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Review Article

Current requirements for polymeric biomaterials in otolaryngology

Abstract

In recent years otolaryngology was strongly influenced by newly developed implants which are based on both, innovative biomaterials and novel implant technologies. Since the biomaterials are integrated into biological systems they have to fulfill all technical requirements and accommodate biological interactions. Technical functionality relating to implant specific mechanical properties, a sufficiently high stability in terms of physiological conditions, and good biocompatibility are the demands with regard to suitability of biomaterials. The goal in applying biomaterials for implants is to maintain biofunctionality over extended periods of time. These general demands to biomaterials are equally valid for use in otolaryngology. Different classes of materials can be utilized as biomaterials. Metals belong to the oldest biomaterials. In addition, alloys, ceramics, inorganic glasses and composites have been tested successfully. Furthermore, natural and synthetic polymers are widely used materials, which will be in the focus of the current article with regard to their properties and usage as cochlear implants, osteosynthesis implants, stents, and matrices for tissue engineering. Due to their application as permanent or temporary implants materials are differentiated into biostable and biodegradable polymers. The here identified general and up to date requirements for biomaterials and the illustrated applications in otolaryngology emphasize ongoing research efforts in this area and at the same time demonstrate the high significance of interdisciplinary cooperation between natural sciences, engineering, and medical sciences.

Keywords: biomaterials, polymers, implants, otolaryngology

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1 Introduction

The tremendous progress in biomaterials research of recent years institutes new possibilities for the development of innovative implants and thus therapeutic options for diseases lacking appropriate treatment options. Aside from all technological challenges the selective organization of the cell-implant interaction is of decisive relevance. The implant may be comprised of polymers, metals, ceramics, or composites (Figure 1). In order to stimulate tissue regeneration biodegradable polymers can be utilized. To improve adhesion and migration of cells structures could be provided with microporous scaffolds [1], [2], [3]. Shape memory materials might be useful to guide cellular differentiation and tissue modeling. Polymermediated drug coatings and chemically modified implant surfaces, combined with nanotechnology, serve as local drug delivery systems and guide cell growth and other cellular functions. The terms active agent and drug are here being used interchangeably.

In the context of drug delivery systems polymer based drug carriers appear to be suited exceptionally well, because drugs can be included by simple protocols. Another advantage is the use of the polymer as a structural component of the implant and, at the same time, as local drug carrier. Biostable polymeric implant materials shall protect the drugs against metabolic processes but guarantee a controlled release of the drug into the host over a defined period of time.

Embedding biologically active agents into the polymer coating of a device is one of the options to produce a local drug delivery system. Polymer solutions containing the active agent are sprayed onto the implant surface or applied onto the implant by dip coating. Drugs that are incorporated into the polymer matrix are released by diffusion or by fragmentation of the polymer provided the polymer is biodegradable.

An alternative to embedding the active substance in the polymer is the coupling of the active substance to the implant surface via chemical synthesis (surface activation and modification). Chemical and/or biological interactions of the surrounding environment or tissue with the modified implant surface realize the release of the active substance. Major targets for local release of biological active substances are the specific inhibition of cell proliferation [4], and inflammation [5], and the prevention of thromboses [6]. A powerful prophylaxis and therapy of implant associated infections is the local delivery of anti-

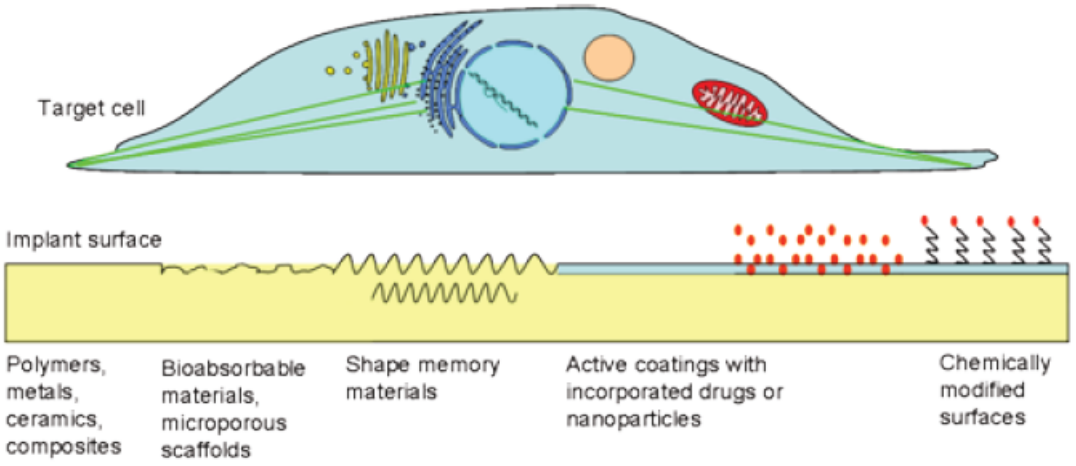

Figure 1: Potential implant modifications for directed control of cell-implant-interaction (schematic).

biotics at the implantation site [7]. Another important topic is the provision of cell specific peptides on the implant surface for preferential cell adhesion [8]. Moreover, cellular responses can be influenced through a myriad of receptors on the cell surface. When appropriate signaling molecules such as growth factors or cytokines [9] are provided on the implant surface the attraction of specific cells can be controlled.

2 Biomaterials as implant materials

Generally, biomaterials are natural or synthetic materials that are utilized in medicine for therapeutic or diagnostic purposes and are in direct contact with the tissue of the organism [10].
These materials interact with the appropriate biological system. In narrower sense biomaterials signify materials that remain, as implants, within the organism for longer periods of time.
The history of biomaterials most likely begins just a few centuries after Common Era when materials foreign to the body were used as therapeutic implants. In ancient medicine biomaterials were applied as rubber soaked linen for the closure of wounds [11]. From Aztec urial sites skulls with gold dental fillings were found. Romans have described the use of urologic catheters. First reports on the applicability of plastics as biomaterial were the usage of a nylon thread for sutures 1941 and cellulose hydrate for haemodialysis in 1943. Modern history of biomaterials commences around 1950 with the development of artificial tissues and organs. In 1952 the first vessel prosthesis was successfully implanted in a human; this was followed in 1960 by replacement of a mitral valve by an artificial implant. During the 1960s the area of research for the development of biomaterials was established in order to specifically influence the functional properties and the biocompatibility of a material to meet medical requirements. Nowadays, biomaterials are widely used for implants in medicine. One example are endoprostheses for joint replacement of chronically inflamed or worn-out joints. Further examples for the replacement of organs or parts of organs are mechanic and biologic heart valve prostheses to treat irreparable heart valve defects, and intraocular lenses for cataract therapy. Stents serve to maintain continuity of lumens, for example of blood vessels, of urethra and ureter, of the bile duct, wind-pipe, and esophagus. Cochlear implants are inserted into the cochlea to stimulate the auditory neurons of deaf or deafened patients on a routine basis.

2.1 General and actual requirements for biomaterials

Biomaterials have to fulfill the following requirements in order to be suitable as implant materials:

- Technical functionality through mechanical properties tuned to the specific implant
- Sufficient stability against physiological media
- Residue-free metabolization for biodegradable biomaterials
- High biocompatibility
- Simple processing
- Sufficiently long shelf-life
- Sterilizable without changes in form and composition

The ideal biomaterial which satisfies all requirements on functional properties, is entirely biocompatible and thus can be applied universally with permanent function is not available up to now despite tremendous progress on biomaterials research. Therefore, today's biomaterials research will continuously be developed with a focus on the design of biomaterials surfaces for functional and biocompatible tissue interaction.
In this context, the use of biomaterials for tissue engineering in otolaryngology is an interesting field of application. Available biomaterials meet functional and biological requirements for tissue engineering only partially. Limitations are found in mechanical properties and in the lack of inducing wanted cellular reactions. In addition, biomaterial cell constructs need to be integrated into the host tissue to prevent loss of transplanted cells.

The functionalization of biomaterial surfaces requires that physicochemical and biophysical properties of the matrix materials are optimized with chemical and physical methods. Of utmost importance are the size, surface charge, hydrophilic and hydrophobic properties, as well as morphology of the material cell/tissue interface. The choice of the matrix material largely depends on the particular application site. To provide for optimal therapeutic results a large variety of matrix systems is necessary for surface functionalization in order to release active agents. In this context, it is advantageous to apply biodegradable and bioabsorbable matrix materials which degrade completely after local release of active agents, and thus avoid an additional surgical procedure for implant removal.

3 Polymers as implant materials

A variety of materials can serve as biomaterials. The first materials used as biomaterials were metals. In particular precious metals such as platinum, gold or titanium, also metal alloys, ceramics, glass, or composites were considered. Prevalent biomaterials are natural polymers such as collagen, alginate, and chitosan as well as synthetic polymers such as polyethylene, polyethylene terephthalate, and polytetrafluorethylene. Polymers are differentiated into biostable and biodegradable polymers with respect to their application as permanent or temporary implant materials.

3.1 Biostable polymers

Biostable materials are needed for long term function of implants. This chapter will focus on biostable polymers which are considered chemically and biologically inert. Biostability has to be considered with caution since most polymers considered as biostable are degraded over the long run due to the "aggressive" physiological conditions of the human organism. Physical degradation processes can be initiated by swelling and embrittlement due to the elution of material plasticizers. Also, chemical degradation processes are known. Oxidation of polyether segments in polyurethane at the α-position to the ether-oxygen [12], or long term hydrolysis of polyamides [13] or polyethylene terephthalate [13], [14] are well documented. These degradation processes proceed over long time periods and finally lead to a loss of material stability known as material fatigue.

Biostable polymers for long term implants have to comply with implant function within the tissue. They should be resistant to abrasive wear when used for artificial joints, show a high mechanical load capacity when used as heart valve replacement, or possess a high compression strength and elasticity when used for bone replacement. Based on implant function the technical requirements for implant materials are very diverse and should be realized by the appropriate choice of polymer(s). Properties of some selected biostable polymers are compiled in Table 1.

3.2 Biodegradable polymers

Biodegradable biomaterials include chemical bonds which are cleaved under the physiological conditions in an organism. Therefore, in many cases polymers are used which contain bonds that can be hydrolyzed. Such bonds are cleaved due to the high content of water within the human body irrespective of the implantation site. Moreover, there are chemical bonds which can be cleaved selectively by enzymes. Since enzyme concentrations vary considerably within an organism, such enzyme cleavable bonds are preferentially used in polymer biomaterials for organ specific local drug delivery applications. Synthetic, biodegradable polymers are normally degraded non-enzymatically by hydrolysis (Table 2), by water mediated cleavage of the polymer chain to oligomers and finally monomers [11].

Polymers which are degraded enzymatically are primarily polypeptides degraded by proteases, polysaccharides such as dextran and amylose degraded by amylases, and biopolyesters which are degraded by esterases (Table 3). P(3HB) one of the biopolyesters has been thoroughly investigated for its potential as implant material by a number of research teams. P(3HB) has been shown to be highly biocompatible and biodegradable. In contrast to synthetically produced biodegradable polymers P(3HB) polymer is a highly pure substance lacking impurities such a remnants of a catalyst or other substances. For its use in manufacturing medical devices it is highly relevant that P(3HB) can be processed with conventional technologies [15]. A variety of structures has been produced for specific medical applications. Porous P(3HB) patches were developed to substitute for the pericard [16], [17] or to seal defects in the vestibular septum [18]. In addition, P(3HB) sleeves served as healing support for tissues and organs [19]. Moreover, it has been shown that P(3HB) membranes served as mechanical barriers to protect organs, nerves, and tendons from newly formed scar tissue [19]. The piezoelectric properties of P(3HB) make it a perfect material for neuronal regeneration [20], [21] which can also be beneficial for bone regeneration. It has been shown that P(3HB) composites stimulate bone growth and bone healing processes [22]. P(3HB) has also been investigated with respect to stent applications [23], [24], [25], [26], [27], [28]. Tantalum stents that were coated with copolymers of 3-hydroxybutyric acid and 3-hydroxyvaleric acid were implanted in porcine coronary arteries. Their biocompatibility was comparable to that of other synthetic polymer coated stents [26] whereas in other animal experiments inflammatory reactions have been reported [27], [28].

The interesting mechanical properties of P(4HB) and the excellent biocompatibility make it a good material for a number of diverse medical applications. P(4HB) suitability was explored as tissue engineering scaffold for heart valves [29], [30], vascular patches [31], suture material

Table 1: Survey of important biostable polymers, their characteristics and medical applications.

Polymers	Properties	Application
Polyethylene (PE - UHMW)	Thermoplastic, semi-crystalline, excellent gliding behavior, low abrasion, very low water uptake	Gliding material in hip and knee joint endoprostheses
Poly(ethylene terephthalate) (PET)	Thermoplastic, semi-crystalline, high bending strength and deformation resistance, excellent gliding behaviour, high abrasion resistance	Suture material, blood vessel prostheses, stent material
Poly(tetrafluorethylene) (PTFE)	Thermoplastic, semi-crystalline, chemically inert, long shelf-life, low surface tension, excellent biocompatibility as implant material	Blood vessel prostheses, material for ligament replacement
Poly(vinylchloride) (PVC)	Thermoplastic, amorphous, very rigid and brittle, for application as implant material addition of plasticizers necessary	Catheters
Poly(methylmethacrylate) (PMMA)	Thermoplastic, amorphous, very rigid and hard	Intraocular lenses, bone-cements, for fastening of hip endoprostheses, dental prostheses
Polyamides (PA)	Thermoplastic (aromatic PA), semi-crystalline, chemically inert, high strength	Artificial tendons and ligaments, suture material
Polyurethanes (PUR), especially polyether urethanes	Soft and entropy elastic	Artificial heart valves, blood vessel prostheses, pacemakers, balloon catheters
Silicon elastomers	Plastic, high resistance under physiological conditions	Soft tissue replacement material in plastic surgery, intraocular lenses, cochlear implants, tracheal prostheses, ear drum perforation cover

Table 2: Survey on a few important synthetic and biodegradable polymers and their degradation mechanisms, primarily non-enzymatic hydrolysis.

Polymer classes	Polymers
Aliphatic polyesters	Poly(α-hydroxycarboxylic acid): Polyglycolide (PGA) Polylactide (PLA) Poly(ω-hydroxycarboxylic acid): Poly(ε-caprolactone) (PCL)
Polyanhydrides	Poly(sebacic anhydride) (PSA)
Polycarbonates	Poly(trimethylene carbonate) (PTMC)
Polyorthoesters	Chronomer™ Alzamer™
Inorganic polymers	Polyphosphazene

[32], [33], orthopedic implants [32], [33], stents [32], [33], [34] and local drug delivery systems [34], [35]. The advantages of biodegradable implant materials are the prevention of secondary surgery and foreign body reactions. Another benefit is that growth processes particularly with children are not hindered.

Table 3: Survey on a few members of natural and biodegradable polymers, which are degraded enzymatically.

Polymer classes	Polymers
Natural polypeptides	Collagen Casein
Synthetic polypeptides	Poly(L-lysine)
Polysaccharides	Amylose Dextran Starch Cellulose Alginate Chitosan
Biopolyesters	Poly(β-hydroxycarboxylic acid): Poly(3-hydroxybutyric acid) (P(3HB)) Poly(γ-hydroxycarboxylic acid): Poly(4-hydroxybutyric acid) (P(4HB))

4 Selected biomaterial applications in otolaryngology

In recent years novel and efficient implants based on the use of innovative biomaterials have been developed for otolaryngology. Such implants not only replace destroyed tissue or restore physiological functions but also compensate for destroyed sensory or neuronal cells by electrical stimulation, which is feasible by the use of biomaterials. One example are the clinically well established cochlear implants, that allow deaf people with intact auditory nerves to perceive individual auditory signals (Chapter 4.1). Another example of biomaterial application is the surgical repair of facial fractures and bony skull defects. For stable osteosynthesis nails, screws, plates, or wires manufactured from surgical stainless steel (316L) or titanium and its alloys are partially replaced by newly developed biodegradable materials (Chapter 4.2).
Furthermore, stenoses of the Eustachian tube are a major cause of chronic middle ear inflammation with consecutive destruction of the sound transmission system, which might be cured by an appropriate stent (Chapter 4.3). Stents might also be used for prevention and treatment of larynx stenoses and to splint intralaryngeal skin or mucosa transplants onto larynx defects.
Of increased importance in otolaryngology is the development of bioartificial tissues by tissue engineering for reconstruction of epithelia (Chapter 4.4). The characteristics of the scaffold material are crucial for the preservation and differentiation of the epithelium. These selected applications will be introduced in more detail in chapters 4.1 to 4.4

4.1 Cochlear implants

The tremendous success story of cochlear implants has advanced this technology into the clinical routine for the treatment of deaf born children or deafened adults [36]. For the implantation of the cochlear implant an electrode array is placed into the cochlea in such a way that numerous electrode contacts allow the electrical stimulation of the auditory nerve. Despite the fact that the technical development of the implant has benefited from the introduction of novel speech processing strategies there are requirements to the implant that cannot be achieved by technical improvements. In particular the interface between electrode and auditory neurons is hampered by pathophysiological processes that can only be controlled by optimized interaction between electrodes and neurons. After cochlear implant insertion fibroblasts migrate into the scaly tympani and produce fibrous material which results in increased impedance. On the other hand, deafness causes a partial loss of neuronal dendrites such that a large gap between electrodes and auditory nerve is the consequence. In order to lower the gap between electrodes and auditory neurons current research focuses on the regeneration of auditory neuron dendrites and preservation of neurons. By local cochlear application of neurotrophic factors such as glial cell-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) it could be demonstrated in vivo that the number of spiral ganglion neurons could be maintaned [37], [38]. To reduce fibrosis around the cochlear electrode a single locally applied dose of glucocorticoids, such as Dexamethasone, clearly reduced electrical impedance [39]. In addition, we could show that drug depots can be accommodated in the silicon carrier of the electrodes [40], [41]. One approach uses cavities that were filled with Dexamethasone whereas another created polymer-Dexamethasone-coatings with a smooth surface (Figure 2).
Investigations on drug release into physiological salt solution conform that such drug depots can generate different drug release profiles (Figure 3). Dexamethasone filled cavities rapidly released Dexamethasone over a short period of time. Incorporation of Dexamethasone in a polymer coating resulted in a long term continuous drug release. The release of Dexamethasone from polymer coatings can be adjusted by the polymer type, the Dexamethasone amount in the coating, the coating thickness and lamination, for example by a drug-free polymer top coat.
Further investigations will show whether functionalization of the electrode carrier with antiproliferative drugs or neurotrophic factors will control fibroblast activity or induce regeneration of auditory neuron dendrites.
Finally, novel concepts are developed that broaden cochlear implant indications towards a bimodal stimulation of the auditory neurons for patients with severe

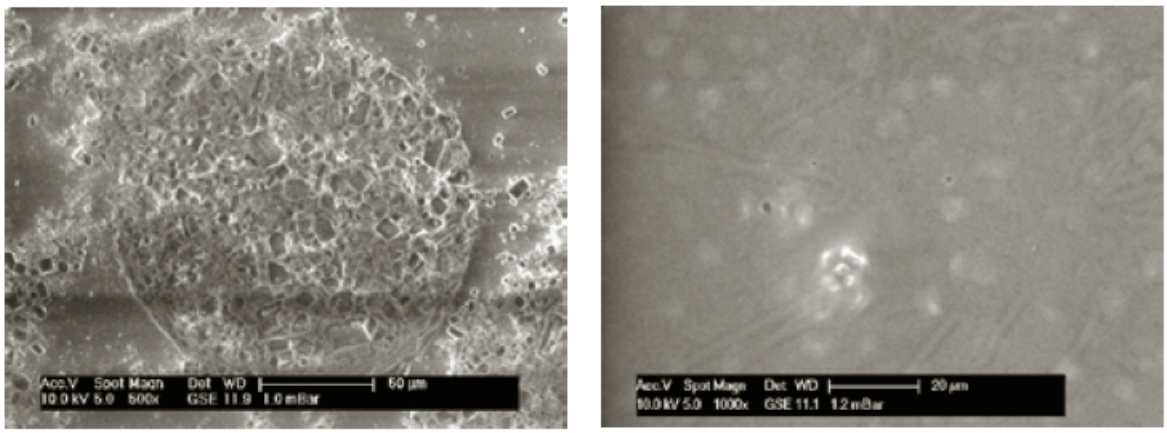

Figure 2: Scanning electron micrograph of a Dexamethasone filled cavity (left) and a polymer/Dexamethasone coating on a silicone matrix (right).

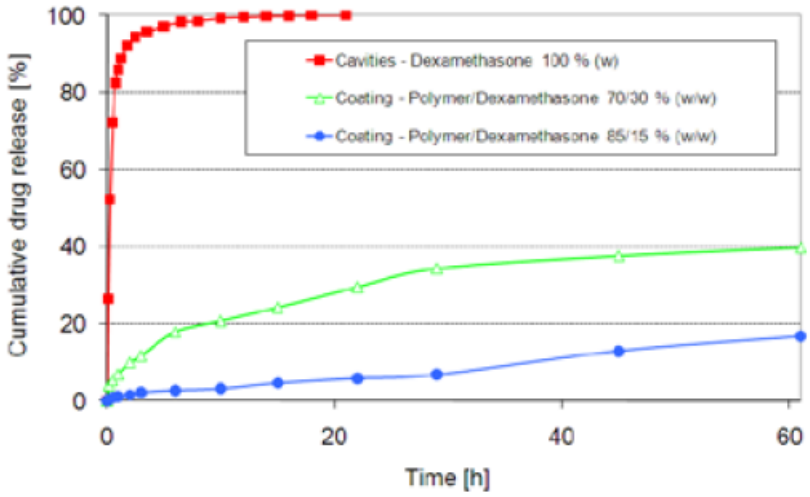

Figure 3: In vitro release of Dexamethasone from cavities and from polymer coatings with different Dexamethasone contents (15 and 30 w%) into physiological sodium chloride solution at 37 °C.

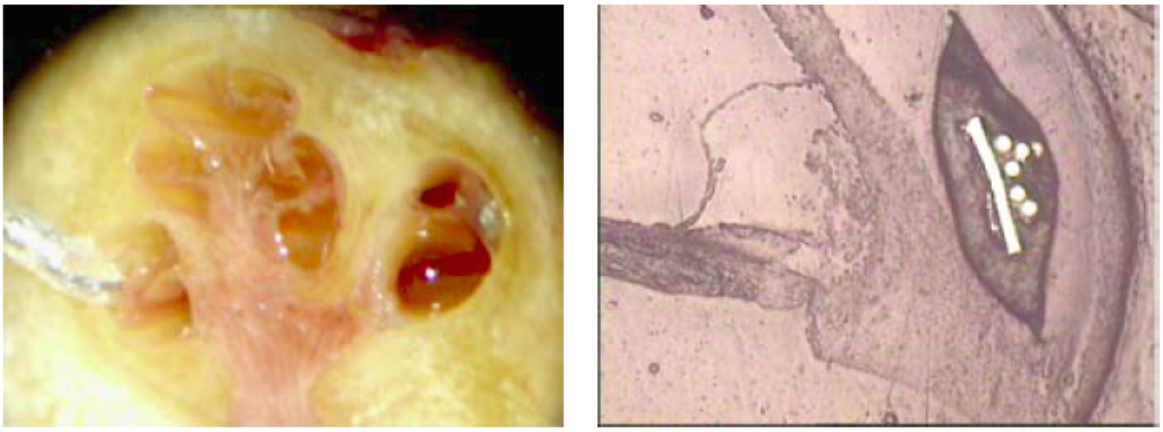

Figure 4: Endosteal electrode (left) and electrode carrier in a petrosal bone model (right).

amblyacousia to acoustically stimulate lower frequencies and electrically higher frequencies. Therefore it is imperative to insert the cochlear electrode atraumatically to prevent damage to intact sensory hair cells and neurons. A novel approach is followed by developing of an endosteal electrode carrier for cochlear stimulation [42], [43], [44] (Figure 4). A flat electrode carrier is inserted endosteal thus preserving the fluid filled cavities of the inner ear and residual hearing.

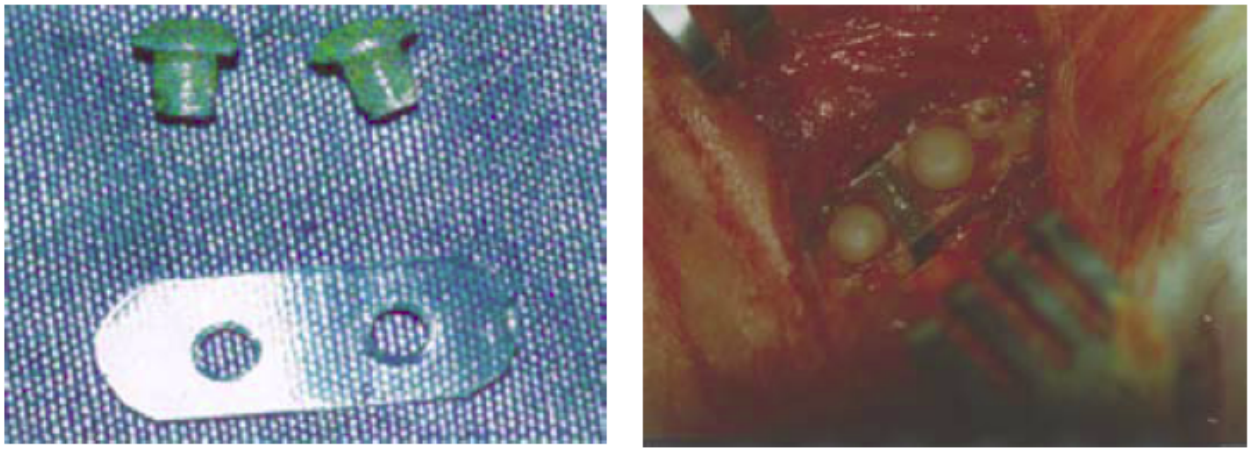

Figure 5: P(3HB) osteosynthesis plate with fixation pins (left) and surgery status in a rabbit model (right).

4.2 Implants for osteosynthesis at the bony skull

Plate osteosyntheses allow three dimensional reconstructions of complex face fractures and the skull base with fortunate aesthetic results. However, these procedures are sometimes accompanied by infections, sensitivity perturbations, and thermo hyperpathies in particular after fractures of the frontal sinus which were repaired by implantation of alloplastic permanent materials such as titanium and titanium alloys and polymethacrylates [45]. In addition, titanium implants caused deposition of abrasions in the surrounding tissue which led to removal of the osseous synthetic material [46]. Other reasons for secondary surgery for implant removal are implant translocation, fixation of fractures in growing bones, or the application of stiff implants in craniofacial surgery which lead to growth perturbations [47]. To overcome the limitations of metallic implants [48] bone replacement materials were developed from biodegradable polymers based on polyglycolide (PGA), polylactide (PLA) and copolymers thereof [49], [50], [51]. Such biodegradable bone replacement systems are preferred for indications in low strain areas of facial bones such as fixation of bone plates after surgical intervention, fractures of the nasoethmoidal and intraorbital areas, fractures of the sinusoidal wall, and for reconstruction of craniofacial structures after facial traumata.

In this context, bone replacement material in form of osteosynthesis plates and membranes made from P(3HB) has been tested. P(3HB) plates including fixation pins have been utilized for reconstruction of the zygomatic arch in White New Zealand rabbits (Figure 5).

Macroscopic evaluation showed that the plates were connate with the bone and the pins firmly fixed in the bone without a detectable fracture crack. Microscopic and histopathologic evaluation showed the characteristic capsule around the implant, with fibroblasts and macrophages, with loose vascularized connective tissue on the outside. After increased times after implantation condensed capsular structures with numerous collagen fibres were visible. Implant induced benign tumors could be excluded. Twelve months postoperatively a 3–6% mass loss of the P(3HB) implant due degradation was observed [52].

P(3HB) membranes for dura mater substitution [53] were placed subperiostal onto the skullcap of White New Zealand rabbits [54] (Figure 5). In the vicinity of the implant no signs of inflammation could be observed. 20 months post implantation no macroscopic signs of biomaterial degradation or absorption were found. 25 months post implantation the subperiostal implant had vanished which was interpreted as sign of complete material absorption. Based on the above observations P(3HB) is well suited for closure of defects in planar areas of the bony skull, or for repair of fractures within the facial area of the skull. The slow degradation of P(3HB) is considered advantageous when compared to that of PLA and PGA [55], [56], because for bone replacement a slowly degrading material is required [57]. Moreover PGA and PLA are not well suited for high mechanical loads [58] as the mechanical strength declines too rapidly due to proceeding material degradation [59]. Another advantage of P(3HB) are its piezoelectric properties which are similar to those of natural bone [60], [61] and one can assume that composites based on P(3HB) stimulate bone growth and regeneration [62].

4.3 Stents for head and neck applications

For numerous medical indications stenoses are dilated minimally invasive and accommodated with a stent. In interventional cardiology drug-eluting stents (DES) are applied for the treatment of atherosclerotic vascular disease [63], [64]. In DES the stent surface is coated with a drug containing polymer which can be biostable or biodegradable. In addition to its primary function as mechanical support of the vessel wall, the stent releases drugs locally into the vessel wall [65], [66].

This technique along with microstructuring of stents opens interesting application perspectives in otolaryngology.

Such microstent systems represent a new generation of stents due to the microscale and their intelligent surface. The modular configuration of such stents comprises the stent body and the drug depot (Figure 6). Particular requirements have to be met by microstents for treatment of Eustachian tube dysfunctions [67]. The diameter (<0.5 mm) has to be considerably smaller than for cardiovascular stents (2.5–5 mm), and the permanent opening of the Eustachian tube should not interfere with the physiological opening and closing mechanism during the deglutition process. Stents for the Eustachian tube must have high mechanical strength and could be produced from shape memory alloys or polymers.

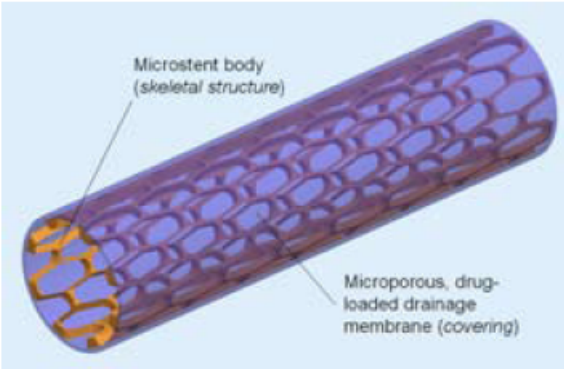

Figure 6: Principle of a modular Eustachian tube stent with drug depot for permanent recanalization.

Hence research efforts include the development of the stent body, and the generation of microporous three-dimensional structures which serve valve control and drug incorporation or covalent coupling. Based on today's view, antibiotics, antiphlogistics, and antiproliferative drugs are relevant for this particular stent application. Stents could further be applied for maintenance of the neoostium [68] in modern frontal sinus surgery, prevention and treatment of laryngeal stenoses, and to splint intralaryngeal skin or mucosa transplants.

4.4 Matrix structures for tissue engineering of epithelia

The generation of bioartificial tissues for reconstruction of epithelia through tissue engineering gains significance in otolaryngology. Actual requirements exist to replace defect or lost respiratory mucosa by novel autologous equivalents, as there are currently no satisfactory therapeutic options to treat extended trachea stenoses. The currently used alloplastic materials based on silicone or polypropylene for trachea prostheses show limitations due to excessive connective tissue growth causing stenoses, poor tissue integration, and risk of implant rejection. For a successful trachea replacement after trauma or resection of malign lesions the backing of the implant with functional respiratory epithelium is imperative.
Another indication is the closure of septum perforations, which are currently treated surgically with low success rates. Since silicone obturators can not completely resolve perforation specific problems [69] the adaptation of such implants might be achieved by implantation of artificial polymer matrices which are seeded with mucosa specific epithelial cells to facilitate adaptation to the biological tissue and at the same time provide a scaffold and mechanical support. Numerous in vitro investigations with respiratory epithelial cells were focused on questions concerning the function of differentiated and undifferentiated cells and to cultivate respiratory epithelial cells on various artificial matrices [70], [71], [72]. In animal experimental models the implantation of membranes or moulds made of various polymers such as polyethylene [73], polypropylene [74], polyetherurethanes [75], polytetrafluorethylene [76], collagen [77] and polypropylene/collagen [78] has been reported. These investigations were aimed to clarify whether the provided structures were repopulated and whether they would differentiate into tissue like structures. The first trachea replacement in humans using tissue engineering showed that a polyethylene mesh covered with spongy collagen is suited to sufficiently accommodate a complication free endothelialization two years post implantation in a 78 year old patient [79]. Results on the long term behavior of such trachea constructs are not yet available.
We were able to show that porous matrices (Figure 7) from the biodegradable polymers PLLA and P(3HB) are suited for recolonization by human respiratory epithelial cells [80]. The differentiation of cells could be shown by the formation of microvilli and in a few cases by the presence of kinocilia.

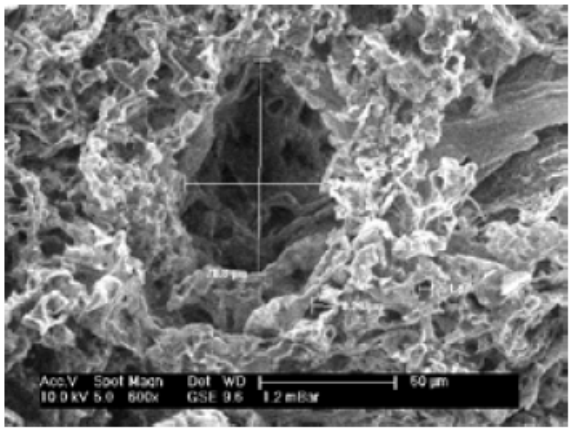

Figure 7: Scanning electron micrograph of an open-celled P(3HB) matrix for tissue engineering of epithelial tissues.

To increase the flexibility of the scaffold materials and to accelerate degradation polymer blends were investigated. The blend of partially crystalline, isotactic natural P(3HB) with more than 30% (w) amorphous, atactic, synthetic P(3HB) resulted in biological incompatibility with numerous dead cells on the scaffold material. Chapter 4 describes in vitro and in vivo investigations which show that the material and its characteristics play important roles for maintenance and differentiation of the epithelium and are the subject of current research in this topic.

5 Trends

The major interest in biomaterials research is the understanding of those cellular mechanisms that guide the interaction with biomaterials at the material/tissue interface. With such knowledge the interaction of cells with implant materials can be optimized by shaping the micro- and nanostructure of the implant surface. The functionalization of the implant surface by drug containing coatings and by chemical surface modifications offer the opportunity of actively govern cellular processes. Such local drug delivery systems facilitate locally and temporally restricted drug release which has great potential for numerous applications due to the modular concept. Of equal importance are currently two research trends. One is the drug targeting and the other the use of micro- and nanotechnologies in biomaterials and implants. A general question regarding biomaterials and implants is the ability of the implants to grow, regenerate and adapt. Such implant characteristics will be realized in the future by tissue engineering approaches.

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