Complications still occur in trauma and orthopedic surgery in spite of improvements in operating techniques and optimization of implants. These complications include delayed fracture healing, non-unions and extensive osseous infections. This may be explained by more complex patterns of injuries, the shift of the population pyramid bringing increased frequencies of complex fractures linked to osteoporosis and more intricate operating procedures.

Growth factors for local application (bone morphogenetic protein [BMP]-2, BMP-7) have been approved by the FDA and CE-marked in Europe, but have not become widely accepted. Reasons may be that, although these proteins are expensive and of limited availability, considerable quantities have to be implanted locally. Furthermore, local release from a bovine collagen carrier in tissue is not evident.

The use of coated implants incorporating active ingredients could release drugs locally and thereby generate a high concentration directly in the area of interest without systemic side-effects. Compounds that could be used in this way include growth factors for the improvement of fracture healing and antibiotics for prophylaxis of implant-related infections.

The coating of implants with biodegradable poly(D,L-lactide) (PDLLA) can facilitate the local controlled release of incorporated growth factors directly into the fracture. The coated implant thus serves both as a fracture stabilization device and as a carrier for active components.

This review presents different models (fracture healing, intervertebral fusion, infection model) demonstrating the efficiency of the coating technology. These findings seem to justify the transfer of this technology into clinical settings.

In a preliminary study, gentamicin-coated intramedullary tibial nails were implanted in six patients exhibiting fractures with severe soft tissue damage. The preliminary findings do not allow conclusions to be drawn in respect of therapy of fractures with severe soft tissue damage or revision surgery. However, the coating seems to be suitable as a “key technology” for the incorporation of active ingredients. In addition, this technology could be helpful in endoprosthesis revisions.

The proper choice of growth factors or suitable antimicrobial substances will require extensive clinical investigations.

Introduction

In spite of improvements in operating techniques and the use of optimized implants in trauma and orthopedic surgery, complications continue to occur. These may result from complex injury patterns, the shift of the population pyramid increasing the occurrence of complex fractures involving osteoporosis and more intricate operating procedures [4]. The complications range from delayed healing and non-union of fractures to extensive bone infections.

Disturbances of fracture healing can be traumatically, mechanically or biologically caused.

Many of the complications are directly correlated with the total duration of treatment, as well as with potential risks such as blood loss, infections, injuries to blood vessels or nerves, compartment syndrome and lasting loss of function. Depending on the duration of the hospital stay, infections resulting from hospital pathogens may also occur, sometimes with lethal consequences [23]. Fractures of the long tubular bones bring the risk of development of proximal deep leg vein thromboses in 30–50% of patients as a result of the prolonged immobilization. In up to 5% of these patients this can lead to a clinically significant lung embolism [2]. Up to 5% of fractures of the lower extremities are affected by delayed healing or remain as non-unions [3]. As the population grows older, fractures related to osteoporosis make up a high proportion of cases involving complications.

For many years attempts have been made to speed up the healing of fractures using either lo-
cally or systemically acting substances. The problems listed above could be reduced by stimulation of fracture healing. The use of hormones or growth factors represents a potential starting point. In vitro and in vivo studies have demonstrated that substances such as parathyroid hormone, growth hormone, and growth factors like insulin-like growth factor-1 (IGF-1), transforming growth factor-β1 (TGF-β1) and BMPs, possess a stimulating effect on osteogenic and chondrogenic cells and could thus stimulate bone healing [19, 26]. The exact mechanism by which growth factors exert this positive effect, and their interaction during the course of fracture healing, has not yet been fully clarified. Animal experiments have already demonstrated positive effects with the systemic use of growth hormone in distraction osteogenesis and healing of bone defects [15, 16]. The use of systemically administered growth hormone in fracture healing is currently being investigated in a clinical study. For patients the use of growth hormone or growth factors and the resulting acceleration of fracture healing could reduce the need for subsequent fracture-related operations and bring a reduction in the treatment period with earlier return to work, as well as reducing limitation of working ability and early retirements. This would represent a major gain in quality of life. At the same time the costs for health services (hospital stays, follow-up treatment and aids) could be reduced.

Coating Process

Systemic treatment with substances such as growth factors and antibiotics can be problematic. It therefore seems useful to progress the development of suitable systems for delivering them locally. Local delivery leads to high local concentrations of the substance without subjecting the whole organism to high systemic doses.

To provide optimal conditions for the action of the substances, and to ensure sufficient biological activity for optimal effects, these local delivery systems need to possess the following qualities. The carrier materials must be bioreabsorbable and replaced by bone [3]. They must also be biocompatible so that immune reactions, toxicity and side-effects are reduced. Neither locally induced inflammatory reactions, nor physical blocking due to incomplete breakdown, can be allowed to inhibit bone growth. The carrier material must also be sterilizable and must permit the substances to be delivered in variable amounts. The incorporated substances must be released in a continuous and controlled way so that they are not resorbed before they can exert their effects. A high level of user-friendliness and easy handling for the operating surgeon are desirable qualities [10]. It should also be possible to apply the substances in closed fractures to avoid incurring the risks associated with the opening of fractures.

The collagen sponge already in clinical use for the local delivery of growth factors and antibiotics, most of them based on bovine collagen, do not adequately fulfill these requirements. The uncontrolled release can lead to very high substance concentrations and allergic reactions to the collagen can occur.

The process being described in the present review uses a bioreabsorbable polylactide coating (PDLLA). It can be applied to metallic surfaces in a “cold” coating process, rendering them “biological”. The osteosynthetic implant itself can thus act as a substance carrier.

The coating process is carried out under clean room conditions at room temperature, which means that thermodilable substances can also be incorporated without their activity being affected. In the investigations presented here, the thickness of the layer, which can be altered, was about 10 μm. Tests of the stability of the coating on metallic surfaces show that it can survive high levels

Fig. 7.2.1. Coating properties on steel and titanium. Significantly more PDLLA can be applied to titanium than to steel implants under the same conditions. After implantation and explantation of the Kirschner wires, the abrasion of the coating mass was shown to be below 5%.