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REVIEW

Osteointegration of orthopaedic devices

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Abstract The different properties of bone must be considered in order to understand the relation between orthopaedic devices and bone. The epi-/metaphyseal areas are defined by their rigidity, their high vascularity and their quick remodelling process. In contrast, the diaphyses of bone are rather elastic and built of dense, scarcely vascularised bone presenting slow remodelling. Implants can integrate by pure mechanical contact without real affinity to bone or, alternatively, they can favour ongrowth of bone, provided that they are osteoconductive. Amongst different bone substitutes, only some of them are absorbable. Only derivates of bone may present the property of osteoinduction, which is the power to create new bone in any region of the body. Orthopaedic devices are characterised by their shape, their stiffness or elasticity and by the characteristic properties of material. They may be osteoconductive such as titanium alloys and some ceramics, allowing integration in bone. Alternatively, other materials such as steel, CoCr alloys and PMMA cements remain separated from bone by a tiny layer of collagen. The surface structure influences the quality of integration. The integration of implants depends on the mutual interaction of the material with the tissue on the implantation site. All implants undergo fatiguing which can lead to fracture of the implant. All implant–bone contacts are threatened by granulation tissue mainly formed because of wear products, infection and other reasons.

Keywords Osteointegration · Orthopaedic implants · Prosthesis · Bone substitutes · Osteoconduction · Osteoinduction

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Introduction

The aim of this article is to analyse the interrelation between bone and orthopaedic devices. To understand the great variability of the reaction of bone towards implants, one has to consider not only the different mechanical properties but also the various remodelling processes of the different regions of bone. On the other hand, orthopaedic implants are extremely variable regarding their material, shape, size, surfaces and overall mechanical properties. It is the purpose of this article to present these different aspects individually. On this basis, the consequences for the relation between implants and bone are presented. In addition, the factors impairing or loosening the mechanical contact will be analysed.

This review is mainly based on clinical experience and experimental activity in the field of development and application of bone substitutes. In order to simplify understanding, most examples illustrated in this article are taken out of the area of hip and femur.

Bone as a recipient for orthopaedic devices

Today, nearly all regions of the skeleton are reached by surgery and therefore are potential sites for an orthopaedic device. However, the mechanical properties are far from being uniform. For physical reasons, the mechanical resistance of bone is much stronger in the lower than in the upper extremity.

The epi-/metaphyseal area of a long bone such as the femur (Fig. 1) is of high rigidity and guarantees the congruency of the joint during function. This stiffness is a result of the diameter of the bone, which is relatively important in the joint region as compared to the diaphysis. The network of bone trabeculae typical for the cancellous

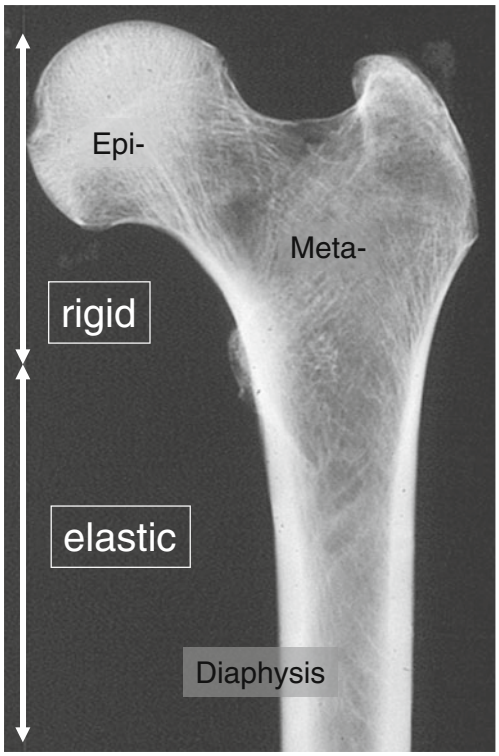

Fig. 1 Changing elasticity in long bones. Radiograph of the proximal femur. Cancellous bone trabeculae form a tight network leading to a rigid system. This architecture gradually changes in the metaphysis in the more elastic cortical tube of the diaphysis

bone adds to a high stiffness requiring only a small quantity of bone. If permanently set under high stress, the trabecular system strengthens [1]. In older people, especially in women, cancellous bone gets thin and brittle, a process which is called osteoporosis. The vascularity of the epi-/metaphyseal region is high, based on an extended system of sinusoids. It is therefore not surprising that remodelling and fracture healing of bone is relatively quick in this region. The remodelling or constant renewing of bone is based on the one side on the gradual absorption of the bone trabeculae by osteoclasts and on the other side on the building of new bone with osteoblasts. Overcharge of the epi-/metaphyseal area results in a combination of fractures and a crush of the trabecular system leading to a loss of substance, which is often prominent in old osteoporotic bone [2]. After reposition of a fracture, frequently gaps are remaining, especially in patients with osteoporosis. Filling of such bone defects has to be considered. On the other hand, restoration of vascularity seems less of a problem. Periarticular bone defects can be filled with nearly any kind of substance, whether it is rigid or elastic, because the surrounding is rigid. A very rigid ceramic block for instance will be accepted in such an environment (Fig. 2). Preferably, one should use substances able to integrate or even to undergo remodelling.

The diaphyseal area is characterised by its tube of relatively small diameter and built of cortical bone, which gradually thickens in the direction of the joints. In contrast, in the meta-/epiphyseal area, the thickness of the bone wall diminishes and later gets dissolved in a cancellous bone structure. The density of cortical bone is high and its resistance remarkable. Nevertheless, the cortical tube shows a remarkable elasticity. It is vascularised by very small vessels. They follow the longitudinal Haver canals of the osteons which are the basic elements of the cortical bone. In addition, they also follow the transverse Volkmann canals. The permanent remodelling consists of a constant new building of osteons. Osteoclasts carve new longitudinal tunnels followed by osteoblasts building and subsequently the bone layers of new osteons. Remodelling in the diaphysis is about ten times slower than in the epiphyseal area. Diaphyseal fractures may consist of a simple fracture line. However, if they are caused by a high-energy trauma, fractures with multiple fragments can occur. Such bone fragments are generally devoid of the periosteum and therefore devascularised and dead [2]. In contrast to the joint area, there is no real loss of substance in the diaphyseal area, but putting the puzzle together would rather lead to a further extension of devascularisation. The bridging of a shattered area is not easy in this elastic region. A rigid implant such as a hydroxyapatite block is only partially integrated in the elastic diaphyseal area (Fig. 3). The reconstruction material must therefore be of adequate elasticity in order to be able to integrate.

As a rule, a device adapts to the place of its integration without major problems if it is of the same or of higher elasticity than the place of its integration. On the other hand, the situation must be forced if more rigid implant is placed in a bone area which is more elastic. This is the case if a CoCr alloy femoral prosthesis is cemented in the medullar canal of the proximal femur (Fig. 4).

Different ways of integration of devices in the bone

Devices can be integrated in the bone in different ways. A device may be linked with bone just by mechanical fit. Examples are screws placed in a predrilled and tapped hole or a prosthesis impacted in the bone after having prepared a cavity in the bone with the corresponding shape of the implant. Between the device and the bone, nature usually forms a thin layer of collagen tissue separating bone and device. The transmission of forces through such a link depends on the interconnection of the rough surface structures of bone and implant. For an optimal result, remaining little gaps between device and bone should be filled. The classic filler is PMMA cement, which leads to

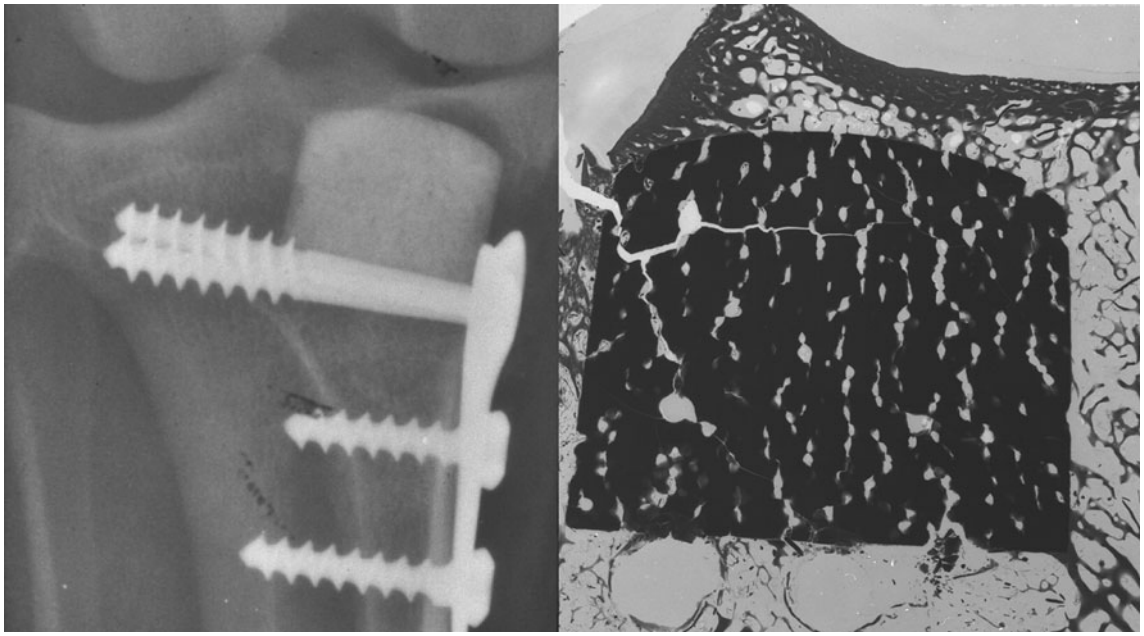

Fig. 2 Rigid implant in a rigid environment. A rigid, mainly dense hydroxyapatite block is placed in the tibial head of a dog and fixed with a plate. The microradiography of the specimen, analysed 3 months after surgery, shows a perfect integration in the rigid epi/metaphyseal area with many bone trabeculae growing on the surface of the block

immediate stability after its polymerisation time of about 10 min (Fig. 4). Force transmission leads to adaptation of the surrounding bone structure to the novel biomechanical situation over the following years after implantation.

A few materials initiate bone to grow over them, thus helping to a much tighter fixation. This phenomenon is called *osteoconduction* [3]. By this process, the device becomes an integrated part of the skeleton without an

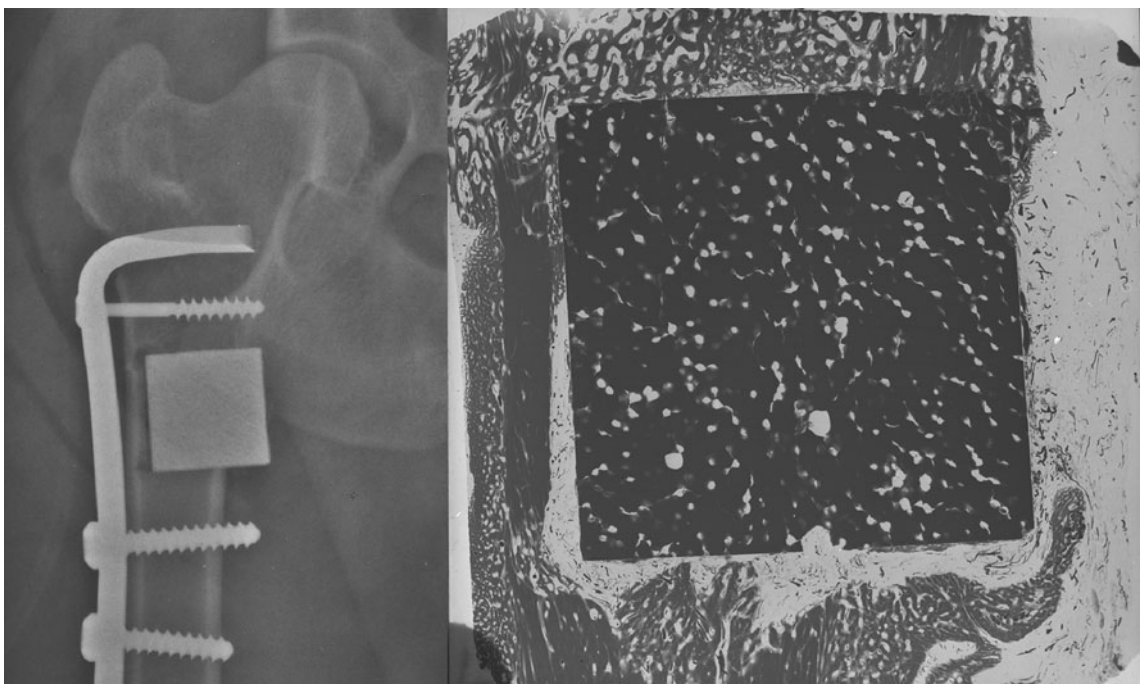

Fig. 3 Rigid implant in an elastic environment. A block of dense hydroxapatite is impacted in a subtrochanteric defect leaving the lateral cortex untouched. The area is bridged by a lateral condylar plate, securing stability but leading to a great elasticity of the defect area. After 3 months, the block is integrated at its proximal border, showing some osteoconduction on the medial surface. However, the lateral and the distal borders are not integrated. There is a non-union due to the rigidity of the block

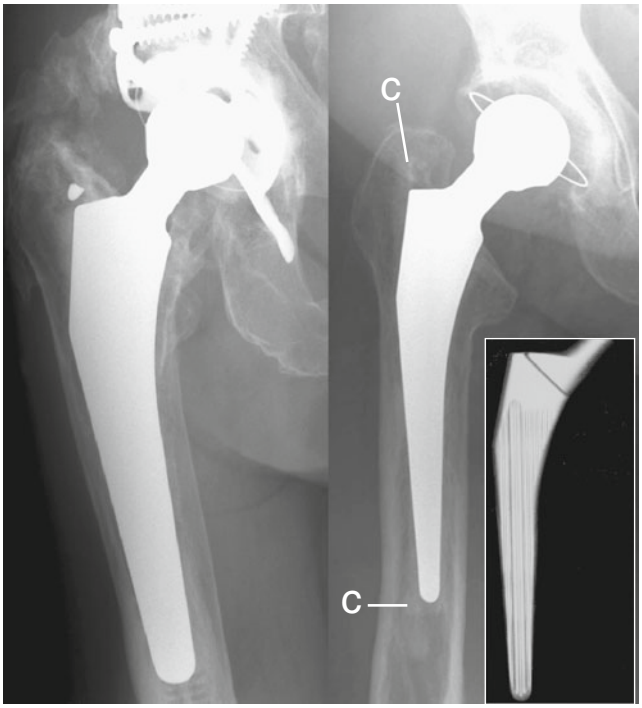

Fig. 4 Device shaped to the bone; different sizes influence the stiffness. Radiographs of a cemented straight stem prosthesis according to ME Müller produced out of the stiff CoMiCrMo alloy (*insert*) in two patients 20 years after implantation. Both prostheses show an excellent result, although the *left* prosthesis is of a much bigger size and therefore much more rigid than the one on the *right*. The thinning of the diaphyseal bone is more pronounced on the left side with the stiffer prosthesis. *C*, cement

intervening layer of collagen tissue. The transmission of forces between bone and device is favoured. This integration process takes time. It is facilitated by a fairly good congruence between bone and device which helps to avoid complications (Fig. 5). The integration of an osteoconductive device follows general rules. Initially, bone grows on the device where there exists direct contact with living bone. Later, bridges are built along loose bone particles being in contact with the living bone and the device. Finally, the bone can further expand on the surface of the device. On the basis of this tight mechanical contact, the load passes through the connecting bone bridges to the device and vice versa. Related to the sustained forces, functional reorientation occurs, a process which is called remodelling of bone. The implant becomes a functional part of the host bone. In this way, integrated plates may take over part of the function of cortical bone (Fig. 6). The acetabular implant can take over the function of the subchondral bone layer and the trabecular bone structure adapts to this situation (Fig. 7, left).

As described above, bone undergoes constant remodelling. Most devices do not take part in this process and remain inert, not changing their structure over time. They are *non-absorbable* and inhibit remodelling with the aim of

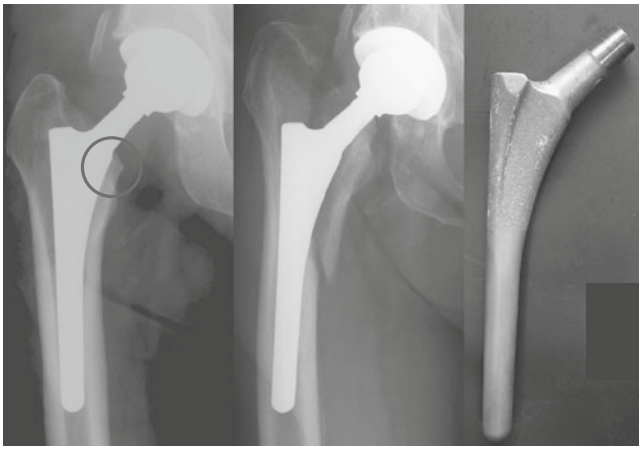

Fig. 5 Insufficient adaptation of the shape of an implant to the bone. This femoral component is more conic and roughly blasted in the upper part but cylindrical and smoothly blasted in the lower half. It is made of the rather elastic and osteoconductive TiAlNb alloy. This shape causes an overcharge by a point contact between the prosthesis and the area of the osteotomy of the collum (*left panel*, *grey circle*). Beginning ongrowth of bone on the roughly blasted part (*right panel*, small white bone islands visible) was too slow to inhibit a fracture due to local overcharge (*middle panel*)

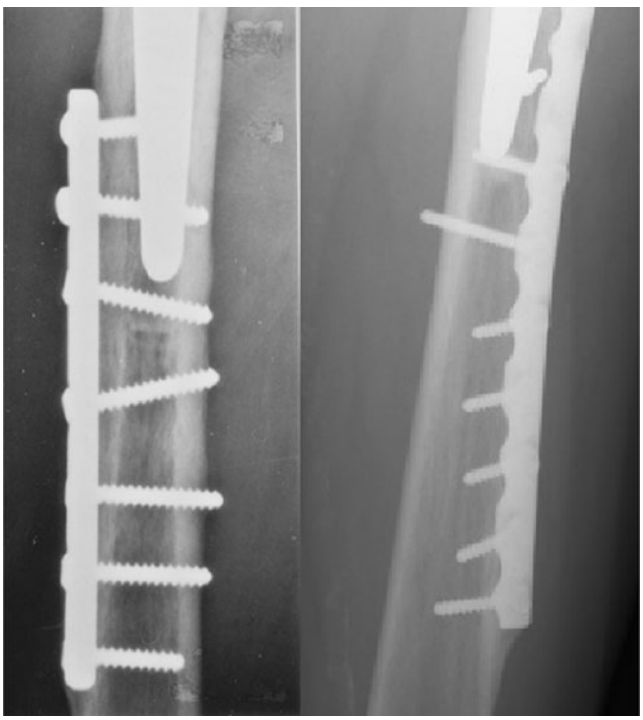

Fig. 6 Ductility of implants. Difference of integration of different metals in bone. Two different plates are used to bridge a periprosthetic femoral fracture. The plate on the *right* had to be shaped to the bone to fit. *Left panel*: radiograph 8 ½ years after plating with a steel plate. *Right panel*: radiograph 9 ½ years after plating with a titanium plate. The steel plate is not fully integrated. It remains separated from the bone by a tiny layer of connective tissue. The original cortex of the diaphysis remains. The titanium plate gets integrated without separating connective tissue and thus gets integrated in the structure of the bone. The cortex of the diapyhsis shows a loss of density in the cortical area under the titanium plate

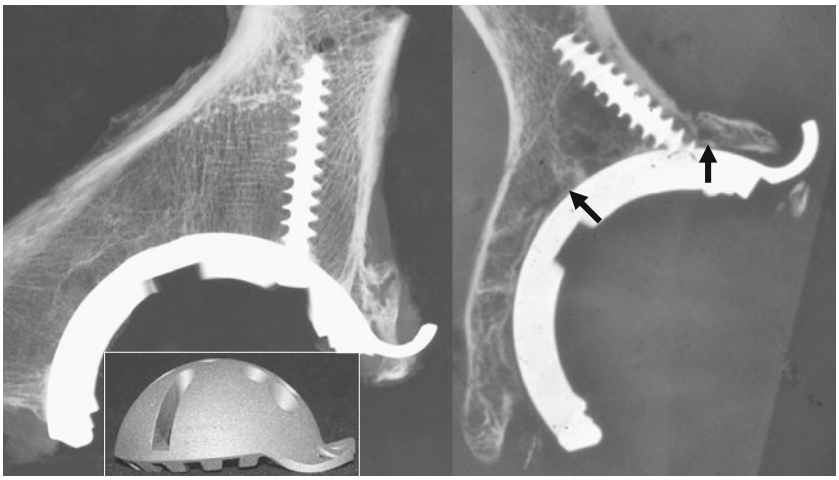

Fig. 7 Variability of bony integration of a SL-cup according to ME Müller out of titanium with roughly blasted surface (*below left*). Radiographs of slices of bone including the prosthesis of two post-mortem specimens with a thickness of 5 mm. *Left panel*: full integration of the whole surface of the implant by many bone trabeculae growing on it. *Right panel*: earlier subchondral sclerosis has vanished. Bony integration only took place between the two *arrows*. In the remaining area, the slightly sclerotic bone is separated from the implant by collagen tissue as analysed in histologic sections. *Screws*: the screws fixing the acetabular implants present a tight contact with the surrounding bone but, being smoothly blasted or polished, they still can be removed quite easily

restoring a fully natural situation. Sintered hydroxyapatite ceramics are a prototype of this category (Figs. 2 and 3).

A few devices are *absorbable* by nature [3]. As a rule, they are products which are preparations or imitations of natural products. This means that they are cleared away by the natural remodelling process. Deproteinised bone or tricalciumphosphate are such substances [4]. This possible absorption is by no way compulsory. It mainly takes place in areas where the skeleton is weight-bearing and where bone remodelling is relatively active.

Osteoinductive materials are able to initiate the formation of bone at the place where they are implanted. This can even be outside of the bone, e.g. after placement in a muscle or in a segmental bone defect. In the presence of such materials, mesenchymal cells are transformed in bone-forming osteoblasts. Osteoinduction is restricted to bone or specific organic fractions of bone (see below).

The term *osteogenicity* is restricted to living osteoblasts being transplanted, for instance, by fresh autologous bone graft in a bone defect, where they remain able to produce bone. Usually, only a minority of osteoblasts survive such a transplantation.

Osteoblasts have a much better chance to survive if they belong to a fragment of living bone placed in a defect. However, contact with the adjacent bone and conservation of the blood circulation by anastomosing at least one artery and one vein are required. In such a free vascular bone graft, the bone forming capacity is conserved including its ability for remodelling. The contact areas between a vascular graft and the host bone bridge the gap, similar as they do it in a vital fracture area.

Various properties of orthopaedic devices

Orthopaedic devices have to be adapted to the mechanical properties of the place of the skeleton they are constructed for and the purpose of their use. Whereas a prosthesis has to resist lifelong against fatiguing, a plate for osteosynthesis of a fracture only temporary takes over the force transmission to allow bone to restore.

The *shape of implants* has to fit with the site of application. As an example, the cemented straight stem prosthesis of ME Müller is the original of hundreds of imitations and further developments. It has been produced to be placed in the proximal femur. Different sizes fit for the various femurs (Fig. 4). Choosing a non-cemented prosthesis, the congruence between bone and prosthesis must be more precise to allow immediate full-weight bearing and to favour ongrowth of bone on the prosthesis. Even apparently little changes of the shape of prosthesis can result in insufficient contact between bone and prosthesis and so to unexpected risks (Fig. 5).

The *ductility* of an orthopaedic device is crucial if it has to be adapted to the bone. This property is required in certain plates produced for osteosynthesis [5]. Such plates require a material allowing a change of shape without substantial loss of resistance against fatigue (Fig. 6).

Different metals have different properties concerning integration with bone. Steel and cobalt–chromium alloys have no osteoconductive power. They are always separated from bone with a layer of collagen tissue. A steel plate used for the osteosynthesis of a fracture does not take over an essential part of weight bearing after healing. The structures of bone remain more or less unchanged. On the other hand,

titanium and some titanium alloys show osteoconduction [5]. Plates, screws or prostheses made of these materials get integrated in the bone without intervening collagen tissue and therefore can take over part of the mechanical function of the host bone. This leads to integration in the mechanical structure of bone. For this reason, a steel plate is much easier to remove than a titanium plate (Fig. 6).

Stability in the contact area between implant and bone is the prerequisite for its osseous integration. The osteoconductive power of an implant is not sufficient to guarantee ongrowth of bone on its whole surface. The distance between implant and bone may be too large or the stability between the touching surfaces may not be achieved (Figs. 2, 3 and 7). The extent of the contact area and the absence of relative movements between bone and implant are crucial for success or failure, respectively (Figs. 5 and 7, right).

Elasticity or rigidity of implants is of great variation. Any given implant increases in rigidity if it is produced out of the same material but in a larger size (Fig. 4). On the other hand, an implant of the same shape can greatly differ in rigidity if it is produced out of different metals (Fig. 8). Not considering the influence of the greater elasticity of TiNbAl versus CoNiCrMo, the cemented Müller Straight Stem was changed to the titanium alloy. After a few years early, loosening was observed especially in small-sized prostheses. Heavy labourer such as farmers and men with small-sized prostheses most frequently suffered from early loosening [6]. Resistance against fatigue of PMMA cement is much lower than the one of metals. Therefore, in cemented prostheses, PMMA cement has to be protected with a rigid prosthesis from precocious degradation by fatigue in order to avoid early loosening of the prosthesis.

The *surface finish* of orthopaedic devices may be polished, smooth blasted or rough blasted. A polished device produced of a non-osteoconductive material does not show osteointegration. The surface remains separated from the bone by a layer of collagen tissue as mentioned above. It locks with the bone by its shape and can usually be removed easily (Fig. 6, left). Prosthesis or screws out of titanium alloys can also be (partially) polished. Such implants undergo osteointegration without intervening collagen tissue but still can be removed—if wanted—with relatively little effort (Figs. 7 and 9). The fixation of bone on rough-blasted surfaces of titanium, on the other hand, is so tight that bone is removed with the device (Fig. 9), whereas rough-blasted steel or CoNiCrMo alloy does not help to ongrowth of bone.

The *surface structure of an orthopaedic device* may be flat or may present longitudinal grooves (Figs. 4 and 5) or ribs (Fig. 9) or pores (Figs. 2 and 3). Such an outside structure may be important for the anchorage of a non-cemented prosthesis in the bone or a cemented prosthesis in the cement [7].

Composite implants are frequently used. Cement and prosthesis form together a combined implant of a particular and unique shape (Figs. 4 and 8). By pushing

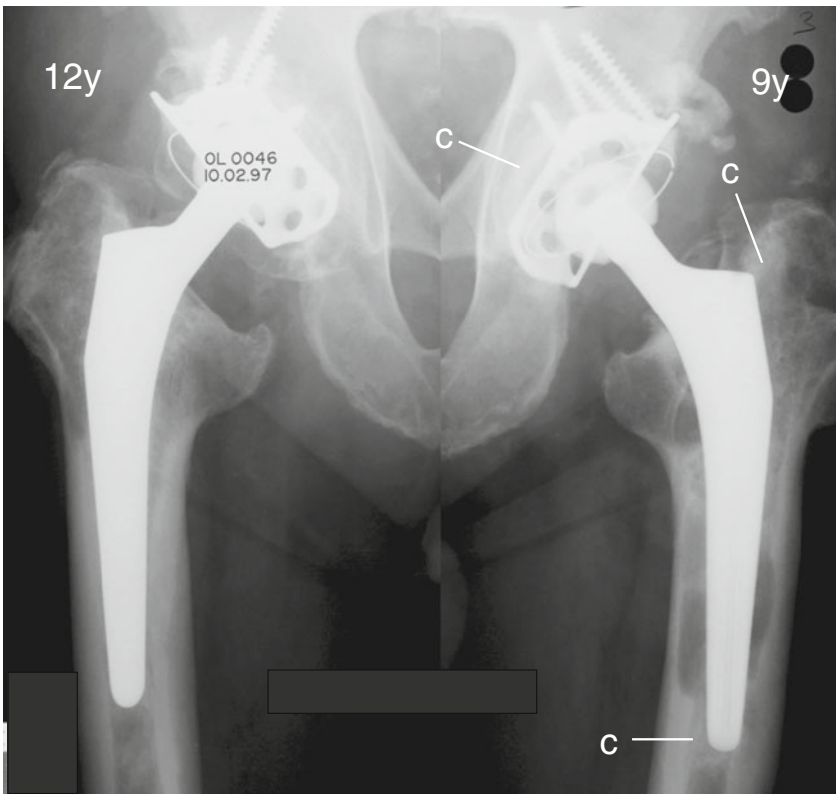

Fig. 8 Influence of metals with different elasticity on the longevity of cemented prostheses. *Left panel*: 12 years after the implantation of a straight stem according to ME Müller forged out of CoNiCrMo with perfect integration. *Right panel*: 9 years after the implantation of an identical stem forged out of TiNbAl with disastrous loosening due to precocious fatiguing of the PMMA cement by the titanium stem which was too elastic for this application. *C*, cement

Fig. 9 Roughly blasted—polished. A well-integrated non-cemented prosthesis out of Ti NbAl had to be removed because of infection. Bone trabeculae remained fixed on the roughly blasted surface, whereas the polished distal end could be removed without adherent bone

the prosthesis in the cement which is previously filled in the medullar cavity, the cement is pressed in between the cancellous trabeculae surrounding the prosthesis (Fig. 10). By this manipulation, a complex implant combined out of metal and cement is created. This cemented implant anchors deeply in the cancellous area, taking advantage of all irregularities of the adjacent bone. Over the years, remodelling of the surrounding bone adapts to the actual force transmission (Fig. 4). This process leads to cortical atrophy of the surrounding bone [8]. The stability between cement and metal is threatened if the PMMA cement undergoes fatiguing (Fig. 8) or if wear particles of the joint partners penetrating in the bone–cement interphase induce loosening in the cement–bone contact area (Fig. 11). Many non-cemented prostheses are covered by a layer of hydroxyapatite. This favours a more rapid and more extensive osteointegration as compared to rough-blasted titanium. On the other hand, the fixation of the ceramics on the titanium surface can fail (Fig. 12). Ceramic particles can get in the artificial joint, causing additional friction and wear. Many other failures of composite devices are known such as breakage of ceramic heads on metallic cones, breakage of prostheses composed out of different modular elements, etc.

Resistance against fatigue has to be guaranteed in a different way for every device. A plate has to bridge a fracture, an osteotomy site or a bone defect until healing is accomplished. The implant is no more under fatigue stress as soon as bone healing is achieved. If unexpectedly a non-union occurs, the plate bridging it may suffer a fatigue fracture because of its insufficient resistance in this situation. In contrast, the physical properties of prostheses should guarantee a lifelong protection against fatigue fracture. However, the extension of granulation tissue caused by wear particles can extend along the prosthesis. This can diminish the area of fixation of the prosthesis to such an extent that a prosthesis is exposed to fatigue in an area of only small diameter, leading to a fatigue fracture. This is rare today because of improved technology (Abb. 11).

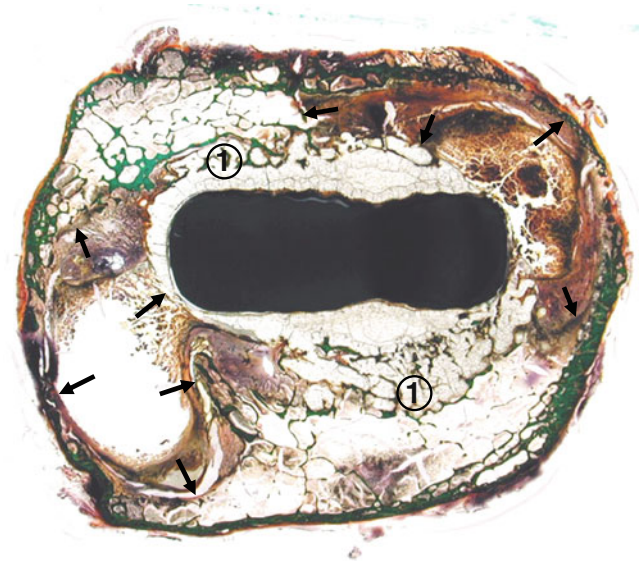

Fig. 10 Integration of cemented prostheses in the metaphyseal area. Non-decalcified sawed section out of the area of the minor trochanter, fixed with Epoxy resin retaining the PMMA cement and the prosthesis, 13 years after implantation in a 71-year-old women. The *line* between prosthesis and cement on the *lower left* is due to an artefact. The stem is encircled by PMMA which interconnects with the surrounding cancellous bone trabeculae labelled as *1*. View under greater magnification (not shown) revealed a tiny connective tissue membrane between the bone and PMMA. From the proximal side, two large cavities filled with granulation tissue containing polyethylene debris are visible. The extension of the cavities is visualised by *arrows*

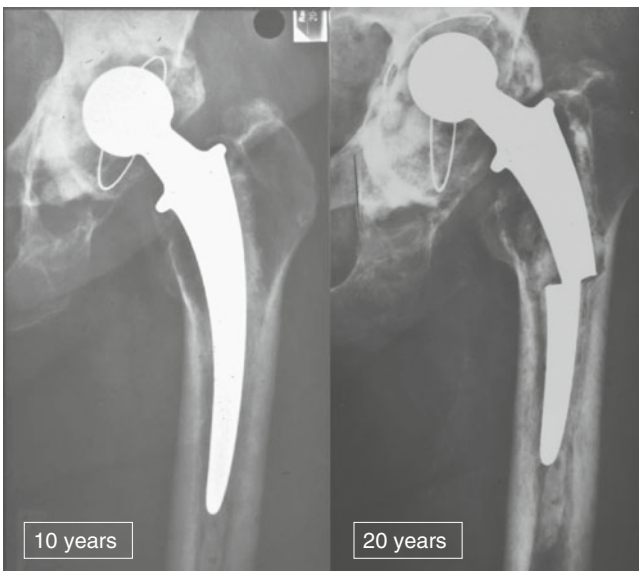

Fig. 11 Fatigue fracture of prosthesis. *Left panel*: at 10 years after the implantation of a curved stem and a polyethylene cup according to ME Müller; remarkable wear and loosening of the cemented cup and osteolysis in the upper part of the stem. *Right panel*: at 10 years later, acute breakage due to fatiguing of the stem immediately proximal of the still well-fixed distal part. The cup did break somewhat before

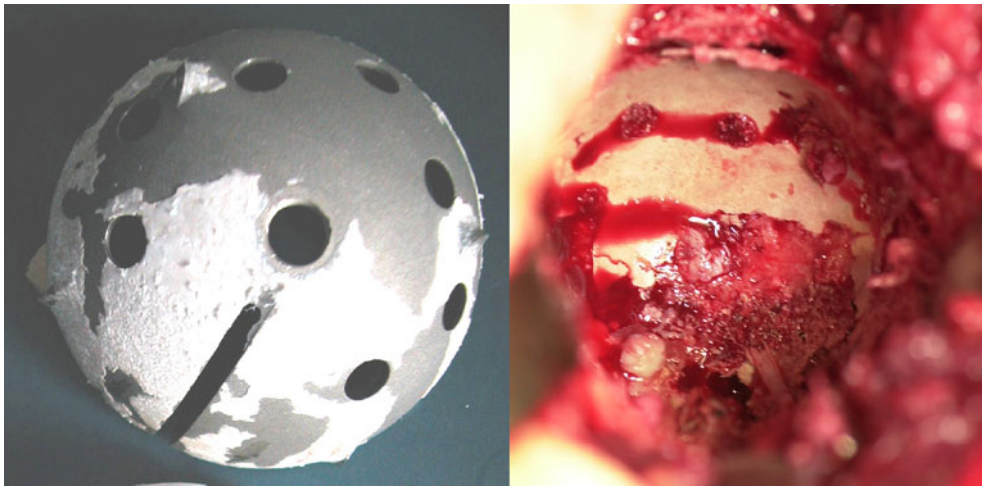

Fig. 12 Problems with fixation of hydroxyapatite on a titanium surface. This acetabular component out of roughly blasted titanium was covered on the outside with hydroxyapatite. There was perfect bony integration on the cranial part, fixed with screws. The implant had to be removed because of infection. *Left panel*: most of the hydroxayapatite was torn from the surface of the implant in the cranial area due to its integration in bone. In the lower region of the cup without osteointegration, the hydroxyapatite remained fixed to the implant. *Right panel*: acetabulum with the layer of ceramics remaining attached to the bone in the area of prior screw fixation

Factors determining the mechanical outcome of orthopaedic devices

Various factors are crucial for the success or failure of healing after total joint replacement, internal fixation of fractures and filling bone defects, respectively.

Prosthetic joint replacement Prostheses replace parts of the skeleton, mainly articulations. The aim is to achieve a long-lasting improvement of function without any complications. Historically, the first joint which has been replaced with long-lasting success was the hip joint [9]. Both parts of the articulation have been replaced, fixing a cup out of soft material and a stem out of metal with PMMA cement to the bone. This method was not only the starting point of modern orthopaedic surgery but also the beginning of serious complications. The first devices did not fulfil the need of longevity of the artificial joints. In the beginning, teflon, the originally used material for the cup, was worn out so quickly that it had to be eliminated. It was replaced by polyethylene which produced much less wear. Poor results motivated the design and production of special instruments allowing standard implantation procedures. Specially shaped prostheses were created to fit for special situations such as congenital dysplastic hips (Fig. 4). Complications have to be analysed in order to find solutions to overcome them [10]. With growing experience, the functional period became longer, but new complications appeared [11]. The anchorage of the PMMA cement in the bone had to be improved by more sophisticated cementing techniques [12]. The penetration of the cement in the cancellous bone could be improved (Fig. 10). Wear particles produced by corresponding joint parts endanger the joint itself which can lead to a breakage of the cup. Wear particles can also provoke a reaction from the side of the tissue. Granulation tissue is formed surrounding the wear particles. This reaction occurs in the joint area as well as in extrusions of the joint capsule. It also has the capacity to find its way in the border area between bone and PMMA cement or between bone and prosthesis [13]. By its further extension (Fig. 10), it leads to progressive loosening of the prosthesis from the joint area to its tip. If the stable anchorage of the prosthesis is restricted to a small area at the tip of the prosthesis, fatiguing of the metal may result in a fracture of the stem (Fig. 11) [14]. The problem of fatiguing cement by the elasticity of titanium has been explained (see above) (Fig. 8). There is a constant search for new friction partners, namely, ceramic to polyethylene, ceramic to ceramic and metal to metal. Polyethylene became more resistant by better linking its molecules consisting of long chains. Non-cemented prostheses were developed, but the majority of the novel models disappeared relatively soon after their introduction. They often fail because of inadequate shape (Fig. 5) or because of the inadequate primary stability between prosthesis and bone not allowing ingrowth. Some models of non-cemented prostheses are implanted since a long time with great success, showing an impressive ongrowth of bone (Figs. 7 and 9). However, they also loosen when they are exposed to granulation tissue of wear products or in case of infection. The loosening begins at the place where there is no osteointegration (Fig. 7, right). Later on, the process continues to attack the osteointegrated part. It may be difficult to differentiate between the various reasons of

loosening. Intraoperative sampling of tissue around the loose prosthesis for histology and bacteriology may allow the diagnosis of a low-grade infection.

Osteosynthesis materials The aim of internal fixation with osteosynthesis materials is to reach adequate stability and reposition to a given fracture site and, as a consequence, to facilitate healing with an adequate functional result. The application should not substantially add to the damage already acquired by the fracture. It should be simple because it is frequently used as an emergency procedure by surgeons with limited surgical experience in the field. As a rule, a permanent integration of the internal fixation device is not wanted because its removal should be easy. The most important fixation devices are nails, plates combined with screws and external fixators. *Nails* placed centrally in the medullar cavity of the bone splint the fracture without creating full stability. This type of osteosynthesis leads to natural healing by callus formation. Nails remain mostly separated from bone by some connective tissue due to a constant slight movement between nail and bone during weight bearing. A full integration is not desired because it would compromise later removal. *Plates* are fixed with screws on the outer surface of the bone with or without a gap between plate and bone, depending on the type of screws used for fixation of the plates. Plates can be used to create a so-called absolute stability, eliminating all relative movements between the fracture fragments and leading to primary bone healing by remodelling [15]. The so-called bridging plates usually do not create anatomic reconstruction. They leave some mobility between the bone fragments, allowing callus healing rather as it is the rule for nails [16]. The degree of integration of the plate in the load flow of the bone after healing of the fracture depends on the material of the device (Fig. 6). The use of the well integrating titanium may even be a disadvantage because of its gradual integration in the mechanics of the bone. Screws fixing the plate to the bone must have a tight fit in order to transmit forces. In a cortical area, the screwholes therefore have to be taped. In a stable fixation, there is a tight fit of the screws in the bone, independent whether they are produced out of steel or titanium (Figs. 6 and 7). The bone structure adapts to their surface. Removal of these screws is facilitated by their smooth or polished surface. An *external fixator* consists of a frame outside the limb connected to the bone by a number of pins with screw tips, wires or metal pins to transmit the load from the bone to the fixator and vice versa. It is meant to bridge a fracture site with comminution and/or with seriously damaged soft tissue. The points of load transmission to the bone are the screws and pins. Tight fit but no ingrowth is mandatory. In case of *delayed union of a fracture,* osteosynthesis material sustains fatigue stress which may result in breaking of nails. In plate osteosynthesis, the plate can undergo the same failure if there is not loosening or breakage of the fixing screws on one side of the fracture.

Healing bone defects Bone defects can be classified in (a) cavitary bone defects being mainly surrounded by living bone (Fig. 2), (b) partial segmental defects, where there still exists a bone bridge or a contact of living bone to secure the length of the site of the defect (Fig. 3) and (c) segmental defects, which are characterised by a total interruption of bone continuity. Whereas healing of a cavitary bone defect is not a major problem, bridging of segmental defects is demanding, especially if they are extended (Fig. 13).

Segmental defects Only three methods can be considered to be safe for bridging a segmental defect. Autologous *bone* is the gold standard for bone reconstruction [17]. Chips of cancellous autograft positioned in any place of the body are able to create bone by osteogenicity (living cells) and by osteoinduction (organic contents). During integration in the living bone structure, they are transformed by "creeping substitution", meaning that the transplanted bone is gradually replaced by living bone [18]. The only way to avoid this substitution is the transplantation of vascularised bone grafts (see above). An alternative method for creating newly formed bone is the so-called callus distraction as first described by Ilizarov [19]. All other methods must be regarded as experimental, based only on case reports. Inorganic ceramics or other matrix substances can be combined with bone morphogenic protein (BMP) extracted from bone and introduced in defect areas such as open tibial fractures. Gustillo IIIB-type fractures better heal when rhBMP-2 is used as compared to standard treatment [20, 21, 22]. However, reaming of the medullar canal has nearly the same effect. There are no systematic proofs for the advantageous use of rhBMP-2 in big segmental defects in man. Countless other substances such as demineralised bone matrix combined or not with inorganic components have no statistically proven effect in human beings [23]. Exceptions are combinations of autologous cancellous autograft with some other filler to augment the activity of the first (Fig. 13).

Partial segmental effects The reconstruction of partial segmental defects depends largely on the size of the remaining bone bridge and its stability. Hypertrophy of this bridge protected by a plate or a nail may create a bone bridge of adequate strength over time. Vascularised bone grafts and cancellous autografts are safe to achieve healing in due time as it is observed in segmental defects (Fig. 13). Sometimes, combination with some organic or inorganic bone substitutes may be helpful.

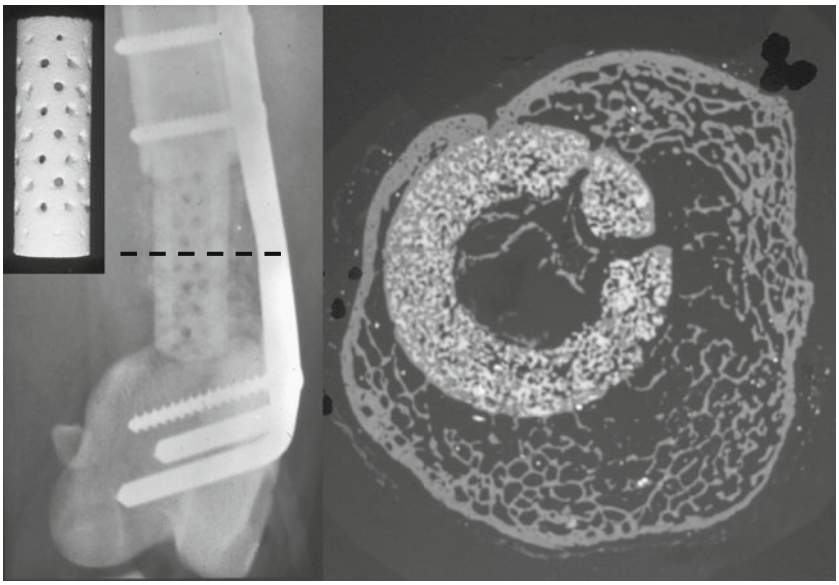

Fig. 13 Integration, remodelling and resorption of tricalcium-phosphate. *Left panel*: postoperative radiograph of the distal femur of a dog. A segmental defect of 3-cm length is bridged by a plate, a porous ceramic tube out of tricalciumphosphate (*insert*) surrounded by an autologous cancellous bone graft kept in place by an absorbable net (Vicryl®). *Right panel*: microradiography of a transverse saw cut on the level marked on the left panel 6 months after surgery. The defect is completely bridged. The ceramic tube (*left insert*) is fully integrated by the new bone (*grey*). The ceramic tube is slowly removed by the remodelling process primarily on the upper left where it is more superficially positioned

Cavitary bone defects Cavitary bone defects can be filled with many bone substitutes, especially if placed in the epi- and metaphyseal area. The classic solution is filling with PMMA cement. It polymerises in the bone defect within 10 min by reaching temperatures up to 90°C. A quantity of cement which is too large can therefore destroy adjacent bone due to overheating. Lined by a thin layer of collagen, it anchors purely by interdentation with the cancellous bone system of the host bone (Fig. 10). It can be loaded with antibiotics to protect itself and the near surroundings from infection for a short time. It can be used as a temporary spacer to fill a defect after resection of a bone tumour of doubtful dignity, later to be replaced if the removed tumour does not recur. In addition, alternative cements containing calcium phosphate can be applied to the defect as a paste, hardening without heating, reaching less stability but being—at least partially—absorbable. Overall remodelling of the bone area remains impaired for a long period.

Filling bone cavities with osteoconductive substances such as deproteinised bone, as well as synthetic hydroxyapatite or tricalcium phosphate is a more permanent solution. The latter is absorbable and therefore can vanish at least partially by remodelling (Fig. 13) [4]. Ceramics such as hydroxyapatite present complete osteointegration if its environment is adapted to its rigidity (Figs. 2, 3 and 13). Fragmented ceramic implants do not necessarily integrate completely, even if they are placed in well-vascularised cavities [17]. The healing result after the use of bone substitutes depend not only on the capacity of osteointegration but also on their inflammatory potential. The formation of foreign body giant cells has to be controlled [24]. The most physiologic procedures still remain the filling with autologous cancellous bone chips, which lead to full remodelling, and avoiding the immunologic problems of allograft material.

Infection and osteointegration of orthopaedic devices

All implants are lifelong endangered by exogenous or hematogenous infection. Microorganisms adhere to the implant surface and form a biofilm. Such an implant-associated infection never heals spontaneously [25]. As a rule, infections extend gradually over the whole surface of the implant by forming a growing biofilm. As a defence reaction of the body, granulation tissue develops around the infected implant. The extension of infection is favoured along parts which are not integrated in bone, such as the joint area of the prosthesis and non-osteointegrated parts of non-cemented implants. If infection occurs immediately after the implantation of a device, osteointegration does not take place at all. The extension of infection is quicker along non-osteoconductive materials and in the areas where osteoconductive implants are not integrated in bone. In addition, the tiny collagen layer around PMMA cement favours the extension of the infected area. The infective granulation tissue leads to bone loss. Loosening takes place

between implant and bone by osteoclastic activity. It is visible as split on radiographs. Loosening also progresses along osteointegrated parts of implants.

Prostheses are usually integrated in healthy, vascular bone. As a rule, this surrounding bone does not show necrosis, not even in the case of an infection. Because of loosening, the infected prosthetic device causes pain and has to be replaced. For different clinical situations and microorganisms, different treatment schedules are adequate [26]. Usually, the bone stock can be preserved. However, bone necrosis can complicate the situation in case of a periprosthetic fracture or if a strut allograft has been used prior to infection.

Internal fixation devices are in tight contact with bone fragments at the fracture site. Bacteria adhere not only to the implant surface but also to dead fracture fragments, which then get surrounded by infective granulation tissue inhibiting fracture healing. If the non-vascularised bone area is restricted, bone healing still can occur. Over time, implant-associated infection spreads over the whole area of the osteosynthesis material. Along nails, infection extends over the whole length of diaphyseal bones. If the medullar cavity is reamed in the narrowest area during osteosynthesis to allow the introduction of a thicker nail with better fit to the surface of the bone, local devascularisation occurs in the inner aspect of the diaphysis [27]. Therefore, this part of the cortical bone is more susceptible to undergo osteomyelitis. Treatment of such infections consists of reaming out the whole inner part of the cortical bone after removing the nail in a consolidated fracture removed [28]. Around plates, the extension of infection is more limited due to their smaller size. Stripping off the periosteum before placing a plate can cause devascularisation and favours local osteomyelitis. *Bone substitutes* such as hydroxyapatite and tricalcium phosphate do not integrate in case of infection. They get embedded in granulation tissue. In contrast, cancellous autografts still have a chance to favour the consolidation of fractures in case of infection.

Conclusions

Orthopaedic devices can be classified as prostheses, bone fixation devices and bone substitutes. Prostheses are designed for the permanent replacement of joints or other parts of the skeleton, fixation devices are used for bridging fractures, nonunions, osteotomies and bone defects in an anatomical shape, and bone substitutes should facilitate healing of bone defects. By using each type of device, numerous mechanical and physiological properties of the specific area of the skeleton have to be considered. For each application, different types of implants with or without the property to undergo osteointegration may be suitable. Every implant presents advantages and disadvantages. Therefore, all factors have to be taken into account for any individual case.

All implants are exposed to fatiguing and infection. Some may vanish by absorption and remodelling. Infection is the most fatal complication threatening the application of an orthopaedic device.

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