Dissertations

Carpal tunnel syndrome—prevalence, electrodiagnosis and outcome instruments

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In an epidemiologic study of carpal tunnel syndrome (CTS), a health questionnaire was mailed to an age- and sex-stratified random population sample of 3000 subjects (25–74 years). Responders with numbness/tingling in the median nerve distribution in the hands and a random sample of nonsymptomatic responders underwent clinical examination as well as portable and conventional median nerve conduction testing. The population prevalence of CTS was estimated for different case definitions.

The agreement between the portable and conventional measurements of median nerve distal motor latency (DML) and wrist-digit distal sensory latency (DSL) was good. Conventional wrist-palm sensory conduction velocity measurement had a better capacity than portable wrist-digit DSL measurement in discriminating subjects judged by the examining physician to have a clinically certain CTS from the controls.

In a prospective study, portable nerve conduction testing showed significantly worse DML and DSL in 42 CTS hands (clinical diagnosis and complete postoperative symptom relief as gold standard) than in 60 nonsymptomatic control hands; portable testing had a sensitivity of 74% and a specificity of 87%.

A study evaluating 129 CTS patients before and 3 and 6 months after unilateral endoscopic carpal tunnel release found prior heavy vibration exposure, normal preoperative DML, and worse activities of daily living score to be associated with patient dissatisfaction with the results of surgery, while sensibility/strength measures did not correlate with patient satisfaction.

In a study of 114 patients presenting with upper-extremity nerve-compression symptoms, the symptom severity scale of the disease-specific CTS outcome instrument was found to discriminate patients classified, on the Katz hand diagram, as having classic/probable CTS from those having possible/unlikely CTS. This was related to the scale's sensory component while the pain component and the functional status scale had no such discriminative capacity.

In a study of 102 CTS patients evaluated before and 3 months after surgical treatment, an expanded Swedish version of the CTS instrument was found to be reliable, valid and responsive to change.

In a study of 58 CTS patients, the CTS instrument symptom severity scale's pain and sensory components and the functional status scale showed large improvement 6 weeks, and 3 and 6 months after surgery. The pain scale of the SF-36 generic (i.e., general health) instrument showed large improvement, and the physical role, physical component summary, and mental health scales showed moderate improvement in health status at 3 months. The sensibility/strength measures showed small to moderate improvements at 3 and 6 months. CTS patients had worse health-related quality of life as compared to the general population norms; improvement had occurred 3 months after surgery.

In a cohort study comparing CTS treatment outcomes in 61 workers' compensation and 161 non-workers' compensation patients, the CTS instrument and the SF-36, administered 7 to 22 months after the initiation of treatment, could not verify any significant differences in the outcomes.

Current concepts and surgical aspects of extremity bone and soft tissue sarcoma

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Over the past 25 years, several factors have contributed to the improved prognosis in patients with bone and soft tissue sarcomas of the extremities.

Effective (neo)adjuvant chemotherapy regimens have led to substantially improved survival in patients with osteosarcoma, MFH of bone, Ewing's sarcoma and rhabdomyosarcoma. Radiotherapy has had a major impact on the local control of soft tissue sarcomas and it is now being routinely combined with conservative "function preserving" resection of the primary tumor. This can prevent local recurrence in up to 90% of cases.

Improvements in imaging techniques, most notably CT and MRI, have enabled accurate preoperative assessment of the type, location, and local extension of the tumor and the proximity or involvement of vital structures. Consequently, far better surgical planning is possible to obtain adequate resection margins and there is also improved potential for limb-sparing surgery. Staging systems for musculoskeletal tumors have proved to be important for the prognosis and a guide for the most optimal treatment for the individual patient. Prognostic clinical factors for tumor recurrence and overall survival are important variables to determine tumor behaviour and to guide treatment of extremity sarcoma. New important prognostic factors are being studied by cytogenetics and molecular biology, and their significance should be taken into account in the design of clinical studies in the future.

Improved surgical techniques and understanding of the influence of surgical margins on local and distant tumor control have undoubtedly had a great influence on patient survival. Adequate surgical resection of the primary tumor with tumor-free margins is crucial for local and systemic control in almost all musculoskeletal sarcomas, even after the addition of chemotherapy or radiotherapy.

Tumor resection with subsequent reconstructive procedures have replaced amputation in approximately 80% of patients with extremity sarcomas.

The two most important criteria for limb-saving procedures are that the tumor must be totally resectable and reconstructive procedures must provide limb function that is equal or superior to the function of a prosthesis.

Most of the patients with extremity sarcomas will now become long-term cancer survivors. Therefore the functional results of the reconstructed limb as well as (late) complications and survival of the reconstruction are becoming increasingly important. The two most frequently used methods to reconstruct the large defect after bone tumor resection are the endoprosthesis and the allograft. Both methods of reconstruction provide good functional results with the same overall and disease-free survival rates as those after limb amputation. However, complication rates are high, approaching 50% in long-term follow-up studies. More than one revision procedure is often necessary and patients frequently out-live the implant that was originally used for reconstruction. Most of the reconstruction-related complications can be resolved without losing the limb or being harmful to extremity function, and without affecting patient survival.

Nowadays, fewer major amputations are performed in patients with extremity sarcomas, but if malignant growth is extensive, amputation may still be a necessary and life-saving operation. The two major ablative surgical procedures are interscapulothoracic amputation and hemipelvectomy. These approaches can be performed with curative and occassionally palliative intent. No postoperative complications occurred after interscapulothoracic amputations in our series. This in contrast with the findings after hemipelvectomy: flap necrosis, wound infection and genito-urinary compications were reported in a considerable number of patients after this procedure. In selected cases, alternative limb-saving or limb-sparing procedures might be feasible, e.g. Tikhoff-Linberg procedure instead of interscapulothoracic amputation, hindfoot amputation instead of below-knee amputation, internal hemipelvectomy with or without reconstruction of the defect and buttockectomy instead of hemipelvectomy.

Pelvic sarcomas still present an enormous problem. Wide surgical margins are often difficult to obtain. In well-selected cases, internal hemipelvectomy with or without reconstruction is an excellent option.

However, complication rates are high in all these procedures. In general, patients with a locally advanced pelvic girdle sarcoma who are unsuitable can-

didates for internal hemipelvectomy have a poor prognosis. Prognosis and treatment regimens vary between different histological subtypes and different grades of tumor. For osteosarcoma of the pelvic region, as described in this thesis, the prognosis remained poor compared to the results of treatment for other extremity osteosarcomas, despite modern multimodality treatment regimens, including neoadjuvant chemotherapy and surgical resection.

The favourable results achieved with bone and soft tissue sarcoma surgery over the past 25 years were achieved by the multidisciplinary approach employed at the University Hospital Groningen.

Absorbable internal fixation of cancellous bone fractures in the lower extremity—a clinical study

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Absorbable self-reinforced rods and screws made of polyglycolide or poly-L-lactide have been developed to replace metallic implants in bone fixation. They have been in clinical use since 1984 with limited indications. In the present study, to expand those indications, 103 fractures in 98 patients were operated on. Absorbable implants were used in 69 fractures and metallic implants in 34 fractures as controls.

In a prospective randomized study of 37 patients aged 65 years and over with displaced malleolar fractures, 16 patients were operated on using SR-PGA rods and screws and 19 patients using metallic screws and plates. In addition, there were 2 patients randomized into the SR-PGA group which were operated on with metallic implants because of peroperative problems. Postoperatively there was one major redisplacement in both groups. During the 1-year follow-up there was no significant difference in the functional or radiologic results between the operative methods used. The results were satisfactory in most patients. The main present limitation is a possible comminution of bone needing a plate for fixation.

In a prospective randomised study of 29 patients with displaced malleolar fractures associated with verified alcohol abuse, 16 patients were operated on using SR-PGA screws and 13 patients using metallic implants. In the SR-PGA group, there were 6 reoperations in 8 redisplaced fractures. In the metallic group there was only 1 redisplacement which needed no reoperation. This difference was statistically significant and caused the discontinuation of the study. Altogether 17 out of 29 patients were lost to follow-up which reflects the poor cooperation of these patients. The present absorbable fixations method was insufficient in this group of patients with lack of cooperation.

6 patients with displaced split-depression type tibial condylar fractures were treated with absorbable SR-PGA screws. 1 patient was reoperated because of an unacceptable primary fracture reduction unrelated to the implant material. The other 5 fractures healed well, with excellent function and excellent or good anatomical results at the 1-year follow-up. The SR-PGA screws yielded a reliable fixation of unicondylar split-depressed fractures when a buttress plate was not needed.

6 patients with a displaced fracture of the neck or body of the talus were treated with absorbable SR-PGA or SR-PLLA screws and rods. During the 2-year follow-up, all the fractures united without redisplacements or collapses due to avascular necrosis. The funtional result was mainly dependent on the other injuries of the patients, being excellent in 4 , good in 1 , and poor in 1 patient who also had bilateral extremely comminuted calcaneal fractures. The absorbable fixation had no adverse effects, and the disadvantages of metallic screws were avoided, such as countersinking of the screw heads below the level of the cartilage surface or a disturbed postoperative CT and MRI.

25 displaced intra-articular calcaneal fractures in 21 patients were operated on with SR-PGA rods and followed up for 2 years. The mean Böhler angle was −12° preoperatively and 20° postoperatively. In 10 fractures, varying degrees of redisplacement occurred during the postoperative period. After the follow-up period 7 patients had an excellent, 5 good, 3 fair, and 6 poor functional result. Subjectively, 15 patients were satisfied and 6 were dissatisfied. These results are similar to those of other operative methods. The postoperative Böhler angle and, later, the appearance or absence of posttraumatic subtalar arthritis seemed to be significant prognostic factors. The absorbable implants offer new possibilities of implant placement especially when the comminution of the medial cortex makes lateral plating troublesome. The removal operations are avoided, even in cases of temporary transarticular fixation. In this indication, new implant designs may be of benefit in the future.

The results of the present study give evidence that osteoporosis as such is not a contraindication to absorbable fixation, but good cooperation of the patients is required. Before this study, intra-articular fractures of weight-bearing joint surfaces treated succesfully with absorbable implants have been reported to be the tibial posterior margin in the ankle and the femoral condyles of adolescents. The present results with fractures of the tibial condyles, talus, and calcaneus give additional evidence that absorbable implants offer sufficient stability to be used for fixation of fractures of the weight-bearing cancellous bones.

Triple osteotomy of the pelvis—an anatomical, biomechanical and clinical study

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Developmental dysplasia of the hip is characterised by a shallow and steeply oriented acetabulum and a valgus ante-torsion deformity of the proximal femur. Dysplasia of the hip can cause hip pain in the young adult, and will eventually lead to degenerative arthritis in the majority, if not all patients. If there are no (or minimal) degenerative changes, then there are many surgical options. From the current literature there would seem to be a preferrence for primarily acetabular re-orientation by pelvic osteotomy. In this manner non weight bearing acetabular cartilage is moved from posterior and medial towards superior and antero-lateral to increase the weight bearing area. Additionally the obliquity of the acetabulum is reduced, resulting in reduced shearing forces in the joint.

The aims of this study were to describe the relevant anatomy of the pelvis for pelvic osteotomies, to report the long term results of triple osteotomy of the pelvis, to analyse the biomechanics and to describe new computer assisted operative techniques.

Results: Anatomy: There are no reports of the detailed surgical techniques. Chapter 3 describes the surgical technique and anatomical structures prone to damage during a triple pelvic osteotomy as first described by Tönnis. Chapter 4 and 5 describe alternative surgical approaches and techniques to osteotomise the pubic bone (chapter 4) and the ischium (chapter 5). The advantages and disadvantages of these alternatives are discussed.

Long term follow-up: A study of 51 hips that underwent a triple osteotomy was undertaken 8 to 15 years post-operative. The results were encouraging. At an average follow-up of 10 years 81% of patients were improved compared with before the operation, and 60% scored good or excellent. Degenerative osteoarthritis progressed by one grade in 21% of the hips over ten years. However, for this group of relatively young patients a still longer follow-up study is required.

Biomechanics: In chapter 7 a computer programme was implemented that calculates the acetabular coverage of the femoral head from conventional antero-posterior radiographs. Acetabular coverage increased significantly, but no clear relation was found between improved acetabular coverage and improved clinical outcome. However, lack of postero-lateral coverage of the femoral head was related to poorer results. This is important, because during the operation, by attempting to improve coverage antero-laterally, the posterolateral coverage may be decreased, thus leading to poorer results.

In chapter 8 a röntgen stereophotogrammetric analysis (RSA) shows that the femoral head and the center of the hip joint is displaced greatly by triple pelvic osteotomy. The greatest displacement was in the posterior direction (average 2,4 centimeters), and interestingly this is exactly the dimension that is impossible to determine from conventional antero-posterior radiographs. This explains why it has not been reported before. The moment arms of the muscles according to the literature are in the order of 2 to 8 centimeters and this displacement posteriorly must therefore have a significant effect on the joint reactive force across the hip joint.

Computer assisted surgery: Finally, in chapter 9 the preliminary results of a new computer assisted operative technique are described. This provides two benefits. First it acts as a navigation aid to help perform the osteotomies more precisely (and therefore more safely) by displaying the osteotomes in real-time on CT images and three dimensional CT reconstructions on a monitor in the operating room. Second, it helps determine acetabular re-orientation by displaying the acetabular re-orientation real-time on a three dimensional CT image of the pelvis.

Conclusion: Triple pelvic osteotomy has been shown to be an effective treatment for dysplasia of the hip in adolescents and young adults with good long-term results.

The anatomy of the pelvis makes the surgical approach for any pelvic osteotomy difficult, and there are many anatomic pitfalls such as the femoral vein, the gluteal, pudendal and obturator neurovascular bundles, and the sciatic nerve.

The two biomechanical studies have shown that the pressure in the joint (load per unit weight bearing area) must change. The load across the hip joint is changed by altering the moment arms of the muscles,

and the weight bearing area (acetabular coverage of the femoral head) is increased. The altered load over an increased weight bearing area combined with an expected reduction of shearing forces in the joint due to the reduced obliquity of the acetabulum probably explain the mechanism by which this operation is effective in providing clinical improvement.

Computer assisted surgical techniques are now under development and promise to be usefull navigation aids when performing the osteotomies and to aid accurate acetabular re-orientation. The preliminary results are reported, and further testing is currently ongoing.

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The role of transforming growth factor-ß (TGF-ß) in mesenchymal tumorigenesis

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The aim of this study was to investigate autocrine loops involving transforming growth factor-beta (TGF-ß) in mesenchymal tumors. TGF-ß is a multipotential polypeptide with known roles in embryology, development, growth and repair, but also in cancer. One of its characteristics is the induction of fibrosis by increased deposition of extracellular matrix. Its presumed role in neoplasia is explained by its effects on cellular proliferation, stroma induction, angiogenesis and immunosuppression.

Two different mesenchymal tumors were studied, first, the benign fibroproliferative lesion of the handpalm called Dupuytren's contracture, and second, the malignant bone tumor osteosarcoma. All components for an autocrine mechanism were shown to be present in both tumors: receptors for TGF-ß on their cell wall (as documented with cross-linking), cellular proliferation in the presence exogenous TGF-ß, TGF-ß production in their microenvironment, and inhibition of autocrine proliferative effects using TGF-ß antibodies.

A potential therapeutic venue by means of interrupting the binding of TGF-ß to the osteosarcoma cell's own receptors was also tested in this thesis. To test this hypothesis, we used suramin, an anti-parasitic drug that has previously been shown to prevent binding of different growth factors. *In vitro* studies indicated that the proliferation of osteosarcoma cells was dose-dependently inhibited by suramin, and that binding of TGF-ß to its receptors was blocked by suramin. Although promising, the clinical use of this medication has been hampered by its severe side-effects and toxicity.

Having established evidence for an autocrine role for TGF-ß in osteosarcoma *in vitro*, the studies were expanded to the *in vivo* situation by correlating the presence of TGF-ß isoforms in high grade osteosarcomas to patient outcome. Using Kaplan-Meier and Cox proportional hazard analysis, it was shown that high expression of TGF-ß3 in osteosarcomas is related to disease-progression.

Lastly, the regulation of homeobox genes by TGF-b superfamily members was evaluated. These genes are known to play a role in skeletal formation, limb patterning and neoplasia, but only limited information is available on their regulation. With a high expression of both the TGF-ß superfamily members and the homeobox genes during the patterning and development of the skeletal system these genes seemed to be plausible target genes for the TGF-ß superfamily. It was indeed shown that in osteosarcoma and neuroblastoma cells certain homeobox genes were up- or down-regulated by TGF-ß superfamily members.

In conclusion, this thesis demonstrates that autocrine mechanisms involving TGF-ß play a role in Dupuytrens's disease and in osteosarcoma. These studies will help elucidate the exact etiopathogenesis of these disease entities. It is expected that the ever-increasing understanding of the roles of TGF-ß in a multitude of diseases ranging from benign to malignant will lead to treatment regimens based on modulation of this growth factor and its receptors in the next century.

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Osteotomy for gonarthrosis with special reference to the tibial callus distraction technique

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Osteotomy is used for correction of the altered load on the gonarthrotic knee joint. It can be performed above or below the knee. Clinical results depend on the correction after bone healing. By tibial closed wedge osteotomy, the deformity is corrected intraoperatively in contrast to tibial hemicallotasis osteotomy (HCO) where the correction is performed after surgery.

Comparing the two methods, the precision was better after HCO but the clinical results were similar at follow-up examination. After one year, the radiographic alignment of the leg was better after HCO, as was the stability of the osteotomy measured by RSA.

In 308 operations, the most common complication after HCO was minor pin-tract infection. It was recorded in 157 cases. Pin-tract care and oral antibiotics were sufficient treatment in most cases.

A loose external pin implies a risk of pin-tract infection. Hydroxyapatite-coating (HA) of the pin threads increased the fixation. HA-coating is recommended for use in metaphyseal locations where the risk of pin loosening is higher.

11 complications requiring reoperation were recorded after 32 distal femoral osteotomies for lateral gonarthrosis. HCO was studied as treatment for lateral gonarthrosis and advanced medial gonarthrosis. The 2-year results after 23 operations were similar to those after treatment for early medial gonarthrosis.

In a matched study of knee arthroplasty, there was no increased radiostereometric migration of the tibial component after a previous tibial osteotomy.

Acute low-back pain—a randomized controlled trial of sick-listed patients, with emphasis on co-morbidity, clinical outcome, predictors and costs

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The general aim of this thesis was to evaluate three treatment options, i.e. a manual treatment program, an intensive training program, and a general practitioner program, in patients sick-listed for acute low-back pain with or without sciatica regarding impairment, pain, functional disability, socioeconomic disability and satisfaction with treatment and explanations of their low-back pain. Additional aims were: (1) to comprehensively characterize patients sick-listed for acute low-back pain with or without sciatica and compare them with referents matched for age, sex and geographic area regarding demographic data, previous sick history, working conditions and psychosocial work environment, (2) to identify factors that might predict outcome at one year, in order to identify patients at risk of significant long-term unfavorable outcome, and (3) to analyze the cost to society of the three different treatment regimes. The thesis is based on study of two materials: 180 patients sick-listed for acute low-back pain with or without sciatica and 668 referents matched for age and sex. The two materials were compared in the first study. In the second study the patients were randomized to one of three conservative treatment programs and followed at 1, 3 and 12 months. The other two studies deal with outcome prediction and cost analysis. The results demonstrate that the patient sick-listed for acute low-back pain does not differ from referents in personality characteristics, he/she smokes more, and is more commonly divorced. He/she estimates high workload. When he/she stays home from work due to low-back pain the perceived pain intensity and disability are moderate. No differences were revealed between the three treatment programs except for satisfaction variables. The manual treatment program and intensive training program groups were more satisfied with treatment, and manual treatment program patients were more satisfied with explanations of the low-back pain episode. The patients who did not complete a conservative treatment program were those with fewer symptoms at the initial visit. Acute low-back pain patients consume a large amount of health care resources. This is because low-back pain is a recurrent problem and low-back pain patients have a considerably increased in co-morbidity compared to referents. The total cost per patient was 47,501 SEK, the most expensive part being indirect costs due to sick leave: about 90% of the total costs. We identified some factors that predicted functional disability, recurrences or chronicity by the end of the follow-up year. These were: sick-listings for low-back pain past two years; high Oswestry score at onset of acute low-back pain episode; lack of stimulating work tasks; increased pain on coughing at first visit and long "duration of pain of the current episode". We suggest that initial examination should focus on these. A patient sick-listed for low-back pain, with a moderate/severe disability at the initial visit and previous sciatica is at high risk of surgery for disc herniation during the following year. A positive Laségue sign at the initial visit does not predict operation during the following year.

Load and movements of the sacroiliac joints

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With radiostereometric analysis (RSA) the movement in the sacroiliac joints (SIJ) of totally 41 patients have been studied.

In a study of 25 patients a constant pattern of movement with different loads was found. The rotations were in all situations small with a mean of 2.5 (0.8–3.9) degrees between extreme positions. There was no difference in movements between symptomatic and asymptomatic joints.

To evaluate whether the standing hip flexion test commonly used reflects movements in the SIJ, 22 patients were analyzed with RSA during the test. The movements registered were very small and support the theory of form and force closure in the SIJ. The self-locking mechanism obstructs the movements in the SIJ and the standing hip flexion test cannot be recommended as a diagnostic tool to evaluate SIJ movement.

The reciprocal straddle position was proposed to show a high degree of SIJ movement. Six women with posterior pelvic pain were analyzed with RSA and a reciprocal movement could be demonstrated. However, it was ten-fold smaller than reported in previous studies and is not detectable by manual methods.

To evaluate the effect of the external Hoffmann-Slätis frame, 10 patients (7 women) with severe posterior pelvic pain were analyzed with RSA with and without the external frame in place. In 8 patients the median reduction in rotation was 55% on the left side and 63% on the right side around the helical (rotational) axes and 74% around the x-axis on the left side and 66% on the right side. The data suggest that external fixation with the HoffmannSlätis frame can be used as a diagnostic tool in evaluating posterior pelvic pain.

In a cross-sectional study of 338 pregnant women, 171 experienced back pain at the time of the examination. A positive outcome of the posterior pelvic pain provocation test was noted in 122 women and 44 of these women experienced a "catching" feeling of the leg when walking, whereas only 1 of 49 women with low back pain had such symptoms. The most probable explanation for the catching is that local nociception disturbs muscular function, since changes in the movements of the SIJ cannot cause these symptoms.

Tissue engineering—a new approach in articular cartilage repair

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The limited potential for articular cartilage to heal after injury is a recognized phenomenon and remains a major clinical problem. Research on strategies to improve the repair of articular cartilage defects currently focuses on the potential of chondrocyte transplantation. The aims of this study were to evaluate the potential use of isolated chondrocytes for the repair of defects in the joint-surface. Both in-vitro and in-vivo experiments were performed using different biodegradable three-dimensional carriers for chondrocyte-transplantation.

The chondrocyte behaviour in different hydrogels, such as collagen type 1, fibrin glue and alginate, was evaluated. Subsequently, an animal model for the regeneration of large fullthickness articular cartilage defects with a chondrocyte-fibrin-glue suspension in goats, was developed. hi a second animal experiment the chondrocyte-fibrin glue suspension was implanted covering a layer of hydroxyapatite, under the hypothesis that this composite graft may reveal a better fixation to the subchondral bone. Follow-up was performed upto one year in both studies and indicated formation of hyaline cartilage-like repair tissue in the defects by the transplanted chondrocytes during the first weeks. From 12 weeks however, early disintegration of the fibrin-glue resulted *in loss of support to the grafted cells and subsequent deterioration of the newly formed repair tissue. One year after surgery no differences from the transplanted group with the sham operated group could be detected anymore, and both defects had been restored with fibrous tissue. Additional use of hydroxyapatite did not stimulate a better fixation of the graft, in fact, early resorption and tilting of the hydroxyapatite did only harm the covering chondrocyte suspension-graft.

Clearly, hydrogels did not offer adequate and long-lasting support to the transplanted chondrocytes and a new set of in-vitro experiments was 'initiated. Chondrocytes were now seeded on porous, highly purified, collagen scaffolds and cultured to create a more structural cartilage implant in-vitro. The influence of linkage of covalently attached cartilage specific glucosaminoglycans (GAGs) to the scaffolds on the chondrocyte metabolic activity was assessed both quantitatively and qualitatively. Chondrocytes cultured in the GAG-loaded scaffolds revealed a higher proliferation rate and a larger total amount of new matrix production, which are both important parameters for the generation of an articular cartilage implant in-vitro. The cartilage specific phenotype of the chondrocytes was preserved in this scaffold, as 'indicated by stabilized RT-PCR profiles on aggrecan, biglycan and decorin.

Sufficient production of new cartilage specific matrix by implanted chondrocytes can possibly be stimulated by additional growth factors. The effects of different growth factors on matrix production was then also evaluated in an atginiate culture system. Transforming Growth Factor ß2 (TGFß2), Insulin-like Growth Factor I (IGF-1) and Bone Morphogenetic Protein-2 (BMP-2) were compared in different concentrations and culture conditions. IGF-1 appeared to have the best and most reproducible dose-response stimulation of new matrix production with a slightly increased RT-PCR profile for aggrecan. This may indicate a potential use of this growth factor as a stimulator for the formation of new articular cartilage.

In conclusion, we believe that the new technique of preculturing a cartilage implant in-vitro, followed by subsequent implantation, is a promising method to stimulate articular cartilage repair. Further understanding of the chondrocyte metabolic interactions with the extra-cellular environment are crucial to eventually improve the clinical results of this transplantation procedure.

The injured anterior cruciate ligament and neuromuscular rehabilitation

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Two prospective, short-term and long-term consecutive randomized studies on non-surgical treated patients with an ACL injury were performed. All patients were practicing recreational sports on a low to moderate activity level. Outcome measures were: isometric muscle strength and isokinetic muscle function, one-leg hop test, single limb balance, Lysholm knee score and Tegner activity level.

In the study on non-acute ACL injured patients, with a late diagnosis of symptomatic anterior cruciate ligament lesion, 26 patients were examined and randomized to open-chain or closed-chain training for a 3 month period. Short term effect after training: Knee extensors improved significantly in both groups, with minor differences. At 3 months standing balance was normalized on the uninjured, but not on the injured side, despite restoration of thigh muscle strength. At 12 months, standing balance was normalized also on the injured side and persisted at the 36-month follow-up. Lysholm knee-score increased significantly during initial 3 months. After 36 months the score was excellent (>83) in 21 out of the 22 remaining patients. Isometric muscle strength values persisted at 36 months. Recreational sports were resumed after training by most patients. Median value in Tegner activity level was still significantly reduced at 36 month-follow-up. Despite improvement 4 patients required ACL reconstruction to return to pre-injury activity level.

In the study on acute ACL-injury in 100 patients, examined with arthroscopy within 10 days from injury, revealed associate lesions in 82% of the cases. Early training and need of supervision in training was evaluated, the patients were randomized to supervised (SV) or self-monitored (SM) training after instruction. At 6 weeks follow-up due to mobility restriction and pain a transferal of nearly 50% of the SM patients was made to SV training, the majority were women. Transferal accelerated the improvement in the male patients with delay the first months. At 36 months isometric muscle strengths and isokinetic work capacities were significantly higher in male patients of original SV group and in men transferred to SV training, than in men remaining in the SM group. In women no differences were observed between SV, transferred or SM patients. Studies on muscle function after ACL injuries in female patients are required.

Giving-way events occurred in 5–10% only of the patients during the follow-up, probably because the treatment allowed cicatrization and preservation of restricted hyperextension.

As part of joint-protection strategy, restriction of hyperextension was preserved in the majority of cases during the period of follow-up.

Isokinetic work was found to have a stronger discriminative power between training modalities than isometric strength.