Current Concepts

Biodegradable Implants in Sports Medicine: The Biological Base

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Summary: Biodegradable implants are increasingly used in the field of operative sports medicine. Today, a tremendous variety of implants such as interference screws, staples, sutures, tacks, suture anchors, and devices for meniscal repair are available. These implants consist of different biodegradable polymers that have substantially different raw material characteristics such as in vivo degradation, host-tissue response, and osseous replacement. Because these devices have become the standard implant for several operative procedures, it is essential to understand their biological base. The purpose of this report is to provide a comprehensive insight into biodegradable implant biology for a better understanding of the advantages and risks associated with using these implants in the field of operative sports medicine. In particular, in vivo degradation, biocompatibility, and the osseous replacement of the implants are discussed. A standardized classification system to document and treat possible adverse tissue reactions is given, with special regard to extra-articular and intra-articular soft-tissue response and to osteolytic lesions. **Key Words:** Biodegradable implants—Clinical application—Sports medicine—Biocompatibility—In vivo degradation.

Materials that disintegrate in the body have been emerging over the past 3 decades, and there are now numerous implants available in the fields of orthopaedic surgery, general surgery, maxillofacial surgery, cardiology, gynecology, and urology. Terms such as absorbable, resorbable, and degradable, with or without the prefix 'bio' are inconsistently used in the literature. We use the term biodegradable to characterize materials that show disintegration after implantation and subsequent complete excretion.

For many years, biodegradable implants have been thought to offer advantages over metal analogs. In orthopaedic practice, metal implants can distort magnetic resonance imaging (MRI),[1,2] and they release metal ions into the surrounding tissue. Further disadvantages include the need for a second surgical procedure for implant removal and complicated revision surgery resulting from the presence of the implant. The intent of biodegradable implants is to provide secure initial fixation strength while allowing degradation and replacement by the host tissue. Therefore, there is no need for implant removal, revision surgery is not compromised, and radiological imaging is not distorted. In addition, functional loads can be assumed earlier by the healing bone while the material is degrading.[3,4]

In sports medicine, the development and use of biodegradable implants has emerged late compared with other fields, such as general orthopaedics, orthopaedic trauma surgery, and maxillofacial surgery. However, the strong interest of joint surgeons in these materials has led to the development of numerous implants becoming available and, as a result, the market has shown a dramatic change within the last few years. Today, we can choose from a large variety

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of biodegradable implants, such as sutures, staples, tacks, anchors, interference screws, and devices for meniscal repair. High mechanical properties of a biodegradable implant may be of primary importance in fracture fixation or other orthopaedic procedures where the implant is exposed to high loads. This may explain the slow progress of biodegradable implant technology in this field. In contrast, as several clinical and biomechanical studies have shown, certain operative procedures in sports medicine do not require implants of high mechanical strength. For interference screw fixation in cruciate ligament reconstruction, the cancellous bone may be the weak link and not the interference screw.[5-7] The fixation strength of a suture anchor construct may be limited by the suture or the bone stock quality.[8,9]

Biodegradable implants consist of different polymeric raw materials that have substantially different material characteristics and tissue response. We believe that it is inappropriate to apply the term biodegradable to all these different materials. Furthermore, it is important to know the basic biology of these materials, such as in vivo degradation, osseous replacement, and biocompatibility, in order to evaluate their appropriateness for the use in operative sports medicine. The purpose of this review is to focus on current developments and to provide the clinician with an insight in biodegradable implant biology.

IN VIVO DEGRADATION

Today, approximately 40 different biodegradable polymers are known.[10,11] Of these, the following materials have been studied to be used in orthopaedic implants:

1. Polyglycolide (PGA) and copolymers such as polyglycolide-co-trimethylene carbonate (PGA-co-TMC), poly-(D,L-lactide-co-glycolide) (PDLLA-co-PGA), and poly-(L-lactide-co-glycolide) (PLLA-co-PGA).
2. Poly-(L-lactide) (PLLA), poly-(D,L-lactide) (PDLLA), and their stereocopolymers with varying ratios of the L and D,L parts.
3. Polydioxanone (PDS).
4. Trimethylene carbonate (TMC).
5. Polyorthoester (POE).
6. Poly-c-capralacton (PCL).

Additionally, composite materials consisting of PLLA/tricalcium phosphate or PLLA/hydroxyapatite have been introduced.[12-15] Of major interest in implant technology in the field of operative sports medicine are the poly-α-hydroxy acids such as PLLA and PGA including their copolymers and stereocopolymers.[16]

In principal, synthetic biodegradable polymers consisting of poly-α-hydroxy acids undergo an unspecific hydrolytic chain scission due to water uptake.[17] Degradation starts at the amorphous phase of the implant leading to fragmentation of the material to smaller parts, which are phagocytosed primarily by macrophages and polymorphonuclear leukocytes.[18-20] Polymeric lactic acid oligomers degrade to monomers which enter the Krebs cycle and get dissimilated to carbon dioxide and water.[17] Beside the hydrolytic chain scission, glycolic acid monomers can be released by unspecific esterases and carboxypeptidases.[21]

Degradation kinetics of different raw materials differ substantially, which may be attributable to the hydrophilic or hydrophobic nature of the different polymers. Furthermore, although the degradation kinetics of biodegradable implants depend primarily on polymer choice, a large variety of additional factors also appear to contribute to this process, including molecular weight, sterilization, implant size, self-reinforcement, and processing techniques.[11,22-30]

We know that in vitro hydrolysis testing could differ markedly from in vivo testing because of the additional influence of environmental conditions. Due to a possible interaction between degrading polymers and the healing tissue, the in vivo degradation characteristics of biodegradable implants should be known. Unfortunately, only a few studies have investigated the in vivo degradation of the different polymers used in biodegradable implants, and these have reported vastly different results because of inconsistent test conditions and different implant processing techniques.[11] Vert et al.[31] tested the tensile strength of different polylactides implanted in sheep tibiae. They reported that PLLA maintains its tensile strength for over 150 weeks. In contrast, Gerlach et al.[24] found that PLLA rods lose approximately 50% of their bending strength within 4 weeks if implanted in rat dorsal muscles. Fischer et al.[14] reported that 2-mm rods made of PDLLA implanted in rat dorsal muscles maintained 90% of their initial bending strength for over 6 weeks with subsequent rapid degradation. In contrast, Mainil-Varlet et al.[32] reported that pushout forces of PDLLA rods implanted in sheep tibiae increased continuously over a period of 6 months and were significantly higher than those of PLLA rods. This may be the result of the implant swelling caused by water uptake of the stereocopolymer. In principal, it is reasonable to assume that slow or intermediate degrading materials such as PLLA, PLLA-co-PDLLA, or PDLLA maintain their mechanical strength at least for the time required

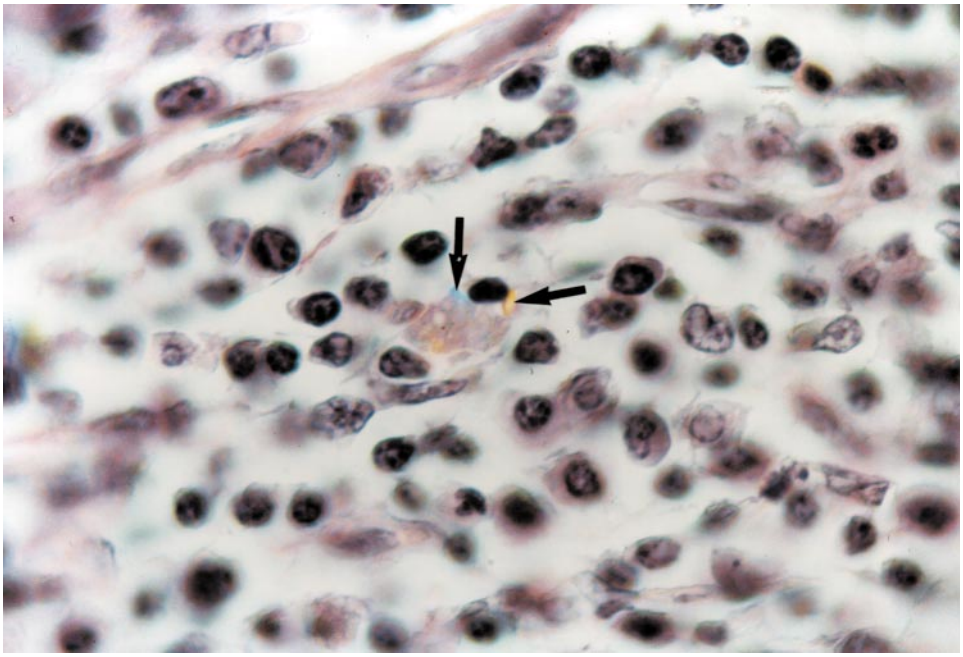

FIGURE 1. Inguinal lymph node of a sheep 6 months after implantation of crystalline self-reinforced PGA pins. Macrophage with intracellularly deposited polymeric particles (black arrows). (Reprinted with permission.[46])

for proper tissue healing. Other materials, such as PDS, PGA, PGA-co-TMC, or PDLLA-co-PGA, which are expected to degrade more quickly, could suffer a significant loss of mechanical strength in vivo within the period of tissue healing. However, clinical studies have not yet reported any healing failure resulting from the use of these materials.[33-39] For long-, intermediate-, and slow-degrading interference screws, different animal studies have proven that these screws withstand the forces until the graft is incorporated.[40-43]

While most reports studied the degradation kinetics of biodegradable implants by measuring strength retention biomechanically, less is known about the long-term fate of implant remnants in the body. Pistner et al.[30] found a large amount of particles of block-polymerized and injection-molded PLLA implants in dorsal rat muscle tissue 112 weeks after implantation, although the material had lost 80% of its bending strength 32 weeks after implantation. Clinical reports have shown that remnants of high molecular-weight PLLA implants could still be found several years after implantation. Bergsma et el.[44] found implant remnants up to 5.7 years after stabilization of midface fractures with PLLA plates and screws.[44] Böstman et al.[45] described the necessity of partial implant removal up to 45 months after stabilization of ankle fractures with highly crystalline self-reinforced PLLA screws. The occurrence of late hydrolytic degradation may depend on the degree of the material's crystallinity. Twelve months after implantation of self-reinforced PGA rods, Weiler et al.[46] found an absence of birefringent material at the implant site, but crystalline PGA remnants were detected in lymph nodes for up to 24 months after implantation (Fig 1). At rearthroscopy, Stähelin et al.[36] found bulky remnants of a highly crystalline PLLA interference screw 20 months after implantation (Fig 2). These reports suggest that a complete degradation of highly crystalline, so-called biodegradable, implants does not occur within an appropriate time. To monitor the complete degradation process of synthetic biodegradable implants in bone tissue, Pistner et al.[47] introduced a scheme of 5 phases of degradation (Table 1).

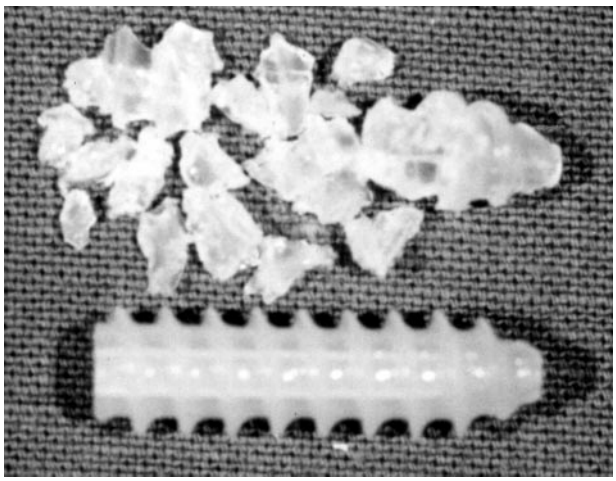

FIGURE 2. Bulky fragments of a highly crystalline PLLA interference screw 20 months after implantation compared with a nonused specimen. (Reprinted with permission.[36])

TABLE 1. *Phases of Degradation of Amorphous Biodegradable Implants and Tissue Reactions According to Pistner et al.*[47]

Phase	Tissue Reaction
1. Healing phase	Unchanged implant, development of a fibrous capsule with a high amount of fibroblasts
2. Latency phase	Unchanged implant, fibrous capsule gets thinner with less cells and more fibers or direct implant contact to bone
3. Protracted resorptive phase	Mainly central degradation of the implant, development of cracks, mild to moderate cellular response with invasion of macrophages and foreign-body giant cells
4. Progressive resorptive phase	Progressive disintegration of the implant with a severe tissue response (macrophages, foreign-body giant cells)
5. Recovery phase	No polymer remnants detectable, development of scar tissue or osseous replacement of the former implant site

OSSEOUS REPLACEMENT

A major intent of biodegradable implants is complete tissue replacement at the former implant site. Although an early replacement with fibrous granulation tissue takes place during degradation,[46,48-53] less is known about the long-term fate of the former implant site and its osseous replacement. Although a complete osseous replacement has been anticipated for all biodegradable implants, it has not yet been shown either experimentally or clinically in most cases. To facilitate uncompromised revision surgery, a complete osseous replacement should occur within a 2- to 3-year time frame to allow for a second interference fit or tack fixation as, for example, in cruciate ligament and shoulder revision surgery.

The osteogenic reaction of the host tissue starts early after implantation of the polymeric material and shows an osseous enclosure within the first few weeks[51,53] (Fig 3). During or following implant degradation, osseous replacement may follow 3 different patterns:

1. There is osseous ingrowth while the implant is degrading (Fig 4). This phenomenon is most desirable but has rarely been found. To our knowledge, it has only been reported to occur during the degradation of PLLA-co-PDLLA (70:30) or self-reinforced PLLA/PDLLA composite rods.[50,51]
2. There is osseous ingrowth in the center of the former implant site after the implant is degraded (Figs 5 and 6).[46]
3. There is an osseous scaring of the former implant site with a slow marginal ingrowth of new bone (Fig 7). This kind of replacement has been found in cases after an osteolytic lesion has occurred and may progress over several months or years.[46]

In general, it is reasonable to assume that the faster a material degrades, the earlier the osseous replacement

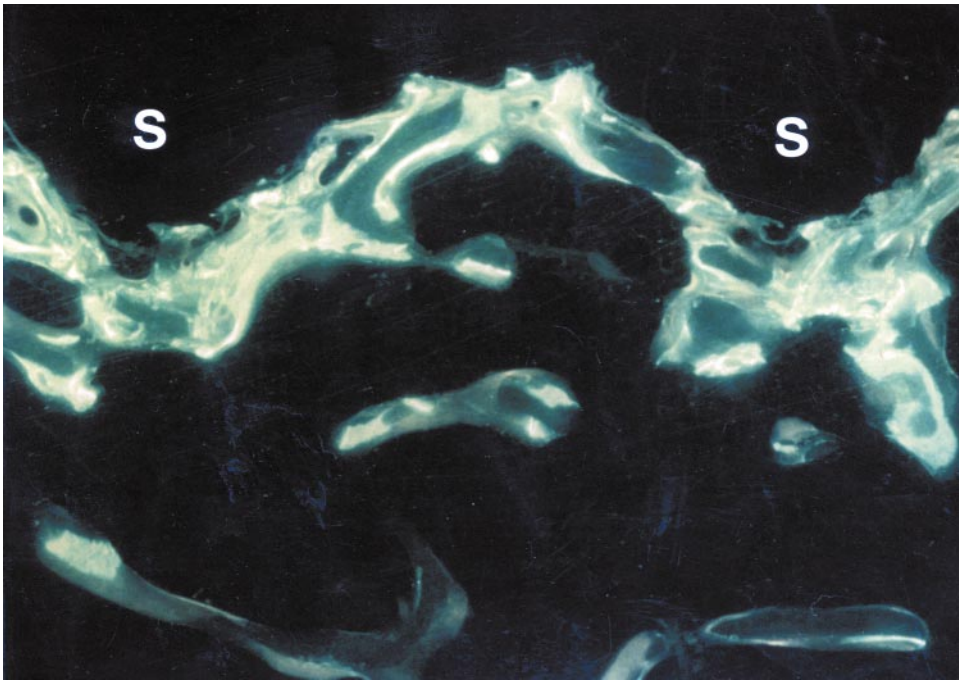

FIGURE 3. Tissue-implant interface 6 weeks after implantation of a PDLLA interference screw in a sheep femur. Polychrome sequential labeling shows activity of the early given fluorochromes (calcein green given at 4 weeks and xylenol orange at 6 weeks) indicating the early osseous enclosure of the implant (S, screw threading).

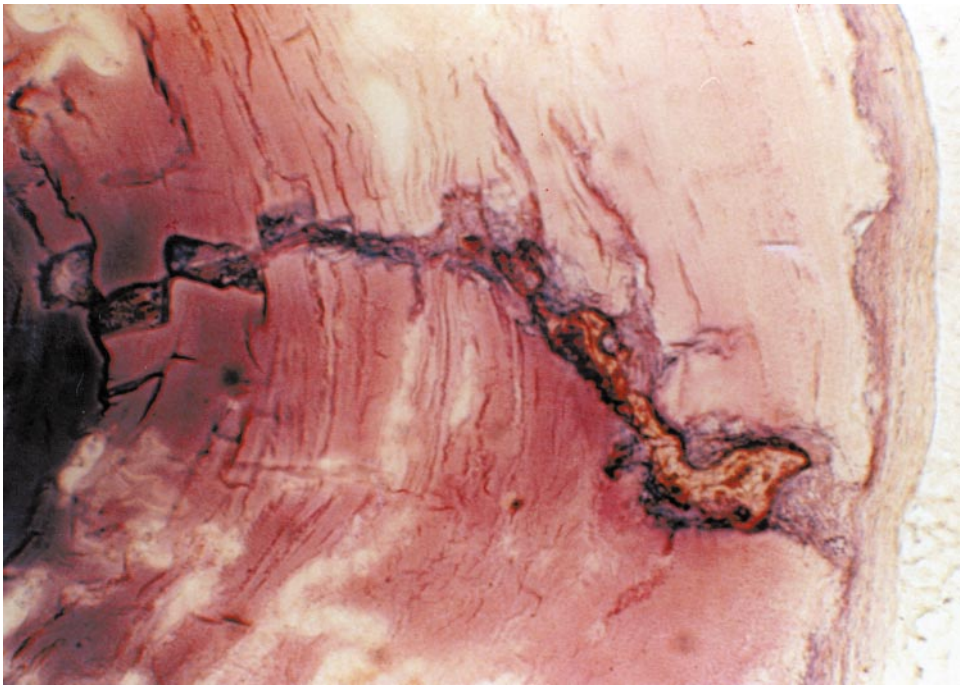

FIGURE 4. Bone trabeculae growing into a PLLA-co-PDLLA pin 15 months after intramedullary implantation in a sheep tibia.

takes place (Figs 8 and 9).[36,54] Materials such as PDLLA-co-PGA, PLLA-co-PDLLA, or PDLLA are considered to degrade faster compared with PLLA implants, for which the degradation process has been described to last for several years.[44,55,56] To our knowledge, no single report has shown complete osseous replacement of a PLLA implant in a clinical or experimental setup (Figs 10 and 11). Several experimental studies have been performed to investigate tissue response and tissue replacement after implantation of PLLA material into bone.[27,49,52,53,57] Unfortunately, their follow-up of 48 to 52 weeks was inappropriate to evaluate either tissue response or tissue replacement, because little or no signs of material degradation had taken place. Gatzka et al.[56] followed a series of patients after stabilization of ankle fractures

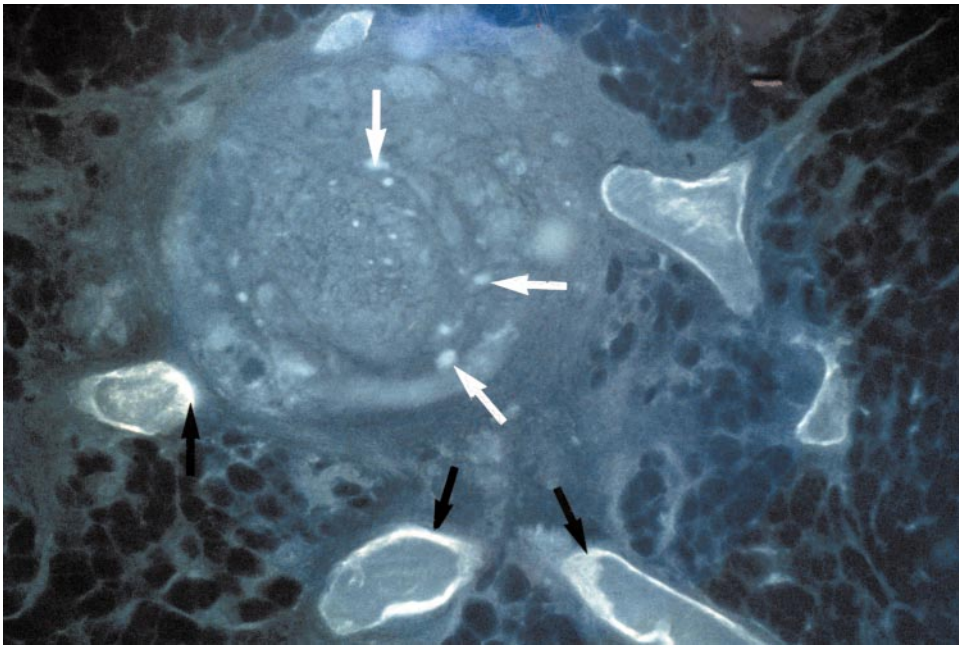

FIGURE 5. New bone trabeculae growing in the center of the former implant site 6 months after implantation of self-reinforced PGA pins in a sheep distal femur. The tetracycline fluorescence (black arrows) indicates the osseous activity. There are implant remnants left (white arrows). (Reprinted with permission.[46])

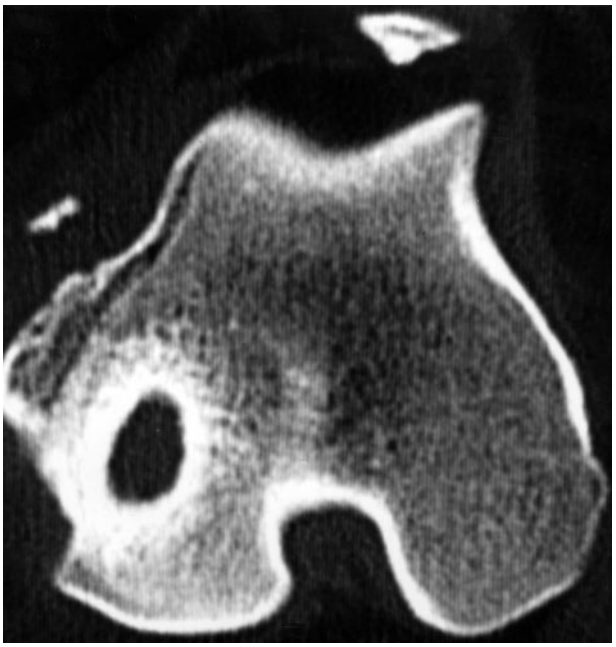

FIGURE 6. CT scan showing severe osseous sclerosis of an implant site 18 months after metaphyseal implantation of PLLA-co-PDLLA pins in a sheep.

with high molecular-weight PLLA screws.[56] In a study of MRI scans, they found that no osseous replacement of the implant had occurred up to 6 years after implantation (Fig 10). Pistner et al.[47] studied the intraosseous long-term fate of injection-molded PLLA and PLLA-co-PDLLA screws inserted in the femur of guinea pigs. After implantation of 150 weeks, they found that osseous replacement of the former implant site had occurred and, therefore, stated that amorphous polylactides are fully biodegradable materials. However, even for faster-degrading implants, the process of osseous replacement may require several years if there has been evidence of an osteolytic lesion during the final stage of degradation (Fig 12).

BIOCOMPATIBILITY AND CLINICAL CLASSIFICATION OF TISSUE RESPONSE

Since the mid 1960s, many studies have been performed to evaluate the suitability of various synthetic biodegradable polymers. Prompted by the results arising out of these investigations, biodegradable implants for various orthopaedic procedures have been introduced. However, the biocompatibility of these materials is still controversial.

The degradation process and tissue response have been documented by many authors. These studies show that biodegradable poly-α-hydroxy acids cause mild, nonspecific tissue response with fibroblast activation and the invasion of macrophages, multinucleated foreign-body giant cells, and neutrophilic polymorphonuclear leukocytes during their final stage of degradation.[47,48,51-53,57-62] The initial euphoria arising out of excellent clinical results was abated by the first reports of foreign-body reactions with biodegradable implants in fracture treatment. In 1987, Böstman et al.[63] re-

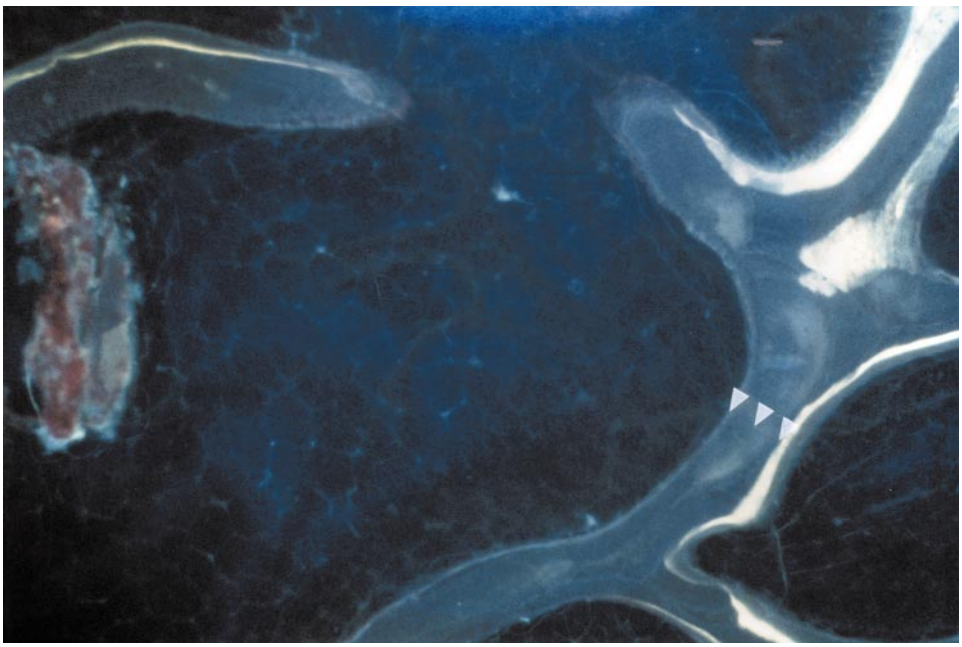

FIGURE 7. Implant site after 18 months of implantation of a self-reinforced PGA rod. Slow bony formation at the margin of the implant site; tetracycline labeling (arrows) 12 months before harvesting the knee (fluorescence microscopy with an almost selective tetracycline presentation).

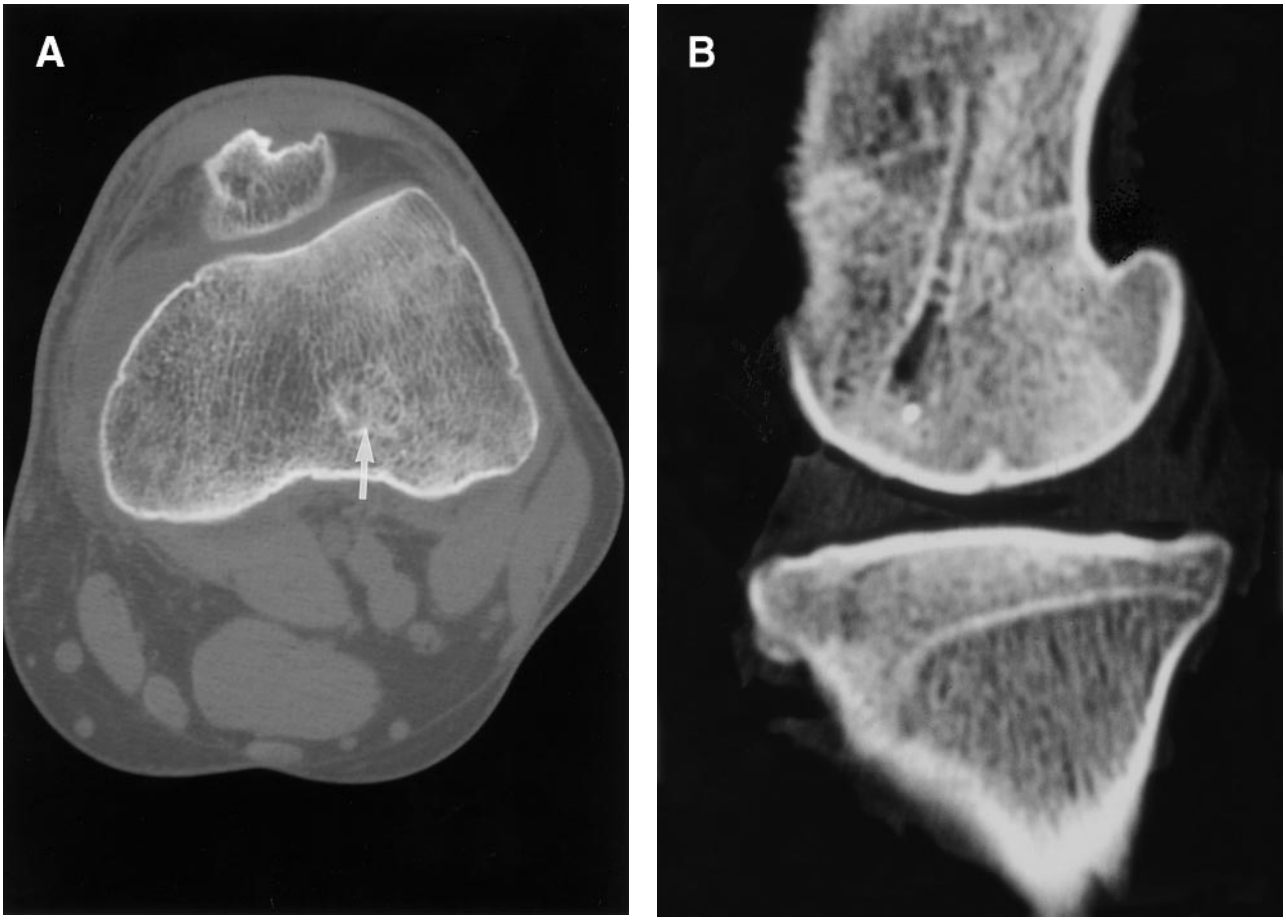

FIGURE 8. (A) CT scan 12 months after anterior cruciate ligament reconstruction with a patellar tendon graft fixed with a PDLLA-co-PGA interference screw. There is a complete osseous replacement of the former implant site (arrow). (B) CT scan 30 months after implantation of a PLLA-co-PDLLA pin in a sheep femur. There is almost a complete osseous restitution of the former implant site.

ported a sterile sinus formation after the use of PGA rods in ankle fractures. Since then, other reports have shown that foreign-body reactions to PGA implants occurred in varying degrees of severity ranging from mild osteolytic changes to intense granulomatous inflammatory soft-tissue lesions necessitating surgical intervention.[46,64-68] This reported intensive inflammatory tissue response was associated with the use of highly crystalline self-reinforced PGA implants, which consequently led to a decrease in their clinical use. However, these experiences led to deep concerns about the suitability of biodegradable implants in orthopaedic surgery.

Many different biodegradable polymers are currently available with better biocompatibility, such as PDS, PLLA including its stereocopolymers and copolymers, and some PGA copolymers. Because many factors contribute to biocompatibility and many different polymers are increasingly implanted, it is essential to have standards to compare the tissue response in experimental or clinical studies and to discuss these reactions strictly individualized for the different materials. Literature reviews on tissue reactions to PGA implants have highlighted the problem of the inability to compare results because of the lack of a well-defined classification system.[16,46] Therefore, we suggest a standardized classification system based on our previous investigations and clinical experiences.[46,51,66,69,70] Such a tool may enable us to gain more standardized information on the incidence and severity of tissue reactions in relation to the choice of polymer, implant design, or anatomic location.

Foreign-body reactions to biodegradable implants should be divided into osseous, extra-articular, and intra-articular synovial inflammatory soft-tissue responses. In each group, tissue responses are differentiated into 4 groups according to the severity of radiological and clinical findings.

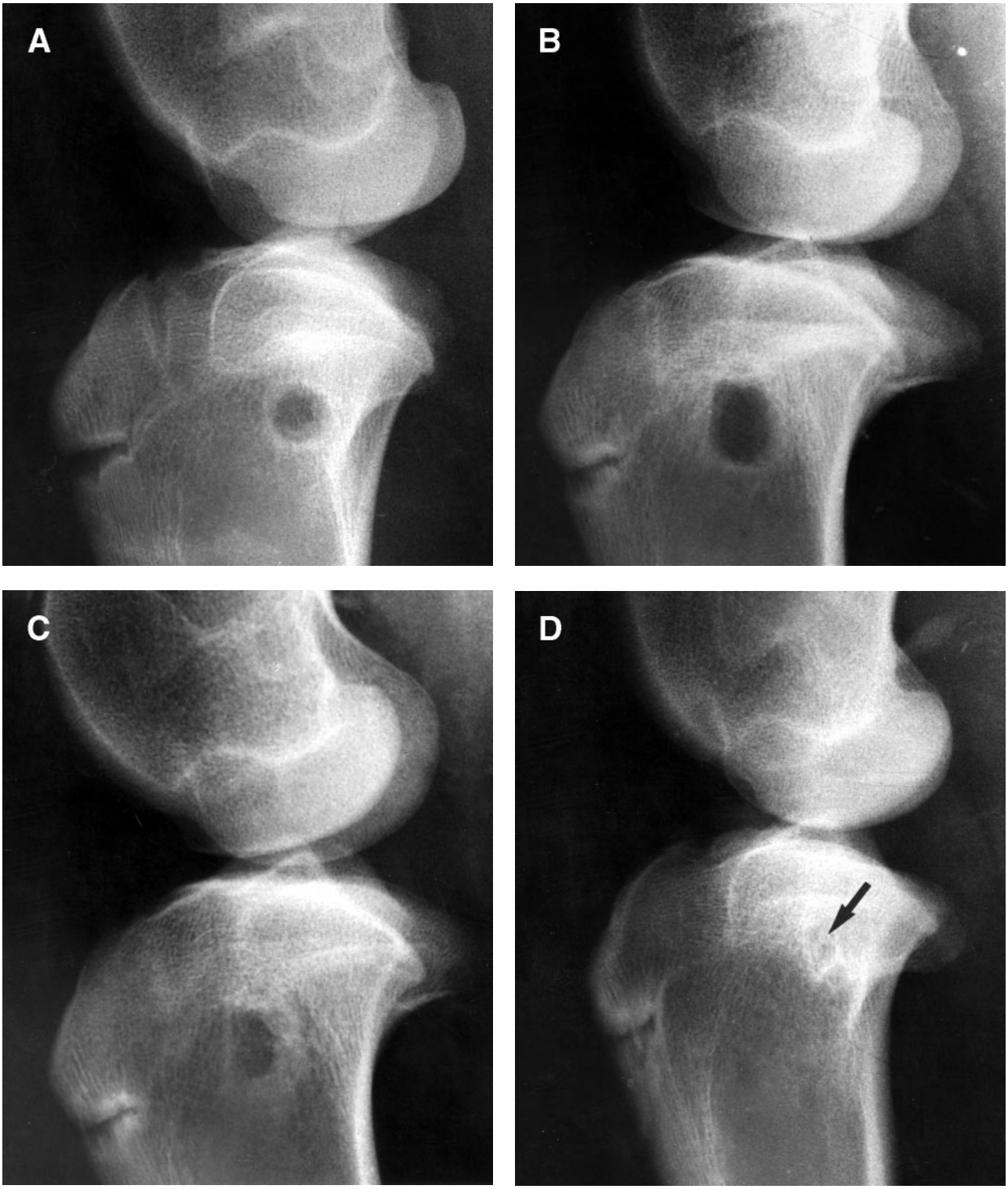

FIGURE 9. Radiographs after metaphyseal implantation of a PDLLA interference screw in a sheep tibia. After 72 weeks, the former implant site appears with an almost complete osseous replacement (arrow) after a transient mild osteolytic change (O-1) at 24 weeks. (A) Postoperative view, (B) after 24 weeks, (C) after 56 weeks, and (D) after 72 weeks.

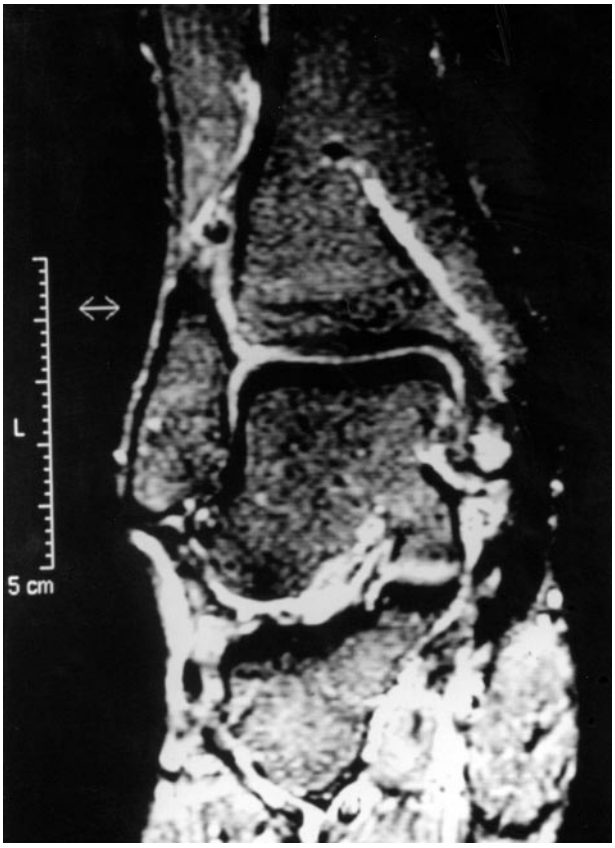

FIGURE 10. MRI 6.5 years after stabilization of a fracture of the medial malleolus with PLLA screws. There are no signs of an osseous replacement, but the hypointense signal indicates the degradation.

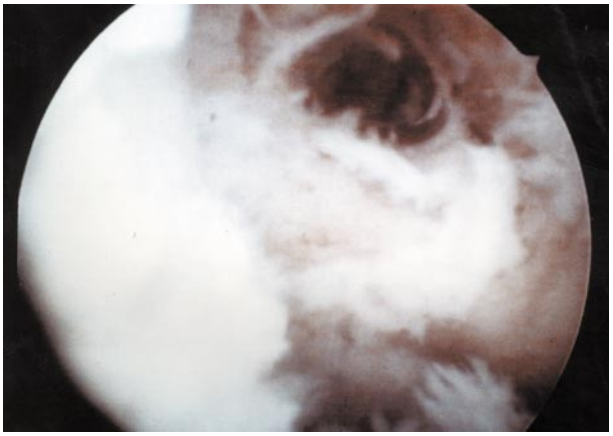

FIGURE 11. Arthroscopic view of the femoral fixation site of a patellar tendon graft 30 months after the use of a PLLA interference screw. Grossly, there are no signs of osseous ingrowth and the threading imprint is still visible.

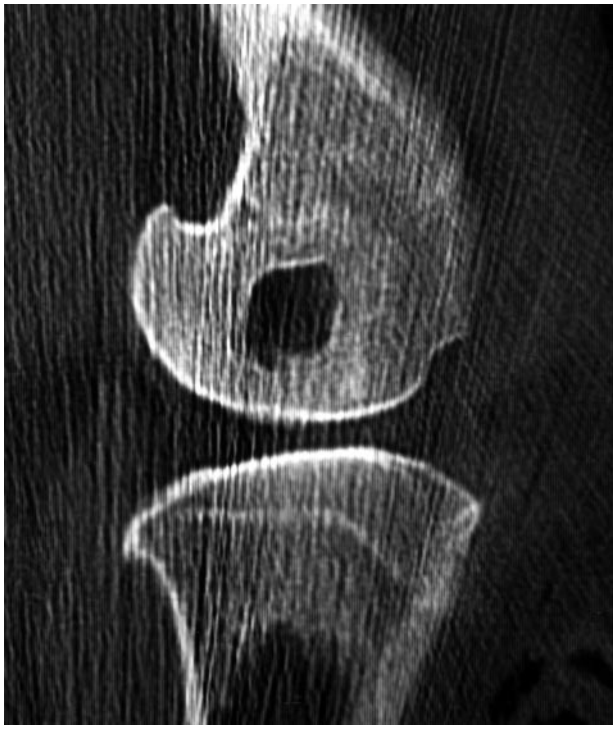

FIGURE 12. CT scan 24 months after implantation of a PGA pin in a distal sheep femur. There is still a moderate osteolytic lesion with no signs of new bone formation, although the implant site contained no PGA material after 6 months. (Reprinted with permission.[46])

Osteolysis

The first reaction at the implant site consists of bone resorption stimulated by the byproducts released during the degradation, and this is visible as radiolucencies on plain radiographs and computed tomography (CT) scans (Table 2). MRI scans are often appropriate to measure these lesions, but interpretation of findings may be difficult because of the reactive surrounding zone accompanying the final implant degradation.[71] Radiolucencies vary from mild osteolytic changes at the implant site to cystic-like extended resorption cavities (Fig 13A). Mild osteolytic changes probably have no effect on fracture healing, soft-tissue fixation, or the static properties of the bone.[71,72] However, if these changes exceed a certain level, they are likely to interfere with fracture healing (Fig 13B)[73] or graft fixation. The predictable osteolytic reaction described for PGA implants[46,65,68,74-77] has also been observed to be associated with the use of PLLA, PDLLA-co-PGA, PGA-co-TMC, and PLLA stereocopolymers, although with a lower incidence and intensity.[51,78-80]

Extra-articular Soft-Tissue Reactions

If the material is applied extra-articularly in soft tissue or in cancellous bone of the metaphysis, such as wrist or

TABLE 2. *Classification of Osteolysis (O) According to Hoffmann et al. and Weiler et al.*[46,69]

Osteolysis		Radiological Findings
O-0	None	No osteolytic changes visible
O-1	Mild	Osteolytic changes at the implant site (osteolysis 1 mm or larger than implant diameter)
O-2	Moderate	Cystic-like extended osteolysis (osteolysis 3 mm or larger than implant diameter, Fig 13A)
O-3	Severe	Confluence of osteolysis into a resorption cavity (if more than 1 implant is used)
O-4	Disturbed healing	Fracture displacement, fragment sequestration, or healing failure of soft tissue due to osteolysis (Fig 13B)

ankle fractures or the tibial interference screw in anterior cruciate ligament reconstruction, the debris accumulated at the implant site during degradation could be expelled into the surrounding soft tissue (Table 3, Fig 14). This can be followed by a progressive inflammatory response, manifesting as a subcutaneous soft-tissue induration or a fluctuant swelling that may perforate the skin and form a sinus (Fig 15). The incidence depends on the anatomic location and ranges from 4% to 14.6% in ankle fractures and from 22.5% to 40% in wrist fractures if self-reinforced PGA implants are used.[66,68,74,81] These reactions have also been observed with a much lower incidence and intensity for PDS or PLLA implants.[45,82-85]

Intra-articular Synovial Reactions

The intra-articular biocompatibility is of special interest in the field of operative sports medicine

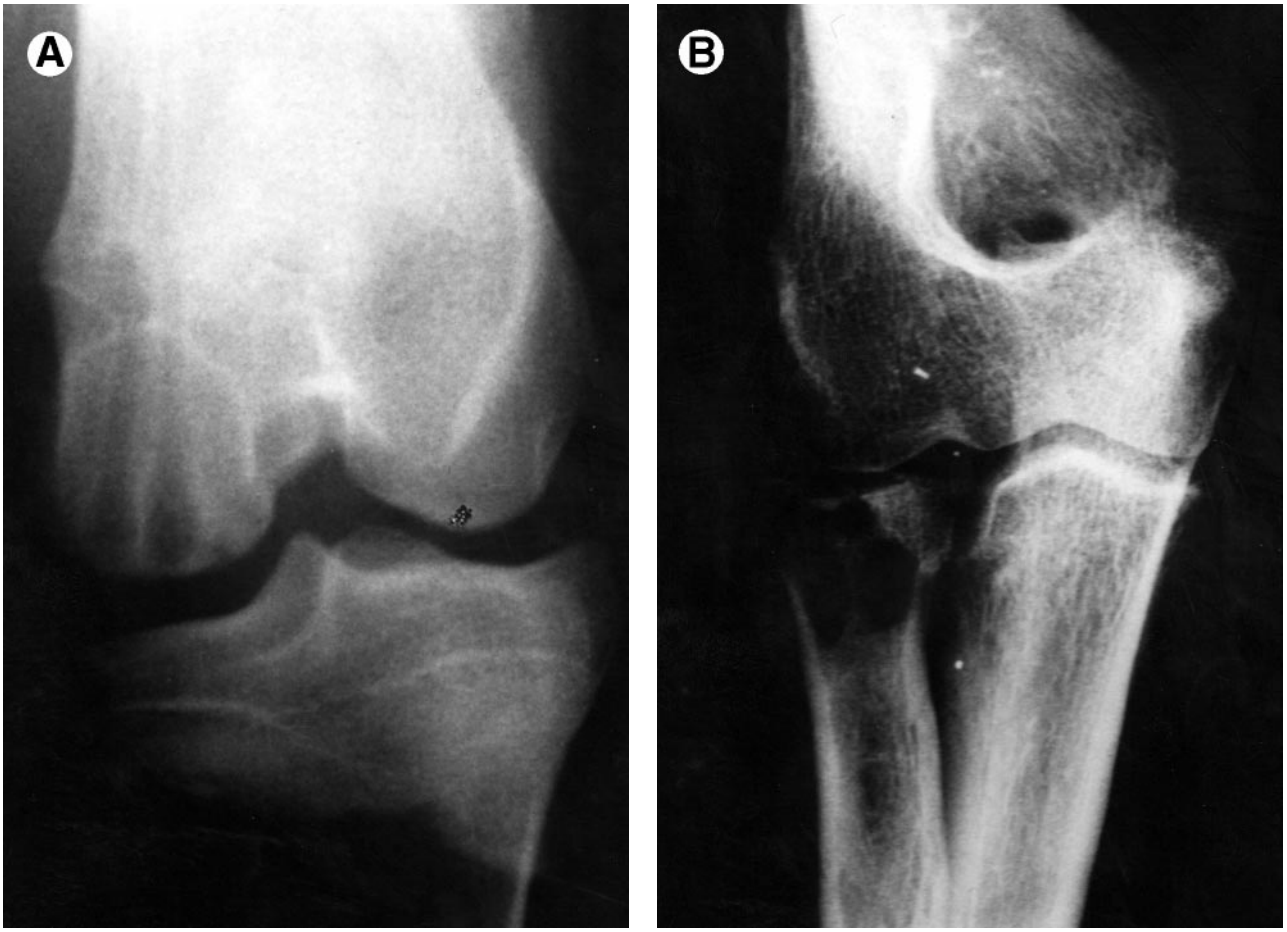

FIGURE 13. (A) Cystically extended resorption cavities (O-2) 12 weeks after osteochondral fragment fixation in a sheep with self-reinforced PGA pins. (Reprinted with permission.[46]) (B) Fracture sequestration (O-4) after stabilization of a multifragmentary radial head fracture with PLLA pins. The fracture situation has been considered to be unstable, and osteolyses occurred 6 months after surgery, although final material degradation is expected to occur later.

TABLE 3. *Classification and Treatment of Extra-articular Soft-Tissue Reactions (EA) According to Hoffmann et al.*[69]

Extra-articular Soft-Tissue Reactions		Symptoms/Findings/Treatment
EA-0	None	No or subclinical reaction
EA-1	Mild	Local, mild soft-tissue induration; no treatment
EA-2	Moderate	Fluctuant swelling, fluid accumulation (ultrasound), local warmth, reddening, swelling, pain; single or repetitive puncture necessary (Fig 15A)
EA-3	Severe	Spontaneous discharge of sinus, primary sterile, secondary possible bacterial contamination; debridement and open wound treatment (Fig 15B)
EA-4	Bacterial superinfection	Deep soft-tissue/bone infection following EA-2 or EA-3; extensive and repetitive debridement

because most implants are applied intra-articularly, such as sutures or tacks for meniscus or labrum repair, or the implant site may be connected with the joint space as in the case of interference screws or suture anchors (Table 4). Whereas osteolysis and extra-articular reactions are associated with the final stage of implant degradation, an inflammatory intra-articular response may also be associated with loosened fragments or wear debris released before implant degradation. This has been shown for the knee and shoulder joint[86,87] and may occur principally with tacks for labrum or meniscus repair. As soon as a connection between the implant site and the joint space exists, the synovial membrane can come into contact with the polymeric debris at the time of final degradation (Fig 16). Barfod and Svendsen[88] and Friden and Rydholm[89] reported cases of severe synovitis following intra-articular use of crystalline self-reinforced PGA rods. In these cases, crystalline polymeric debris surrounded by foreign-body giant cells could be identified as the cause. Recent reports describe a high incidence of loss of motion with synovial adhesions attributable to the inflammatory response after the use of PGA-co-TMC tacks in the shoulder joint.[39,90-92] Intra-articular synovial reactions vary from mild joint effusions to severe synovitis with the necessity of surgical intervention (Table 4).

As compromised biocompatibility is most commonly detected in the latter stages of implant decomposition, it is well accepted that the degradation byproducts are responsible for tissue reactions. Consequently, this implies that a large amount of byproducts being released per time unit from the implant cannot be adequately handled by the clearing capacity of the surrounding tissue. This mainly depends on the degradation kinetics of the implant. This process can last up to several years and influences the time schedule for experimental or clinical follow-up studies. Maximum extent of foreign-body reactions associated with PGA implants should occur approximately 12 weeks after

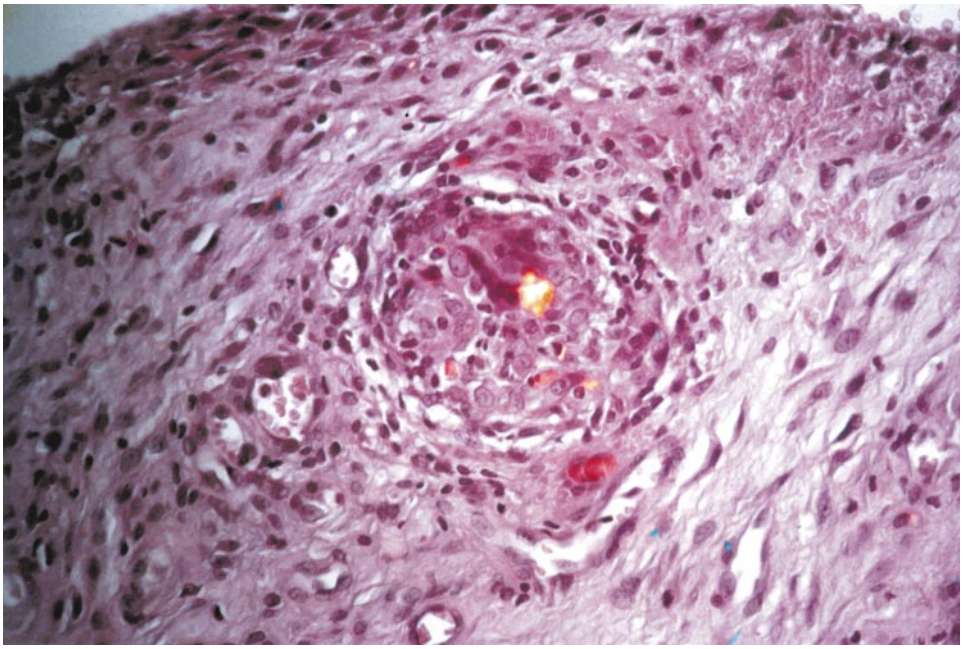

FIGURE 14. Histology of the discharge after a sterile sinus formation shows leukocytes and foreign-body giant cells surrounding the birefringent PGA particles (polarized light).

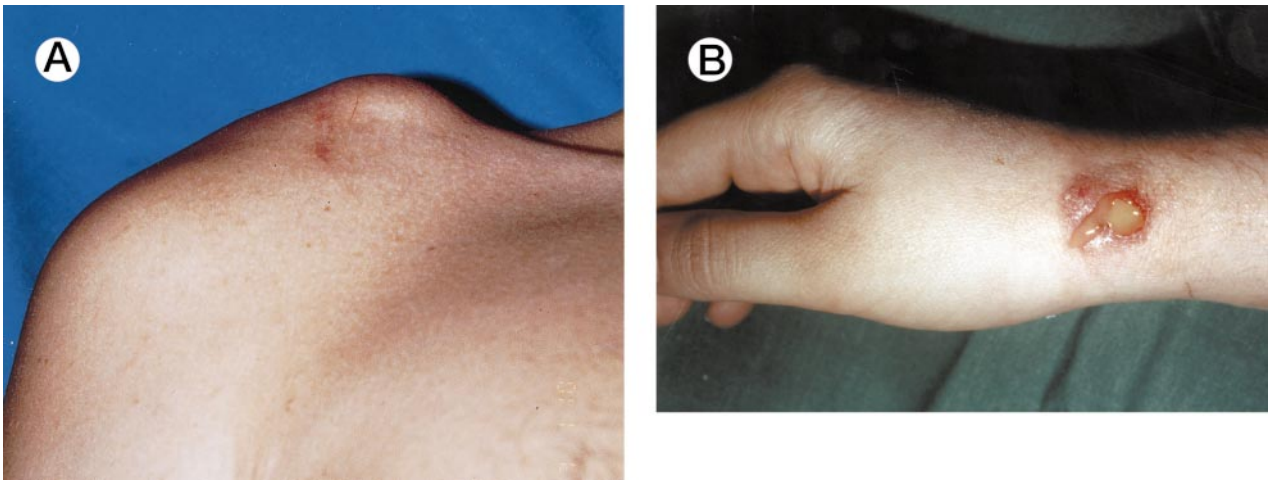

FIGURE 15. (A) Subcutaneous fluctuant swelling (EA-2) after reduction of a Rockwood type V acromioclavicular joint separation with a PDS band. (B) Spontaneous discharge of debris (EA-3) after stabilization of a wrist fracture with self-reinforced PGA rods. (Reprinted with permission.[69] Copyright 1997 by Springer-Verlag.)

surgery.[46,57] Those accompanied with PDS, PGA-co-TMC, or PDLLA-co-PGA may occur between 8 and 24 weeks after implantation. With the few reported cases of foreign-body reactions associated with PLLA or PLLA-co-PDLLA implants, they may occur between 1 and 2 years at the earliest but normally occur later, depending on implant processing techniques, stereocopolymer composition, implant design, and molecular weight.[51,82,85,93]

As for soft-tissue reactions, it is reasonable to assume that fast accumulation of implant fragments or low molecular-weight byproducts cannot be handled adequately by the clearing capacity of the tissue, represented by macrophages and polymorphonuclear leukocytes. Therefore, soft-tissue reactions are mostly associated with fast-degrading implants, such as those composed of PGA. However, they may also be observed for PLLA if the implant volume exceeds a certain level and the local clearing capacity of the tissue is overloaded.[82]

It is known that debris of degradable or nondegradable materials, such as polyethylene or polymethylmethacrylate, leads to an inflammatory tissue response if the particles get phagocytosed by macrophages.[18,62,94,95] In addition, macrophage activation leads to bone resorption via mediator release, which results in osteoclast activation.[96-98] This may account for the appearance of osteolytic changes with the use of biodegradable implants, because maximum macrophage accumulation at the tissue-implant interface correlates with the maximum expansion of osteolysis, as it has been described for PGA implants.[46,57]

As an important factor, there are several reports that the local decrease in pH at the implant site during the degradation is 1 of the main reasons for the inflammatory tissue response.[99-101] On the contrary, in a recent

TABLE 4. *Classification and Treatment of Intra-articular Synovial Reactions (IA) According to Hoffmann et al.*[69]

Intra-articular Synovial Reactions		Symptoms/Findings/Treatment
IA-0	None	No or subclinical reaction
IA-1	Mild	Mild (sterile) joint effusion, no additional local or systemic signs of inflammation, single need for puncture, foreign-body giant cells, round cells, or implant remnants in puncture fluid or synovial membrane
IA-2	Moderate	Significant (sterile) joint effusion, no other additional local or systemic signs of inflammation, need for recurrent puncture, foreign-body giant cells, round cells, or implant remnants in puncture fluid or synovial membrane; administration of nonsteroidal anti-inflammatory drugs, partial weight-bearing until disappearance of symptoms
IA-3	Severe	Significant (sterile) joint effusion with local signs of inflammation (pain, reddening, warmth), need for recurrent punction or surgical revision (e.g., arthroscopic synovectomy), foreign-body giant cells, round cells, or implant remnants in puncture fluid or synovial membrane
IA-4	Bacterial superinfection	IA-1 to IA-3 and positive microbiological examination, arthroscopic or open debridement with lavage and synovectomy

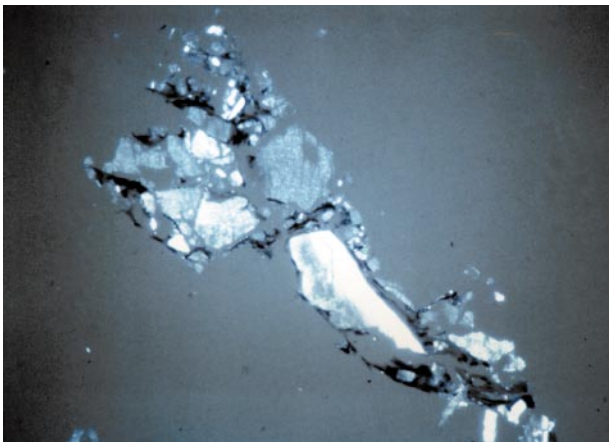

FIGURE 16. Synovium of a patient at rearthroscopy 30 months after implantation of a highly crystalline PLLA interference screw. There are birefringent implant remnants, although the implant site grossly showed no material remaining (see Fig 11).

study, Ignatius and Claes[102] were able to show that the accumulation of PLLA-co-PDLLA or PLLA-co-PGA degradation products itself may reduce growth in cell culture. The toxic influence was dependent on a high concentration of degradation products after pH adjustment.

It is reasonable to assume that a protracted degradation is of primary importance in increasing the biocompatibility of a biodegradable implant, especially with regard to the soft-tissue response. But even slow-degrading and amorphous polymers may provoke osteolytic changes if there is insufficient drainage of byproducts in the surrounding tissues or when the cellular clearing capacity may be overloaded.

However, other factors appear to contribute to biocompatibility. Matlaga et al.[103] and Lam et al.[104] showed that even the implant shape affects the intensity of an inflammatory response using degradable and nondegradable polymers. This has largely been discussed for the self-reinforcement of PGA implants but has not yet been proved. Additionally, mechanical instability at the implant site may accelerate degradation and may consequently lead to a higher amount of degradation products being released per unit of time, thus possibly increasing the host-tissue response. Furthermore, the crystallinity of a biodegradable implant, which prevents late hydrolytic degradation, can result in a foreign-body reaction.[44,104-106] Thus, use of materials with low crystallinity has been advocated for medical purposes.[107]

Synovial reactions are associated with the release of implant fragments into the joint space. This rare but severe complication was observed with the use of PGA, PGA-co-TMC, or PLLA implants in the knee and shoulder joints.[39,46,86,88-92,108,109] This specific synovial reaction to polymeric particles also occurred with a high incidence using artificial nondegradable ligaments for cruciate ligament reconstruction.[110-114] Ligament wear particles were identified as the cause,[115-117] and recent clinical observations and an experimental study have shown that these wear particles are deposited in the draining lymph nodes.[118,119] This phenomenon has also been described for crystalline PGA and PLLA implants, which suggests that only incomplete degradation of highly crystalline materials occurs[46,120] (Fig 1). Future studies should take into consideration the fact that crystalline implant remnants may provoke late synovial reactions; for example, if highly crystalline PGA, PLLA, or PGA-co-TMC implants, such as tacks and pins for labrum and meniscus repair, are used intra-articularly. The fatal long-term results of these reactions after stabilization of ankle fractures with PGA rods has recently been described.[108] Böstman[108] reported the development of a moderate to severe osteoarthritis of the ankle that occurred 36 to 109 months after surgery in 10 of 74 patients who had previous inflammatory soft-tissue reactions. He concluded that the joint damage seemed to be caused by polymeric debris entering the articular cavity through an osteolytic lesion.

CONCLUSION

The use of biodegradable implants offers distinct advantages in the field of operative sports medicine. Thus, research and development of biodegradable implants should be given high priority. The research on these devices should be encouraged by the will to define and solve problems and to find technical solutions, rather than driven by the desire for quick results.

Concerns about the poor biocompatibility of self-reinforced PGA implants do not necessarily apply to other materials with an appropriate tissue response. Biocompatibility depends on a large variety of factors. Therefore, each biodegradable implant should be tested regarding its intraosseous, soft-tissue, and intra-articular biocompatibility, and discussion of the results should be strictly individualized for each of the different polymers, copolymers, and stereocopolymers. Furthermore, in vivo long-term studies are necessary, with follow-up until implant remnants have disappeared and an osseous replacement has taken place. To gain more information on biocompatibility according to the specific choice on polymer and

implantation site, the clinical use of biodegradable implants is recommended to be performed under study conditions, and all results concerning tissue response should be evaluated with a standardized classification system.

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