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Experimental orthopedics

The effect of immobilization on rabbit limb muscles

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In previous studies, manipulation of immobilized rabbit legs had resulted in heterotopic cartilage and bone formation, especially in the deep portion of the vastus intermedius muscle. The aim of this study was to examine the changes in the muscle of the rabbit limb following immobilization alone. Morphologic changes were observed already within a few days of immobilization especially in the deep portion of the vastus intermedius muscle when immobilized in a shortened position. In this muscle the vascular permeability was also significantly increased as studied using Evans' blue albumin. Serum creatine kinase activity increased significantly during the first day of the immobilization period. It seems that the deep portion of the vastus intermedius muscle, composed almost exclusively of type I fibers, is exceptionally prone to damage when immobilized in a shortened position. Additional trauma caused by daily manipulation is needed for the myositis ossificans-like bone formation.

Local stimulation of proteoglycan synthesis in articular cartilage explants by cyclic compression in vitro

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Articular cartilage plugs (Ø 5–10 mm) from the patellar surface of bovine femur were subjected under tissue culture conditions to 1.5-hour cyclic compressive loading with a plain-ended stainless steel loading head controlled by a microprocessor-based apparatus. Synthesis of proteoglycans was monitored by 35SO₄ incorporation, and the deposition site of the labeled macromolecules was localized by quantitative autoradiography of tissue sections. Proteoglycan synthesis was stimulated by 0.5 MPa peak pressures repeated either at 2- or 4-second intervals, whereas lengthening of the intervals to 20 and 60 seconds abolished the stimulation. Raising the pressure to 1 MPa also abolished the stimulation in experiments with 2-second intervals, but not with 4-second intervals, suggesting that cyclic loading with too high pressure or frequency lacks the stimulating effect on articular cartilage proteoglycan synthesis. With a 8-mm-diameter plug, the central tissue directly under the head was analyzed separately from the margin area of the explant. It appeared that in the central tissue proteoglycan synthesis stimulation occurred in the intermediate, but not in the superficial, zone of cartilage, while the margin area of the plug showed a stimulation in the superficial zone.

The present data would indicate that the synthesis stimulation of articular cartilage proteoglycans associated with cyclic compressive loading is limited to certain cycle frequencies and pressure values, and that there is a specific topographic distribution of the stimulation under and around the loaded site of the cartilage.
Effects of perivascular sympathectomy on peripheral adrenergic innervation

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Perivascular sympathectomy has been accepted as a method for the treatment of vasospastic disorder in the hand area. We did perivascular sympathectomy in the saphenous vessels of rat, in central vessels of rabbit’s ear, and in metacarpal vessels of rabbit’s paw. In a glyoxylic acid-induced fluorescence method examination, the perivascular sympathectomy removed adrenergic innervation only from the operated on site, while the innervation was normal distally. Based on our experiment, we suggest that the effects of perivascular sympathectomy should be reexamined.

Effects of early physiologic dynamic compression on fracture healing

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The effects of early physiologic dynamic compression on fracture healing and remodeling was studied in the dog. Bilateral transverse middribial osteotomies were stabilized with rigid external fixation. One osteotomy of each animal was subjected to dynamic compression by release of the fixator telescoping mechanism (axial dynamization) at 2 weeks, while the other side remained unchanged and served as the control. The quality of bone union between the two sides was compared at 12 weeks. Both osteotomies reached the torsional strength and stiffness of the intact tibia. Dynamic compression reduced the interfragmentary gap and resulted in contact healing. The control osteotomies united through a gap-type cortical healing mechanism. Both sides showed low intracortical porosity and high intracortical new bone formation. No statistical differences were observed in quantitative two-phase bone scanning and in osteotomy-site blood flow. Axial dynamization of an external fixation device may not provide significant benefits if fracture union is progressing uneventfully under stable mechanical conditions.

Effect of clodronate on bone in oophorectomized dogs

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The effect of clodronate on bone was studied in 9 oophorectomized beagle dogs. In the beginning of the study, bone mineral density was measured in the lumbar spine using dual-energy x-ray absorptiometry and computed tomography. Clodronate, 20 mg/kg body weight/day, was started orally for 3 dogs and 40 mg/kg body weight/day for 3 dogs; the remaining 3 dogs served as controls. After 4 months of dual-energy x-ray densitometry, there was a significant increase ($P < 0.05$; paired t-test) in the bone density after treatment with the higher dose of clodronate. Computed tomography did not reveal significant changes in any of the groups examined.

Fibrillations and regeneration following partial muscle rupture: An electromyographic and histologic study in rats

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The electrophysiologic events in correlation with morphologically detectable nerve and muscle-fiber damage in the rat gastrocnemius muscle were studied after a standard contusion injury. The injury was about 1-cm distal to the point at which the nerve branches to the muscle from the tibial nerve. The examinations were performed 2-56 days after injury. Two untreated rats and two completely denervated gastrocnemius muscles after transectioning the sciatic nerve from the thigh served as controls. Electromyographic recordings were done with a concentric needle electrode (Dantec 13L23), with an external diameter of 0.35 mm and recording surface of 0.04 mm². The fibrillations of gastrocnemius muscle were recorded under ether anesthesia, and the compound motor activation potential (CMAP) by stimulating of the sciatic nerve in the thigh using supramaximal stimulation intensity with a monopolar needle electrode (Dantec 13L49). In the injured muscle the first signs of fibrillation were seen 5 days after injury. The fibrillations were seen both proximally and distally to the injury after 7 and 10 days, and only distally 14 days after injury. Twenty-one days after injury, the fibrillations had disappeared also distally indicating reinnervation of the muscle segment. In intact muscle the CMAP had no late components. Ten days after injury, late components were observed proximally, and 14 days after injury also distally. Fifty-six days after injury, numerous late components were seen. This indicates reinnervation of the regenerating new muscle fibers, the organization of which was still histologically somewhat complex.
Electromyography reveals the pathophysiology of muscle injury and may be used in the diagnosis and follow-up of muscle injuries.

Experimental lumbar interbody fusion with poly-L/DL-lactide reinforced coralline hydroxyapatite

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Poly-L/DL-lactide-reinforced coralline hydroxyapatite (HA) blocks, 3 x 8 x 12 mm in size, were used in experimental lumbar ventral interbody implantation for fusion in growing pigs. For implantation the disc material was evacuated and the endplate cartilages were excised. The follow-up times were 3, 6, 12, and 16 weeks; and 21 pigs were analyzed. The implants remained in place until the 16-week follow-up. Radiographically, resorption and fragmentation were seen from 12 weeks on. Solid radiographic fusion was not revealed in any case, and gross examination confirmed minor mobility in the operated on disc space of every case. Collagen strands were histologically seen around and inside the HA implant; no inflammatory reaction was encountered. Only separate islets of calcified bone tissue were seen in 12- and 16-week specimens.

Fixation of cancellous bone osteotomies of the distal femur with absorbable polylactic screws in rabbits.

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Polyactic acid (PLA) is a synthetic, absorbable material. In vivo, PLA undergoes hydrolytic deesterification into the lactic acid, which becomes incorporated into the tricarboxylic acid cycle after transformation into pyruvate.

In the present study, polylactic screws (length 20 mm, diam. 3.2 mm) made of self-reinforced poly-L-lactic acid (SR-PLLA) and poly-DL/L-lactic acid (SR-PDLLA/PLLA) were used in fixation of osteotomies in rabbits. Osteotomies were done in the cancellous region of the distal femur, and were fixed with polylactic screws (Figure 1). The molecular weight of SR-PLLA is 260,000 and of SR-PDLLA/PLLA 100,000. The implants were gamma sterilized, dose 2.8 Mrad. The follow-up times were 1, 3, 6, 12, 24, 36, and 48 weeks, and there were 5 rabbits in each group. Seventy rabbits were operated on—35 in the PLLA group and 35 in the PDLLA/PLLA group. Radiographic, microradiographic, and oxytetracycline-fluorescence analyses were performed after killing the animals.

Results: In the PLLA group, 34/35 fixations were firm, and there was only one failure of fixation at 12 weeks. At 3 weeks and later, all the osteotomies, except 1 at 6 weeks, showed bony union in radiographic and microradiographic analyses. More than 10° of angulational deformity was observed in 2 cases in the PLLA group—in 1 case at 12 weeks and in 1 at 48 weeks. Strong external callus formation was observed at 3–6 weeks, and the amount of external callus decreased during the follow-up period.

In the PDLLA/PLLA group, 33/35 fixations were stable and there were two failures: one at 3 and one at 6 weeks. At 6 weeks, only one osteotomy revealed bony union in radiographic and microradiographic analyses. At 12 weeks and later, all the osteotomies were clinically and radiographically consolidated.

More than 10° of angular deformity was noticed in the PDLLA/PLLA group in 4 cases—one at 3 and 1 at 12 weeks—and in 2 cases in the 48 weeks’ follow-up group. The external callus formation was abundant at 6–12 weeks and decreased during time.

No sinus formation or infection was noticed during the follow-up. In the PDLLA/PLLA group, the OTC fluorescence inside the implant showed increased intensity, and thus there was new bone formation at 24 weeks and later.

This study demonstrates that the mechanical properties of SR-polylactic screws were sufficient for fixation of osteotomies of weight-bearing bones. On the basis of the promising results of this and a previous investigation, clinical research where SR-PLLA screws are being used for fixation of ankle fractures has started.

Figure 1. A schematic view of the right distal femur of rabbit showing the operative technique. Anterior (A) and lateral (B) view. A horizontal osteotomy was cut in the cancellous part of the distal femur. The osteotomy was fixed with an absorbable polylactic screw. The head of the screw was removed after fixation. The rabbits were allowed to use their limbs after the operation, and no external support was used.
Fixation of an experimental canine femoral shaft osteotomy with an intramedullary biodegradable rod

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Biodegradable rod as an internal fixation device has been successfully used for fixation of cancellous bone fractures since 1984. However, all the attempts at intramedullary fixation of diaphyseal fractures with biodegradable rods have failed to date. The main cause of failure has been the relatively rapid loss of the load-carrying capacity of the implants. The purpose of the present study was to examine the healing of an experimental femoral osteotomy after intramedullary fixation with a self-reinforced (SR-) PGA rod in growing dogs.

Material and methods: A proximal diaphyseal osteotomy of the right femur was made in 14 twelve-week-old beagle dogs. After accurate reduction, fixation of the osteotomy was achieved with an intramedullary 4.5 mm × 60 mm SR-PGA rod. No external support was used after the operation. The follow-up intervals were 3, 6, 12, 24, and 48 weeks. Femurs were analyzed by radiographic, microradiographic, oxytetracycline (OTC) fluorescence and histologic studies.

Results: The consolidation of the osteotomy was evident in all the animals in 6 weeks. There were no significant growth disturbances or angular deformities.

Conclusions: An intramedullary SR-PGA rod provided sufficient stability for rapid healing of a proximal femoral osteotomy in growing dogs. The biodegradable fixation of diaphyseal fractures of growing animals needs specific consideration, and further experimental studies are in progress.

Fixation of mandibular osteotomies with self-reinforced polylactide screws and plates: An experimental study in sheep

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It has been revealed in many histologic, histomorphometric, OTC fluorescent, and microradiographic studies that new bone modeling and calcification are normal after fixing cancellous bone osteotomies with biodegradable self-reinforced polyglycolic acid (SR-PGA) or poly-L-lactic acid (SR-PLLA) rods. The purpose of this study was to find out whether there is any difference in cancellous bone mechanical healing after osteotomy fixed with biodegradable rods compared with classical metallic rod fixation.

The right distal femurs of 30 adult rabbits were osteotomized. The osteotomies were fixed with two 1.5-mm metallic (Kirschner), SR-PGA (Biofix CC®), or SR-PLLA (BI, MW 250,000) rods. There were 10 animals in each group. The follow-up times were 6 and 12 weeks.

The shear strength of the osteotomized femurs was compared with the nonosteotomized control femurs. After 6 weeks, the osteotomized femurs had reached 72 percent, 69 percent, and 71 percent shear strength in metallic, SR-PGA, and SR-PLLA groups, respectively. After 12 weeks, the shear strength percentages were 76 percent, 80 percent, and 73 percent. There was no appreciable difference in shear strength values between these groups.

Radiographically, it was found that all the fixations had succeeded. External callus formation was strongest in the maxillary fixation. Fixation of fractures of cancellous bone with biodegradable rods has given good clinical results, which encouraged us to study the possibility of biodegradable fixation of mandibular fractures.

Methods: A total of 36 osteotomies of sheep's mandibular condyle and corpus were fixed with biodegradable self-reinforced poly-L-lactic (SR-PLLA) screws or SR-PLLA plates with metallic screws. In the control group (36), similar metallic screws and plates were used. Two osteotomies in the condylar area were left unfixed.

Results: Early results of all the experiments carried out clearly indicate that SR-PLLA screws and plates provide sufficient fixation for healing.

Conclusion: Based on these findings, we found it worthwhile to continue developing a combination of SR-PLLA screws and plates to be used together as a totally biodegradable fixation device.
Table. Shear strength of osteotomized and control femurs

<table>
<thead>
<tr>
<th>Fixation</th>
<th>FH</th>
<th>HG</th>
<th>PLLA</th>
<th>FG</th>
<th>LG</th>
<th>PLLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (weeks)</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Number of animals</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Osteotomized femur, mean shear strength (MPa)</td>
<td>4.3</td>
<td>3.7</td>
<td>4.0</td>
<td>4.9</td>
<td>5.9</td>
<td>4.2</td>
</tr>
<tr>
<td>Control femur, mean shear strength (MPa)</td>
<td>6.0</td>
<td>5.4</td>
<td>5.6</td>
<td>6.7</td>
<td>7.4</td>
<td>5.8</td>
</tr>
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Met = metallic rod, PGA = polyglycolic acid rod, PLLA = poly-L-lactic acid rod.

SR-PGA group. The osteotomy line disappeared better in the SR-PLLA group than in the other groups.

We conclude that the shear strength of the healing cancellous bone after experimental osteotomy is as good with the SR-PGA and SR-PLLA rod fixations as with the classical metallic rod fixation. Radiographically, it seemed that the PGA rods did not keep the fixation as exact as the metallic and PLLA rods.

The chondrogenic potential of rib perichondrium in connection with biodegradable material

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The chondrogenic potential of rib perichondrium was investigated in rabbits. The fifth rib cartilage was resected subperichondrially from both sides and was replaced with a 10-mm x 1.5-mm polyglycolic acid rod on the contralateral side, the other side serving as a control. The maintained perichondrium was sutured around the PGA implant. Samples were taken 4, 12, and 20 weeks postoperatively. A strong neocartilage formation was seen on both the implant and the control side. On the implant side the neocartilage grew to form a tubelike structure around the PGA rod. Also, new bone formation was observed. The chondrogenic potential of rib perichondrium in connection with biodegradable material proved to be good. This gives a possibility to mold regenerating cartilage tissue with biodegrading implants to a certain shape for use in reconstructive surgery.

Varia

Late results of birth brachial palsy

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The early operations on birth brachial palsy were made in the beginning of the century, but the results were uncertain or unpredictable (3). The introduction of microsurgery and the development of anesthesiologic techniques on small children have made operations on traumatic lesions of the brachial plexus feasible. Exploration and operation are currently indicated if the biceps brachii muscle is not functioning at the age of 3 months (2).

Between 1971 and 1985, 23 children with birth brachial palsy were operated on at the pediatric surgery departments at Helsinki and Turku University Central Hospitals; 3 additional patients were operated on at the Orthopedic Hospital of the Invalid Foundation in Helsinki. The mean age of the patients was 3 months at the time of the operation. The indication for the operation was unsatisfactory recovery of the palsy within 3 months of life. Between 1980 and 1985, 51 birth palsies were treated conservatively at the Children’s Hospital of Turku and the University Central Hospital. In both series the degree of recovery was evaluated 1–14 years after birth as described by Mallet (1, 4).

In conservatively treated patients the result was very good in 15 after a follow-up of 1–5 years, good in 20, fairly good in 13, and poor in 4. In the operated on group, the result was good in 6 after 1–14 years follow-up, fairly good in 17, and poor in 3. The most common operative finding was a traumatic neuroma at Erb’s point (the roots of C5 and C6). There were nine root avulsions in 67 roots explored (13.4 percent).

References
Treatment of femoral shaft fractures in children

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Femoral shaft fractures in children are treated nonoperatively whenever possible, and operative treatment is usually considered avoidable. The purpose of the present study was to find out long-term results of the conservative and operative treatment of these fractures in children.

Patients and methods: Totally, 131 patients, 0–15 years of age, suffering from femoral shaft fractures were treated at Kuopio University Central Hospital from 1976 through 1985.

Results: In all, 114 (87 percent) of these patients were reexamined after an average follow-up of 8 (3–12) years. The mean age of the patients was 15 (4–27) years at control. The conservative treatment included Bryant’s tibial, and femoral tractions (92 patients, 81 percent). The length of the traction treatment and hospitalization were on average 26 (5–35) days and 32 (10–55) days, respectively. The operative treatment included plating, intramedullary nailing according to Rush or Kuntscher (22 patients, 19 percent); the hospitalization was 23 (6–99) days. After conservative treatment the injured leg was 0.15 mm shorter than the opposite leg. In the operatively treated group, the injured leg was 8 (–15 to +23) mm longer than the opposite leg. The mean correction of angular deformities during the follow-up interval in the Bryant’s and tibial traction groups was 6°–7°.

Conclusions: The hospitalization associated with the conservative treatment was remarkably longer than with the operative treatment. The operative treatment of a femoral shaft fracture of a child should be considered more often.

Conservative treatment in lumbar spinal stenosis

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The prognosis of lumbar spinal stenosis is usually considered poor, and the treatment of these patients is often surgical decompression. The long-term outcome of operated on spinal stenosis patients is not very encouraging.

In some clinical studies, calcitonin has been reported to increase functional capacity and to alleviate clinical symptoms of spinal stenosis. This placebo-controlled, randomized, double-blind, cross-over, 1-year study (40 patients) showed that there were some beneficial effects on the patients without appreciable side effects. Calcitonin had a powerful analgesic effect ($P < 0.001$). Calcitonin therapy can be used as a conservative treatment of lumbar spinal stenosis in elderly patients with a high surgical risk.

Results of revision after cemented total hip replacement (THR) with the Lubinus endoprosthesis

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From 1979 to 1984, 147 patients with 159 cemented total hip arthroplasties (THR) had revisions with a cemented Lubinus hip arthroplasty at the Orthopedic Hospital of the Invalid Foundation. The average age of the patients at primary arthroplasty was 60 years and at revision 66 years.

Totally, 101 hips were followed for an average of 6 (4–9) years after the revision. Radiographic evidence of loosening of the femoral component was found in 36 percent of the hips and of the acetabular component in 19 percent of the hips. At the time of follow-up, 21 hips (17 percent) had been revised a second time. The clinical overall results were satisfactory, with 53 percent of the hips free from significant pain.

Short-term results of rehabilitation after cruciate ligament reconstruction using a Kennedy LAD

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A good intraarticular procedure is often needed in cases of old rupture of the anterior cruciate ligament (ACL). Favorable results have been obtained with a composite autograft augmented with polypropylene braid. The aim of the present study was to evaluate the short-term results and the rehabilitation results after augmented ACL reconstruction.

Patients and methods: Twenty-one patients (mean age 31 years) with old ACL injuries reconstructed using a Kennedy LAD (ligament augmentation device) were evaluated after a mean follow-up time of 16 (8–24) months. The mean interval from the injury to the reconstruction was 41 months. The knee function was determined with a functional score described by Lysholm and Gillquist. The maximal peak torque of extension and flexion forces were determined isometrically by a David Rehab System device at 60° of knee flexion.
**Results:** Twelve patients had excellent or good and 9 patients had a fair functional result. Four patients had a positive anterior drawer sign. The mean of maximum peak torque of extension was 255 ± 22 kpm in the uninjured leg, but only 189 ± 23 kpm in the injured leg (P < 0.01).

**Discussion:** The intraarticular augmented reconstruction of the ACL gives fairly good function over the short term. The effect of the thigh muscle training on the disability caused by a cruciate ligament injury has long been well documented. Even after reconstruction a good muscle strength evidently decreases the risk of recurrent minor injury. The results of the present study showed that an insufficient rehabilitation of the injured leg was obtained with formal physical therapy, thus suggesting the importance of a more individual training program.

**Effect of ACL reconstruction with patellar tendon or prosthetic ligament on the morphology of the other ligaments in the knee joint**

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The healing of knee ligament injuries is a great problem in everyday traumatology today. Much research is being carried out to clarify the healing of repaired ligaments. The aim of this study was to investigate the effect of ACL reconstruction on the other ligaments of the knee joint in dog.

**Material and methods:** Eleven adult mongrel dogs were used. In 9 dogs, one hind limb had resection of the ACL, in 4 dogs replacement with the medial third of the patella tendon was performed, and in 5 dogs the ACL was replaced with double-bended prosthetic ligament (Johnson-Johnson). In 2 dogs, only a large arthrotomy was performed. The contralateral limb served as a control. Thereafter, the dogs were caged in small runs for 12 weeks, then killed, and both hind limbs were removed. Frozen, and kept at −30 °C until the day of biomechanical testing. Before testing ACL, the other ligaments (MCL, LCL, PCL) were removed, fixed in 10 percent neutral formalin, embedded in paraffin, and sectioned longitudinally at 6 μ for histologic analysis. The sections were stained with Masson's trichrome, Alcian blue-PAS, picrosirius, and PAS-Hematoxylin stains. The following pathologic changes were recorded: collagenolysis, collagen necrosis, granulation, metachromasia with Masson's staining as an indicator of collagen denaturation, glycosaminoglycan (GAG) accumulation, lipomatosis, chondrocyte metaplasia, fiber atrophy, mucoid degeneration, hyalinization, chronic inflammation, and foreign-body reaction.

**Results:** Macroscopic observations. In all of the dogs the operated on knee was found to have a thickening of the anterior joint capsule especially on the medial side where the arthrotomy was performed. In many knees a small amount of synovial fluid was found as an indication of synovitis. The adjacent ligaments were macroscopically normal.

Microscopic observations. In all the ligaments of operated on knees, numerous pathologic alterations were found. In general, the pathologic changes in MCL ligaments were more rarely seen (mean 3.8) than in the other ligaments. In LCL and PCL ligaments the pathologic changes were more frequent (mean 4.8 and 6.0, respectively). Also, in all the ligaments of both knees with a sham operation, some pathologic changes were found (mean values 3.0, 2.5, and 4.6 in LCL, MCL, and PCL, respectively). In the control knees the corresponding pathologic changes were not found.

**Conclusion:** The large medial arthrotomy with or without ACL reconstruction is followed by numerous pathologic changes in the other ligaments of the dog knee.

**Intraarticular distal humeral fractures in adults**

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Intraarticular distal humeral fractures are uncommon and difficult to treat. They often occur in osteoporotic bone or as a result of a high-energy trauma. Surgical treatment consists of exposure with an osteotomy of the olecranon, of restoration of the joint surfaces, and stabilization of the fracture enough to allow early mobilization of the elbow joint (1). Sixty-one patients from a 10-year period were followed up for at least 2 years. A mechanical failure of the osteosynthesis occurred in 18 patients. Mechanical failures were due to biomechanically inadequate fixation in 12 patients. A poor functional outcome was noticed in 6 of these patients. In the whole series, there was a poor functional outcome in 22 patients.

**Reference**

Calcitonin decreases bone resorption in rheumatoid arthritis

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Rheumatoid arthritis (RA) is associated with the development of both generalized and periarticular osteoporosis. The cellular basis of the bone loss is unknown. Synthetic salmon calcitonin (SCT) is known to inhibit bone resorption, and several studies have suggested its efficacy in the treatment of postmenopausal osteoporosis. Thus, it might also be effective in treatment of osteoporosis associated with RA.

Twenty-two women (mean age ± SD 49 ± 11 yrs) with classical or definite rheumatoid arthritis (disease duration 15 ± 8 years) were treated with calcitonin nasal spray (SCT) 200 IU 3 times a week for 3 months. Bone biopsies from the iliac crest were taken before and after SCT treatment. Histomorphometric quantification of undecalcified bone sections was made using a manual point-counting method. The pin index (VAS) was evaluated before and after calcitonin treatment.

SCT decreased the resorption surface of trabecular bone (RS) significantly (P < 0.001). There was also a significant increase (P < 0.05) in trabecular bone volume (TBV) after 3 months of treatment. No significant changes were found in osteoid parameters. SCT had no effect on the pain indices. We conclude that SCT has a favorable effect on bone mass in RA.