

Description

BACKGROUND

The present invention provides articles for treatment of bony defects. Although examples described herein relate to bone defects in the mouth, similar treatment is applicable throughout the human body.

A bony defect is any unnatural or irregular anatomy of the bone structure, particularly where bone is missing from the natural anatomy. Bone defects are commonly found in the oral cavity including the jaw bone, and are often the result of traumatic injury to the teeth and bone, disease affecting pulp canals of the teeth, periodontal disease, tooth root fractures, tumors, cancer, or congenital defects.

These defects may be functional or aesthetic in nature and have been treated in the past by grafting either natural or synthetic materials to increase tissue volume. The natural grafting materials include iliac, rib, or oral bone harvested from the patient who will receive the graft (i.e. autogenous), cortical or cancellous bone harvested from an individual different from the patient (i.e., allogenuous), or cortical or cancellous bone harvested from a different mammalian species (i.e. xenogenous). Synthetic materials include particles or blocks of either solid or porous hydroxylapatite, particles or blocks of synthetic polymers such as poly (methylmethacrylate) or processed collagenous material usually obtained from a bovine source.

There are two major difficulties associated with the use of the above materials. First, none of the above-mentioned materials predictably result in resolution of the bony defect with viable bone tissue. Autogenous iliac grafts result in the most predictable bone healing, but require a painful surgical procedure to harvest the iliac graft material.

After surgical placement of any of the above-mentioned graft materials into a bone defect, bone cells and fibrous connective tissue cells compete to fill the void space within the graft material or to replace the graft material as it resorbs. Because fibrous connective tissue can grow and form faster than bone tissue, the above-mentioned graft materials may attach or be partly ingrown with bone; however, the majority of healing is accomplished by ingrowth of soft connective tissue. In addition, with particulate materials, the particles tend to migrate over time through the soft tissue beyond the margins of the bone defect thereby reducing or minimizing therapeutic results.

The second major problem is that all of the above-mentioned materials are prone to either dehiscence of the suture line due to stretching the gingival tissue over them during closure of the

surgical site or perforation of the graft material through the gingival tissue at some point after initial healing has occurred. In either case, exposure of the graft material occurs with subsequent infection and loss of graft material.

WO-A-86-00517 describes an article for use in prosthetic implants and capable of supporting preferential connective tissue growth and/or attachment for treating bone defects. The article comprises a flexible, flattened member, respective portions defining first and second juxtaposed surfaces. The second surface, which is impermeable, surrounds the first surface which is porous and capable of supporting connective tissue ingrowth and/or attachment.

SUMMARY OF THE INVENTION

The invention is defined in appended claim 1.

In contrast to the article described in WO-A-86/00517, the permeable first surface surrounds the second surface which is impermeable to connective tissue ingrowth and/or attachment and to bacteria.

The invention provides a biocompatible porous article for successful treatment of bony defects particularly in the jaw bone of the mouth. Treatment involves placement of the article over the bony defect thus creating a space between the article and the bone in the region of the defect into which bone cells proliferate. The article itself protects the defect space thus created from epithelium, fibrous connective tissue, and bacteria all of which would normally be detrimental to bone tissue healing within the defect region. The article thus allows predictable resolution of bony defects even in the event of exposure of the article to the oral or outside environment through dehiscence of the suture line, perforation of the overlying soft tissue or inability to obtain primary or complete closure of the soft tissue.

It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

Additional advantages of the invention will be set forth in part in the detailed description which follows, and in part will be obvious from the description or may be learned by practice of the invention. The advantages of the invention may be realized and attained by means of the instrumentalities and combinations particularly pointed out in the appended claims.

The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate embodiments of the invention and, together with the description, serve to explain the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a three-dimensional view of uniaxially expanded polytetrafluoroethylene.

Figure 2 is a three-dimensional view of an embodiment of a prior art article described in Examples 1 and 2 wherein a first portion of the article is porous and a second portion of the article is substantially impermeable to oral tissues.

Figure 2A is a cross-sectional view of the embodiment of Figure 2 taken along line A-B.

Figure 3 is a three-dimensional view of a bony defect in the alveolar ridge wherein the mucoperiosteal flaps have been elevated thereby leaving the alveolar bone ridge exposed.

Figure 4 is a three-dimensional view of a bony defect in the alveolar ridge similar to that of Figure 3 repaired with an embodiment of the invention.

Figure 5 is a bucco-lingual cross-sectional view of the inventive embodiment placed over the alveolar ridge bony defect and mucoperiosteal flap resutured over the article.

Figure 5A is a view similar to that in Figure 5 but showing the addition of bone filler material to the defect.

Figure 5B is a view similar to that in Figure 5 but showing dehiscence at the juncture of the mucoperiosteal flaps.

Figure 6 is a surface view of the inventive embodiment and configured for treatment of bony defects wherein a first peripheral surface of the article is capable of supporting tissue ingrowth and a second central surface of the article is impermeable to tissue ingrowth.

Figure 6A is a cross-sectional view of Figure 6 taken along line E-F.

Figure 6B shows an alternative construction similar to that in Figure 6 but having wire reinforcements.

Figure 6C is a cross-sectional view of the construction shown in Figure 6B taken along line C-C.

Figure 7 is a bucco-lingual cross-sectional view of the inventive embodiment wherein a dental implant is placed within the alveolar ridge defect underlying the article.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Reference will now be made in detail to the present preferred embodiments of the invention, examples of which are illustrated in the accompanying drawings.

The present invention provides articles for the treatment of defects in bones, particularly in the jaw bone of the mouth. For use of the article, as shown in Figure 3, the mucoperiosteal flaps 101 including the gingival epithelium 103 and gingival

connection tissue 105 are separated from the alveolar ridge of the jaw bone 107 leaving exposed the bony defect 109. As shown in Figure 4, one embodiment of the article 120 comprising a flexible, flattened member having first and second juxtaposed surfaces meeting at a boundary is positioned over the affected region of the bone and is fixed in a laminar relationship to a portion of the alveolar ridge. In the most preferred embodiment, the first surface 121 is formed of a porous, biocompatible material capable of supporting the ingrowth of connective tissue and thus preventing or retarding the migration of gingival epithelium into the defect region. This first surface is configured to be peripheral to a second surface and sized and configured so as to surround the perimeter of the defect area, and adapt closely to the contours of the bone adjacent to the defect area when the article is in place. The second surface 123 is preferably configured so that it is surrounded by the first surface. The second surface is formed of a material substantially impermeable to oral tissues and bacteria and configured to fully cover the bony defect. The second surface also creates a space (e.g. Figure 5, space 131) between the surface and bone defect to allow bone cells to proliferate within the space without competition from cells originating from the fibrous connective tissue and epithelium. This results in filling of the defect space by viable bone tissue. Because the article will protect the defect space from epithelium, gingival connective tissue, and bacteria, bone tissue will fill the space even in the event that the article is exposed to the outside environment due to suture line dehiscence, perforation, or inability to obtain primary or complete closure of the overlying tissue. In some situations, complete closure of the tissue may not be possible (e.g., sites where a tooth is extracted leaving a gap in the soft tissue). In these cases the tissue should be closed as much as possible and stabilized with sutures. Also, allogeneous, autogenous, or alloplastic materials 134 (Figure 5A) can optionally be used to help fill the bony defect by providing a matrix for bone cell growth and/or to prevent collapse of the article into the defect space.

Finally, as shown in Figure 5 and 5A, the mucoperiosteal flaps are repositioned so that soft tissue completely covers the implanted material 121 and 123, and the flaps are sutured closed 133. The article may be further secured in the area of the defect with various biocompatible glues, sutures, filaments and the like. However, the present invention is intended to function satisfactorily even in the event of dehiscence of the flaps at their juncture, as is depicted at 137 in Figure 5B.

It is intended that the materials comprising either of the articles for treatment of bony defects

be similar to those described in WO-A-86/00517 and be made from biocompatible materials. The porous material must also allow for the rapid ingrowth of gingival connective tissue to inhibit the apical migration of gingival epithelium along the surface of the material. Preferably the porous material is soft and flexible so that it will conform to the curvature of the tooth and surrounding bone and not cause tissue necrosis in the tissues against which it is placed. Suitable biocompatible materials which can be made porous include, but are not limited to, silicones, polyurethanes, polyethylenes, polysulfones, polyacrylics, polycarboxylates, polyesters, polypropylenes, poly(hydroxyethylmethacrylates), and perfluorinated polymers, such as fluorinated ethylene propylene, and polytetrafluoroethylene.

The above-mentioned may be made porous by any techniques known to those of ordinary skill in the art which will render the materials capable of supporting gingival connective tissue ingrowth while preventing apical migration of gingival epithelium. Such techniques include, but are not limited to, sintering carefully controlled sizes of beads; combining the materials with a partially resorbable implant that would resorb or could be resorbed, *in vivo* or *in vitro*, to leave a porous surface; weaving or knitting fibers together to form a fabric-like material; or using a foaming agent during processing to cause bubbles to form and leave pores as the material hardens.

The porous material may be treated or filled with biologically active substances such as antibiotics, fibrin, thrombin, and collagen. These substances may enhance connective tissue formation within the porous material and inhibit infection during healing.

Each of the articles may be comprised of a suitable bioresorbable, biodegradable, or hydrolyzable material so that the article dissolves over a period of time. It is most preferred, however, that the porous material be expanded polytetrafluoroethylene (PTFE) which is subsequently processed to a desired microstructure such as by application of heat and pressure. Expanded PTFE is an extremely inert and biocompatible material with a history of medical implant use. U.S. Patent Numbers 3,953,566 and 4,187,390, the disclosures of which are incorporated herein by reference, teach methods for producing expanded PTFE and characterize its porous structure. The porous structure of expanded PTFE is further illustrated in Figure 1. The microstructure of expanded PTFE is a three-dimensional matrix of nodes 9, connected by fibrils 10.

The pore size of expanded PTFE can be characterized by determining the bubble point and the mean flow pressure of the material. Bubble point

and mean flow pressure are measured according to the American Society for Testing and Materials Standard F316-80 using ethanol.

The density of expanded PTFE determines the amount of void space in the material which may become ingrown with connective tissue. The density of expanded PTFE is the ratio of the mass of a given sample of expanded PTFE to its volume.

The fibril length of expanded PTFE is defined herein as the average of ten measurements between nodes connected by fibrils in the direction of expansion. Although Figure 1 illustrates material expanded in one direction only, PTFE expanded in more than one direction is thought to be equally applicable to the invention. In order to measure the average fibril length of expanded PTFE, two parallel lines are drawn across a photomicrograph of about 40 to 50 times magnification of the surface of the material so as to divide the photograph into three equal areas. If the material has been uniaxially expanded, these lines are drawn in the direction of expansion (i.e., direction of orientation of fibrils). Measuring from left to right, five measurements of fibril length are made along the top line in the photograph beginning with the first node to intersect the line near the left edge of the photograph and continuing with consecutive nodes intersecting the line. Five more measurements are made along the other line from right to left beginning with the first node to intersect the line on the right hand side of the photograph. If the material is expanded in more than one direction, the lines are drawn and fibril lengths measured as above, except when a node is not attached by fibrils to a node intersecting the drawn line. In this case, the fibril length from the node to a node which creates the least angle with the drawn line is measured along the fibril's axial orientation. The ten measurements obtained by this method are averaged to obtain the average fibril length of material.

Starting materials of expanded PTFE with average fibril lengths greater than about 60 microns, and preferably greater than 100 microns, densities less than 1 g/cc and preferably about 0.3 to 0.1 g/cc and a wall thickness of about 1mm are most preferred and are subsequently compressed in certain regions to achieve desired microstructures.

When expanded PTFE is compressed by the application of heat and pressure, the microstructure of nodes and fibrils distorts so that characterization by fibril length becomes impractical. Nodes become positioned more closely together as the amount of compression is applied to the point where the material begins to approach a state where there are no void spaces between the nodes. In situations such as these, a preferred parameter used to characterize the microstructure is the internodal distance of expanded PTFE rather

than fibril length. Internodal distance is defined herein as the average distance between edges of nodes in the direction of expansion based on at least 20 random measurements of internodal distance from three fields of view at 200X. Measurements were made on a Nikon medical research microscope.

The articles of the invention include one embodiment, which comprises a layered structure wherein a first layer having a porous surface capable of supporting ingrowth or attachment of connective tissue is arranged in laminar relationship with a second support layer which is substantially impermeable and incapable of penetration by tissues or bacteria. Here the first porous layer allows fibrous connective tissue ingrowth into the porous material or attachment along the outer surface of the porous material to inhibit or retard epithelial migration. The backing layer substantially prevents undesirable tissue and bacteria from entering the space of the bony defect and allows desirable bone cells to proliferate in the space created by the layered article.

The second embodiment, and the most preferred article, for treatment of bony defects is shown in Figures 6, 6A, 6B and 6C and comprises an integral member having a portion with a first porous compressed surface 121 with an average internodal distance greater than 8 microns and preferably in the range of 15-20 microns, a wall thickness of about 0.20mm (0.008 inches) and a density of about 1.0 g/cc. The member also has a second surface 123 positioned to be central to and surrounded by the first surface which is juxtaposed in planar relationship thus forming a boundary encircling the second surface. The portion of the member forming the second surface is more greatly compressed so that it is substantially impermeable to oral tissues and bacteria; however there may be some tissue attachment topically along the second surface. The portion of the member forming the second surface preferably has an average internodal distance of less than 5 microns, a density of about 1.5 g/cc and a wall thickness of about 0.13mm (0.005 inches). These articles may be of laminar or integral construction.

To construct the member portions having the representative first and second surfaces of this embodiment, application of heat and pressure to the starting expanded PTFE material similar to that previously described is used. The degree of compression to achieve each of the surfaces is controlled by the use of plates designed to be separated at predetermined distances. Similar to the previous embodiments for treatment of periodontal disease, because the two surfaces are compressed from the same starting material, no means for attachment of the first and second surface are

required.

Figure 6 shows the preferred shape for the article for treating a bone defect wherein the article has a rectangular shape, the center of which has a further compressed oval shaped region. Figure 6A shows the member in cross-section with the more compressed region in the center. Alternative shapes, sizes and configurations are intended to be within the scope of the articles of this invention for treatment of bony defects.

The article used in the treatment of bony defects may be used in conjunction with bone filler materials including but not limited to autogenous, allogeneous, or xenogeneous bone; synthetic bone materials such as hydroxylapatite, tricalcium phosphates or polymeric materials including bioresorbable, biodegradable, or hydrolyzable sponges, particles, gels or blocks of material.

Additionally, the articles for treatment of bony defects may be used in conjunction with biologically active materials or molecules including but not limited to cell activators, antibiotics, or materials which serve as a structural framework for cellular migration such as collagen, fibronectin, or fibrin. The biologically active materials may be bound to the surface of the article, incorporated into it so that they may be released in a controlled fashion over a period of time, or placed within the bony defect space protected by the article.

The articles for the treatment of bony defects may also incorporate biocompatible reinforcement components such as metallic (e.g., titanium) or polymeric wires, struts, or meshes to allow molding or shaping of the article to specific configurations or to support the article and prevent its collapse into the defect space. Such reinforcement means can, for example, comprise optional wire supports at least partially attached to article 120, as shown in Figures 6B and 6C.

Finally, the article may be used in conjunction with a dental implant as shown in Figure 7 and described in Example 3 wherein the implant 150 is placed in the defect region and the article 120 of the invention is placed over it and extends over the bone ridge.

All articles of the present invention are preferably sterilized prior to insertion into a periodontal pocket or covering a bone defect. Preferably, the articles are sterilized and are contained in a package, the interior environment of which is sterile.

The following examples were designed to elucidate the teachings of the present invention and not to limit the scope of the invention. Various other modifications and equivalents of the examples will readily suggest themselves to those of ordinary skill in the art, particularly after issuance of this patent, without departing from the present claimed invention.

Example 1 (Prior Art)

Ponchos similar to that shown in Figure 9 of WO-A-86/00517 illustrated in Figure 2 were made with a starting material of expanded PTFE made in accordance with the description in Patent Nos. 4,187,390 and 3,953,566. The poncho had a center 18 which forms a first porous surface and an outer circumference 20 which forms a second impermeable surface. The starting material had an ethanol bubble point of below about 5.17×10^4 dyne/cm² (0.75 psi), an ethanol mean flow pressure below about 2.07×10^5 dyne/cm² (3 psi), an average fibril length greater than 100 microns, a density of about 0.3 to 0.1 g/cc, and a wall thickness of about 1mm.

A sheet of the starting material was clamped into a metal frame to hold the material in place. The frame was positioned between two plates that had been fixed on a pneumatic press. Each plate was machined so that a rectangular central portion having dimensions of 4mm x 12mm was relieved such that compression of the expanded PTFE would take place peripheral to the central relieved area but not within the central relieved area. The central relieved area remained porous with an open structure. Shims were used in the press as stops to control the degree of compression. The shims were arranged to prevent the plates from contacting each other by about 0.007 inches. The plates were heated to between 300°F and 400°F and the expanded PTFE was compressed between the heated plates for about thirty seconds.

The resulting compressed region of expanded PTFE had a density of about 1.0 g/cc and a wall thickness of about 0.18mm (0.007 inches). The compressed region also had internodal distances ranging from about 5 microns to 50 microns with an estimated mean internodal distance of about 15 to 20 microns.

The resulting membrane was thus similar in shape to the poncho illustrated in Figure 2 with a central surface of open-structured porous PTFE and a peripheral surface of compressed expanded PTFE.

Six of these ponches were implanted into five dogs. Buccal and lingual full-thickness mucoperiosteal flaps were elevated and buccal or circumferential periodontal defects were surgically created on mandibular pre-molar teeth. Each poncho was placed over the teeth with the open-structure porous region adapted closely to the tooth surface at or just apical to the cemento-enamel junction. The compressed, less porous, peripheral portion of each poncho was carefully trimmed so that the defined surface completely covered the bony margins of the defect.

After placement of the poncho, the mucoperiosteal flaps were repositioned so that the

soft tissue completely covered the implanted material and the flaps were sutured closed.

The dogs were sacrificed at various time intervals between one and three months post-operatively and the experimental teeth were removed en bloc for histological processing and evaluation. When analyzed histologically, it was found that the epithelium had not migrated past the porous central region of the ponchos and that the porous central regions were extensively ingrown with connective tissue and mononuclear cells. It was found also that some connective tissue had grown within the compressed peripheral region where the internodal distances were greater than 8-10 microns with more tissue ingrown where the internodal distances were greater than 15 microns. In many instances, the connective tissue penetrated the full wall thickness of this peripheral region. However, because of the ingrowth of connective tissue in this compressed peripheral region, epithelium could not migrate along the compressed region in the event that the open-structured porous region became exposed to the oral environment.

New cementum with collagen fibers was present on the previously denuded root surface and varying amounts of new bone tissue had healed into the defect space between the patch and the tooth root.

Example 2 (Prior Art)

Expanded PTFE ponchos with integral two-part constructions were made similar to that described in Example 1. In this case, compression of the compressed peripheral region was increased by reducing the shim stop thickness to 0.005 inches. This resulted in a poncho member having a porous central region surrounded by a compressed peripheral region having a wall thickness of 0.005 inches, a density of about 1.5 g/cc and an internodal distance ranging from 0 to 40 microns with an estimated mean internodal distance of about 5 to 10 microns.

Ponchos of this type were implanted into surgically created periodontal defects on dog premolars similar to that described in Example 1. The dogs were sacrificed at various time intervals between one and three months post-operatively and the experimental teeth removed en bloc and processed for histological evaluation.

Histologically, the experimental sites showed the epithelium had halted its apical migration at or coronal to the open-structured porous central regions of the ponchos the surface of which central porous regions ponchos were extensively ingrown with connective tissue and mononuclear cells.

In one case, the coronal margin of the flap was located apical to the porous region of the poncho

thereby exposing this region and a portion of the compressed region to the oral environment. The epithelium was located about 1.5 to 2 mm apical to the junction between the porous region and the compressed region of the ponchos. A Brown-Brenn bacteria stain showed the presence of gram positive bacteria throughout the interstices of the open-structured porous regions and on the surface of the compressed portion of the ponchos which was exposed to the oral environment. In addition, there was localized penetration by bacteria into the compressed region exposed to the oral environment but the bacteria did not penetrate through the entire wall thickness.

Since the compressed region was more compressed than that of the material described in Example 1, the presence of connective tissue was markedly less although there was some connective tissue attachment to PTFE fibrils on the surface of this compressed region. It was noted however that this localized presence of connective tissue elements and attachment to the surface aided in retarding epithelial migration.

In the site where 2 to 3mm of the porous region and compressed region had become exposed to the oral environment, the space between the poncho and the tooth surface coronal to the flap margin was filled with viable connective tissue which showed evidence of collagen deposition, this in spite of moderate acute inflammation. The presence of viable connective tissue indicated that bacteria were unable to permeate the compressed portion in a sufficient amount to produce infection and cause necrosis. It appeared that the larger the internodal distance, the greater the susceptibility to bacterial penetration through the wall thickness of the material.

Example 3

Expanded PTFE patches were made with the starting material made according to the description in Patent Nos. 4,187,390 and 3,953,566 as follows: A mixture of PTF resin in a liquid lubricant was extruded into a tubular form. The extruded tubular form was dried for approximately 96 hours at about 300°C, which removed the lubricant. The tubular form, held at a temperature of about 295°C, was then stretched at a constant velocity along the central axis of the tube at a rate of about 75% per second until it was approximately 10 times its original length, where rate was defined as

$$\frac{l_f - l_i}{l_i(t)} \times 100\%$$

where l_f = final length, l_i = initial length, and t = total time of expansion. Subsequent to stretching, the tube was restrained longitudinally and heat treated about 375°C for about 75 seconds. The expanded PTFE tube was then slit longitudinally through its walls and laid flat. The wall was about 1mm thick and had nodes passing through its wall thickness. The ethanol bubble point of the material was about 3.45×10^4 dyne/cm² (0.5 psi) and the ethanol mean flow pressure was about 6.89×10^4 dyne/cm² (1.0 psi). The average fibril length was about 200 microns and the density was approximately 0.2 g/cc.

In this example, the patch did not have two juxtaposed surfaces formed by materials of different relative porosity but the entire patch was compressed so that the article implanted in each subject consisted of compressed expanded PTFE with a density of about 1.5 g/cc and a wall thickness of about 0.13mm (0.005 inches). The internodal distance was about 5 to 10 microns. The dimensions of each article were about 30mm x 40mm.

The articles were implanted into six sites in humans where bony alveolar ridge defects were present and prevented or compromised placement of dental implants. Vertical incisions were made across the alveolar ridge crest mesial to the bony ridge defect and distal to sites proposed for dental implant placement. These incisions were connected on the labial side of the ridge by a horizontal incision placed apical to the mucogingival junction. Full thickness mucoperiosteal pedicle flaps were elevated and receptor holes drilled in the bone to accept dental implants. The dental implants were then placed into the prepared receptor sites. In each case a portion of the implant was not surrounded by bone because of the bony defect. In three cases, a particulate hydroxyapatite material was used as a filler in the defect to prevent the article from collapsing into the defect and space below. In the other three cases, no filler or support was provided.

The sterile patches were trimmed to the appropriate size and were draped over the bony defect and surrounding area and the dental implant. The flaps were replaced and sutured to enclose the patches.

Post-operative healing events were uneventful in 4 of the 6 sites. At one month post-operative, two of the sites showed perforation of the gingival tissue by the patches. Each article was removed by elevating the gingival tissue and peeling the patch off of the bony surface. Upon removal of each patch, it was observed that the defect space had filled with a hard, apparently calcified, bone-like tissue. The gingival tissue flaps were replaced and sutured and the sites were allowed to heal for

an additional two to five months prior to placement of abutment posts and bridgework.

The remaining four patches were removed at between 1 and 3 months post-operatively. Removal was similar to the removal of similar cases with elevation of the gingival tissue and observation of the defect sites. In all cases, a hard, apparently calcified, bone-like tissue had filled each defect space. These sites were allowed to heal for an additional one to five months prior to placement of the abutment posts and bridgework. All cases were restored with bridgework and functioned assymptomatically.

In these cases, the patches were used to create and protect a bony defect space into which viable bone tissue could grow. Had there been no patch, the defect space would have filled with fibrous connective or scar tissue, thus compromising the function of the dental implant. These cases were ideal because enough space existed mesial and distal to the defect sites to prepare the pedicle flaps. This prevented any suture lines from being located directly over the articles. In many cases, it is not possible to make pedicle flaps and the incision must be placed on the ridge crest. In such instances, the patch must be capable of both limiting the migration of epithelium and protecting the defect site from bacteria.

Example 4

Based on the results of Examples 1, 2 and 3, the following article is theorized to be the most preferable embodiment. The article has been constructed but has not been implanted in any subjects.

As Examples 1 and 2 showed, patches having regions of compressed expanded PTFE with internodal distances greater than or equal to 8 microns showed predictable connective tissue ingrowth with greater permeation as the internodal distances increased (i.e., leaving the membrane more porous) and corresponding increased potential for permeation of bacteria.

The preferred article for treating bony defects, particularly where exposure of at least a portion of the article to the oral cavity is a possibility, is comprised of an integral flexible flattened patch or member, preferably of expanded PTFE having two juxtaposed surfaces exhibiting differing average internodal spacings. To construct the member, and as shown in Figure 6, a central region 123 of the member was compressed to a sufficient degree, such that it was made substantially impermeable to oral tissues and bacteria. The compressed region of which would be placed directly over the bony alveolar ridge defect. It has been found that compressed expanded PTFE having an internodal dis-

tance less than 8 microns and a density of 1.5 g/cc is preferred. The second region less compressed and thus more porous is peripheral to the central, highly compressed region. This peripheral region would be capable of preferential connective tissue ingrowth for inhibition of epithelial migration and should extend beyond the margins of the bony alveolar ridge defect. It has been found that compressed expanded PTFE with an internodal distance greater than about 8 microns and density of about 1.0 g/cc is preferred for the peripheral region.

To construct such a two-part member, preferential compression was used rendering a central portion that was highly compressed compared to a peripheral region with relatively less compression. This is in contrast to the patches in Examples 8 and 9 which utilized a non-compressed center region and a compressed peripheral region. Although preferential compression of an integral expanded PTFE member is the preferred method of making such a member, bonding a central portion substantially impermeable to tissue ingrowth to a peripheral more porous region capable of supporting connective tissue ingrowth could also be used.

By placing the more compressed region 123 over the bony alveolar defect as shown in Figure 4 so that it extends 1 to 2mm beyond the margins of the defect and the peripheral (more porous) region 121 capable of supporting tissue ingrowth extends beyond the more compressed region, a defect space can be created and protected from invasion by gingival connective and epithelial tissues and bacteria. This protected space thus creates an opportunity for bone cells to proliferate and fill the defect with viable bone tissue.

The two-part member is designed to be removed after adequate healing has occurred, generally after 1 month; however, in applications where exposure of the article is unlikely the two-part member may remain in place for the life of the patient.

It will be apparent to those skilled in the art that various modifications and variations can be made in the articles and processes of the present invention. Thus, it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims.

Claims

1. An article (120) of manufacture for use in prosthetic implants and capable of supporting preferential connective tissue ingrowth and/or attachment for treating bone defects, the article comprising a flexible, flattened member having respective portions defining first (121) and sec-



an additional two to five months prior to placement of abutment posts and bridgework.

The remaining four patches were removed at between 1 and 3 months post-operatively. Removal was similar to the removal of similar cases with elevation of the gingival tissue and observation of the defect sites. In all cases, a hard, apparently calcified, bone-like tissue had filled each defect space. These sites were allowed to heal for an additional one to five months prior to placement of the abutment posts and bridgework. All cases were restored with bridgework and functioned asymptotically.

In these cases, the patches were used to create and protect a bony defect space into which viable bone tissue could grow. Had there been no patch, the defect space would have filled with fibrous connective or scar tissue, thus compromising the function of the dental implant. These cases were ideal because enough space existed mesial and distal to the defect sites to prepare the pedicle flaps. This prevented any suture lines from being located directly over the articles. In many cases, it is not possible to make pedicle flaps and the incision must be placed on the ridge crest. In such instances, the patch must be capable of both limiting the migration of epithelium and protecting the defect site from bacteria.

Example 4

Based on the results of Examples 1, 2 and 3, the following article is theorized to be the most preferable embodiment. The article has been constructed but has not been implanted in any subjects.

As Examples 1 and 2 showed, patches having regions of compressed expanded PTFE with internodal distances greater than or equal to 8 microns showed predictable connective tissue ingrowth with greater permeation as the internodal distances increased (i.e., leaving the membrane more porous) and corresponding increased potential for permeation of bacteria.

The preferred article for treating bony defects, particularly where exposure of at least a portion of the article to the oral cavity is a possibility, is comprised of an integral flexible flattened patch or member, preferably of expanded PTFE having two juxtaposed surfaces exhibiting differing average internodal spacings. To construct the member, and as shown in Figure 6, a central region 123 of the member was compressed to a sufficient degree, such that it was made substantially impermeable to oral tissues and bacteria. The compressed region of which would be placed directly over the bony alveolar ridge defect. It has been found that compressed expanded PTFE having an internodal dis-

tance less than 8 microns and a density of 1.5 g/cc is preferred. The second region, less compressed and thus more porous is peripheral to the central, highly compressed region. This peripheral region would be capable of preferential connective tissue ingrowth for inhibition of epithelial migration and should extend beyond the margins of the bony alveolar ridge defect. It has been found that compressed expanded PTFE with an internodal distance greater than about 8 microns and density of about 1.0 g/cc is preferred for the peripheral region.

To construct such a two-part member, preferential compression was used rendering a central portion that was highly compressed compared to a peripheral region with relatively less compression. This is in contrast to the patches in Examples 8 and 9 which utilized a non-compressed center region and a compressed peripheral region. Although preferential compression of an integral expanded PTFE member is the preferred method of making such a member, bonding a central portion substantially impermeable to tissue ingrowth to a peripheral more porous region capable of supporting connective tissue ingrowth could also be used.

By placing the more compressed region 123 over the bony alveolar defect as shown in Figure 4 so that it extends 1 to 2mm beyond the margins of the defect and the peripheral (more porous) region 121 capable of supporting tissue ingrowth extends beyond the more compressed region, a defect space can be created and protected from invasion by gingival connective and epithelial tissues and bacteria. This protected space thus creates an opportunity for bone cells to proliferate and fill the defect with viable bone tissue.

The two-part member is designed to be removed after adequate healing has occurred, generally after 1 month; however, in applications where exposure of the article is unlikely the two-part member may remain in place for the life of the patient.

It will be apparent to those skilled in the art that various modifications and variations can be made in the articles and processes of the present invention. Thus, it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims.

Claims

1. An article (120) of manufacture for use in prosthetic implants and capable of supporting preferential connective tissue ingrowth and/or attachment for treating bone defects, the article comprising a flexible, flattened member having respective portions defining first (121) and sec-



- ond (123) juxtaposed surfaces, said first surface (121) totally surrounding said second surface characterised in that said first surface is capable of supporting connective tissue ingrowth and/or attachment and the first surface has a permeability to connective tissue ingrowth which is greater than that of the second surface and said second surface has a permeability to bacteria different to that of said first surface and is substantially impermeable to bacteria and connective tissue ingrowth.
2. The article of claim 1 wherein said member (120) is an integral member.
 3. The article of claim 1 further including means (135) for supporting said member in conforming relation to the bone in the vicinity of the defect.
 4. The article of claim 3 wherein said support means (135) includes wire means embedded in said member.
 5. The article of claim 4 wherein said wire means (135) includes titanium wire.
 6. The article of claim 1 wherein said first surface is formed by an expanded polytetrafluoroethylene material having an inter-nodal distance of greater than or equal to 8 microns and a density of about 1.0 g/cc.
 7. The article of claim 6 wherein said member is integrally formed, and wherein the thickness of said member portions forming said first (121) and second (123) surfaces is about 0.20mm (0.008 inches) and about 0.13mm (0.005 inches) respectively.
 8. The article of claim 1 wherein a biologically active substance is releasably contained in said member.
 9. The article of claim 1 wherein at least the member portions (121) having the greater permeability are made from one or more biocompatible materials selected from the group consisting of silicones, polyurethanes, polyethylenes, polysulfones, polyacrylics, polycarboxylates, polyesters, polypropylenes, poly(hydroxyethyl) methacrylates, and perfluorinated polymers.
 10. The article of claim 5 wherein said support means (135) include a polymeric mesh.

11. The article of claim 1 wherein said member portion defining said second surface (123) is made from one or more biocompatible materials selected from the group consisting of silicones, polyurethanes, polyethylenes, polysulfones, polyacrylics, polycarboxylates, polyesters, polypropylenes, poly(hydroxyethyl) methacrylates and polyfluorinated polymers.
12. The article of claim 1 wherein said second surface is centrally located with respect of said first surface.

Patentansprüche

1. Ein Erzeugnis (120) zur Verwendung in prothetischen Implantaten und mit der Fähigkeit zum Unterstützen eines bevorzugten Bindegewebs-Hineinwachstums und/oder einer bevorzugten Bindegewebs-Anheftung zur Behandlung von Knochendefekten, wobei das Erzeugnis ein biegsames, abgeflachtes Element aufweist, das jeweilige Abschnitte besitzt, die erste (121) und zweite (123) nebeneinander angeordnete Oberflächen definieren, wobei die genannte erste Oberfläche (121) vollständig die genannte Zweite Oberfläche umgibt, dadurch gekennzeichnet, daß die genannte erste Oberfläche dazu befähigt ist, das Bindegewebs-Hineinwachstum und/oder die Bindegewebs-Anheftung zu unterstützen, und die erste Oberfläche eine Permeabilität für das Bindegewebs-Hineinwachstum aufweist, welche größer als diejenige der zweiten Oberfläche ist, und daß die genannte zweite Oberfläche eine Bakterienpermeabilität aufweist, die gegenüber derjenigen der ersten Oberfläche unterschiedlich ist, und für Bakterien und für Bindegewebs-Hineinwachstum im wesentlichen undurchlässig ist.
2. Das Erzeugnis gemäß Anspruch 1, bei welchem das genannte Element (120) ein einstückiges Element ist.
3. Das Erzeugnis gemäß Anspruch 1, weiterhin umfassend Mittel (135) zum Tragen des genannten Elementes in einer sich anpassenden Beziehung zu dem Knochen in der Umgebung des Defektes.
4. Das Erzeugnis gemäß Anspruch 3, bei welchem die genannten Träger-Mittel (135) Draht-Mittel aufweisen, welche in dem genannten Element eingebettet sind.
5. Das Erzeugnis gemäß Anspruch 4, bei welchem die genannten Draht-Mittel (135) Titan-



draht umfassen.

Das Erzeugnis gemäß Anspruch 1, bei welchem die genannte erste Oberfläche durch ein Material aus expandiertem Polytetrafluorethylen gebildet ist, das einen Zwischenknoten-Abstand von größer als oder gleich zu 8 Mikron und eine Dichte von ungefähr 1,0 g/cm³ aufweist.

7. Das Erzeugnis gemäß Anspruch 6, bei welchem das genannte Element einstückig ausgeformt ist, und bei welchem die Stärke der genannten Abschnitte der Elemente, welche die erste Oberfläche (121) und die zweite Oberfläche (123) bilden, jeweils ungefähr 0,20 mm (0,008 inches) und ungefähr 0,13 mm (0,005 inches) beträgt.

8. Das Erzeugnis gemäß Anspruch 1, bei welchem eine biologisch wirksame Substanz in freisetzbarer Weise in dem genannten Element vorhanden ist.

9. Das Erzeugnis gemäß Anspruch 1, bei welchem zumindest die Elementen-Abschnitte (121) mit der größeren Permeabilität aus einem oder mehreren bioverträglichen Materialien hergestellt sind, die ausgewählt sind aus der Gruppe bestehend aus Silikonen, Polyurethanen, Polyethylenen, Polysulfonen, Polyacryl-Werkstoffen, Polycarboxylaten, Polyestern, Polypropylenen, Poly(Hydroxyethyl)-Methacrylaten, und perfluorierten Polymeren.

10. Das Erzeugnis gemäß Anspruch 5, bei welchem die genannten Träger-Mittel (135) ein polymeres Netz umfassen.

11. Das Erzeugnis gemäß Anspruch 1, bei welchem der genannte, die genannte zweite Oberfläche (123) definierende Abschnitt des Elementes aus einem oder mehreren bioverträglichen Materialien hergestellt ist, die aus der Gruppe ausgewählt sind, bestehend aus Silikonen, Polyurethanen, Polyethylenen, Polysulfonen, Polyacryl-Werkstoffen, Polycarboxylaten, Polyestern, Polypropylenen, Poly(Hydroxyethyl)-Methacrylaten und polyfluorierten Polymeren.

12. Das Erzeugnis gemäß Anspruch 1, bei welchem die genannte zweite Oberfläche in Bezug auf die genannte erste Oberfläche mittig angeordnet ist.

Revendications

1. Article de fabrication (120) destiné à être utilisé dans des implants prothétiques et à même de supporter la pénétration d'un tissu conjonctif préférentiel et/ou sa fixation, pour traiter des défauts osseux, l'article comprenant un élément aplati souple ayant différentes parties définissant une première (121) et une deuxième (123) surfaces juxtaposées, la première surface (121) entourant totalement la deuxième surface, caractérisé en ce que la première surface peut supporter la pénétration par un tissu conjonctif et/ou sa fixation, et que la première surface présente une perméabilité vis-à-vis de la pénétration par un tissu conjonctif, qui est supérieure à celle de la deuxième surface, la deuxième surface ayant une perméabilité aux bactéries différente de celle de la première surface et étant essentiellement imperméable aux bactéries et à la pénétration du tissu conjonctif.

2. Article selon la revendication 1, dans lequel l'élément (120) est un élément intégral.

3. Article selon la revendication 1, qui comprend en outre un moyen (135) pour supporter l'élément de façon qu'il épouse l'os au voisinage du défaut.

4. Article selon la revendication 3, dans lequel le moyen de support (135) comprend des moyens de fil métallique noyés dans l'élément.

5. Article selon la revendication 4, dans lequel les moyens de fil métallique (135) comprennent un fil de titane.

6. Article selon la revendication 1, dans lequel la première surface est formée d'un matériau de polytétrafluoréthylène expansé ayant une distance internodale supérieure ou égale à 8 micromètres et une masse volumique d'environ 1,0 g/cm³.

7. Article selon la revendication 6, dans lequel l'élément est formé d'une manière intégrale, et où l'épaisseur des parties de l'élément formant la première surface (121) et la deuxième surface (123) est respectivement d'environ 0,20 mm (0,008 inch) et d'environ 0,13 mm (0,005 inch).

8. article selon la revendication 1, dans lequel une substance biologiquement active est contenue dans l'élément de façon à pouvoir s'en libérer.



9. Article selon la revendication 1, dans lequel au moins les parties d'élément (121) ayant la perméabilité la plus grande sont constituées d'un ou plusieurs matériaux biocompatibles choisis parmi l'ensemble comprenant les silicones, les polyuréthanes, les polyéthylènes, les polysulfones, les polyacryliques, les polycarboxylates, les polyesters, les polypropylènes, les poly(méthacrylates d'hydroxyéthyle) et les polymères perfluorés.

5

10

10. Article selon la revendication 5, dans lequel le moyen de support (135) comprend un tamis polymère.

15

11. Article selon la revendication 1, dans lequel la partie d'élément définissant la deuxième surface (123) est constituée d'un ou plusieurs matériaux biocompatibles choisis parmi l'ensemble comprenant les silicones, les polyuréthanes, les polyéthylènes, les polysulfones, les polyacryliques, les polycarboxylates, les polyesters, les polypropylènes, les poly(méthacrylates d'hydroxyéthyle) et les polymères polyfluorés.

20

25

12. Article selon la revendication 1, dans lequel la deuxième surface est disposée en position centrale par rapport à la première surface.

30

35

40

45

50

55