Behavior of trabecular bone

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Metabolism

Mechanisms of ^{99m}Tc-MDP uptake in bone

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The mechanism underlying the binding of the bone-seeking isotopes to skeletal tissue has long been a subject of discussion, and several fundamentally different hypotheses concerning the determining factors have been proposed: viz., local bone perfusion, bone mineral, immature collagen, and enzyme systems.

In view of the uncertainty that is still attached to the mechanism underlying the binding of bone-seeking isotopes to skeletal tissue, the localization was elucidated by means of autoradiography, comparison of the latter with the distribution of alkaline phosphatase activity, collagen formation, tetracycline labeling, and evaluation of the affinity of the bone-seeking isotopes for the inorganic phase of the skeletal tissue by studying the decalcification of sections labeled in vivo.

^{99m}Tc-MDP was administered intravenously to 4–5-week-old rats 3 hours before they were killed. The knee region was freeze-embedded and cut on a hard-tissue cryostat by Ullberg's technique (1954). Furthermore, microautoradiography was carried out by the dip method.

To investigate the hypothesis on the binding of bone-seeking isotopes to immature collagen, the uptake of bone-seeking agents was compared with the collagen formation, visualized autoradiographically by labeling with ^{3}H-proline (Weinstock & LeBlond 1974).

The radionuclide uptake of ^{99m}Tc-MDP was compared with the flow distribution in the epiphyseal region, the latter being visualized autoradiographically by using a diffusible radioactive isotope administered intravenously ^{99m}Tc-pertechnetate was administered 15 sec and 5 min, respectively, prior to flow stoppage with a tourniquet at the thigh. Thereafter, contact autoradiography on the freeze-out block was performed.

With the purpose of elucidating the affinity of ^{99m}Tc-MDP to the mineral phase of the bony tissue, labeled sections were mounted on tape, counted in a gamma spectrometer before and after incubation for 10 min. in water or in 4 per cent EDTA, which decalcifies the sections. The activity released from the sections was examined chromatographically in four chromatographic systems, and the R_F values were compared with those for ^{99m}Tc-MDP, ^{99m}Tc-pertechnetate, ^{99m}Tc-Sn colloid, ^{99m}Tc-albumin, and ^{99m}Tc-EDTA in the corresponding systems.

Contact autoradiography afforded a good survey of the distribution of Tc-MDP, which exhibited a narrow belt of particularly high activity at the junction of epiphysis and metaphysis. This uptake was microradiographically located in that part of the provisional calcification in the cartilage matrix that was situated at the end of the vascular invasion into the cartilage. Under low magnification, there was good agreement between the radionuclide distribution and the distribution of alkaline phosphatase activity, at least in the bony tissue. On the other hand, there was no uptake of ^{99m}Tc-MDP in the alkaline phosphatase-active hypertrophic chondrocytes, and the provisional calcification with high radionuclide uptake did not show a high enzyme activity. This militates against the enzyme itself from being the target of the Tc-phosphatase complexes. There was a patchy increase in uptake in the periosteal area below the metaphysis, where a particularly marked osteoclastic activity was found, visualized by their acid phosphatase activity. At this site, the uptake was localized predominantly in the walls of Howship's lacunae, but there was some uptake also in the osteoclasts themselves.

The tetracyline labeling with short labeling showed fluorescence of both formative areas, in particular the provisional calcifications and of the resorptive surfaces in Howship's lacunae. There was good agreement between the fluorescence of tetracyline and the autoradiographic uptake of ^{99m}Tc-MDP within the same section.

In contrast, there was poor correlation between the distribution of bone-seeking isotopes and collagen formation, assessed by labeling. In this labeling the uptake did not show a maximum at the zone of provisional calcification, but osteoid formation increased just below the vascular coil at the vascular invasion into the epiphyseal cartilage. This militated against collagen formation as the factor determining the uptake of bone-seeking isotopes.

Visualization of the flow distribution at a flow stop 15 seconds after administration of pertechnetate showed a marked flow in the metaphyseal bone, but not a distribution that could afford the sole explanation of the high uptake of ^{99m}Tc-MDP in the zone of provisional calcification. Thus, it must be assumed that factors other than the flow also influence the uptake of the bone-seeking isotopes.

In the decalcification experiments on in vivo-labeled sections, only 1.6 per cent of the radionuclide uptake remained on the sections after 10 minutes' incubation in EDTA, whereas 98.8 per cent of the activity remained on the sections after incubation in water.

The released activity could not, in the four systems, be chromatographically distinguished from ^{99m}Tc-MDP, indicating that ^{99m}Tc-MDP labels the mineral phase of the bony tissue, and that no dissociation occurs on the crystal surface.

The present studies have demonstrated an increased uptake of the bone-seeking agents on formative as well as on resorptive surfaces, including in particular areas showing provisional calcification in the enchondral ossification. Even though the perfusion has some influence upon the quantitative uptake, local factors on the bony surface must be responsible for differing extraction of the bone-seeking isotopes.

The ^{99m}Tc-phosphate complexes bind to the inorganic phase. It is most reasonable to assume that it is the area of free crystal surface available to adsorption that differs.

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Growth plate and subchondral bone metabolism in experimental arthritis

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The significance of changed uptake of bone-seeking isotopes in various arthritic conditions in children is yet not well defined. By the development of scintimetric techniques, quantitated measurements of the uptake can be performed in immature joints within circumscribed regions of the bone (Hansen et al. 1986, Wingstrand 1986). Further, repeated scintimetry may provide a precise description of the combined vascular and metabolic lesions in arthritis with respect to time.

We studied the uptake pattern of ^{99m}Tc-DPD in experimental models of nonspecific synovitis, hemarthrosis, and septic arthritis in dog knees.

Materials and methods. Ten mongrel puppies were scheduled for nonspecific arthritis (NSA). Unilateral arthritis of the knee was induced from the age of 8 weeks by weekly injections of a Carragheenan solution for 12 weeks. In 6 mongrel puppies, unilateral chronic hemarthrosis (HA) was induced also from the age of 8 weeks by biweekly intraarticular injections of autologous blood for 12 weeks. In both groups, joint scintigraphy was performed 2 hours after injection of 15 mCi ^{99m}Tc-DPD by means of a large field gamma camera equipped with a converging collimator, initially and every 2 weeks during induction of arthritis and monthly in a postarthritic phase of another 12 weeks.

Unilateral septic arthritis (SA) was induced in 12 puppies aged 8 weeks by intraarticular inoculation of 1.0×10^8 *Staphylococcus aureus*. Scintigraphy was performed initially and after 48 hours followed by bilateral intraarticular pressure measurements (IAP).

All the scanning procedures and IAP measurements were performed under Immobilon (vet) anesthesia. The scintimetric analysis included three regions bilaterally obtained from sagittal scans: the femoral and tibial

growth plates (FGP and TGP) and the femoral epiphysis (FE) by means of a General Electric Star data processing system. Count ratio (CR) between experimental and control limbs was calculated. In control studies the interindividual and intraindividual coefficients of variation of the scintimetric technique applied were 0.08 and 0.05, respectively.

Results. In NSA, altered uptake was noted after 2 weeks. The induction phase was characterized by a decreased tracer uptake in the growth plates, i.e., CR 0.4 in the FGP and 0.6 in the TGP ($P < 0.05$), whereas a slight increase with a CR of 1.1 was measured in FE (NS). In the postarthritic phase the growth plate activity normalized in contrast to a marked increase in tracer uptake in FE to a CR of 1.8 ($P < 0.01$).

The uptake pattern in hemarthrosis followed the pattern found in the NSA group in the induction period. In the postinduction period a temporary increase in FE uptake was encountered. The uptake pattern normalized at the end of the experiments.

Following septic arthritis, 10 dogs showed significantly decreased uptake in the growth plates (Figure 1). No constant pattern of uptake was present in FE. An aberrant uptake pattern in 1 dog included a grossly increased growth plate uptake (Figure 1, No. 2), probably due to infectious spread to the bone. In another dog (Figure 1, No. 1) a total absence of tracer uptake in FE was attributed to an obliterated blood supply of the FE secondary to septic thrombosis. The IAPs of the infected knees ranged from 13 to 30 mmHg. No relationship between IAP and static uptake in FGP ($r = -0.22$), in TGP ($r = -0.17$), or in FE ($r = 0.32$) could be demonstrated.

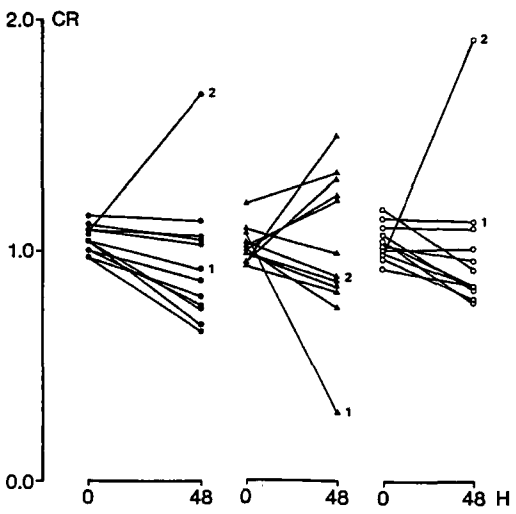

Figure 1. Scintimetry in septic arthritis. • Femoral growth plate △ Femoral epiphysis ○ Tibial growth plate.

Comments and conclusions.

1. Early synovitis of both nonseptic and septic origins caused a decreased uptake of ^{99m}Tc-DPD, probably due to inhibition of growth plate metabolism.

2. In early septic arthritis, negative bone scans may be encountered in spite of fulminant joint infections.

3. A radionuclide examination of a juvenile arthritic condition should include regional scintimetry, because the change of uptake within different regions of a joint may counterbalance each other. Repeated scans may carry additional information.

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Vasoactive substances in normal subchondral bone

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The principal mechanisms in local control of blood flow are of either metabolic or neurogenic origin. The presence of local vasoactive substances in the regulation of epiphyseal bone blood flow has previously been suggested (Bünger et al. 1983a). The nature of these substances in normal and diseased bone is largely unknown. Increased arterial CO_2 tension and a low pH induce vasodilatation in bones (Gross et al. 1979). In addition, intraarterial administration of lactic acid increases nutrient arterial blood flow (Woodhouse 1963). Resting bone blood flow is not influenced by inhibition of prostaglandin synthesis (Hierton 1981), suggesting that prostaglandins play no role in maintaining resting bone blood flow.

We studied changes in local vasoactive substances and the influence of prostaglandin synthesis inhibition on the hemodynamics in normal epiphyseal bone during elevated joint pressure.

Materials and methods. Group A. In 6 anesthetized (Fentanyle, N_2O, O_2) mongrel dogs (aged 3 months),

pO_2, pCO_2, pH, lactate, and potassium were measured in blood withdrawn from the brachial artery and the distal femoral epiphyses during steady state 30 minutes after elevation of the joint pressure (P_J in the right knee to 50 per cent of the mean arterial blood pressure (MAP) and subsequently 30 minutes after elevating the P_J in the right knee to 150 per cent of MAP. Thirty minutes after evacuation of the right knee joint cavity, indomethacin, 7.5 mg/kg, was administered i.v.; and after 1 hour of recovery, the same procedure was repeated in the left knee.

Group B. In another group of 6 anesthetized dogs, the regional bone blood flow (RBF) was determined by the tracer microsphere technique before and 30 minutes after elevation of P_J to 50 per cent of MAP in the right knee. Sixty minutes after indomethacin blockade, the procedure was repeated on the left side. In both groups, MAP and the intraosseous pressure in the distal femoral epiphyses (IOP) were continuously recorded.

Results. Elevation of P_J to 50 per cent of MAP caused no changes in either pO_2, pCO_2, pH, lactate, and potassium in epiphyseal blood or RBF, whereas both the IOP and the IOP amplitude were significantly increased. Elevation of P_J to 150 per cent of MAP resulted in a significant lowering of epiphyseal blood pO_2 and an increase in epiphyseal blood lactate. These changes were not affected by administration of indomethacin.

Discussion. The initial levels of pO_2, pCO_2, pH, IOP, and RBF are comparable to values published by others, whereas, to our knowledge, no reports have so far been made on lactate and potassium in epiphyseal blood. Previous studies (Bünger et al. 1983b) have shown an increase in RBF during venous knee joint tamponade, in contrast to the present results; however use of different anesthetic agents may account for this discrepancy. Elevation of P_J to 50 per cent of MAP impairs the venous drainage from the distal femoral epiphysis as illustrated by the increase in IOP. In spite of this, the local metabolic milieu and the RBF were maintained at a normal level, probably through vasodilatation, as suggested by the increased IOP amplitude.

It is not possible to conclude from the present data whether one or more of the vasoactive substances measured are responsible for this regulation. However, considering that the vasoactive substances, the RBF, and the vasodilatation were unchanged following administration of indomethacin, it seems likely to assume that vasodilatating prostaglandins are of minor or no importance in maintaining epiphyseal metabolic equilibrium during elevated knee joint pressure.

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Subchondral bone metabolism in arthrosis: In situ measurement of respiratory gases

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The arthrotic process has been thoroughly investigated with respect to histologic and histochemical features in both humans and animals. The hemodynamics of the arthrotic process have been evaluated in man and animals by means of bone marrow pressure, intraosseous phlebography, and radionuclide uptake. However, direct measurements of respiratory gases in the tissues involved in the arthrotic process have not been performed previously. This would seem essential in order to judge the nutritional possibilities for the subchondral bone in early and late stages of the process.

Recently, mass spectrometry was introduced for in situ measurement of respiratory gases in subchondral bone (Kofoed et al. 1983). This method has been used to study certain steps in the experimental arthrotic process in the rabbit knee. The experimental model was described by Telhag & Lindberg (1972).

Simulated joint effusion. Because joint effusion has been considered one of the initiating steps in the arthrotic process (Arnoldi & Reimann 1979, Christensen 1985), the influence of simulated joint effusion on respiratory gases in subchondral bone was studied in adult rabbits. In addition to measurement of partial oxygen pressure (pO_2) and partial carbon dioxide pressure (pCO_2), the intraosseous pressure and the qualitative bone blood flow (the relative argon signal) were measured simultaneously. The joint effusion was obtained by intraarticular infusion of an isotonic sodium chloride solution and the intraarticular pressure was maintained at 75 mmHg for 30 minutes, after which it was released under continuous measurements in order to study the effect of "decompression" of the joint. The simulated joint effusion resulted in subchondral hypoxia, hypercapnia, increased intraosseous pressure,

and decreased blood flow. During 30 minutes of joint effusion, there were no signs of active regulation reversing these changes. However, when the increased intraarticular pressure was released, all the parameters returned to their initial values within 15 minutes (Kofoed & Lindenberg 1986). These findings seem to indicate that regulatory mechanisms in the subchondral bone, which might counteract the increased regional pressure, do not respond to such changes immediately. Thereby, a metabolically different and probably toxic environment may be maintained for a considerable period, giving rise to osteonecrosis.

Three-week synovitis. For further evaluation of this possibility, a 3-week model of synovitis was investigated. The model of experimental arthrosis (Telhag & Lindberg 1972) was incured with synovitis for the first 3 weeks. pO_2, pCO_2, and pH were measured in situ in the subchondral bone. Significant hypoxia, hypercapnia, and acidosis were found (Kofoed 1986a). This emphasizes the effect of joint effusion.

Four-month arthrosis. At the 4-month stage of the experimental arthrotic process, pO_2 and pCO_2 in the subchondral bone were not significantly different from the respiratory gases in normal subchondral bone, although there was a tendency for pO_2 to be increased in arthrotic bone (Svalastoga et al. 1984). By that time, the synovial effusion had disappeared.

Eleven-month arthrosis. In an 11-month model of arthrosis, the increase in pO_2 in arthrotic subchondral bone was significant. At the same time, increased intraosseous pressure was demonstrated, and histologically the subchondral bone lamellae were enlarged (Kofoed 1986b).

Figure 1 shows the "arthrotic/normal" index of subchondral pO_2 and pCO_2 in the four situations described above. From this figure, it could be anticipated that profound changes in the respiratory gases of subchondral bone are occurring throughout the arthrotic process. Initially, these are dominated by hypoxia and acidity. The hypoxia in the subchondral bone environment may indicate an increased metabolism. However, the simultaneous finding of acidosis speaks in favor of decreased nutrition. After about 3 months, pO_2 and pCO_2 seemed to be normal. This indicates that initially at least partial bone necrosis may have been present, but that revascularization takes over and normalizes the environment. When, in spite of that, pO_2 subsequently increased further, this could be explained either by a hypervascularization process that cannot be called off or by a reduced metabolism. A continued hypervascularization is the most probable explanation, as new bone formation is a prominent feature of arthrosis. This could not be explained under conditions with diminished metabolism. The demonstrated increase in the amount of subchondral bone (sclerosis) could therefore be explained by revascularization with apposition of new bone on the dead trabeculae.

The serial measurements show subchondral bone to be a metabolically reactive tissue, but compared with other tissues the changes seem to occur relatively slowly. This is in agreement with the well-known clinical observation that arthrosis is a slowly developing process. The series of experiments do not answer the question why the arthrotic process is not reversed when revascularization has taken over and respiratory gases are normal. Maybe the answer should not be looked for in the subchondral bone, but rather in the joint cavity.

("Arthrotic"/normal) index of subchondral pO_2 and pCO_2 throughout the experimental arthrotic process.

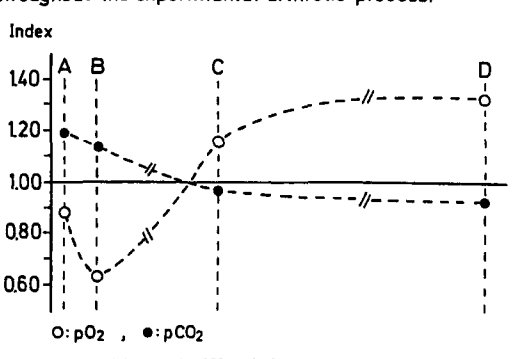

Figure 1.

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The relationship between dynamic and static bone scans in arthritis

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Joint scintigraphy traditionally visualizes the mineralization front areas of the juxtaarticular bones 2 hours after injection of bone-seeking isotopes (Einhorn et al. 1986). In immature joints, the binding preferentially takes place in the subchondral bone layer and in the calcification zone of the growth plates. By scintimetric technique the uptake can be quantitated within different regions of the joints (Hansen et al. 1986). Further information might be obtained from dynamic scintigraphy by quantitated analysis of the tracer accumulation during the first 30 seconds after bolus injection, i.e., the angiographic phase, and the following 3.5 minutes, i.e., the blood-pool phase.

We have compared dynamic and static scintimetry in juvenile septic and nonseptic arthritis of the knee in puppies in order to determine whether dynamic scintimetry provides additional information compared with conventional delayed joint scintigraphy.

Chronic nonseptic arthritis. Unilateral arthritis of the knee was induced for 3 months by weekly intraarticular injections of a Carragheenan solution. Dynamic and static scintimetry were performed after 14 days and again after 3 months when the chronic arthritis was fully developed (Bünger et al. 1984). At 3 months, the characteristic feature of the joint imaging was a reduced uptake of ^{99m}Tc-DPD in the growth plates evident in both the dynamic and static studies. Thus, the angiography and the blood pool phase both had scintimetric growth plate ratios between arthritic and control joints of 0.75, whereas the static uptake was further depressed to a ratio of 0.60. The epiphyseal uptake was insignificantly changed in the angiographic phase. During the blood-pool phase the epiphyseal uptake increased to a ratio of 1.2 , whereas the static uptake was unchanged. In the early scintimetry at 14 days, similar tendencies were detectable, but the only significant change was a reduction in the static growth plate uptake to a ratio of 0.80.

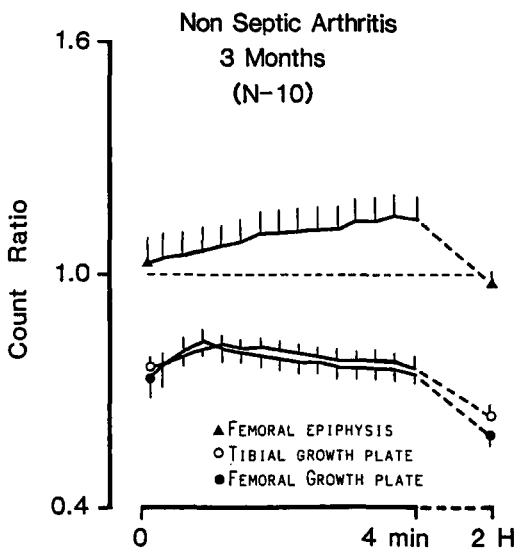

Figure 1.

These scintimetric findings are corroborated by our earlier observations in the same model on regional changes in the intraosseous microcirculation (Bünger et al. 1986). The main characteristics of the arthritic epiphyses were an increased vascular volume, an unchanged total epiphyseal blood flow and hence a prolonged transit time of blood. The increased permeable surface area between blood and bone facilitates the diffusion of ^{99m}Tc-DPD across the capillary membrane and accounts for the increased uptake of tracer in the blood-pool phase. By contact autoradiography, an increased uptake of diphosphonate was present in a very thin subchondral bone layer, while the central epiphyseal bone seemed osteopenic, with a reduced tracer uptake (Hansen et al. 1986). These regional differences in epiphyseal metabolism may counterbalance each other in the scintimetric analysis and account for the absence of epiphyseal changes in the static scintimetriy. In the metaphyses, both the blood flow and the microvascular volume tended to decrease in accordance with the decreased growth-plate uptake in all three phases of the scinitimetry. By contact autoradiography, the growth-plate uptake could be located to a narrow rim of metaphyseal bone corresponding to the layer of provisional calcification (Hansen et al. 1986, Christensen & Krogsgård 1981). The size of the bone biopsies needed for tracer studies on the microvasculature far exceeds the width of this bone layer (Bünger et al. 1986), which probably explains the greater sensitivity of the scintimetry to changes in this region.

Septic arthritis. A septic gonarthritis developed rapidly in 9 puppies following a single inoculation of *Staphylococcus aureus*. After 2 days, the joint infection was prominent with an intraarticular effusion at a pressure of between 15 and 30 mm Hg and a severe limb edema. A three-phase scintimetry was then performed.

The scintimetric results showed high variability, but in 7 of the 9 cases, a constant pattern could be recognized. In the septic joints, the most characteristic finding was a dynamic ratio curve in the epiphyseal region with a nearly doubled uptake in the angiographic phase and a blood-pool uptake ratio of 1.3. In contrast,

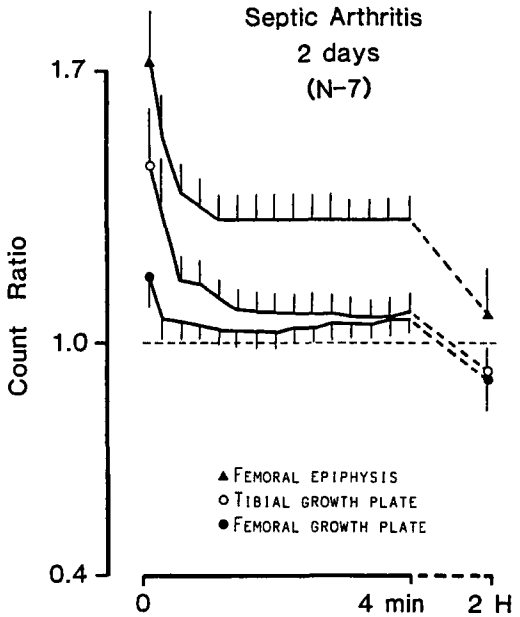

Figure 2

the static epiphyseal uptake ratios varied around unity. In the juxtaarticular growth plates, the angiographic phase was hyperemic, but no major alterations could be demonstrated in the blood-pool phase. The static growth-plate uptake, however, was slightly reduced. Two cases showed aberrant dynamic uptake curves in all three anatomic locations with a severely depressed uptake in both the angiographic and the blood-pool phases. This probably was an expression of a blood-flow reduction to the entire extremity due to a severe limb edema. In these two cases the static scintimetries did not differ from the rest.

Discussion and conclusion

The outstanding feature of scintimetry in nonseptic arthritis was a reduced growth plate metabolism, which was most clearly demonstrated in the static studies. The early septic arthritis was characterized by a significantly abnormal scan, most often including an increased epiphyseal uptake and – surprisingly – normal or even slightly "cold" static joint images due to a depressed growth plate metabolism, which seems to be a consequence of synovitis. The use of dynamic scintigraphy and regional scintimetry thus improves the diagnostic potential of conventional joint scintigraphy in juvenile arthritic conditions, especially with reference to the early septic arthritis not yet complicated by infectious bone involvement or major intraosseous circulation disorders, such as septic thrombosis.

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Reactions to implants

Bone-implant interface characteristics

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The ideal bone implant would be the one that functions adequately and results in the most naturelike tissue reactions for a long enough period of time, which in most cases is the remaining lifetime of the patient. From this, it follows that an inert material is not to be regarded as ideal, as naturelike biological reactions do not occur to neutral substances, neither is a bioactive or a biodegradeable implant necessarily ideal per se, as natural tissue reactions and adequate long-term function may not be the result of such implantations. In search of the optimal bone implant, it is essential to perform interfacial evaluations on various levels of resolution. It is well known that the implant interface characteristics are dependent on *peri-implant parameters*, such as the surgical technique, as well as on *post-implantation parameters* exemplified by the loading conditions (Albrektsson et al. 1981). A successful outcome of any implantation procedure is, in fact, related to the control of such factors. However, there are in addition several *pre-implantation* factors of utmost importance for the subsequently developing interfacial characteristics after insertion of a foreign device. Baier et al. (1984) have demonstrated that the surface conditions of the implant

prior to implantation are related to its successful integration or not afterwards. According to Baier et al., implants with high surface energy are capable of becoming truly incorporated in bone with a bonding strength at least equivalent to the strength of the bone itself, in contrast to low surface energy materials that lack this capacity. The surface energy in turn is dependent not only on the biomaterial chosen, but also on the way of manufacturing and cleaning before insertion (Kasemo & Lausmaa 1985).

Today's implants in the clinical reality are far from reaching the above proposed ideals of adequate function and naturelike tissue reactions. In the cemented joint replacement, for example, there is an inevitable degree of traumatizing surgery in combination with heat and toxic monomer release that result in a fibrous tissue anchorage of the arthroplasty. Irrespective of that, some authors have described patches of bone cement in direct contact with bone tissue (Linder & Hansson 1983). We know that a fibrous-tissue encapsulation is the body's predominant way of reacting to a material that is nonself rather than self. Because of these soft-tissue interfacial characteristics, the cemented implant is not and will not become the ideal way of joint repair, but it may yet remain as a clinical alternative in certain types of joint arthroplasties in the senior patient for many decades to come. The obvious alternative, the cementless joint arthroplasty, does not necessarily end up with better clinical results than the cemented one. From a biological point of view, this is far from surprising. We know that currently used noncemented hip replacements, such as the Lord prosthesis, are anchored in fibrous tissue and are not directly bonded to bone. The same is true of cementless knee arthroplasties of different designs that have been demonstrated to migrate for years after insertion (Ryd 1986).

The osseointegrated bone implant (Brånemark et al. 1977) has presented a new approach to tackle the long-term anchorage problem of metallic devices. At the resolution level of the electron microscope, osseointegrated implants have experimentally been found to elicit fairly naturelike tissue reactions (Albrektsson 1985). In the natural state, without the presence of any implant, there is a collagen-free zone in the 100–200 Å border region around, for instance, an epithelial cell. In the case of c.p. titanium, a similar zone devoid of collagen of the order of 200–400 Å wide has been described. No other metal has demonstrated such a naturelike tissue reaction (Albrektsson & Jacobsson 1987). Titanium implants used for the anchorage of knee arthroplasties in the dog have been found to be integrated in bone tissue without any interposed soft tissue (Röstlund et al. 1987). Steinemann et al. (1986) have measured the resistance to shear and tensile forces in the case of an osseointegrated implant. It was found that a shear stress of more than 20 N/mm^2 had to be applied for loosening of the experimental titanium implant 100 days after its insertion, whereas a tear-off strength of approximately 3.5 N/mm^2 was measured at 100–200 days after implant insertion. A tear-off strength of this magnitude is comparable to the strength of trabecular bone. This is of a particular interest since Steinemann et al. (1986) used an experimental design that permitted the evaluation of the true tensile forces acting over the interface, as the findings indicate the presence of some type of adhesion with physical or chemical forces acting over the bone-to-titanium interface.

In the case of oral implants, osseointegrated replacements have received considerable recognition; and this approach has, in fact, become the first scientifically recognized implant treatment in dentistry. However, it is far too early to state whether osseointegration will receive a similar treatment success in the case of joint arthroplasties. The main reason why osseointegration should be of a potential interest to the orthopedic surgeon is the fact that the losses observed in the mandible have almost exclusively occurred during the first year of implantation and depended on primary failure to achieve osseointegration. If osseointegration has been verified at 1 year after insertion of the implant, it seems to be a very valid prognostic sign for successful implantation also 20 years later, as evidenced by the clinical material of Brånemark et al. (1977).

In essence, osseointegration may represent a fairly naturelike implant fixation type that also has lead to highly improved success rates in dental surgery. We will, nevertheless, need 5- and 10-year clinical follow-up figures of a similar positive outcome in the case of joint arthroplasties before we know if the results of Brånemark are to be generalized to the orthopedic field.

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Bone reaction to glass ceramics

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By contrast to the crystalline ceramics (i.e., calcium phosphates and aluminum oxides), the glass ceramics are a composite of an amorphous, "glassy" network of silicon oxide in which submicroscopic crystals of other oxides are stored. They are alkaline and have a controlled reactive surface. Their binding to bone is postulated to be of a chemical nature and to depend on a certain dissolution of ions from their crystal phase. The solubility of the crystal phase depends on the amount of network formed, and the bioactivity of these Bioglasses® has been defined as the time it takes for a known amount of glass ceramic to override a pH of 5.4 in a buffered solution and reach an equilibrium pH of 10 (Hench & Clark 1978). The Bioglasses® reportedly do not undergo fibrous encapsulation upon implantation in living bone. Gross & Strunz (1985) have described an amorphous substance on the surface of glass ceramics in bone that possibly contains fibronectin and provides a basis for attachment of collagen. Subsequently, a primary ossification may occur at the bone-implant interface. It remains a problem to limit a progressive dissolution of these glass ceramics in vivo, and an uncontrollable dissolution may elicit a continuous inflammatory response to the dissolution products with fibrous tissue encapsulation of the implant (Barth et al. 1985). Ceravital® is a potassium- and magnesium-containing glass ceramic with reduced solubility in vitro. However, recent studies indicate that the solubility of glass ceramics cannot be directly related to their bone-bonding capability (Gross & Strunz 1985). The release of constituents such as Al_2O_3, Ta_2O_5, ZrO_2, or phosphates from the material may inhibit normal mineralization and result in fibrous or chondroid tissue formation at the bone-implant interface.

The maximal bone strength between bioactive glass ceramics and bone is apparently obtained by 6 weeks' implantation. The reported bond strength of the glass ceramic to bone interface under *static* load is (0.6–2.4)MN/m^2. This is rather low compared with the strength expected from chemical bonds (range 30–100 MN/m^{2}1., Hero & Syverud 1985), and physical forces acting between the bone surface and the glass ceramic surface may be of greater importance than hitherto recognized.

The glass ceramics have limited strength, fracture toughness, and fatigue properties. The bulk material is therefore unsuitable for use in highly stressed orthopedic implants unless it is applied as a coating on a metal substratum or as a metal fiber reinforced glass. Strengthening of the bulk material through different recrystallization procedures has also been attempted (Nakamura et al. 1985). Even when these precautions are taken, the brittle glass remains mechanically incompatible with the ductile bone and does not allow a distributed load transfer at the bone-implant interface under *dynamic* load. The resulting stress concentration at the bone-implant interface may exceed the strength of the glass ceramic to bone bond so that the bony fixation of the implant fails (Barth et al. 1986).

At present, the bioactive glass ceramics are being used in dental replacement and reconstructive plastic surgery, and also as total ossicle replacement prostheses in the middle ear.

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Reaction of bone to PMMA and metal ions: an in vitro human and animal study

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In later years, several new prostheses based on noncemented fixation have been offered to the orthopedic surgeon. The reason has been the increased awareness of the possible toxicity of acrylic bone cement combined with poor mechanical properties. With the use of a cemented prosthesis, there will be a rather high leakage of monomer especially during polymerization and possibly a small long-term leakage of metal ions due to corrosion (Ferguson et al. 1960). The leakage of monomer from cement has been estimated both in vitro and in vivo (Lee & Ling 1975, Crout et al. 1979), whereas the leakage of metal ions most often has been investigated in vitro or by the appearance of these ions in the urine, though lately in vivo tissue concentrations have been studied (Woodman et al. 1983, Ducheyne et al. 1984).

In order to separate the various factors that may play a role for bone turnover in connection with prosthetic replacement, we have developed two in vitro systems allowing the study of the effect of one factor at a time. The animal model used calvaries from 2–4 day mice with very high bone tissue turnover allowing effects to be recorded within 2 days. Calvaries from mice injected subcutaneously 2 days previously with ^{45}calcium were divided into two pieces and cultured for 2 days as paired halves in separate tubes. To the medium of one half, the test substance was added; and after culturing, each calvaria was decalcified in hydrochloric acid. Liquid scintillation was then performed on both medium and acid.

Release was expressed as the percentage of total isotope found in the medium, and results were calculated as a ratio between treated and control. Other calvaries were cultured in the same manner, but were homogenized after culturing. Triple determinations of alkaline phosphatase activity were performed on the homogenate, and the results were corrected for differences in tissue mass by measurement of the DNA content in the homogenate. To investigate whether there is a difference in the response of mice bone and human bone, we evaluated the effects on human osteoblast-like cells in a culture.

Fresh cancellous bones were cut into pieces of the size of chips and placed in a 25-cm^2 cultivating flask with 8-ml culture medium and left in an incubator at 37° and 5 per cent CO_2. Half the medium was replaced every week. After 3–5 weeks, cells from the pieces of bone had invaded the bottom of the flask and as a result of proliferation covered approximately 70 per cent of the surface, forming a monolayer and comprising approximately 1 million cells. The pieces of bone were removed and the cells were released from the bottom by trypsination. The cells were recovered by centrifugation and resuspended and transferred to new flasks. After another week, a new monolayer had formed. The flasks were divided into controls and test flasks receiving test substance dissolved in the medium.

Evaluation of calcium turnover in these cells is not possible, but after 3 days with the test substance, the cells can be homogenized by ultrasonication and determination of alkaline phosphatase activity and DNA content can be made. The effect of the various test substances on the ability of the cells to synthesize DNA was studied by measuring tritiated thymidine incorporation. Totally, 10^4 cells were cultured with and without the test substance for 17 hours in a tritiated thymidine-containing medium, and the cells were harvested. The amount of incorporated tritiated thymidine was determined by liquid scintillation.

Results. In the calvaria model, a dose-dependent depression on both ^{45}calcium release and alkaline phosphatase activity was found when monomer was added. The minimal concentration capable of significant depression was below in vivo concentrations (Crout et al. 1979).

The toxicity of monomer was confirmed on the human osteoblast-like cells. A depression of both alkaline phosphatase activity and the ability to incorporate thymidine was recorded.

Chromium in the 3-valent form and nickel and cobalt, both in the 2-valent form, were used as chloride salts as test substances. This should be the valency of these ions released from implants in vivo.

In the calvaria model, chromium had little effect on ^{45}calcium release, whereas both nickel and cobalt depressed the release almost to the same extent. Alkaline phosphatase activity was reduced by all three ions. These results were paralleled in the human osteoblast-like cell system with a depression of alkaline phosphatase activity by all the ions. Nickel and cobalt both reduced tritiated thymidine incorporation, whereas chromium was without significant effect.

Conclusions. In vitro monomer is toxic to bone tissue with an overall depression of bone turnover. This can be demonstrated both in young mice bone tissue and in osteoblast-like cells of human origin. Chromium, nickel,

and cobalt exhibit perhaps more specific effects on bone tissue found both in mice and in human osteoblast-like cells, with a significant depression or with no effect on some of the parameters studied.

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Bone ingrowth in glassy carbon implants

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Advantageous properties (biocompatibility, elasticity) have made glassy carbon an interesting material for orthopedic implantation. Rautavuori & Törmälä (1979) published a method that enables the preparation of bulky, strong, microporous glassy carbon bodies up to 20-mm wide. Because the pore size of microporous carbon is far too small for ingrowth of bone tissue, the implants of glassy carbon have been coated with a porous layer (pore size 200–300 μm) of the same material)

Histology and microradiography. Glassy carbon bodies were implanted into the femoral metaphyses of 30 rabbits. The amount of bone tissue in the pores increased and reached a maximum at 12 weeks, 45 per cent of the total pore volume being filled with bone tissue (Figure 1). Fluorochrome uptake was seen in the pores indicating new bone growth originating from surrounding bone. Microradiographs revealed new bone formation in the pores of implants after 3 weeks, and the density of bone spicules increased with time. Because glassy carbon is radiolucent, we could not evaluate the portion of bone of the pore volume microradiographically (Tarvainen et al. 1985).

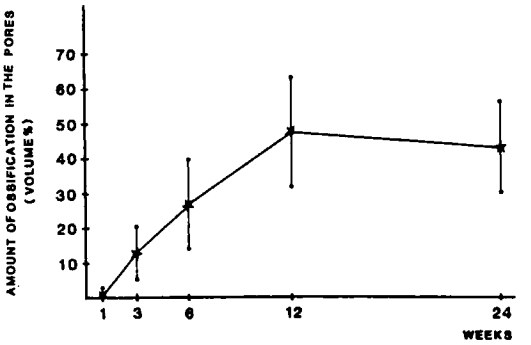

Figure 1.

Shear strength. For study of shear strength of porous carbon, the cylinders were implanted into drill holes made through the medial articular surface of the tibia of 15 rabbits. The fixation strength increased significantly from 1 to 6 weeks and reached a maximum of 4.6 MN/m^2 at 6 weeks (Figure 2). The microscopic examination of the sheared surfaces revealed that at 1 and 2 weeks shearing occurred in the tissue surrounding the implant and at 3, 6, and 12 weeks in the porous coating of the implant. Thus, the fragility of the porous carbon coating itself seemed to be the major limiting factor of the shear strength (Tarvainen et al. 1986).

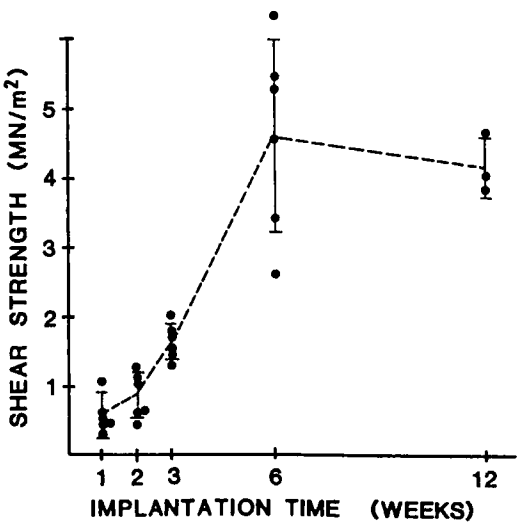

Figure 2.

Discussion. The macroporous coating is characterized by inferior mechanical properties compared with the microporous core. The implants were loaded, but by the exact press fit of the implant during the operation, all shear movement in the bone/implant interface presumably was avoided in spite of early, unlimited mobilization of the animals.

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Bone ingrowth into porous fiber titanium implants

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Prosthetic fixation methods that circumvent the cement related problems have attracted an increasing interest. The efforts have followed two main paths: attempts to achieve a chemical bonding between implant and tissue (i.e., bioreactive systems) and mechanical interlock by bone ingrowth in porous coatings on the implants. Various ceramics, polymers, and metal have been manufactured to porous structures that allow bone ingrowth.

We have used specially designed titanium implants made from a 0.25-μm wire and compressed to a relative density of 50 per cent. The structure has irregularly shaped and sized interconnected pores in the 250–450-μm range, suitably sized for bone ingrowth (Galante 1983). These implants have mechanical properties in the same range as trabecular bone. Titanium has repeatedly been found to be a biocompatible metal.

Previously, bone ingrowth has been assessed mechanically and morphologically. Rønningen et al. (1983) found that the invading bone remodels from immature to lamellar bone and concluded that the ingrown bone attains the same pattern as in healing fractures, morphologically, as well as chronologically. In the studies to be reported, we have applied chemistry and radiotracer methods using collagen and mineral analyses and isotopes to obtain data on ingrowing bone.

Experiment 1. Nonweight-bearing cylindrical implants were placed in the proximal femurs of cats for 4–26 weeks, and the ingrowth was compared to repair of a standardized bone defect in the contralateral femurs (Rønningen et al. 1984). During the first 12 weeks, there was a rapid ingrowth that leveled out during the ensuing weeks. The chemical composition of the ingrown bone was biologically normal and similar to bone in the healing defects.

Experiment 2. In a weight-bearing model in rats, a segment of the proximal tibia was replaced by a disc-shaped implant and compared with the healing of corresponding metaphyseal osteotomies after 3–26 weeks. The ultimate bending moments of the fiber titanium-bone interfaces and the osteotomies had reached about 45 per cent and the osteotomies (Table 1) increased with time and approached the level of the contralateral intact tibias at the 12th week, whereas after 26 weeks the ultimate bending stresses of the titanium-bone interfaces had reached about 45 per cent and the osteotomies about 75 per cent of the strength of the intact tibias (Barth et al. 1986a). When the amount and composition of the ingrown bone in the titanium implants were related to the strength of fixation, it was

Table 1. Ultimate bending moments (I) and stresses (II) of controls, osteotomies and the distal fiber titanium to bone interfaces (Mean±SD)

		3 wk		12 wk		26 wk
I	Control	0.50±0.10	*	0.7± 0.2		0.7± 0.1
		***				**
	Osteotomy	0.20±0.05	***	0.6± 0.1	***	0.8± 0.1
		***		**		
	Fiber	0.10±0.04	***	0.4± 0.2	***	0.7± 0.2
II	Control	105±54.6		140±45.9		114±45.4
		***				**
	Osteotomy	8.4± 5.1	***	76.0±19.2		79.8±14.6
				***		***
	Fiber	5.8± 0.8	***	35.0±13.6	*	48.3±14.9

Significantly different: *** $P<0.0005$, ** $P<0.005$, * P 0.05.

shown that the absolute amounts of bone constituents per se, and not their relative amounts, were the determinations of fixation strength (Barth et al. 1986b).

Experiment 3. Femora of cats were osteotomized and osteosynthesized by means of intramedullary rods made of porous fiber titanium. After 8 months the invading bone had a rich blood supply. The results also indicated that more extensive bone ingrowth can be achieved using a gentle reaming procedure that leaves some endosteum with adjacent marrow cells intact (Rønningen et al. 1984).

In *experiment 4*, remedies that may enhance bone formation within porous fiber titanium were investigated. Implants were placed in the musculature of rats together with bone grafts, marrow, and matrix. The combination of bone marrow grafts and matrix was an efficient bone producer, and the bone production paralleled that obtained in autografts (Rønningen et al. 1985, 1986).

Conclusion. Bone that invades porous fiber titanium implants behaves like bone in a fracture defect repair, in a way that can be utilized for fixation of weight-bearing skeletal prostheses.

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Mechanical properties

Quantitative computed tomography and axial compressive strength of tibial trabecular bone

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Several radiologic methods have been utilized for noninvasive quantitation of bone properties, e.g., radiogrammetry, photodensitometry, photon absorptiometry, and computed tomography (CT). However, the only noninvasive technique that offers three-dimensional spatial resolution is CT. This means that trabecular bone is immediately separated from cortical bone and offers the possibility of studying local variations in bone strength in normal and pathological bone.

Because bone strength is dependent on both material properties and architecture, it is by no means self-evident that a method like CT-which cannot resolve trabecular architecture-will be an adequate means of predicting mechanical bone properties. In the present paper the basis of the CT bone strength assay will be discussed and data on the obtainable accuracy will be presented.

The contrast parameter in a CT image is the so-called CT value, H, which is derived from the material characteristic linear attenuation coefficient, μ, by the equation:

$$H = 1000 \times (\mu/\mu_0 - 1)$$

where μ_0 is the linear attenuation coefficient of water. For a specific matter, μ is a complicated function of electron density and chemical composition (Bentzen 1986). Furthermore, μ depends on the spectral (energy) distribution of the x-rays used for the measurement.

Table 1. QCT bone strength assay: scan parameters for EMI 7070

Spatial resolution	1.6mm
Splice width	2mm
Image noise	0.5% c.v.
Scan time	3sec
Tube current	50mA
Multi-slice surface dose	11mGy
Pixel size	0.375mm
Image matrix size	320×320 pixels
Nominal energy	140 kVp + filter
Effective energy	83keV

Table 1 shows the performance characteristics of a typical whole-body scanner (the EMI 7070 at Aarhus Kommunehospital) when used for trabecular bone quantitative CT, QCT. Pixel size is the actual dimension

of the individual picture elements, slice width, the thickness (orthogonal to the scan plane) of the slice, and spatial resolution is a measure of the smallest resolvable structures in the image. The magnitude of these parameters is of an order quite adequate for studying bone mechanical parameters. As an example, an estimate of the relevant spatial resolution in the study of bone mechanical parameters may be obtained from experimental biomechanical work where it has been shown that trabecular bone may be treated as a continuum in regions of a radius greater than or equal to approximately 2.5 mm (Harrigan et al. 1985). Absorbed dose to the patient, a factor of obvious importance in any procedure involving ionizing radiation, is around 10 mGy and is delivered locally, thus representing a negligible risk for the individual patient.

Due to preferential absorption of low energy x-ray photons (internal filtration), the spectral distribution is changed to yield an increased effective energy. This effective energy shift, changing the μ value or the CT value, is known as beam hardening, and represents an inherent problem in QCT. Beam hardening is especially pronounced in the presence of cortical bone having a relatively high effective atomic number. In addition, to beam hardening, several other physical effects exist that may influence the CT values (Bentzen 1986).

Despite these theoretical limitations, actual correlation coefficients from experimental work (Table 2) have been quite high (Bentzen et al. 1987), a partial explanation being that geometry and internal inhomogeneities, to a large extent, are comparable in different human knees. However, as a consequence of the large spatial gradients in the distribution of both QCT and mechanical parameters in human trabecular bone, an experiment comparing these must follow a protocol ensuring optimal spatial agreement between measuring sites in the two situations. Spatial variation is probably a major cause of the residual 25–35 per cent variation in mechanical parameters not described by a regression equation on QCT data.

A somewhat lower correlation between ultimate strength of human lumbar vertebrae and CT (r = 0.68) was published by McBroom et al. (1985). Again, spatial variation is presumably a partial explanation; but at the same time, it must be expected that other trabecular bones having a structure different from the tibia will also have another CT-strength dependency.

Table 2. Correlation coefficients between QCT and mechanical parameters derived from a compression tests of 165 bone specimens*

	Linear	Power	P
Ultimate strength	0.80	0.84	N.S.
Yield strength	0.79	0.85	0.10
Elastic Modulus	0.73	0.78	N.S.
Ultimate energy	7.78	0.83	N.S.
Yield energy	0.72	0.81	0.05
Ultimate strain	−0.24	−0.17	N.S.
Yield strain	−0.17	−0.11	N.S.

P=P-value for equal correlation with linear and power law fits.
* From Bentzen et al. (1986).

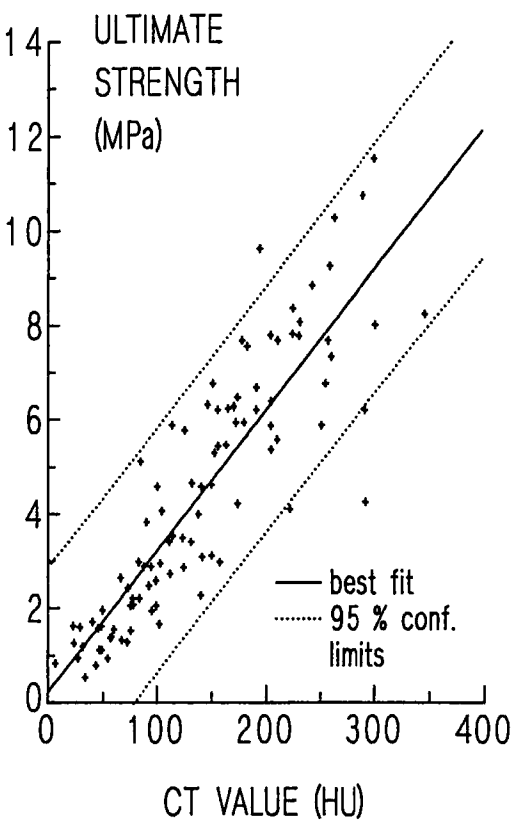

Figure 1. Ultimate strength versus CT value in a series of 97 bone specimens excised from the proximal tibial epiphysis of 10 human cadaver knees. The linear correlation coefficient is 0.87

A calculation of the 95 per cent confidence limits on the QCT estimated ultimate strength of tibial trabecular bone yields a value of 2.3 MPa, with a somewhat narrower interval for low strength (below 3 MPa) specimens (Figure 1). An accuracy in this range allows meaningful application of the QCT bone strength assay in clinical work (Bentzen et al. 1985, Hvid et al. 1986).

In conclusion, QCT has been shown to be a valuable tool in noninvasive investigation of mechanical parameters in tibial trabecular bone.

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Clinical remodeling studies

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The potential of trabecular bone to remodel in response to permanent alterations in the local biomechanical environment was suggested by Wolff (1892), and a quantitative relationship between distributed joint loads (stresses) and trabecular bone density and architecture has been established (Hayes & Snyder 1981). Current theory on bone remodeling emphasizes mechanical stimuli as the factor in control of the remodeling process (e.g., strain-sensitive cells initiate the process above a threshold value, the minimum effective strain) (Frost 1986). A permanent increase in local strain would thus be expected to eventually result in an increase in bone strength as a result of positive balance between bone formation and bone resorption. Very low local strains, on the other hand, seem to favor a negative balance leading to loss of local strength (Behrens et al. 1974, Hvid 1987).

Remodeling in degenerative disease of the knee joint. At the knee joint, degenerative diseases (e.g., arthrosis (A) and rheumatoid arthritis (RA)) are commonly accompanied by progressive malalignment with its associated redistribution of the joint load (Harrington 1983). A close correspondence has been documented between the distribution of load as assessed by gait analysis (Harrington 1983) and the distribution of axial compressive strength of subchondral bone (Behrens et al. 1974, Hvid 1987, Hvid & Hansen 1986) in response to varus and valgus deformities. Varus knees invariably exhibit relatively higher strength at the medial tibial condyle with the highest strength towards the margin of the condyle in severe varus. Valgus knees are less predictable with regard to mediolateral strength distribution, although the typical case shows higher lateral strength (Hvid 1987, Hvid & Hansen 1986).

Remodeling after total knee replacement. Trabecular bone-strength assay utilizing quantitative computed tomography (QCT) offers acceptable accuracy, good precision, and a spatial resolution not obtainable by any other noninvasive method (Bentzen et al. 1987). Topographic strength profiles of the normal and arthritic proximal tibia obtained by QCT (Bentzen et al. 1985) correspond closely to those obtained by direct mechanical methods (Hvid & Hansen 1985, 1986).

The method was applied to a series of total knee replacements (TKR) followed for 2 years after operation. Twenty patients entered the study, but 2 were excluded, 1 because of complications in connection with ankle replacement and 1 because of a large cement-filled cyst in one of the tibial condyles. Of the remaining 18 TKRs, nine were performed for A and nine for RA. All the patients had their walking ability improved by the operation. Preoperative alignment was neutral in three knees (all with RA), varus (5 to 20 degrees) in nine knees (six with A) and valgus (5 to 22 degrees) in six knees (three with A). Postoperative alignment was neutral in 15 knees and slightly valgus in three knees. Computed tomographies were carried out using 120 keV, 90 mA, and a 3-second scan time. Three consecutive 3-mm slices were obtained from the proximal tibia, the most proximal slice being just deep and parallel to the cement-bone interface. Using appropriately sized templates, two areas were defined for data collection anteriorly and posteriorly at each condyle. In the following results, the two condylar measurements were averaged from the proximal scan level.

The changes recorded in QCT with time after TKR are shown in Figures 1 and 2. The findings at the time of operation are in agreement with previous reports on the distribution of mechanical strength at the tibia (Behrens et al. 1974, Hvid 1987, Hvid & Hansen 1986). At 2 years postoperatively, densities were significantly decreased at the medial condyles of varus knees and at the lateral condyles of valgus knees. The condyles that were weak at the time of operation tended towards an increase in densities, but, although this response was pronounced in some patients, the overall results were not statistically significant. The abnormal mediolateral density distributions at the time of operation were normal after 2 years, but the absolute densities were lower in the valgus group. The general trends were apparent already after 3 months postoperatively. There was no significant difference of response in the A and RA groups.

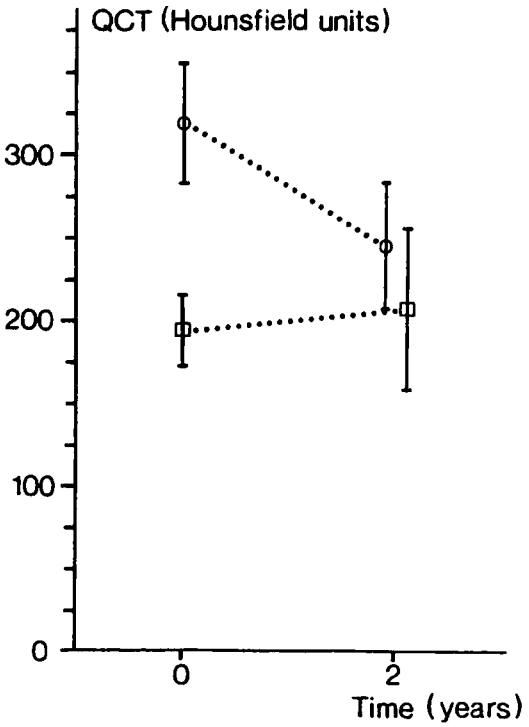

Figure 1. QCT in varus knees at operation and 2 years postoperatively. Vertical bars correspond to ±1 SEM. On the QCT scale, 100 Hounsfield units are equivalent to approximately 3 MPa compressive strength (Bentzen et al. 1987). ○ = medial tibia. □ = lateral tibia.

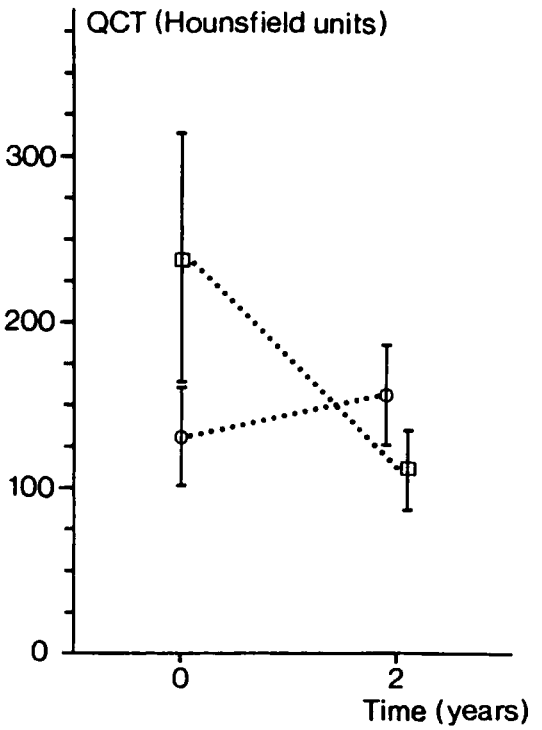

Figure 2. QCT in valgus knees at operation and 2 years postoperatively. ○ = medial tibia. □ = lateral tibia.

The findings of this study suggest that epiphyseal trabecular bone has a significant capacity to remodel in response to alterations of mechanical demands. It is noteworthy that the densities obtained from the weaker condyles at the time of operation were not critically low on an average (Hvid 1987), which accounts for the magnitude of the response.

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Time-dependent properties of trabecular bone

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Hardly any biological material has pure elastic properties. Nevertheless, Swanson & Freeman (1966) and Pugh et al. (1973) failed to demonstrate any significant viscoelasticity of trabecular bone by ultrasonic technique. However, typical viscoelastic phenomena, such as stress relaxation, creep, and energy dissipation, were later demonstrated by Schoenfeld et al. (1974), Walker et al. (1976), and Zilch et al. (1980).

Effect of strain rate. Any model on a viscoelastic solid must include at least one elastic element (a spring element) and one viscous element (a damping element). The Kelvin solid is a typical, and the most simple, viscoelastic model. It consists of a spring element connected parallel with a damping element, and expresses the fundamental time dependency by a simple equation:

$$\sigma = E\varepsilon + \lambda d\varepsilon/dt$$

(σ = stress, ε = strain, $d\varepsilon/dt$ = strain rate, and E and λ are constants (coefficient of elasticity and coefficient of viscosity, respectively).

From this equation, it is seen that determinaton of "nonviscous" properties, such as strength or modulus of elasticity, must be performed at an infinite low strain rate to avoid interference from viscosity. This dependence on strain rate of ultimate strength and stiffness has been investigated by Carter & Hayes (1977), who found that both strength and stiffness inside the strain rate range 10^{-2}–1 sec^{-1} were approximately proportional to the strain rate raised to the 0.06 power.

Cyclic loading. Another effect of viscoelasticity is seen by conditioning, i.e., preloading before the real test. Preloading of trabecular bone specimens 10 times to 50 per cent of predicted ultimate strength has been shown to cause a 50 per cent increase in the stiffness from the first to the tenth loading cycle, and a 35 per cent drop of the energy dissipation (Linde et al. 1985). Cyclic loading (700 times) of femoral heads showed a 200 per cent increase of stiffness and a 70 per cent decrease of energy dissipation during the test sequence (Walker et al. 1976). However, the cartilage was not removed from these specimens, and this may have affected the results considerably.

Measurements at infinite low strain rate are not applicable for most experimental studies, and "time independent" mechanical properties should instead be determined in a reproducible manner by achieving steady state concerning viscosity. This can be done by 10 conditioning cycles with a 0.1 Hz frequency (Linde & Hvid 1987).

Strain delaying. Besides making stiffness measurements and determination of ultimate properties troublesome, viscoelasticity has great physiologic importance. Strain is probably a far more important factor than stress in physiologic bone processes (modeling, remodeling) (Frost 1983) and may appear to be so in pathologic bone processes (fractures, microfractures, local bone loss, arthrosis) as well. The strain-delaying effect of viscosity protects the bone structure from reaching failure strains when a high load is applied for a short time (Figure 1). Further, trabecular bone exhibits energy absorptive properties as a consequence of viscosity. This energy absorption seems different in arthrotic bone compared with normal trabecular bone (Walker et al. 1976), and this property may have major importance in the pathogenesis of arthrosis and other load-related diseases, such as overuse injury.

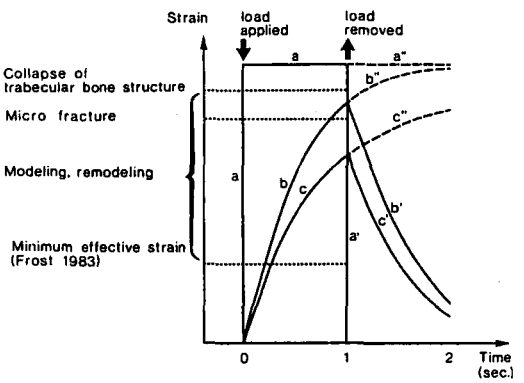

Figure 1. The physiologic effect of viscoelasticity illustrated by an example where a high load is applied to a trabecular bone specimen for 1 second: a) pure elastic properties, b) viscoelastic properties, c) viscoelastic properties with more pronounced viscosity. a, b, c) specimen under loading, a', b', c')specimen during relaxation, a", b", c") specimen under continued loading.

Rheologic models. Hitherto, rheologic models on the behavior of trabecular bone have been based mainly on theoretical considerations. The available experimental data are, however, very sparse. Schoenfeld et al. (1974) performed stress relaxation experiments to four different load levels on three specimens from a femoral head and found about 10 per cent stress reduction after 10 seconds and 15 per cent after 100 seconds. The percentage of stress relaxation seemed independent of the load level. Zilch et al. (1980) investigated femoral specimens from different locations of five pairs of cadaveric femora. The mean stress relaxation (at steady state) was about 18 per cent and the creep about 4 per cent, but

with a large variation between individuals and topographic locations.

Much more experimental data are necessary for creating and testing appropriate rheologic models. There are, however, technical problems because of the fragility of trabecular bone and because the effects on the measurements of viscoelastic properties by machining, storage mode, testing environment, and the test set-up, are almost unknown. Furthermore, testing must be carried out nondestructively, and the magnitude of the applied load ought to be related to the ultimate strength or strain, or to the stiffness of the bone rather than selected to a uniform load independent of the strength of the bone. This demands high accuracy of techniques used for prediction of stiffness or ultimate strength.

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Mechanical properties of normal avascular and revascularizing cancellous bone: An animal experiment

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Several researchers have attempted to evaluate the material properties of cancellous bone (stiffness, strength) (Behrens et al. 1974, Carter & Hayes 1977, Galante et al. 1970, McElhaney et al. 1970, Townsend et al. 1975). Of considerable interest in clinical practice is the question of how the material properties are affected in avascular and revascularizing trabecular bone when compared with normal trabecular bone.

Material and methods. Using a sterile surgical procedure, the anterosuperior segments of the left femoral heads of African Pygmy Goats were devascularized and isolated, but kept in situ, using acrylic cement. Forty-four goats were used and divided into six groups. The control group was not operated on. Three avascular groups were killed 6, 12, and 24 weeks after the operation. The fifth group was operated on twice: first, to devascularize and isolate the segment and, secondly, to revascularize the same segment by drilling a hole through the acrylic cement barrier. The last group was also operated on twice, similar to the fifth group, but in addition an arteriovenous bundle was transplanted into the segment through the drill hole (Hori 1981). Eleven goats in this group were killed after 12 weeks and 5 goats after 24 weeks.

Specimens for mechanical tests were obtained from all the material of the first five groups. All the test specimens were cylindric, 5 mm in diameter and 4-mm thick and cored from the anterosuperior segments in the principal trabecular direction. Each specimen was subjected to unconfined compression to failure on a Zwick testing machine at a cross-head speed of 1 mm/min. Yield strength and Young's modulus were determined. The apparent density of each sample was assessed (Carter & Hayes 1977). Histologic examinations were carried out to check avascularity and revascularization using normal and UV light microscopy. No specimens were obtained from the last group, which was subjected to loading in vivo and evaluated only histologically.

Three human postmortem femoral heads were used, and a total of 45 specimens were obtained for testing to assess the validity of the testing methods and as a means of comparison.

Results. The results confirm that the mechanical properties of cancellous bone, both human and goat, are principally functions of apparent density (Carter & Hayes 1977, Galante et al. 1970, McElhaney et al. 1970) (App. dens. goat 0.59–1.48 g/cm^3). No differences in strength were observed between normal, 6-, 12-, and 24-week avascular cancellous bone in goats (Figure 1) (yield strength: 4.7–54.6 MPa). This was also true for the stiffness, Young's modulus (E: 84–1,434 MPa). The strength and stiffness obtained in the human specimens were generally in agreement with those published earlier (Behrens et al. 1974, Carter & Hayes 1977, Galante et al. 1970 McElhaney et al. 1970). Decreasing strength

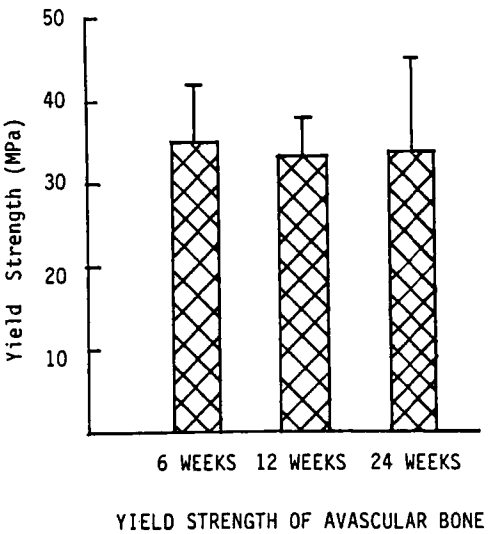

Figure 1. Yield strength of avascular trabecular bone as a function of time.

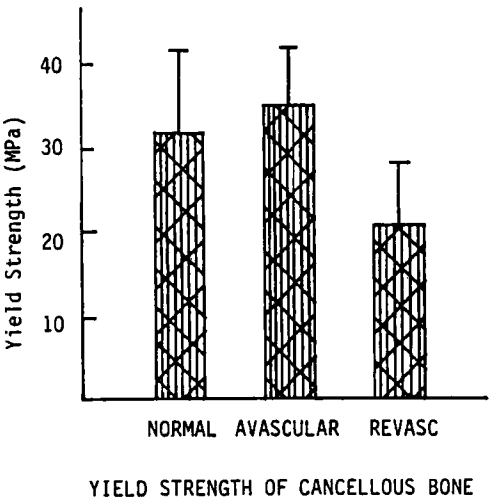

Figure 2. Comparison of yield strength in normal, avascular and revascularized trabecular bone.

and stiffness with increasing age were also observed (Weaver & Chalmers 1966). Very different results were obtained for the revascularizing specimens of group 5. The average yield strength was found to be significantly less than in the normal and avascular specimens (Figure 2). The corresponding apparent density was essentially equal, on an average.

In the last group, 16 goats with an arteriovenous bundle transplantation, all the anterosuperior segments were loaded in vivo during a period of 13 weeks (11 goats) and 24 weeks (5 goats). Of the first 11 goats (1 infected excluded), eight segments showed no signs of collapse and two displayed a small partial collapse. In the 24-week group (3 infected excluded), the remaining two segments showed no signs of collapse.

Conclusions

1. The quality of the cancellous bone matrix if isolated in vivo under normal loading conditions remains unchanged.

2. Collapse of the femoral head during avascular necrosis is due to the revascularizing process.

3. Transplantation of an arteriovenous bundle may prevent collapse.

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