand Surgery, Maricopa Medical Center
Phoenix, Arizona, US

Dr. Zidel is a hand surgeon in Phoenix, Arizona. He is Chief of the Hand Surgery Service at the Maricopa Medical Center and the Maricopa Integrated Health System and also Assistant Professor of Plastic Surgery at the Mayo Clinic, Scottsdale, Arizona. Dr. Zidel has been a Hand Fellowship Director at Wayne State University, Detroit, Michigan as well as the Director of the Burn Center at Detroit Receiving Hospital. Besides his M. D. degree, he has a Master’s Degree in Physiology and has been a Research Fellow at the Hospital for Joint Diseases Orthopaedic Institute in New York. He completed his Plastic and Reconstructive Residency at Wayne State University and his Hand Fellowship at New York University. He is a founding member of the Dupuytren Foundation.
Research, education and global collaboration to find better treatment for Dupuytren's and related conditions.