JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 5 (1994) 59–66

Fluorapatite-coated implants in experimental arthritis: the response of rabbit trabecular bone

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Fluorapatite-coated implants have been studied for the first time under non-optimal tissue conditions and have shown promising results. The influence of arthritis on the tissue response to implants coated with fluorapatite (FA) was studied in an arthritis model. Immune complex-induced arthritis was elicited in the right knee-joint of eight rabbits while the contralateral joint served as control. Ti–6Al–4V cylinders, plasma-spray coated with FA were implanted in the patellar groove (PG) and medial femoral condyle (MC) in each knee for 6 weeks. Histology showed a close bone-to-implant contact at the lateral surface of the implants without any intervening soft tissue or inflammatory cells. Histomorphometry revealed no differences in bone apposition between control and arthritic joints, but the MC-implants showed more bone apposition than the PG-implants. Parts of the implant surface were not covered by bone, but were in contact with bone marrow. The FA coating on the implant sides did not show signs of resorption in the control and arthritic joints, but the coating on the upper surface of the implants was partially resorbed in both the control and arthritic joints. The arrangement and composition of the regenerating tissue in this location was profoundly influenced by the inflammatory process in the arthritic joints. In a previous study, using the same arthritis model, an impaired bone formation was found around commercially pure titanium implants in arthritic joints. In the present study, the unimpaired bone formation around FA-implants in the arthritic joints indicates that an FA coating adds advantageous properties to metal implants used in tissues influenced by an on-going inflammation.

1. Introduction

The promising clinical application of hydroxylapatite (HA)-coated hip implants has recently been reported [1–3]. The introduction of HA plasma-sprayed coatings for clinical purposes is based upon extensive animal experiments [4–10]. Fluorapatite (FA) is a ceramic with a high stability with respect to the extreme temperatures in the plasma-spray process [11]. In a recent implant study in healthy goats, we compared the mechanical fixation, stability and histological characteristics of plasma-sprayed coatings of HA, FA, and magnesiumwhitlockite (MW), and non-coated Ti–6Al–4V (Ti) alloy [12, 13]. FA coated implants showed, after 12 and 25 weeks implantation, a fixation in the cortical bone that was comparable with HA-coated implants. After 25 weeks, the FA coating appeared to be largely intact, while the HA coating had almost completely disappeared. In addition, the FA-coated implants showed more apposition of mineralized bone at the implant surface than the HA-implants. These results formed the basis for further research on the application of FA plasma-sprayed coatings in orthopaedic surgery [14, 15].

Animal experiments of hard tissue implants are usually performed under optimal conditions, namely in the healthy bone of relatively young animals. The situation in clinical practice is more complex. Not only are patients usually older, but in many patients the healing capacity of their bone tissue is decreased due to osteopenia as seen in rheumatoid arthritis or osteoarthritis. It is therefore important to perform an experimental study to examine the behaviour of implants under biologically non-optimal conditions, as for instance in arthritic joints. Several arthritis models in laboratory animals have been developed. Thomsen *et al.* [16] described a model of proliferative synovitis in rabbit knee-joints, induced by antigen and preformed immune complexes. Using this model, it was found that implants of commercially pure titanium had a lower degree of mineralized bone–implant contact in arthritic joints compared to implants in healthy control joints [17]. Similarly, using a canine

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experimental arthritis model, Søballe *et al.* [18, 19] described an impaired incorporation of alloyed titanium implants compared to hydroxylapatite-coated implants in osteopenic bone (carrageenin-induced arthritis).

The purpose of the present investigation was to analyse the response of trabecular bone to fluorapatite plasma-spray coated implants in a rabbit experimental arthritis model. In addition, the stability of the fluorapatite coating under these pathological conditions was examined.

2. Materials and methods

2.1. Implants

Thirty-two cylindrical plugs of commercially available Ti–6Al–4V (Krupp-Klöckner GMBH, Essen, Germany) alloy were manufactured. All plugs measured 5.0 mm long and 3.2 mm diameter. The plugs were grit-blasted to a roughness of $R_a = 4.5$–5.0 μm, cleaned, and plasma-spray coated on the sides and top with fluorapatite using previously described conditions [12]. The coating thickness on the implant sides was 50 μm, giving a final implant diameter of 3.3 mm. The thickness of the coating on the implant top was approximately 20 μm. The plugs were cleaned ultrasonically in 100% ethanol, dried at 50 °C, and sterilized in an autoclave. Scanning electron microscopical evaluation demonstrated that the autoclaving procedure did not alter the surface structure of the implants. Fig. 1 shows a scanning electron micrograph of the FA coating.

2.2. Animals and induction of arthritis

Eight adult, female New Zealand White rabbits, weighing 3.5–5.2 kg were used. The animals were fed *ad libitum* on standard pelleted food and water. The protocol for the immune-complex induced arthritis has previously been described in detail [16, 17]. In brief, the rabbits were immunized by a subcutaneous injection in the neck with bovine serum albumin (BSA, Boeringer-Mannheim GMBH, Germany) mixed with Freund's adjuvant (Difco Laboratories, Detroit, Michigan, USA). Fourteen days after immunization, a schedule of intra-articular injections in the knee-joints started. During 4 weeks the right knee-joints were challenged weekly with 0.5 ml antigen solution (25 mg BSA ml^{-1}) while the left (control) knee-joints were injected with 0.5 ml saline.

Prior to each intra-articular injection and at the times of surgery and sacrifice, clinical signs of arthritis were evaluated by macroscopic observation of joint swelling and measurement of skin temperature above the knee-joints. Peripheral blood was obtained from an ear vein prior to and at different periods after immunization to assess the presence of antibodies against BSA (precipitation in gel), and for a lymphocyte proliferation test [16]. Synovial fluid was harvested under sterile conditions at surgery and sacrifice. The number of leucocytes in the exudate and differential counts were determined. Smears of synovial fluid were incubated on blood agar at 37 °C for 48 h to detect possible bacterial infection.

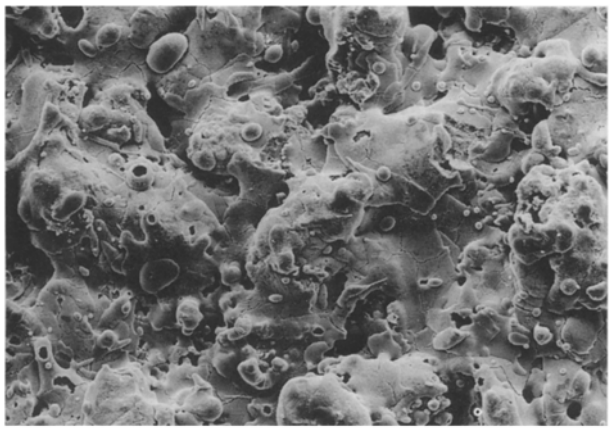


Figure 1 Scanning electron micrograph, showing the surface structure of the FA coating.

2.3. Surgical procedures

The animals were operated upon 1 week after the last intra-articular injections. Surgery was performed under general anaesthesia induced and maintained by intramuscular injections of fluanizone (Hypnorm®, Jenssens, Brussels, Belgium, 0.7 mg kg^{-1} body weight) and diazepam (Stesolid®, Dumex, Copenhagen, Denmark, 1.5 mg kg^{-1} body weight). The hind-limbs were shaved, washed and disinfected with povidone–iodine. Under sterile conditions, the knee-joint was opened through medial parapatellar skin and capsule incisions. After the synovial fluid was collected the patella was dislocated laterally. Holes were drilled (diameter 3.3 mm; depth 6.0 mm) in the patellar groove and medial femoral condyle, using low-speed dental drills with increasing diameter, and under generous cooling with saline. The sharp cartilage rim at the proximal edge of the holes was removed with a scalpel, and the implants were press-fit inserted into the holes with the upper implant surface at the level of the bone–cartilage border. To remove possible drilling debris the joints were carefully flushed with saline. The joint capsule and fascia were closed with Vicryl® 5–0 and the skin with silk 5–0 sutures (Ethicon®, Johnson and Johnson AB, Sollentuna, Sweden).

To minimize the peri-operative infection risk, the animals received daily benzylpenicillin (Intencillin®, LEO, Sweden, 2.250.00 IE/5 ml) from 2 days before until 1 day after surgery. An injection of buprenorphin (Temgesic®, Reckitt and Coleman, USA, 0.05 mg kg^{-1} body weight) was given once as post-operative analgesic.

2.4. Animal sacrifice

All animals were sacrificed 6 weeks after surgery. First, blood was obtained via a marginal ear vein under anaesthesia. The knee-joints were carefully opened and synovial fluid was collected by washing the joints with 0.5 ml of Hanks' balanced salt solution (HBBS) using an automatic pipette and attached syringe. Fresh biopsies were taken of the tissue grown on top of the patellar groove (PG)-implants. These biopsies

were used for other purposes and are not included in this study. Then, the rabbits were given an overdose of phenobarbital (Mebumal®, Aco Läkemedel AB, Solna, Sweden) and fixed with 2.5% glutaraldehyde in 0.05 M sodium cacodylate (pH 7.4), by perfusion via the left heart ventricle. The implants and the surrounding bone were removed, and the medial condyle (MC) and patellar groove (PG) implants were separated from each other using a circular dental saw. All specimens were then immersed in glutaraldehyde.

The MC-implants were dehydrated by graded series of ethanol and embedded in polymethylmethacrylate. After polymerization, nondecalcified sections of approximately 10 μm thickness were cut parallel to the length axis of the femur using a modified sawing microtome [20]. The sections were stained in alternating order with basic fuchsine/methylene blue, safranine-O, and masson-trichrome, and evaluated with a light microscope.

The PG-implants were post-fixed in 2% osmium tetroxide for 1 h, dehydrated by graded series of ethanol and embedded in LR-White® (London Resin Co. Ltd, Hampshire, UK). The implants were divided longitudinally by sawing. One part of the specimen was used to prepare approximately 10 μm thick ground sections [21]. These sections were stained with 1% toluidine blue and evaluated with a light microscope. The remaining part of the specimen was used for other purposes and is not included in this study.

Histomorphometrical evaluation was performed for each implant on two sections close to the central axis of the implants, using a light microscope coupled to a VIDAS Image Analysis System (Kontron Electronic Bildanalyse GMBH, Munich, Germany). The following parameters were measured: (1) the percentage of bone apposition on the implant sides for both the MC- and PG-implants. This was defined as the percentage of implant length at which there was a direct bone-to-implant contact (magnification X100), (2) the percentage of bone area next to the MC-implants. This area was separated into five zones of each 200 μm thick, and in addition, the first 200 μm zone next to the implant was divided into five zones of each 40 μm thick (Fig. 2). Bone area measurements were performed using a magnification of X25. The histomorphometrical data of the right (arthritis) and left (control) knees were compared with each other using paired t-tests. Differences were accepted as being significant at $p \leq 0.05$.

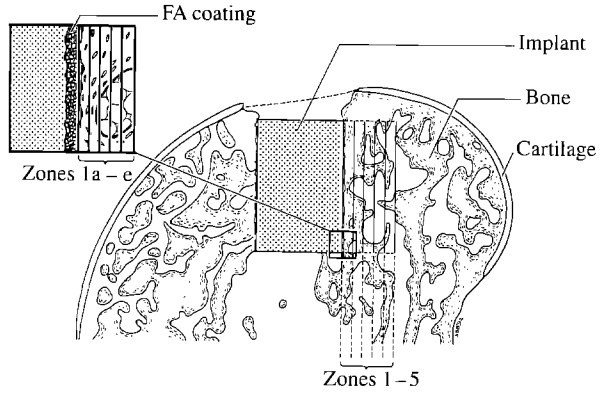


Figure 2 Schematic representation of five zones of 200 μm width used for bone area measurements next to the MC-implants. Zone 1 is separated into five sub-zones (a–e) of each 40 μm width.

3. Results

3.1. Development of the arthritis

Two weeks after the first intra-articular injection, a humoral and cellular immune response was evidenced by the presence of precipitating antibodies in the serum and a raised lymphocyte stimulation index (reaching a maximum at the time of surgery). Antibodies to BSA were detectable in the serum throughout the complete post-operative period of 6 weeks.

Clinical signs of inflammation were present 28 days after immunization as indicated by an elevated skin temperature and by swelling of the (antigen-challenged) right knees in comparison with the left (control) knees. These parameters reached maximum values at the time of surgery. At surgery, 1 week after the last intra-articular injection, a fibrinous exudate was retrieved from the arthritic joints whereas a very small amount of a clear fluid could be washed out from the control joints. The number of inflammatory cells was markedly higher in the antigen-challenged joint than in the contra-lateral control joint. At sacrifice, the number of cells in the arthritic joint exudate had decreased considerably. In both the arthritic and control joints polymorphonuclear granulocytes predominated. All samples of the joint fluid at surgery and sacrifice were sterile. The parameters with respect to the assessment of the arthritis are summarized in Table I.

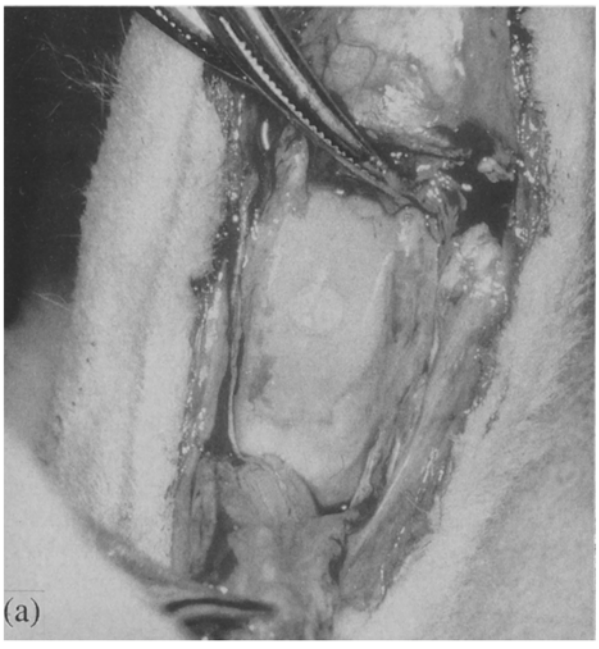
3.2. Macroscopical observations

No pathological findings were noted in the control joints. The right (arthritic) joints had a swollen, hyperaemic and easily bleeding synovial capsule. The cartilage surface was yellowish and had numerous erosions. Furthermore, a lower resistance of the underlying bone during drilling was noticed in comparison with the control joints. Although all animals showed an arthritis of their right knees, the degree of arthritis varied.

All implants were at sacrifice still *in situ*. The majority of implants were totally or partially overgrown with a whitish tissue, but in the right (arthritic) joints the overgrown tissue appeared more irregular (Fig. 3). Synovial adhesions were found in one arthritic joint.

TABLE I Summarized data on evaluation of arthritis regarding skin temperature, lymphocyte stimulation index, antibodies in sera and joint swelling.

	Surgery	Sacrifice
Difference in skin temperature (°C, right–left)	1.6 ± 0.8	0.7 ± 0.9
Lymphocyte stimulation index	0.7 ± 0.5	0.5 ± 0.3
No. animals with precipitating antibodies	8/8	8/8
No. animals with joint swelling (right knee)	8/8	5/8



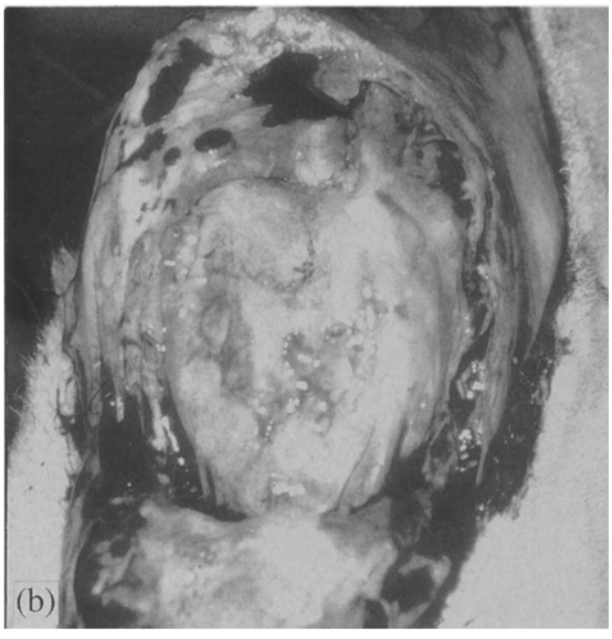


Figure 3 Macroscopical appearance of PG-implants at sacrifice: (a) left (control) joint showing whitish repair tissue on implant top; (b) right (arthritic) joint of the same animal, showing swelling of capsule and synovial tissue. Irregular appearance of articular cartilage and repair tissue on top of implant.

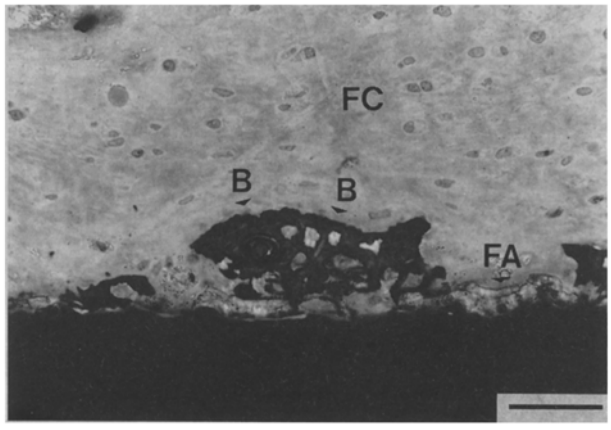


Figure 4 Light micrograph of tissue grown on top of PG-implant (control), showing fibrocartilage (FC) and newly formed bone (B) on top of FA coating (FA) (staining toluidine blue). Bar = 50 μm.

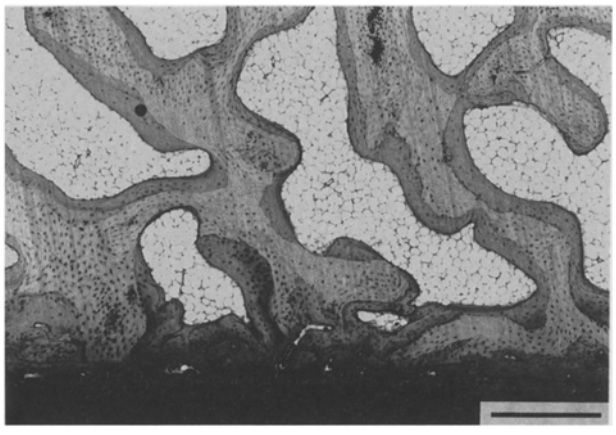


Figure 5 Survey light micrograph of MC-implant and surrounding bone in control joint. A "collar" of bone, almost forming a continuous layer along the lateral implant sides is visible (staining basic fuchsin/methylene blue). Bar = 500 μm.

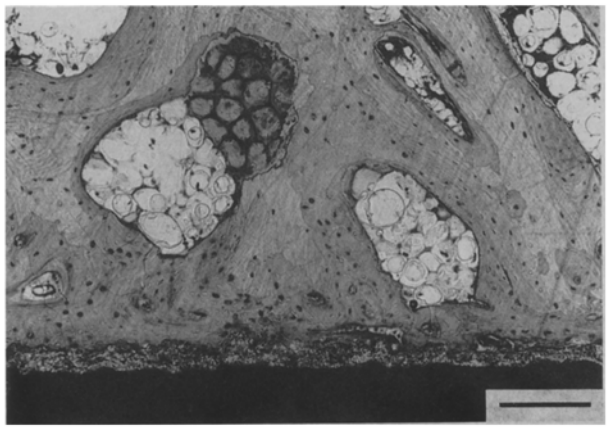


Figure 6 Histological appearance of PG-implant in control joint showing bone in close apposition to the FA coating (staining toluidine blue). Bar = 200 μm.

3.3. Histology

3.3.1. Control joints

In the control joints, the upper surface of the implants was covered by bone and cartilage. The main part of the regenerated tissue facing the joint cavity was either fibrocartilage or hyaline cartilage. Clusters of chondrocytes were commonly observed, whereas blood vessels were rarely detected. In seven of the eight MC-implants, the tissue on the upper surface of the implants was continuous with the cartilage surface. Beneath the cartilage, the tissue on top of the implants frequently consisted of mineralized bone. In general, the bone formed a rim in direct continuity with the subchondral bone lateral to the implant. A general impression was that this bone was growing centripetally over the upper implant surface. However, areas of apparently newly formed mineralized bone not in continuity with the subchondral bone, were also observed on the implant top (Fig. 4). The surrounding

articular cartilage appeared normal without signs of inflammation or mechanical damage.

The major morphological findings in the tissues around the implants were firstly, the presence of a collar of bone (Fig. 5), almost forming a continuous layer along the lateral implant sides, and secondly, a close apposition of this bone to the FA coating on the implants sides (Fig. 6). The apposed bone collar was laterally connected to bone trabeculae. In areas without bone apposition, bone marrow or fibroblasts were in contact with the FA. A fibrous encapsulation of the implant was never observed and inflammatory cells were rarely detected.

3.3.2. *Arthritic joints*

The morphology of the tissue in the antigen-challenged joints differed from that in the control joints although variations in the degree of inflammatory cell infiltration and tissue derangement was noted between the arthritic joints. In general, the most striking differences were observed in the tissues directly related to the joint cavity: synovial tissue, articular cartilage and the tissue on top of the implants.

The cartilage appeared thinner than in the control joints. In some areas, pannus tissue with a large number of inflammatory cells was located on the edges of the partly eroded cartilage as well as between the cartilage and the subchondral bone (Fig. 7). In these areas, macrophages and multinuclear giant cells were observed in direct contact with the cartilage. All PG-implants were covered with tissue, but because biopsies had been taken, the continuity with the joint surface could not be evaluated for this location. Five of the eight MC-implants were completely covered with whitish tissue, and in none of the specimens was this tissue continuous with the joint surface. This tissue consisted of fibrocartilage or granulation tissue, although areas of hyaline cartilage also were observed. The granulation tissue contained numerous blood vessels and inflammatory cells, mainly macrophages, lymphocytes and plasmacells (Figs 8 and 9). Similarly to the control joints, mineralized bone was present in direct contact with the upper surface of the implants. Laterally, this bone was frequently in contact with the subchondral bone.

A consistent finding in the arthritic joints was the large amount of bone in close apposition with the FA on the implant sides (Fig. 10). In areas without bone apposition, either bone marrow or loose connective tissue was present at the implant surface (Fig. 11). In one of the arthritic joints, a thin layer of inflammatory tissue was present between the FA coating and the surrounding subchondral bone (Fig. 12). A fibrous encapsulation of the implants was never observed.

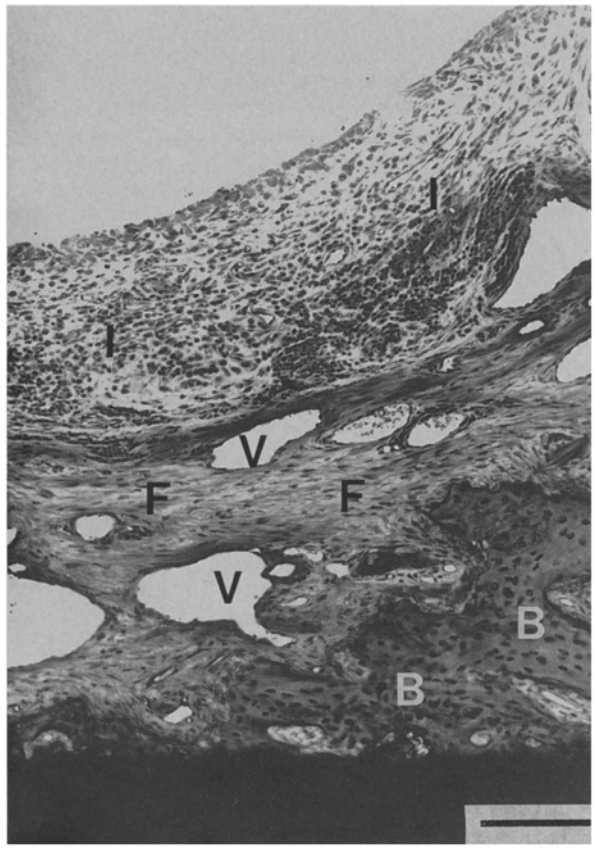


Figure 8 Histological appearance of tissue grown on top of MC-implant (arthritis), showing inflammatory (I) and fibrous (F) tissue, vessels (V) and newly formed bone (B) on top of the FA coating (staining basic fuchsin/methylene blue). Bar = 150 μm.

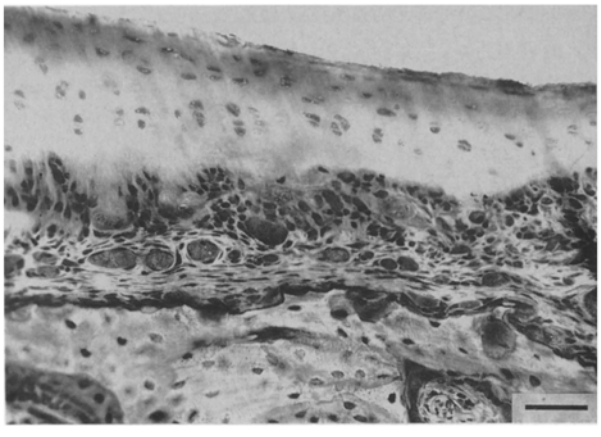


Figure 7 Light micrograph of the border between cartilage and bone in an arthritic joint (PG). Inflammatory tissue is located between cartilage and subchondral bone (staining basic fuchsin/methylene blue). Bar = 50 μm.

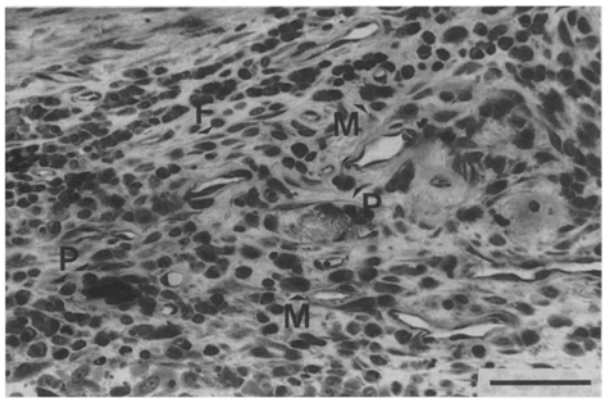


Figure 9 Detail of inflammatory tissue on top of MC-implant; P, plasmacell; M, macrophage; F, fibroblast (staining basic fuchsin/methylene blue). Bar = 50 μm.

3.4. Histomorphometry

Light microscopic observation revealed a large degree of direct bone-to-implant contact for all implants in both the control and arthritic joints. The quantification of bone apposition for the various implants is presented in Table II. No significant differences in bone apposition between the control and the arthritis joints were found for the MC- and PG-implants. The MC-implants had a significantly higher amount of bone apposition than the PG-implants in both the control and arthritic joints.

Measurements of relative bone areas in the zones lateral to the MC-implants are presented in Table III. The control joints showed a higher percentage of bone area up to 400 μm from the interface (zones 1A-2). At larger distances from the interface, no significant differences were found between the control and arthritic joints.

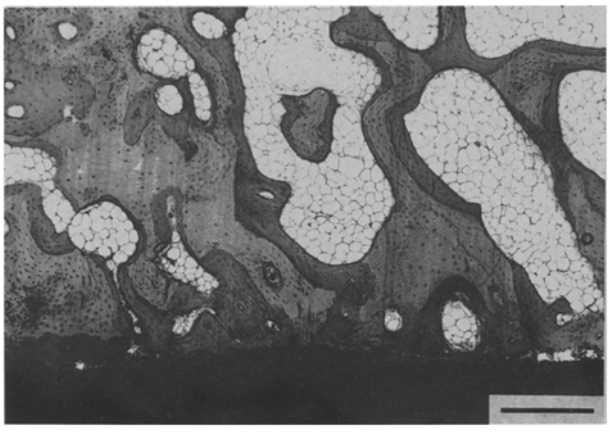


Figure 10 Survey light micrograph of MC-implant and surrounding bone in arthritic joint showing bone in contact with the FA coating (staining basic fuchsin/methylene blue). Bar = 500 μm.

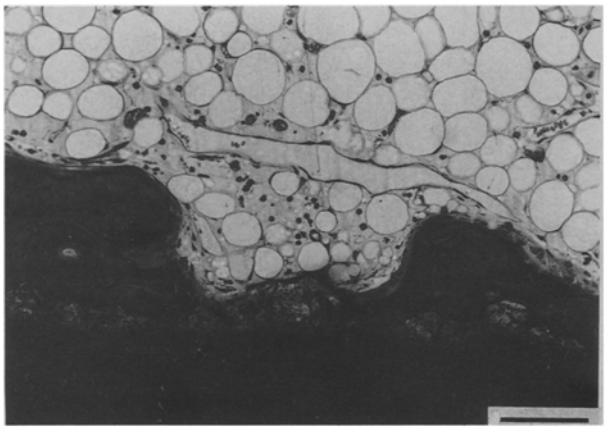


Figure 11 Histological appearance of MC-implant in arthritic joint showing bone apposition and marrow cells/osteoblasts in contact with the FA coating (staining basic fuchsin/methylene blue). Bar = 100 μm.

TABLE II Mean bone apposition (%) ± standard deviation for the MC- and PG-implants in the control and arthritic joints ($n = 8$)

	Medial condyle	Patellar groove
Control	77.4 ± 8.1[a]	55.7 ± 12.2[a]
Arthritis	74.6 ± 4.4[b]	54.3 ± 8.1[b]

No significant differences in bone apposition between control and arthritic joints. Significant difference between MC- and PG-implants for both the control and arthritic joints, [a]$p < 0.005$, [b]$p < 0.001$.

3.5. Fluorapatite coating stability

In both the arthritic and control joints, the FA coating on the sides of the PG- and MC-implants did not show any signs of resorption, and had a uniform thickness of approximately 50 μm. However, on top of the implants, where the coating was originally thinner (approximately 20 μm), the FA coating had partially disappeared in both the control and arthritic joints.

4. Discussion

In the present study, a mono-articular arthritis was induced in rabbits by immune complexes. This model was used to study the tissue response to intra-articular inserted FA-implants. A major reason for studying an

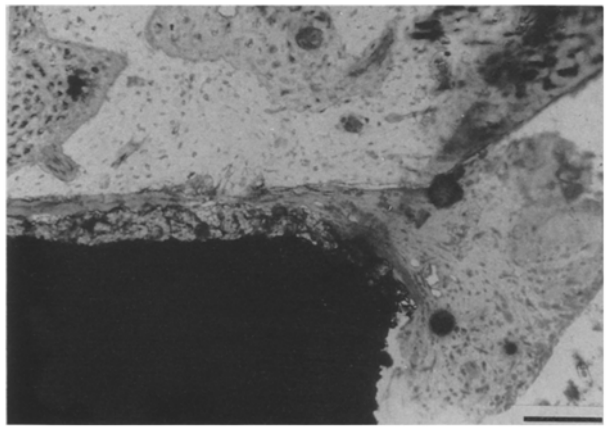


Figure 12 Micrograph showing a thin layer of inflammatory tissue between the FA coating and the surrounding bone (staining basic fuchsin/methylene blue). Bar = 100 μm.

TABLE III Mean bone areas (%) ± standard deviation in various zones adjacent to the medial condyle implants for the control and arthritic joints ($n = 8$)

	Zone 1A	Zone 1B	Zone 1C	Zone 1D	Zone 1E	Zone 2	Zone 3	Zone 4	Zone 5
Distance from implant surface (μm)	0–40	41–80	81–120	121–160	161–200	201–400	401–600	601–800	801–1000
Control	85.1 ± 9.2	80.9 ± 10.3	77 ± 11.5	72.6 ± 11.2	69.7 ± 9.7	61.3 ± 6.9	51.1 ± 9.0	50.7 ± 10.4	47.8 ± 6.9
p[a]	⩽ 0.05	⩽ 0.025	⩽ 0.025	⩽ 0.025	⩽ 0.001	⩽ 0.05	n.s[a]	n.s.	n.s.
Arthritis	78.5 ± 5.3	70.0 ± 7.9	66.3 ± 7.8	64.4 ± 7.4	61.4 ± 8.9	54.3 ± 7.4	47.7 ± 6.6	48.1 ± 8.7	49.5 ± 8.0

[a] Results from paired t-tests on differences between control and arthritic joints: n.s., not significant.

implant in such a location is that in clinical practice intra-articular implants are often used under conditions where the host tissue in joints and bone are affected by an on-going inflammatory disease, as for instance in rheumatoid arthritis. In the present study, the induction of the arthritis followed essentially the same protocol as that previously described [16, 17]: a cellular and humoral immune response, paralleled by clinical and morphological signs of inflammation, was elicited in the animals by repeated intra-articular injections of antigen. An arthritis was present in all antigen-challenged joints, although the inflammatory response differed between individual rabbits.

The major finding in the present study was that no significant difference in bone apposition to FA-coated implants was detected between normal and arthritic joints. In the local inflammatory environment, irrespective of implantation site (medial condyle or patellar groove), a large amount of bone was observed in direct contact with the FA surface. This is in contrast to previous findings with commercially pure titanium [17] or Ti–6Al–4V [19] in which an impaired bone response was observed in the arthritic joints. The mechanisms behind these differences is yet uncertain. One crucial factor for bone formation and subsequent remodelling of bone adjacent to an implant surface may be the presence of osteoblasts or inflammatory cells and their activity at the implant–tissue interface. As previously shown [17], a direct continuity between the joint cavity and the bone surrounding the implant may promote the migration of inflammatory cells from the joint cavity and synovial pannus tissue along the implant surface. These inflammatory cells at the implant surface then prevent bone regenerating and making contact with the surface. In the present study, mineralized bone was in direct contact with the FA-coated implant sides. Inflammatory cell infiltration and fibrous capsule formation was generally not observed, indicating that migration of inflammatory cells along the implant–tissue interface did not occur. One possible mechanism explaining the differences described for FA-implants and titanium implants is that bone formation occurs with different intensity and at different sites in relation to surfaces of FA or titanium. Kinetic studies of the bone formation around threaded pure titanium implants in cortical bone have shown that bone-forming osteoblasts are not directly related to the implant surface and that the interface zone close to the implants is the last part of the bone next to the implant which is mineralized [22]. Although we have not yet examined the early healing of FA-coated implants, the present morphological findings of mineralized bone and osteocytes in intimate contact with the FA in the subchondral cancellous bone as well as on top of the implant, indicate that bone may have been formed directly on the fluorapatite surface. Such a process might then lead to an early sealing of the interface zone from the joint cavity, and thus preventing invasion of inflammatory and bone-resorbing cells. These possible mechanisms will be the topic of a future investigation.

The amount of bone apposition varied between implants in the medial condyle and patellar groove (MC-implants 77.4% and 74.6%, respectively, for the control and arthritis joints, and for the PG-implants 55.7% and 54.3%, respectively). These values for bone apposition are generally higher than values previously obtained for implants in rabbit bone. In a previous study of screw-shaped titanium implants in the patellar groove in rabbits [17], the overall bone apposition varied after 6 weeks from 45.3% in the control joints to 31.1% in the arthritic joints. Johansson and Albrektsson [23] found 37.2% bone apposition, 12 weeks after implantation of screw-shaped titanium implants in healthy rabbit trabecular bone (tibial metaphysis and femoral head). In another study by Sennerby *et al.* [24], 38.5% bone apposition was measured for titanium screws after 6 weeks implantation in healthy rabbit trabecular bone (patellar groove). Because differences exist with regard to the surgical procedure, implant location, implant size and design in these studies, no firm conclusions can be drawn on the high bone-apposition values measured in this study for FA-implants and the lower values obtained for titanium implants in previous studies. However, as discussed above, differences in mechanisms of bone formation on the titanium and FA surfaces may lead to an earlier and more extensive bone formation around FA-implants. We also found differences in the degree of bone apposition between implants in the patellar groove and medial condyle. Although the PG- and MC-implants with surrounding tissue were embedded and sectioned using different techniques, we do not believe that these factors may account for the differences. For instance, the section thickness did not vary between the two techniques. Previous studies have shown that the rate of bone formation and the amount of bone formed around implants are related to the implant site, e.g. cortical versus cancellous bone [24, 25]. It is, therefore, possible that bone apposition to implants may be influenced by pre-existing variations in the bone structure as well as different biomechanical conditions, even within the same joint. Consequently, the influence of the implant location has to be taken into account when comparing results from different studies.

In a previous study on goats [12, 13], plasma-sprayed FA coatings were found to have a superior stability compared with plasma-sprayed HA coatings. In the present study we found that the FA coating on the implant sides did not show signs of resorption, which confirms our previous observations on the stability of the FA coating in a biological environment. On the other hand, the initially thinner FA coating on the upper surface of the implants, facing the joint cavity, had partially disappeared after 6 weeks in both the control and arthritic joints. *In vitro* studies have already shown that under a physiological pH, the solubility of FA plasma-sprayed coatings is lower than that of HA plasma-sprayed coatings [26]. A low pH may increase the solubility of the FA coating. Previous observations indicate that an acidosis can prevail in arthritic joints due to synovial effusion and circulatory imbalance [27–30]. For that reason it might be expected that the FA coating should be more

extensively resorbed in arthritic joints. However, we did not find any clear evidence for this and the degree of resorption of the FA coating on the implant top appeared to be about the same in the control and arthritic joints. At present, we do not know why the coating on the upper, but not at the lateral surface of the implant is partially resorbed. Possible factors of importance are mechanical trauma related to joint movements, contact with the synovial fluid during the initial healing phase, and a difference in properties between a thin (20 μm) and thicker (50 μm) FA coating.

In animal experiments, non-loaded implants of several types of biomaterials inserted in bone have been shown to heal with a direct bone-to-implant contact. In clinical orthopaedic applications, e.g. metal hip prosthesis, the implants can be surrounded by inflammatory cells, a fibrous capsule and resorbed bone [31, 32]. In such applications a rapid establishment of a direct bone-to-implant contact may be crucial for avoiding the appearance of inflammatory cells and fibrous tissue around the implants, which might lead to failure of the implant. The present findings of a large amount of mineralized bone in intimate contact with the implants in normal as well as in arthritic joints indicate that a coating with FA is a useful surface modification of currently used metal implants for prosthetic treatment in normal and pathological conditions.

Acknowledgements

The authors thank L. Emanuelsson, C. Gretzer, J.G.C. Wolke, R.C. Vriesde and J.P.C.M. van der Waerden for technical assistance. Financial support was received from the Netherlands Technology Foundation (STW, grant LGN99.1984), the Swedish Medical Research Council (grants 9289 and 9495), the King Gustaf V 80-year Fund, and the National Swedish Board for Technical Development (NUTEK, grants 90-00536 and 90-01480).

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Received 2 September
and accepted 9 November 1992