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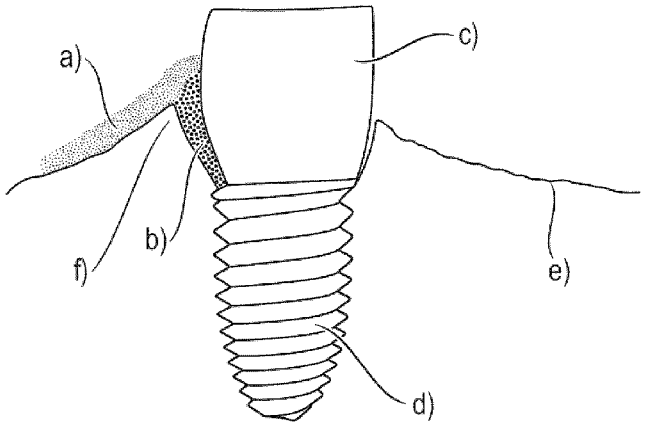
(54) Title: COMPOSITIONS AND FILMS FOR APPLICATION TO DENTAL SUBSTRATES

Fig. 4



(57) Abstract: The Invention provides products comprising compositions which may be applied to natural teeth and dental substrates such as implantable devices, prosthetic components and combinations thereof. The product comprises a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl- based resins such as acrylate-based resin, silane terminated polymers and mixtures thereof; and a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof. The invention also relates to products comprising compositions of the invention for use in methods of treating peri-implantitis and periodontitis in a subject. The invention further relates to a dental substrate coated with a polymer and to a dental substrate having a polymer film attached thereto, wherein the attached polymer has one or more relief features on at least a portion of the film.

[Continued on next page]

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Compositions and films for application to dental substrates

Field of the invention

The present disclosure relates to products comprising compositions which may be applied to natural teeth and dental substrates such as implantable devices, prosthetic components and combinations thereof. Once applied, the product comprising compositions is able to facilitate the attachment and growth of connective tissue to the natural tooth and the dental substrate thereby improving soft tissue barrier formation. The present disclosure also relates to products comprising compositions for use in treating conditions associated with the introduction of a dental substrate into the oral cavity of a subject and depletion of gingiva tissue, such as peri-implantitis and peridontitis. The present disclosure also relates to a dental substrate coated with a polymer and to a dental substrate having a polymer attached thereto, wherein the polymer has one or more relief features on at least a portion of the film. These dental substrates may also be used in the treatment or prevention of peri-implantitis and periodontitis.

Background

The introduction of dental substrates such as implantable devices, prosthetic components and combinations thereof into the oral cavity, are common procedures performed by dentists and surgeons to replace damaged or lost natural teeth. For example, a synthetic dental implant is often constructed by first inserting an implant into the jaw bone to act as a natural tooth root and then attaching an abutment to the implant, which extends above the gum-line in the oral cavity. A tooth-related prosthesis such as a crown may then be attached to the abutment.

When introducing medical implants into the body, there is a risk that pathogenic germs may also be introduced which may result in infection or inflammation. Furthermore, if the medical implant is bio-incompatible then adverse effects may be observed. If these adverse effects persist they can lead to the development of serious conditions and can result in the implant

having to be removed. When introducing dental substrates into the oral cavity, the risk of infection is high as the oral cavity provides an accessible and suitable environment for pathogens.

Peri-implantitis is a site-specific infectious disease that causes an inflammatory process in soft tissues, and bone loss around an osseointegrated implant in function. In compound implants (when the abutment is a separate piece from the implant), between the actual implant and the superstructure (abutment) are gaps and cavities into which bacteria can penetrate from the oral cavity. Later these bacteria can return into the adjacent tissue and can cause peri-implantitis. Peri-implantitis differs from periodontitis in that it has different pathological manifestations. For example, peri-implantitis has a much more prominent inflammatory component (PMID:22967131). Diagnosis is based on changes of color in the gingiva, bleeding and probing depth of peri-implant pockets, suppuration, X-ray, and gradual loss of bone height around the tooth.

Dental substrates, when placed in a site in the oral cavity, will lack the soft tissue barrier (or seal) that natural teeth have and will therefore have a greater chance of being exposed to pathogens. In fact, poor quality soft tissue barrier at the site of the treatment or the placement of the dental substrate can lead to periodontal as well as post-implant complications.

A natural tooth has gingival fibres attached to the surface layer of its root (the cementum). The barrier formation around natural teeth towards the oral cavity is provided by the junctional epithelium via hemidesmosomes and is supported by functionally oriented collagen fibres of the connective tissue, which are firmly anchored in the mineralized root cementum.

Cementum forms the surface layer of the bone. Its composition is similar albeit not identical to that of bone. It is secreted by specialized cells called cementoblasts which may become entrapped by the cementum they produce and thus become cementocytes. The

cementoblasts that do not become entrapped in cementum line up along the cemental surface along the length of the outer covering of the periodontal ligament. These cementoblasts can form subsequent layers of cementum if the tooth is injured, thus, as for most biological materials; cementum is continuously renewed to prevent the surface from aging.

After the placement of a dental substrate in a site in the oral cavity, an attachment is established that consists of barrier epithelium and a zone of connective tissue (Abrahamsson I., J Clin Periodontol. 2002 May, 29(5), 448-55). This kind of attachment is vulnerable, and may be compared to that of an adhesive. Furthermore, unlike an untreated natural tooth, a dental substrate introduced into a site in the oral cavity is not surrounded by strong fibres, which provide a barrier.

When a dental substrate is introduced into a site in the oral cavity, the soft tissue adjacent to the site includes junctional epithelium that is similar to that found around a natural tooth (Bosshardt D.D. *et al.*, J Dent Res. 2005; 84(1): 9-20). However, the implantable medical device does not have cementum and therefore does not provide an anchorage site for proper fibre attachment Furthermore, the 'attachment' fibres in the supracrestal soft tissue compartment are parallel to the implant surface and perpendicular to the periosteum of the marginal bone crest (Abrahamsson I., J Clin Periodontol. 2002 May, 29(5), 448-55). This results in the implantable medical device having weaker mechanical resistance as compared to that of a natural tooth. A natural tooth has fibres which connect to the outer cementum leading to a ring-shaped arrangement of fibres surrounding the tooth. The fibres are anchored in the cementum and result in a strong attachment of the soft tissue to the tooth's surface. (See Figure 1 for a comparison of a natural tooth and a synthetic tooth).

If a dental probe is guided along the enamel of a natural tooth in the direction of the root, there is resistance due to the strong barrier. The tissue of the gingiva is firmly anchored in the cementum of the tooth. The surface of an implanted dental substrate such as an implant

and/or abutment is not so firmly attached to the tissue of the gingiva. Consequently, the gingiva can be separated from the tooth much more easily. As mentioned above, the weaker barrier facilitates the intrusion of pathogenic germs and leads to a greater risk of inflammation.

In order to address the problem of a weak barrier existing between the tissue of the gingiva and a dental substrate, a number of procedures have been developed to attempt to regenerate the gingiva. For example, dentists generally attempt to bring the tissue of the gingiva in close proximity with the implantable device and fix it with sutures. However, whether this results in the formation of an adequate barrier depends on the condition of the tissue, the tissue biotype, the suturing technique used and the experience of the performing dentist. Furthermore, if non-resorbable sutures are used then a subsequent visit to the dentist will be needed.

Other treatment procedures involve the application of autologous soft tissue grafts (GBR (guided bone regeneration)/GTR (guided tissue regeneration) techniques) at the affected site. However, the use of autologous grafts will generally require donor sites to be treated in addition to the affected treatment site and this will result in additional pain and discomfort for the patient.

Another approach, based on the assumption that healthy gingival tissue will establish the best attachment, includes the removal of all inflammatory signs and sources. Following this approach, the dentist will clean the affected site by using curettes, lasers, ultrasound or abrasion techniques and/or will flush the site with sodium chloride, hydrogen peroxide, chlorhexidine or similar solutions; apply chips loaded with chlorhexidine or similar agents; or apply gels containing microspheres or fibres which comprise filler molecules such as tetracycline and chlorhexidine.

Another approach to creating a strong barrier between the gingiva tissue and a dental substrate is to prepare an autologous fibrin tissue glue (like PRF) and inject it into the gap formed between the soft tissue and the dental substrate (or tooth in periodontology). The intended function of the fibrin gel is to improve bone formation (for deep defects) and/or to act as a membrane between the healing tissue and external factors (like saliva, oral microbiome etc). However, this approach has one major drawback which is that in order to produce the fibrin gel; 100 ml of fresh blood from the patient to be treated is needed (J. Cutan. Aesthet. Surg., 2014 Oct-Dec, 7(4), 189–197).

A further approach to creating a strong barrier between the gingiva tissue and a dental substrate is to mimic the natural tooth matrix (J. Adv. Prosthodont., 2014 Oct, 6(5), 406-14). Such an approach was used in the development of the product Emdogain® (Straumann), which is an enamel matrix derivative product (EMD). Such products comprise an extract of porcine fetal tooth material. Emdogain® is described as being able to regenerate a patient's own periodontal attachment as well as having the ability to stimulate periodontal regeneration on the tissue surrounding an implantable device.

Together with surface mimicking, other strategies have been used which are directed to creating a nano-structured surface. For example, MetAlive have developed MetAlive® technology which enables protein-mediated attachment of the gingival tissue to the surface of an abutment. Both connective and junctional epithelial tissue have been found to display an improved attachment to this titanium surface of an abutment. This method is based on the anodization of the medical device surface. However, this process cannot be used during surgery directly at the wound site.

Despite the different methods and treatments currently available for improving the barrier between the tissue of the gingiva and a dental substrate, there are several drawbacks to the current approaches. There thus exists a need for a simple and effective means of for improving the barrier between the tissue of the gingiva and a dental substrate which is

versatile, and which can be used to treat or prevent peri-implantitis and periodontitis in a subject.

The embodiments of the present invention address this need by substituting the function of the cementum by modifying of the surface of the dental substrate in order to foster the attachment of gingival tissue and fibers. Advantageously, the embodiments disclosed herein can be applied pre and post implantation of the implant and abutment and therefore can be used to treat patients irrespective of implant system and without the necessity of removing/replacing the system the patient is using. This has practical advantages as the embodiments of the present invention can be applied during the first abutment placement and also during post-implant treatments (e.g. like peri-implant complications) without the need to remove the abutment. Additionally, the embodiments disclosed herein can be applied after an abutment replacement due to a prosthesis exchange.

Summary

The inventors of the present disclosure have surprisingly found that a product comprising a first composition and a second composition, as described herein, may be applied to a dental substrate or a natural tooth located in the oral cavity to promote attachment of gingival tissue and fibres. The inventors of the present disclosure have also found that by attaching a polymer to a dental substrate or applying a polymer coating to a dental substrate, attachment of gingival tissue and fibres to the dental substrate is promoted. Furthermore, the inventors of the present disclosure have also found that by attaching a polymer having one or more relief features on at least a portion of the film to a dental substrate, attachment of gingival tissue and fibres to the dental substrate is promoted. The product, the polymer and the polymer having one or more relief features on at least a portion of the film as disclosed herein, act by modifying the surface of a dental substrate and encourage gingival tissue and fibres to affix to it. The product comprising a first composition and a second composition may be applied to a dental substrate as a single layer. Alternatively, multiple layers of the product comprising a first composition and a second composition may be applied to the dental substrate.

The product comprising a first composition and a second composition comprises a resin in the first composition and a filler in the second composition. However, rather than combining the first and second composition and applying them to a dental substrate as a single layer, the first composition may be applied to the dental substrate in a first layer and the second composition may be applied in a second layer. Between the first layer and the second layer one or more additional layers may be present.

The product comprising a first composition and a second composition and multi-layered coatings as described herein may be applied *in situ* during the placement of the dental substrate. Further applications may be applied without the need to remove the dental substrate. Alternatively, the product comprising a first composition and a second composition and multi-layered coatings may be applied to the dental substrate before the dental substrate is introduced into the oral cavity.

In a first aspect of the present disclosure is provided a product comprising:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixtures thereof.

In a second aspect of the present disclosure is provided a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers and mixtures thereof; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixtures thereof.

The product according to the second aspect of the present disclosure can be used to coat a natural tooth or a dental substrate wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In one embodiment of the second aspect of the present disclosure the product comprises one or more layers between the first layer and the second layer. The one of more layers between the first layer and the second layer are formulated to bond two dissimilar materials together that would otherwise have poor adhesion to each other. In the present case, the one or more layers are formulated to form a first bond with the first layer of the product according to the second aspect of the present disclosure and a second bond with the second layer of the product according to the second aspect of the present disclosure, wherein the strength of the first bond and strength of the second bond are each greater than the strength of the bond formed between said first layer and said second layer. As a result, products comprising multilayer structures can be produced that combine the key properties of the first composition and the second composition.

In a third aspect of the present disclosure is provided a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In one embodiment of the third aspect of the present disclosure the product is applied to a dental substrate *ex vivo*.

In another embodiment of the third aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In a further embodiment of the third aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer one or more layers are present between the first layer and the second layer. Preferably, the one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

A fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;
and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In one embodiment of the fourth aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In another embodiment of the fourth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer, one or more layers are present between the first layer and the second layer. Preferably, the one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

A fifth aspect of the present invention is a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat.

In one embodiment of the fifth aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In another embodiment of the fifth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer one or more layers are present between the first layer and the second layer. Preferably, the one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

A sixth aspect of the present disclosure is a dental substrate coated with a polymer coating, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof. The polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and pH responsive polymers.

In a seventh aspect of the present disclosure is provided a dental substrate coated with a polymer coating according to the sixth aspect of the present disclosure for use in a method of treating or preventing peri-implantitis or periodontitis in a subject.

An eighth aspect of the present disclosure is the use of a polymer coating for coating a dental substrate *ex vivo*, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof. The polymer coating

comprises at least one polymer selected from the group consisting of thermoresponsive polymers and a pH responsive polymer.

In one embodiment of the eighth aspect of the present disclosure, the polymer coating is coated on the surface of the dental substrate to which gingiva tissue attaches.

A ninth aspect of the present disclosure is a polymer coating for use in a method of treating or preventing peri-implantitis or periodontitis in a subject, wherein the polymer coating is applied on a natural tooth or a dental substrate in the oral cavity;
wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and pH responsive polymers.

In an tenth aspect of the present disclosure is a dental substrate having an outer surface to which a polymer film is attached, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

In one embodiment of the tenth aspect of the present disclosure, the polymer film is attached to the outer surface of the dental substrate to which gingiva tissue attaches.

In an eleventh aspect of the present disclosure is provided a dental substrate having an outer surface to which a polymer film is attached according to the tenth aspect of the present disclosure for use in a method of treating or preventing peri-implantitis or periodontitis in a subject.

A twelfth aspect of the present disclosure is a polymer film for use in a method of treating or preventing peri-implantitis or periodontitis in a subject, wherein the polymer film is applied on a natural tooth or a dental substrate in the oral cavity;
wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

A thirteenth aspect of the present disclosure is the use of a polymer film for application on a dental substrate *ex vivo*, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof. The polymer film has one or more relief features on at least a portion of the film.

A fourteenth aspect of the present disclosure is a method of making a dental substrate having an outer surface to which a polymer film is attached, comprising the steps of:

a) forming one or more relief features on a polymer film by embossing the film; and

b) attaching the polymer film to the outer surface of the dental substrate by one or more layers of adhesives or by thermal shrinking.

The embodiments of the present invention function by filling the soft tissue gap between the dental implant (e.g. an abutment) and remain stable until soft tissue recovery. They also prevent epithelial cell ongrowth/overgrowth. They additionally represent a suitable environment for fibroblast migration and soft tissue formation and closely adhere/bind to the dental substrate (e.g. implant and/or abutment).

Description of the Figures

Figure 1:

Figure 1 provides a comparison of the structural features of a natural tooth in the oral cavity and an artificial tooth.

Figure 2:

Figure 2 illustrates the different layers which may be present in the product according to the second aspect of the present disclosure.

Figure 3:

Figure 3 shows a film which has been subjected to a flocking process. During flocking, fibres are arranged perpendicular to the film surface.

Figure 4:

Figure 4 illustrates how the gap between a dental substrate and the surrounding tissue may be filled with a glue, wherein a) is a glue; b) is a coating of a product according to the present disclosure; c) is an abutment; d) is an implant; e) is the normal soft tissue of the gingiva; and f) is soft tissue that is not attached to the abutment surface.

Figure 5:

Figure 5 illustrates how the gap between a dental substrate and the surrounding tissue may be filled with a glue and a bone substitute material, wherein a) is a glue; b) is a coating of a product according to the present disclosure; c) is an abutment; d) is an implant; e) is the normal soft tissue of the gingiva; f) is soft tissue that is not attached to the abutment surface; and g) is bone substitute material.

Figure 6:

Figure 6 illustrates how the gap between a dental substrate and the surrounding tissue may be filled with a glue, a bone substitute material and a soft tissue scaffold, wherein a) is a glue; b) is a coating of a product according to the present disclosure; c) is an abutment; d) is an

implant; e) is the normal soft tissue of the gingiva; f) is soft tissue that is not attached to the abutment surface; g) is bone substitute material; and h) is a soft tissue scaffold.

Detailed Description

The present disclosure relates to products comprising a first composition and a second composition and products having a first layer comprising a first composition and a second layer comprising a second composition, which may be used to coat a natural tooth or a dental substrate. The dental substrate may be coated *in situ*, i.e. after being placed in a site in the oral cavity, or it may be coated *ex vivo*, i.e. outside the subject's body.

The present disclosure also relates to a dental substrate coated with a polymer and to a dental substrate having a polymer attached thereto wherein the polymer has one or more relief features on at least a portion of the film.

As used herein, the term "natural tooth" refers to a whole tooth or a part of a tooth in the oral cavity.

As used herein, the term "dental substrate" refers to an artificial tooth or components thereof. Such components of an artificial tooth include implantable devices and prosthetic components.

As used herein, the term "implantable device" refers to a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component.

As used herein, the term "implant" refers to an artificial replacement for a tooth's root.

As used herein, the term “abutment” refers to a connecting element which may be used to connect an implant to a crown.

As used herein, the term “prosthetic component” refers to a crown and a bridge

The product according to one aspect of the present disclosure comprises at least one resin and at least one filler. Specifically, a first aspect of the present disclosure provides a product comprising:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixtures thereof.

In a preferred embodiment of the first aspect of the present disclosure, the resin is selected from the group consisting of polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers, epoxy resin and mixtures thereof. More preferably the resin is selected from the group consisting of polyurethane-based resin, acrylate-based resin and mixtures thereof. Most preferably the resin is acrylate-based resin.

The amount of the resin present in the product is from 5 wt.% to 95 wt%, preferably from 60 wt.% to 80 wt.%, based on the total weight of the product.

As indicated in the first aspect of the present disclosure, mixtures of resins may also be employed in the first composition. Such resins may create micro-domains of different adhesives having different adhesive properties.

In one embodiment of the first aspect of the present disclosure, the filler is selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In an embodiment of the first aspect of the present invention, the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment of the present invention, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the product may be present in an amount from 5 to 95 wt. %, preferably, 20 to 95 wt.%, more preferably 60 to 80 wt.% based on the total weight of the product.

One or more fillers as mentioned in the embodiment, the another embodiment, the further embodiment and the alternative embodiment mentioned above, may be combined with any of the preferred, more preferred, or most preferred resins, or combinations thereof. For example, the product according to the first aspect of the present disclosure may comprise a most preferred acrylate-based resin and a filler such as hydroxylapatite mentioned in the further embodiment. Alternatively, the product according to the first aspect of the present

disclosure may comprise a more preferred polyurethane-based resin and a filler such as microspheres mentioned in the alternative embodiment.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product. The product according to the present disclosure may comprise other components such as additives. These other components may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

For the filler component of the second composition of the product, a salt may be employed. The skilled person would understand that any salt can be used that is biocompatible and non-toxic. Examples of salts that may be used as the filler component in the second composition described herein include salts based on alkaline and alkaline earth metals as cations. The corresponding anions of these salts may be non-metal ionic or halogenic compounds. In one embodiment, the cation is selected from the group consisting of Na^+, Mg^{2+}, Ca^{2+} and K^+. In one embodiment the anion may comprise Cl, P, O, N, and mixtures thereof. In one embodiment the salt is selected from the group consisting of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, sodium citrate, sodium sulfate, sodium bisulfate, sodium phosphate, monosodium phosphate, disodium phosphate, potassium phosphate, monopotassium phosphate, dipotassium phosphate, sodium ammonium chloride, sodium carbonate, sodium hydroxide, sodium iodide, sodium nitrate, sodium nitrite, sodium phosphate and ammonium nitrate.

For the filler component of the second composition of the product, chitosan may be employed. The chitosan for use in accordance with the present disclosure may have a degree of deacetylation (DDA) of 0 to 100%, preferably in the range of 0 to 25%, preferably in the range of 75 to 100%. In one embodiment, the chitosan has a degree of deacetylation in the range of 0 to 25% or 75 to 100%. Preferably the chitosan does not have a degree of deacetylation in the range of 26% to 74%.

For the filler component of the second composition of the product, micropheres may be employed. The microspheres may comprise resorbable and/or non-resorbable materials. The microspheres can be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range (mean value) of 1 to 500 µm, preferably 3 to 150 µm.

For the filler component of the second composition of the product, hydrogel polymers may be employed. The term "hydrogel polymers" refers to any polymeric material that has the ability to swell and retain a significant fraction of water within its structure, but that will not dissolve in water and that is biocompatible. These hydrogels can further be described as either homopolymeric, copolymeric or multipolymer interpenetrating polymeric hydrogels.

For the filler component of the second composition of the product, bioglasses may be employed. The bioglass may be selected from the group consisting of silicate-based glasses, phosphate-based glasses and borate-based glasses.

For the filler component of the second composition of the product, autologous fat may be employed. Autologous fat is fat which has been obtained from the same subject. It can be collected from any suitable site, which can be patient-specific. Autologous fat is typically composed of a mixture of fat stem cells, vasculature, tissue residues, and other cells.

In a particular embodiment of the first aspect of the present disclosure is provided a product comprising:

a first composition comprising at least one resin selected from the group consisting of polyurethane-based resin, acrylate-based resin, and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof.

In a further particular embodiment of the first aspect of the present disclosure is provided a product comprising:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof.

In a further particular embodiment of the first aspect of the present disclosure is provided a product comprising:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof.

In a further particular embodiment of the first aspect of the present disclosure is a product comprising:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product.

The product according to the first aspect of the present disclosure may further comprise at least one additive. Such additives may be selected from rheology modifiers, coupling agents, anti-foaming agents, antimicrobial agents, growth factors and bioactive agents.

These additives may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

Examples of rheology modifiers include: fumed silica, polymer solutions and clays.

Examples of coupling agents include: silanes, titanates and zirconates.

In one embodiment of the present disclosure, the coupling agent is selected from the group consisting of silanes, titanates, zirconates and phosphonates. Preferably the coupling agent is a silane.

Examples of anti- foaming agents include: mono- and diglycerides, siloxanes and esters of phosphoric acid.

Examples of antimicrobial agents include: silver particles, antibiotics (such as penicillins and cephalosporins), or bacteriostatic/bacteriocidal agents such as quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofurantoin) or tetracyclines, aminoglycosides, macrolides, sulphonamides. Others include antiseptics like hydrogen peroxide, iodine, polyhexanide, chlorhexidine, sodium bicarbonate and the like.

Examples of growth factors and bioactive agents include the families and derivatives of: PDGF (platelet-derived growth factor), EGF (epidermal growth factor), HB-EGF (heparin-binding epidermal growth factor), IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor), FGF (fibroblast growth factor), and the like.

The product according to the first aspect of the present disclosure may further comprise at least one peptide. Such peptides may be selected from peptide amphiphiles, consisting of a short hydrophobic domain at one end and a hydrophilic oligopeptide sequence at the other, or RAD-peptides (modification of RGD-peptides). Examples of RAD-peptides include e.g RAD-16 (Nanomedicine, 2013, 8(5), 823–847).

The product of the first aspect of the present disclosure preferably has a Young's modulus in the range of 0.1 kPa to 100 GPa, preferably in the range of 20 kPa to 100 GPa, preferably in the range of 50 kPa to 100 GPa, more preferably in the range of 70 kPa to 100 GPa. For measuring methods see "Study of Elastic Modulus and Yield Strength of Polymer Thin Films Using Atomic Force Microscopy", Binyang Du , Ophelia K. C. Tsui ,Qingling Zhang and Tianbai He, Langmuir, 2001, *17* (11), pp 3286–3291 and references therein.

The product according to the first aspect of the present disclosure may be in the form of a film or a sleeve.

The product according to the first aspect of the present disclosure may be a dental substrate selected from an implantable device such as a dental implant, an implant abutment, a

personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The first and second compositions of the product according to the first aspect of the present disclosure may be combined to form a single composition. The product according to the first aspect of the present disclosure that is a single composition may be in the form of a powder, a liquid, a hydrogel, a paste, a fiber or a thread. Preferably the product according to the first aspect of the present disclosure that is a single composition is in the form of a paste, a liquid, or a hydrogel.

In a second aspect of the present disclosure is provided a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers and mixtures thereof; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixtures thereof.

In a preferred embodiment of the second aspect of the present disclosure, the resin is selected from the group consisting of polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers, epoxy resin and mixtures thereof. More preferably

the resin is selected from the group consisting of polyurethane-based resin, acrylate-based resin and mixtures thereof. Most preferably the resin is acrylate-based resin.

The amount of the resin present in the product is from 5 wt.% to 95 wt%, preferably from 60 wt.% to 80 wt.%, based on the total weight of the product.

As indicated in the second aspect of the present disclosure, mixtures of resins may also be employed in the first composition. Such resins may create micro-domains of different adhesives having different adhesive properties.

In one embodiment of the second aspect of the present disclosure, the filler is selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In an embodiment of the second aspect of the present invention, the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment of the present invention, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the product may be present in an amount from 5 to 95 wt. %, preferably, 20 to 95 wt.%, more preferably 60 to 80 wt.% based on the total weight of the product.

One or more fillers as mentioned in the embodiment, the another embodiment, the further embodiment and the alternative embodiment mentioned above, may be included in the second layer of the product and any of the preferred, more preferred, or most preferred resins, or combinations thereof may be included in the first layer of the product. For example, the product according to the second aspect of the present disclosure may comprise a most preferred acrylate-based resin in the first layer and a filler such as hydroxylapatite mentioned in the further embodiment in the second layer. Alternatively, the product according to the first aspect of the present disclosure may comprise a more preferred polyurethane-based resin in the first layer and a filler such as microspheres mentioned in the alternative embodiment in the second layer.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product. The product according to the present disclosure may comprise other components such as additives. These other components may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

For the filler component of the second composition in the second layer of the product, a salt may be employed. The skilled person would understand that any salt can be used that is biocompatible and non-toxic. Examples of salts that may be used as the filler component in the second composition described herein include salts based on alkaline and alkaline earth metals as cations. The corresponding anions of these salts may be non-metal ionic or halogenic compounds. In one embodiment, the cation is selected from the group consisting of Na^+, Mg^{2+}, Ca^{2+} and K^+. In one embodiment the anion may comprise Cl, P, O, N, and mixtures thereof. In one embodiment the salt is selected from the group consisting of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, sodium citrate, sodium sulfate, sodium bisulfate, sodium phosphate, monosodium phosphate, disodium phosphate, potassium phosphate, monopotassium phosphate, dipotassium

phosphate, sodium ammonium chloride, sodium carbonate, sodium hydroxide, sodium iodide, sodium nitrate, sodium nitrite, sodium phosphate and ammonium nitrate.

For the filler component of the second composition in the second layer of the product, chitosan may be employed. The chitosan for use in accordance with the present disclosure may have a degree of deacetylation (DDA) of 0 to 100%, preferably in the range of 0 to 25%, preferably in the range of 75 to 100%. In one embodiment, the chitosan has a degree of deacetylation in the range of 0 to 25% or 75 to 100%. Preferably the chitosan does not have a degree of deacetylation in the range of 26% to 74%.

For the filler component of the second composition in the second layer of the product, micropheres may be employed. The microspheres may comprise resorbable and/or non-resorbable materials. The microspheres can be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range (mean value) of 1 to 500 µm, preferably 3 to 150 µm .

For the filler component of the second composition in the second layer of the product, hydrogel polymers may be employed. The term “hydrogel polymers” refers to any polymeric material that has the ability to swell and retain a significant fraction of water within its structure, but that will not dissolve in water and that is biocompatible. These hydrogels can further be described as either homopolymeric, copolymeric or multipolymer interpenetrating polymeric hydrogels.

For the filler component of the second composition in the second layer of the product, bioglasses may be employed. The bioglass may be selected from the group consisting of silicate-based glasses, phosphate-based glasses and borate-based glasses.

For the filler component of the second composition in the second layer of the product, autologous fat may be employed. Autologous fat is fat which has been obtained from the same subject. It can be collected from any suitable site, which can be patient-specific. Autologous fat is typically composed of a mixture of fat stem cells, vasculature, tissue residues, and other cells.

In a particular embodiment of the second aspect of the present disclosure is provided a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of polyurethane-based resin, acrylate-based resin, and mixtures thereof; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof.

In a further particular embodiment of the second aspect of the present disclosure is provided a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of acrylate-based resin; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof.

In a further particular embodiment of the second aspect of the present disclosure is provided a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of acrylate-based resin; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof.

In a further particular embodiment of the second aspect of the present disclosure is a product comprising:

a first layer comprising a first composition which comprises at least one resin selected from the group consisting of acrylate-based resin; and

a second layer comprising a second composition which comprises at least one filler selected from the group consisting of hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product.

The product according to the second aspect of the present disclosure may further comprise at least one additive. The additive may be present in the first layer and/or the second layer. Such additives may be selected from rheology modifiers, coupling agents, anti-foaming agents, antimicrobial agents, growth factors and bioactive agents.

These additives may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

Examples of rheology modifiers include: fumed silica, polymer solutions and clays.

Examples of coupling agents include: silanes, titanates and zirconates.

In one embodiment of the present disclosure, the coupling agent is selected from the group consisting of silanes, titanates, zirconates and phosphonates. Preferably the coupling agent is a silane.

Examples of anti-foaming agents include: mono- and diglycerides, siloxanes and esters of phosphoric acid.

Examples of antimicrobial agents include: silver particles, antibiotics (such as penicillins and cephalosporins), or bacteriostatic/bacteriocidal agents such as quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofurantoin) or tetracyclines, aminoglycosides, macrolides, sulphonamides. Others include antiseptics like hydrogen peroxide, iodine, polyhexanide, chlorhexidine, sodium bicarbonate and the like.

Examples of growth factors and bioactive agents include the families and derivatives of: PDGF (platelet-derived growth factor), EGF (epidermal growth factor), HB-EGF (heparin-binding epidermal growth factor), IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor), FGF (fibroblast growth factor), and the like.

The product according to the second aspect of the present disclosure may further comprise at least one peptide. The at least one peptide may be present in the first layer and/or the second layer. Such peptides may be selected from peptide amphiphiles, consisting of a short

hydrophobic domain at one end and a hydrophilic oligopeptide sequence at the other, or RAD-peptides. Examples of RAD-peptides include e.g RAD-16 (Nanomedicine, 2013, 8(5), 823–847).

The product according to the second aspect of the present disclosure may be in the form of a film or a sleeve.

The product according to the second aspect of the present disclosure may be a dental substrate selected from an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The first and second layers of the product according to the second aspect of the present disclosure may be each independently in the form of a powder, a liquid, a hydrogel, a paste, a fiber or a thread. Preferably the first and second layers of the product according to the second aspect of the present disclosure are each independently in the form of a paste, a liquid, or a hydrogel.

In one embodiment of the second aspect of the present disclosure the product comprises one or more layers between the first layer and the second layer.

The one of more layers between the first layer and the second layer are formulated to bond two dissimilar materials together that would otherwise have poor adhesion to each other. In the present case, the one or more layers are formulated to form a first bond with the first layer of the product according to the second aspect of the present disclosure and a second bond with the second layer of the product according to the second aspect of the present

disclosure, wherein the strength of the first bond and strength of the second bond are each greater than the strength of the bond formed between said first layer and said second layer

The one or more layers between the first layer and the second layer are formulated to have surface energy that is between the surface properties of the first layer and the second layer.

The product according to the second aspect of the present disclosure can be used to coat a natural tooth or a dental substrate wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

The one or more layers between the first layer and the second layer may comprise: an adhesive formulation based on a polymer, optionally a tackifier resin, fillers, stabilizing and/or rheology modifying additives.

In a third aspect of the present disclosure is provided a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In a preferred embodiment of the third aspect of the present disclosure, the resin is selected from the group consisting of polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers, epoxy resin and mixtures thereof. More preferably the resin is selected from the group consisting of polyurethane-based resin, acrylate-based resin and mixtures thereof. Most preferably the resin is acrylate-based resin.

The amount of the resin present in the product is from 5 wt.% to 95 wt%, preferably from 60 wt.% to 80 wt.%, based on the total weight of the product.

As indicated in the third aspect of the present disclosure, mixtures of resins may also be employed in the first composition. Such resins may create micro-domains of different adhesives having different adhesive properties.

In one embodiment of the third aspect of the present disclosure, the filler is selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In an embodiment of the third aspect of the present invention, the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment of the present invention, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the product may be present in an amount from 5 to 95 wt. %, preferably, 20 to 95 wt.%, more preferably 60 to 80 wt.% based on the total weight of the product.

One or more fillers as mentioned in the embodiment, the another embodiment, the further embodiment and the alternative embodiment mentioned above, may be combined with any of the preferred, more preferred, or most preferred resins, or combinations thereof. For example, the product according to the third aspect of the present disclosure may comprise a most preferred acrylate-based resin and a filler such as hydroxylapatite mentioned in the further embodiment. Alternatively, the product according to the third aspect of the present disclosure may comprise a more preferred polyurethane-based resin and a filler such as microspheres mentioned in the alternative embodiment.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product. The product according to the present disclosure may comprise other components such as additives. These other components may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

For the filler component of the second composition of the product, a salt may be employed. The skilled person would understand that any salt can be used that is biocompatible and non-toxic. Examples of salts that may be used as the filler component in the second composition described herein include salts based on alkaline and alkaline earth metals as cations. The corresponding anions of these salts may be non-metal ionic or halogenic compounds. In one embodiment, the cation is selected from the group consisting of Na^+, Mg^{2+}, Ca^{2+} and K^+. In one embodiment the anion may comprise Cl, P, O, N, and mixtures thereof. In one embodiment the salt is selected from the group consisting of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, sodium citrate, sodium sulfate, sodium bisulfate, sodium phosphate, monosodium phosphate,

disodium phosphate, potassium phosphate, monopotassium phosphate, dipotassium phosphate, sodium ammonium chloride, sodium carbonate, sodium hydroxide, sodium iodide, sodium nitrate, sodium nitrite, sodium phosphate and ammonium nitrate.

For the filler component of the second composition of the product, chitosan may be employed. The chitosan for use in accordance with the present disclosure may have a degree of deacetylation (DDA) of 0 to 100%, preferably in the range of 0 to 25%, preferably in the range of 75 to 100%. In one embodiment, the chitosan has a degree of deacetylation in the range of 0 to 25% or 75 to 100%. Preferably the chitosan does not have a degree of deacetylation in the range of 26% to 74%.

For the filler component of the second composition of the product, micropheres may be employed. The microspheres may comprise resorbable and/or non-resorbable materials. The microspheres can be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range (mean value) of 1 to 500 µm, preferably 3 to 150 µm.

For the filler component of the second composition of the product, hydrogel polymers may be employed. These hydrogels can further be described as either homopolymeric, copolymeric or multipolymer interpenetrating polymeric hydrogels.

For the filler component of the second composition of the product, bioglasses may be employed. The bioglass may be selected from the group consisting of silicate-based glasses, phosphate-based glasses and borate-based glasses.

For the filler component of the second composition of the product, autologous fat may be employed. Autologous fat is typically composed of a mixture of fat stem cells, vasculature, tissue residues, and other cells.

In a particular embodiment of the third aspect of the present disclosure is provided a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of polyurethane-based resin, acrylate-based resin, and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In a further particular embodiment of the third aspect of the present disclosure is provided a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In a further particular embodiment of the third aspect of the present disclosure is provided a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In a further particular embodiment of the third aspect of the present disclosure is a method of applying a product to a dental substrate or a natural tooth *in vivo* or *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product.

The product according to the third aspect of the present disclosure may further comprise at least one additive. Such additives may be selected from rheology modifiers, coupling agents, anti-foaming agents, antimicrobial agents, growth factors and bioactive agents.

These additives may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

Examples of rheology modifiers include: fumed silica, polymer solutions and clays.

Examples of coupling agents include: silanes, titanates and zirconates. In one embodiment, the coupling agent is selected from the group consisting of silanes, titanates, zirconates and phosphonates. Preferably the coupling agent is a silane.

Examples of anti- foaming agents include: mono- and diglycerides, siloxanes and esters of phosphoric acid.

Examples of antimicrobial agents include: silver particles, antibiotics (such as penicillins and cephalosporins), or bacteriostatic/bacteriocidal agents such as quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofurantoin) or tetracyclines, aminoglycosides, macrolides, sulphonamides. Others include antiseptics like hydrogen peroxide, iodine, polyhexanide, chlorhexidine, sodium bicarbonate and the like.

Examples of growth factors and bioactive agents include the families and derivatives of: PDGF (platelet-derived growth factor), EGF (epidermal growth factor), HB-EGF (heparin-

binding epidermal growth factor), IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor), FGF (fibroblast growth factor), and the like.

The product according to the third aspect of the present disclosure may further comprise at least one peptide. Such peptides may be selected from peptide amphiphiles, consisting of a short hydrophobic domain at one end and a hydrophilic oligopeptide sequence at the other, or RAD-peptides. Examples of RAD-peptides include e.g RAD-16 (Nanomedicine, 2013, 8(5), 823–847).

The product of the third aspect of the present disclosure preferably has a Young's modulus in the range of 0.1 kPa to 100 GPa, preferably in the range of 20 kPa to 100 GPa, preferably in the range of 50 kPa to 100 GPa, more preferably in the range of 70 kPa to 100 GPa. For measuring methods see "Study of Elastic Modulus and Yield Strength of Polymer Thin Films Using Atomic Force Microscopy", Binyang Du , Ophelia K. C. Tsui ,Qingling Zhang and Tianbai He, Langmuir, 2001, *17* (11), pp 3286–3291 and references therein.

In one embodiment of the third aspect of the present disclosure the product is applied to a dental substrate *ex vivo*.

In another embodiment of the third aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In a further embodiment of the third aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer one or more layers are present between the first layer and the second layer. Preferably, the one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

In a first embodiment of the third aspect of the present disclosure, the product is applied to a dental substrate, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The product according to the third aspect of the present disclosure may be in the form of a film or a sleeve. The film and sleeve can be formed by extrusion processes such as flatbed or blow extrusion, or by casting. The sleeve may also be formed by blow-extrusion of a tubular film. The term "sleeve" as used herein, describes a tubular film having at least one opening.

In an embodiment of the third aspect of the present disclosure, the product in the form of a film or sleeve may be applied to a natural tooth or a dental substrate by means of thermal shrinking. Thermal shrinking may be conducted at maximum temperatures of 45°C. Thermal shrinking may be performed *in vivo* or *ex vivo* if the film or sleeve is applied to a dental substrate.

The film or sleeve may have a thickness in the range of 15 µm – 200 µm, preferably a thickness in the range of 15 µm and 100 µm, most preferably a thickness in the range of 15 µm – 50 µm.

The films and sleeves as described herein may be subjected to further processes carried out *ex vivo*. Such processes include micro-embossing and flocking.

During micro-embossing, a polymer film is treated with a heated engraved roll to emboss a pattern on the film. The micro-embossing of polymer films may be used to increase the

surface area of the film and to provide for sites for mechanical anchoring. Such sites include pillars, mushroom shaped structures and cavities.

During flocking, fibres are arranged perpendicular to the film surface (see Figure 3). The flocking process involves applying short mono-filament fibres directly on a surface that has been previously coated with an adhesive by means of electrostatic forces. Such an adhesive are known as “flock adhesives” and are typically based on polymer dispersions.

In a further embodiment of the third aspect of the present disclosure, the product in the form of an injectable liquid, a hydrogel or a paste is applied to a natural tooth or a dental substrate.

In a further embodiment of the third aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer the first layer and/or the second layer are each independently in the form of an injectable liquid, a hydrogel or a paste, wherein the first layer is applied to a natural tooth or a dental substrate and the second layer is applied to the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. The one or more layers may optionally be in the form of an injectable liquid, a hydrogel or a paste.

The one of more layers applied to the first layer are formulated to bond two dissimilar materials together that would otherwise have poor adhesion to each other. In the present case, the one or more layers are formulated to form a first bond with the first layer of the product and a second bond with the second layer of the product, wherein the strength of the first bond and strength of the second bond are each greater than the strength of the bond formed between said first layer and said second layer.

The one or more layers between the first layer and the second layer are formulated to have surface energy that is between the surface properties of the first layer and the second layer.

The injectable liquid preferably has a viscosity of between 100 cP and 50'000cP, preferably of between 200 and 5000 cP.

All viscosities mentioned herein were measured according to the Brookfield method as specified in DIN EN ISO 2555 or ISO 1652.

The injectable hydrogel preferably has a viscosity in the range of 100 cP and 50'000cP, preferably in the range of 200 and 5000 cP.

In a further embodiment, when contacted with a fluid such as water or saliva at a site in the oral cavity, the hydrogel becomes solid. Preferably the hydrogel solidifies within 0.5-10 minutes of being contacted with a fluid. Preferably the hydrogel solidifies within 0.5-5 minutes of being contacted with a fluid. Most preferably the hydrogel solidifies within 0.5-2 minutes of being contacted with a fluid.

In a further embodiment of the third aspect of the present disclosure, the product is in the form of a fibre which is applied to a natural tooth or a dental substrate by spinning the fibre around the natural tooth or dental substrate. When the fibre is applied to a dental substrate, it may be spun around the dental substrate *in vivo* or *ex vivo*.

In a further embodiment of the third aspect of the present disclosure, the first layer and the second layer of the product are each in the form of a fibre, wherein the first layer is applied to a natural tooth or a dental substrate by spinning the fibre around the natural tooth or dental substrate and the second layer is applied to the first layer by spinning the fibre around the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of fibres.

The fibre may have a diameter in the range of 20 nm and 400 nm, preferably in the range of 30 nm and 100 nm. The length of the fibre needed will depend on the surface area of the natural tooth or dental substrate to be covered by the fibre. This skilled person would be able to determine this. The term “fibre” as used herein means one or more fibres.

In a further embodiment of the third aspect of the present disclosure, the product is comprised in microspheres which are applied to a natural tooth or a dental substrate.

In a further embodiment of the third aspect of the present disclosure, the first composition of the product is comprised in a first layer of microspheres and the second composition of the product is comprised in a second layer of microspheres, wherein the microspheres comprising the first layer are applied to a natural tooth or a dental substrate and the microspheres comprising the second layer are applied to the first layer. Prior to application of the microspheres comprising the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of microspheres.

The microspheres may be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range of 1- 500 µm, preferably preferably 3 to 150 µm.

In another embodiment of the third aspect of the present disclosure the product is applied to a natural tooth or dental substrate by sprinkling the product on a natural tooth or dental substrate to which adhesive has been applied and then curing.

In a further embodiment of the third aspect of the present disclosure, the first layer of the product is applied to a natural tooth or a dental substrate by sprinkling the first layer of the product on the natural tooth or dental substrate and then curing, and the second layer of the

product is applied to the cured first layer by sprinkling the second layer of the product on the first layer and then curing. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be applied by sprinkling onto the first layer and then curing.

Prior to the application of the products according to the third aspect of the present disclosure, the natural tooth and dental substrate may first be cleaned. The natural tooth and dental substrate may be cleaned mechanically, for example by using ultrasound, curettes or a specialised brush such as a TiBrush (a brush comprising titanium bristles). The natural tooth and dental substrate may be cleaned chemically, for example etching with hydrogen peroxide, hydrogen fluoride, plasma, laser or blasting. The natural tooth and dental substrate may be cleaned mechanically and chemically.

In a further embodiment of the third aspect of the present disclosure, together with the application of the product to a natural tooth or a dental substrate, a cyanoacrylate-based glue may be applied on the external part of the gingiva that surrounds the natural tooth or dental substrate. For example, the gap between the dental substrate and the surrounding tissue may be filled with a glue. This is illustrated in Figure 4. The glue may comprise cyanoacrylate monomers. The glue preferably functions by radical, anionic or photo-induced curing.

In a further embodiment of the third aspect of the present disclosure, together with the application of the product to a natural tooth or a dental substrate, the gap between the natural tooth or dental substrate and the surrounding tissue may be filled with a glue and a bone substitute material. This is illustrated in Figure 5. The bone substitute material may comprise autologous, allogenic (such as “Creos Allograft”), xenogenic (such as “Creos Xenograft”) or synthetic materials (such as “NovaBone Dental” or CeraSorb).

In a further embodiment of the third aspect of the present disclosure, together with the application of the product to a natural tooth or a dental substrate, the gap between the

natural tooth or dental substrate and the surrounding tissue may be filled with a glue, a bone substitute material and a soft tissue scaffold. This is illustrated in Figure 6. The soft tissue scaffold may comprise materials originating from an autologous, allogenic, xenogenic or synthetic source, such as different forms of collagens but not limited to such. The soft tissue scaffold remains stable until soft tissue recovery is completed. The soft tissue scaffold represents a suitable environment for fibroblast migration and soft tissue formation and closely adheres/binds to the product that has been applied to the natural tooth or dental substrate.

A fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;
and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

In a preferred embodiment of the fourth aspect of the present disclosure, the resin is selected from the group consisting of polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers, epoxy resin and mixtures thereof. More preferably the resin is selected from the group consisting of polyurethane-based resin, acrylate-based resin and mixtures thereof. Most preferably the resin is acrylate-based resin.

The amount of the resin present in the product is from 5 wt.% to 95 wt%, preferably from 60 wt.% to 80 wt.%, based on the total weight of the product.

As indicated in the fourth aspect of the present disclosure, mixtures of resins may also be employed in the first composition. Such resins may create micro-domains of different adhesives having different adhesive properties.

In one embodiment of the fourth aspect of the present disclosure, the filler is selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In an embodiment of the fourth aspect of the present invention, the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment of the present invention, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the product may be present in an amount from 5 to 95 wt. %, preferably, 20 to 95 wt.%, more preferably 60 to 80 wt.% based on the total weight of the product.

One or more fillers as mentioned in the embodiment, the another embodiment, the further embodiment and the alternative embodiment mentioned above, may be combined with any of the preferred, more preferred, or most preferred resins, or combinations thereof. For example, the product according to the fourth aspect of the present disclosure may comprise

a most preferred acrylate-based resin and a filler such as hydroxylapatite mentioned in the further embodiment. Alternatively, the product according to the fourth aspect of the present disclosure may comprise a more preferred polyurethane-based resin and a filler such as microspheres mentioned in the alternative embodiment.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product. The product according to the present disclosure may comprise other components such as additives. These other components may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

For the filler component of the second composition of the product, a salt may be employed. The skilled person would understand that any salt can be used that is biocompatible and non-toxic. Examples of salts that may be used as the filler component in the second composition described herein include salts based on alkaline and alkaline earth metals as cations. The corresponding anions of these salts may be non-metal ionic or halogenic compounds. In one embodiment, the cation is selected from the group consisting of Na^+, Mg^{2+}, Ca^{2+} and K^+. In one embodiment the anion may comprise Cl, P, O, N, and mixtures thereof. In one embodiment the salt is selected from the group consisting of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, sodium citrate, sodium sulfate, sodium bisulfate, sodium phosphate, monosodium phosphate, disodium phosphate, potassium phosphate, monopotassium phosphate, dipotassium phosphate, sodium ammonium chloride, sodium carbonate, sodium hydroxide, sodium iodide, sodium nitrate, sodium nitrite, sodium phosphate and ammonium nitrate.

For the filler component of the second composition of the product, chitosan may be employed. The chitosan for use in accordance with the present disclosure may have a degree of deacetylation (DDA) of 0 to 100%, preferably in the range of 0 to 25%, preferably in the range of 75 to 100%. In one embodiment, the chitosan has a degree of deacetylation in the

range of 0 to 25% or 75 to 100%. Preferably the chitosan does not have a degree of deacetylation in the range of 26% to 74%.

For the filler component of the second composition of the product, micropheres may be employed. The microspheres may comprise resorbable and/or non-resorbable materials. The microspheres can be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range (mean value) of 1 to 500 µm, preferably 3 to 150 µm.

For the filler component of the second composition of the product, hydrogel polymers may be employed. These hydrogels can further be described as either homopolymeric, copolymeric or multipolymer interpenetrating polymeric hydrogels.

For the filler component of the second composition of the product, bioglasses may be employed. The bioglass may be selected from the group consisting of silicate-based glasses, phosphate-based glasses and borate-based glasses.

For the filler component of the second composition of the product, autologous fat may be employed. Autologous fat is typically composed of a mixture of fat stem cells, vasculature, tissue residues, and other cells.

A particular embodiment of the fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of polyurethane-based resin, acrylate-based resin, and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

A further particular embodiment of the fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

A further particular embodiment of the fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

A further particular embodiment of the fourth aspect of the present disclosure is the use of a product for coating a dental substrate *ex vivo*, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product.

The product according to the fourth aspect of the present disclosure may further comprise at least one additive. Such additives may be selected from rheology modifiers, coupling agents, anti-foaming agents, antimicrobial agents, growth factors and bioactive agents.

These additives may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

Examples of rheology modifiers include: fumed silica, polymer solutions and clays.

Examples of coupling agents include: silanes, titanates and zirconates. In one embodiment, the coupling agent is selected from the group consisting of silanes, titanates, zirconates and phosphonates. Preferably the coupling agent is a silane.

Examples of anti- foaming agents include: mono- and diglycerides, siloxanes and esters of phosphoric acid.

Examples of antimicrobial agents include: silver particles, antibiotics (such as penicillins and cephalosporins), or bacteriostatic/bacteriocidal agents such as quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofurantoin) or tetracyclines, aminoglycosides, macrolides, sulphonamides. Others include antiseptics like hydrogen peroxide, iodine, polyhexanide, chlorhexidine, sodium bicarbonate and the like.

Examples of growth factors and bioactive agents include the families and derivatives of: PDGF (platelet-derived growth factor), EGF (epidermal growth factor), HB-EGF (heparin-binding epidermal growth factor), IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor), FGF (fibroblast growth factor), and the like.

The product according to the fourth aspect of the present disclosure may further comprise at least one peptide. Such peptides may be selected from peptide amphiphiles, consisting of a short hydrophobic domain at one end and a hydrophilic oligopeptide sequence at the other, or RAD-peptides. Examples of RAD-peptides include e.g RAD-16 (Nanomedicine, 2013, 8(5), 823–847).

The product of the fourth aspect of the present disclosure preferably has a Young's modulus in the range of 0.1 kPa to 100 GPa, preferably in the range of 20 kPa to 100 GPa, preferably in the range of 50 kPa to 100 GPa, more preferably in the range of 70 kPa to 100 GPa. For measuring methods see "Study of Elastic Modulus and Yield Strength of Polymer Thin Films Using Atomic Force Microscopy", Binyang Du , Ophelia K. C. Tsui ,Qingling Zhang and Tianbai He, Langmuir, 2001, *17* (11), pp 3286–3291 and references therein.

In another embodiment of the fourth aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In a further embodiment of the fourth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer one or more layers are present between the first layer and the second layer. Preferably, the one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

In a first embodiment of the fourth aspect of the present disclosure, the product is applied to a dental substrate, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The product according to the fourth aspect of the present disclosure may be in the form of a film or a sleeve. The film and sleeve can be formed by extrusion processes such as flatbed or

blow extrusion, or by casting. The sleeve may also be formed by blow-extrusion of a tubular film. The term “sleeve” as used herein, describes a tubular film having at least one opening.

In an embodiment of the fourth aspect of the present disclosure, the product in the form of a film or sleeve may be applied to a dental substrate by means of thermal shrinking. Thermal shrinking may be conducted at maximum temperatures of 45°C.

The film or sleeve may have a thickness in the range of 15 µm – 200 µm, preferably a thickness in the range of 15 µm and 100 µm, most preferably a thickness in the range of 15 µm – 50 µm.

The films and sleeves as described herein may be subjected to further processes carried out *ex vivo*. Such processes include micro-embossing and flocking.

During micro-embossing, a polymer film is treated with a heated engraved roll to emboss a pattern on the film. The micro-embossing of polymer films may be used to increase the surface area of the film and to provide for sites for mechanical anchoring. Such sites include pillars, mushroom shaped structures and cavities.

During flocking, fibres are arranged perpendicular to the film surface (see Figure 3). The flocking process involves applying short mono-filament fibres directly on a surface that has been previously coated with an adhesive by means of electrostatic forces. Such an adhesive are known as “flock adhesives” and are typically based on polymer dispersions.

In a further embodiment of the fourth aspect of the present disclosure, the product in the form of an injectable liquid, a hydrogel or a paste is applied to a dental substrate.

In a further embodiment of the fourth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer the first layer and/or the second layer are each independently in the form of an injectable

liquid, a hydrogel or a paste, wherein the first layer is applied to a dental substrate and the second layer is applied to the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. The one or more layers may optionally be in the form of an injectable liquid, a hydrogel or a paste.

The one of more layers applied to the first layer are formulated to bond two dissimilar materials together that would otherwise have poor adhesion to each other. In the present case, the one or more layers are formulated to form a first bond with the first layer of the product and a second bond with the second layer of the product, wherein the strength of the first bond and strength of the second bond are each greater than the strength of the bond formed between said first layer and said second layer.

The one or more layers between the first layer and the second layer are formulated to have surface energy that is between the surface properties of the first layer and the second layer.

The injectable liquid preferably has a viscosity of between 100 cP and 50'000cP, preferably of between 200 and 5000 cP.

All viscosities mentioned herein were measured according to the Brookfield method as specified in DIN EN ISO 2555 or ISO 1652.

The injectable hydrogel preferably has a viscosity in the range of 100 cP and 50'000cP, preferably in the range of 200 and 5000 cP.

In a further embodiment, when contacted with a fluid such as water or saliva at a site in the oral cavity, the hydrogel becomes solid. Preferably the hydrogel solidifies within 0.5-10 minutes of being contacted with a fluid. Preferably the hydrogel solidifies within 0.5-5 minutes of being contacted with a fluid. Most preferably the hydrogel solidifies within 0.5-2 minutes of being contacted with a fluid.

In a further embodiment of the third aspect of the present disclosure, the product is in the form of a fibre which is applied to a dental substrate by spinning the fibre around the dental substrate.

In a further embodiment of the fourth aspect of the present disclosure, the first layer and the second layer of the product are each in the form of a fibre, wherein the first layer is applied to a dental substrate by spinning the fibre around the dental substrate and the second layer is applied to the first layer by spinning the fibre around the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of fibres.

The fibre may have a diameter in the range of 20 nm and 400 nm, preferably in the range of 30 nm and 100 nm. The length of the fibre needed will depend on the surface area of the dental substrate to be covered by the fibre. This skilled person would be able to determine this. The term "fibre" as used herein means one or more fibres.

In a further embodiment of the fourth aspect of the present disclosure, the product is comprised in microspheres which are applied to a dental substrate.

In a further embodiment of the fourth aspect of the present disclosure, the first composition of the product is comprised in a first layer of microspheres and the second composition of the product is comprised in a second layer of microspheres, wherein the microspheres comprising the first layer are applied to a dental substrate and the microspheres comprising the second layer are applied to the first layer. Prior to application of the microspheres comprising the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of microspheres.

The microspheres may be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range of 1- 500 µm, preferably preferably 3 to 150 µm.

In another embodiment of the fourth aspect of the present disclosure the product is applied to a dental substrate by sprinkling the product on a dental substrate to which adhesive has been applied and then curing.

In a further embodiment of the fourth aspect of the present disclosure, the first layer of the product is applied to a dental substrate by sprinkling the first layer of the product on the dental substrate and then curing, and the second layer of the product is applied to the cured first layer by sprinkling the second layer of the product on the first layer and then curing. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be applied by sprinkling onto the first layer and then curing.

Prior to the application of the products according to the fourth aspect of the present disclosure, the dental substrate may first be cleaned. The dental substrate may be cleaned mechanically, for example by using ultrasound, curettes or a specialised brush such as a TiBrush (a brush comprising titanium bristles). The dental substrate may be cleaned chemically, for example etching with hydrogen peroxide, hydrogen fluoride, plasma, laser or blasting. The dental substrate may be cleaned mechanically and chemically.

A fifth aspect of the present invention is a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat.

In one embodiment of the fifth aspect of the present invention, the subject is a mammal. The subject may be selected from the group consisting of a human, a dog, a horse, a sheep, a cow. Preferably the subject is a human.

In a preferred embodiment of the fifth aspect of the present disclosure, the resin is selected from the group consisting of polyurethane-based resin, vinyl-based resins such as acrylate-based resin, silane terminated polymers, epoxy resin and mixtures thereof. More preferably the resin is selected from the group consisting of polyurethane-based resin, acrylate-based resin and mixtures thereof. Most preferably the resin is acrylate-based resin.

The amount of the resin present in the product is from 5 wt.% to 95 wt%, preferably from 60 wt.% to 80 wt.%, based on the total weight of the product.

As indicated in the fifth aspect of the present disclosure, mixtures of resins may also be employed in the first composition. Such resins may create micro-domains of different adhesives having different adhesive properties.

In one embodiment of the fifth aspect of the present disclosure, the filler is selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another

embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In an embodiment of the fifth aspect of the present invention, the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment of the present invention, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the product may be present in an amount from 5 to 95 wt. %, preferably, 20 to 95 wt.%, more preferably 60 to 80 wt.% based on the total weight of the product.

One or more fillers as mentioned in the embodiment, the another embodiment, the further embodiment and the alternative embodiment mentioned above, may be combined with any of the preferred, more preferred, or most preferred resins, or combinations thereof. For example, the product according to the fifth aspect of the present disclosure may comprise a most preferred acrylate-based resin and a filler such as hydroxylapatite mentioned in the further embodiment. Alternatively, the product according to the fifth aspect of the present disclosure may comprise a more preferred polyurethane-based resin and a filler such as microspheres mentioned in the alternative embodiment.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product. The product according to the present disclosure may comprise other

components such as additives. These other components may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

For the filler component of the second composition of the product, a salt may be employed. The skilled person would understand that any salt can be used that is biocompatible and non-toxic. Examples of salts that may be used as the filler component in the second composition described herein include salts based on alkaline and alkaline earth metals as cations. The corresponding anions of these salts may be non-metal ionic or halogenic compounds. In one embodiment, the cation is selected from the group consisting of Na^+, Mg^{2+}, Ca^{2+} and K^+. In one embodiment the anion may comprise Cl, P, O, N, and mixtures thereof. In one embodiment the salt is selected from the group consisting of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, sodium citrate, sodium sulfate, sodium bisulfate, sodium phosphate, monosodium phosphate, disodium phosphate, potassium phosphate, monopotassium phosphate, dipotassium phosphate, sodium ammonium chloride, sodium carbonate, sodium hydroxide, sodium iodide, sodium nitrate, sodium nitrite, sodium phosphate and ammonium nitrate.

For the filler component of the second composition of the product, chitosan may be employed. The chitosan for use in accordance with the present disclosure may have a degree of deacetylation (DDA) of 0 to 100%, preferably in the range of 0 to 25%, preferably in the range of 75 to 100%. In one embodiment, the chitosan has a degree of deacetylation in the range of 0 to 25% or 75 to 100%. Preferably the chitosan does not have a degree of deacetylation in the range of 26% to 74%.

For the filler component of the second composition of the product, micropheres may be employed. The microspheres may comprise resorbable and/or non-resorbable materials. The microspheres can be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural:

proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range (mean value) of 1 to 500 µm, preferably 3 to 150 µm.

For the filler component of the second composition of the product, hydrogel polymers may be employed. These hydrogels can further be described as either homopolymeric, copolymeric or multipolymer interpenetrating polymeric hydrogels.

For the filler component of the second composition of the product, bioglasses may be employed. The bioglass may be selected from the group consisting of silicate-based glasses, phosphate-based glasses and borate-based glasses.

For the filler component of the second composition of the product, autologous fat may be employed. Autologous fat is typically composed of a mixture of fat stem cells, vasculature, tissue residues, and other cells.

In a particular embodiment of the fifth aspect of the present disclosure is provided a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of polyurethane-based resin, acrylate-based resin, and mixtures thereof; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microspheres, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, autologous fat and mixture thereof.

In a further particular embodiment of the fifth aspect of the present disclosure is provided a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof.

In a further particular embodiment of the fifth aspect of the present disclosure is provided a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof.

In a further particular embodiment of the fifth aspect of the present disclosure is a product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of acrylate-based resin; and

a second composition comprising at least one filler selected from the group consisting of hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

The combined weight of the filler and resin in the product is preferably at least 85 wt.% based on the total weight of the product, more preferably at least 90 wt.% based on the total weight of the product.

The product according to the fifth aspect of the present disclosure may further comprise at least one additive. Such additives may be selected from rheology modifiers, coupling agents, anti-foaming agents, antimicrobial agents, growth factors and bioactive agents.

These additives may be present in less than 15 wt.%, preferably less than 10 wt.% based on the total weight of the product.

Examples of rheology modifiers include: fumed silica, polymer solutions and clays.

Examples of coupling agents include: silanes, titanates and zirconates. In one embodiment, the coupling agent is selected from the group consisting of silanes, titanates, zirconates and phosphonates. Preferably the coupling agent is a silane.

Examples of anti- foaming agents include: mono- and diglycerides, siloxanes and esters of phosphoric acid.

Examples of antimicrobial agents include: silver particles, antibiotics (such as penicillins and cephalosporins), or bacteriostatic/bacteriocidal agents such as quinolones (ciprofloxacin), rifamycins (rifampin), nitroimidazoles (metronidazole), and nitrofurans (nitrofurantoin) or

tetracyclines, aminoglycosides, macrolides, sulphonamides. Others include antiseptics like hydrogen peroxide, iodine, polyhexanide, chlorhexidine, sodium bicarbonate and the like.

Examples of growth factors and bioactive agents include the families and derivatives of: PDGF (platelet-derived growth factor), EGF (epidermal growth factor), HB-EGF (heparin-binding epidermal growth factor), IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor), FGF (fibroblast growth factor), and the like.

The product according to the fifth aspect of the present disclosure may further comprise at least one peptide. Such peptides may be selected from peptide amphiphiles, consisting of a short hydrophobic domain at one end and a hydrophilic oligopeptide sequence at the other, or RAD-peptides. Examples of RAD-peptides include e.g RAD-16 (Nanomedicine, 2013, 8(5), 823–847).

The product of the fifth aspect of the present disclosure preferably has a Young's modulus in the range of 0.1 kPa to 100 GPa, preferably in the range of 20 kPa to 100 GPa, preferably in the range of 50 kPa to 100 GPa, more preferably in the range of 70 kPa to 100 GPa. For measuring methods see "Study of Elastic Modulus and Yield Strength of Polymer Thin Films Using Atomic Force Microscopy", Binyang Du , Ophelia K. C. Tsui ,Qingling Zhang and Tianbai He, Langmuir, 2001, *17* (11), pp 3286–3291 and references therein.

In one embodiment of the fifth aspect of the present disclosure, the first composition and the second composition are combined to form a single composition. Alternatively, the first composition is present in a first layer and the second composition is present in a second layer.

In a further embodiment of the fifth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer one or more layers are present between the first layer and the second layer. Preferably, the

one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

In one embodiment of the fifth aspect of the present disclosure the method of treating comprises applying the product to a natural tooth or a dental substrate.

In a first embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product to a dental substrate, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The product according to the fifth aspect of the present disclosure may be in the form of a film or a sleeve. The film and sleeve can be formed by extrusion processes such as flatbed or blow extrusion, or by casting. The sleeve may also be formed by blow-extrusion of a tubular film. The term “sleeve” as used herein, describes a tubular film having at least one opening.

In an embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product in the form of a film or sleeve to a natural tooth or a dental substrate by means of thermal shrinking. Thermal shrinking may be conducted at maximum temperatures of 45°C.

The film or sleeve may have a thickness in the range of 15 µm – 200 µm, preferably a thickness in the range of 15 µm and 100 µm, most preferably a thickness in the range of 15 µm – 50 µm.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product in the form of an injectable liquid, a hydrogel or a paste to a natural tooth or a dental substrate.

In a further embodiment of the fifth aspect of the present disclosure, when the first composition is present in a first layer and the second composition is present in a second layer, the method of treating comprises applying the first layer in the form of an injectable liquid, a hydrogel or a paste to a natural tooth or a dental substrate, and then applying the second layer in the form of an injectable liquid, a hydrogel or a paste to the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. The one or more layers may optionally be in the form of an injectable liquid, a hydrogel or a paste.

The one of more layers applied to the first layer are formulated to bond two dissimilar materials together that would otherwise have poor adhesion to each other. In the present case, the one or more layers are formulated to form a first bond with the first layer of the product and a second bond with the second layer of the product, wherein the strength of the first bond and strength of the second bond are each greater than the strength of the bond formed between said first layer and said second layer.

The one or more layers between the first layer and the second layer are formulated to have surface energy that is between the surface properties of the first layer and the second layer.

The injectable liquid preferably has a viscosity of between 100 cP and 50'000cP, preferably of between 200 and 5000 cP.

All viscosities mentioned herein were measured according to the Brookfield method as specified in DIN EN ISO 2555 or ISO 1652.

The injectable hydrogel preferably has a viscosity in the range of 100 cP and 50'000cP, preferably in the range of 200 and 5000 cP.

In a further embodiment, when contacted with a fluid such as water or saliva at a site in the oral cavity, the hydrogel becomes solid. Preferably the hydrogel solidifies within 0.5-10 minutes of being contacted with a fluid. Preferably the hydrogel solidifies within 0.5-5 minutes of being contacted with a fluid. Most preferably the hydrogel solidifies within 0.5-2 minutes of being contacted with a fluid.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product in the form of a fibre to a natural tooth or a dental substrate by spinning the fibre around the natural tooth or dental substrate.

In a further embodiment of the fifth aspect of the present disclosure, the first layer and the second layer of the product are each in the form of a fibre and the method of treating comprises applying first layer in the form of a fibre to a natural tooth or a dental substrate by spinning the fibre around the natural tooth or dental substrate, and applying the second layer in the form of a fibre to the first layer by spinning the fibre around the first layer. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of fibres.

The fibre may have a diameter in the range of 20 nm and 400 nm, preferably in the range of 30 nm and 100 nm. The length of the fibre needed will depend on the surface area of the natural tooth or dental substrate to be covered by the fibre. This skilled person would be able to determine this. The term "fibre" as used herein means one or more fibres.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product comprised in microspheres to a natural tooth or a dental substrate.

In a further embodiment of the fifth aspect of the present disclosure, the first composition of the product is comprised in a first layer of microspheres and the second composition of the product is comprised in a second layer of microspheres and the method of treating comprises applying the first layer of microspheres to a natural tooth or a dental substrate and then applying the second layer of microspheres to the first layer. Prior to application of the second layer of microspheres, one or more layers may be applied to the first layer. These one or more layers are formulated as described above and may optionally be in the form of microspheres.

The microspheres may be comprised of bioglass (silicate-based glasses, phosphate-based glasses and borate-based glasses), ceramics, polymers (synthetic: PLA, PCL, PGA, PLGA, PLLA) (natural: proteins, collagen, alginates, chitosane, HA, Gelatin) and mixtures thereof. The microspheres may have a diameter range of 1- 500 µm, preferably preferably 3 to 150 µm.

In another embodiment of the fifth aspect of the present disclosure the method of treating comprises applying the product to a natural tooth or dental substrate by sprinkling the product on a natural tooth or dental substrate to which adhesive has been applied and then curing.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying a first layer of the product comprising the first composition to a natural tooth or a dental substrate by sprinkling the first layer of the product on the natural tooth or dental substrate and then curing, and then applying the second layer of the product comprising the second composition to the cured first layer by sprinkling the second layer of the product on the first layer and then curing. Prior to application of the second layer, one or more layers may be applied to the first layer. These one or more layers are formulated as

described above and may optionally be applied by sprinkling onto the first layer and then curing.

Prior to the application of the products, the natural tooth and dental substrate may first be cleaned. The natural tooth and dental substrate may be cleaned mechanically, for example by using ultrasound, curettes or a specialised brush such as a TiBrush (a brush comprising titanium bristles). The natural tooth and dental substrate may be cleaned chemically, for example etching with hydrogen peroxide, hydrogen fluoride, plasma, laser or blasting. The natural tooth and dental substrate may be cleaned mechanically and chemically.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product to a natural tooth or a dental substrate and applying a cyanoacrylate-based glue on the external part of the gingiva that surrounds the natural tooth or dental substrate. For example, the gap between the dental substrate and the surrounding tissue may be filled with a glue. This is illustrated in Figure 4. The glue may comprise cyanoacrylate monomers. The glue preferably functions by radical, anionic or photo-induced curing.

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product to a natural tooth or a dental substrate and filling the gap between the natural tooth or dental substrate and the surrounding tissue with a glue and a bone substitute material. This is illustrated in Figure 5. The bone substitute material may comprise autologous, allogenic (such as “Creos Allograft”), xenogenic (such as “Creos Xenograft”) or synthetic materials (such as “NovaBone Dental” or CeraSorb).

In a further embodiment of the fifth aspect of the present disclosure, the method of treating comprises applying the product to a natural tooth or a dental substrate and filling the gap between the natural tooth or dental substrate and the surrounding tissue with a glue, a bone substitute material and a soft tissue scaffold. This is illustrated in Figure 6. The soft tissue

scaffold may comprise materials originating from an autologous, allogenic, xenogenic or synthetic source, such as different forms of collagens but not limited to such. The soft tissue scaffold remains stable until soft tissue recovery and may be employed to prevent epithelial cell ongrowth/overgrowth. The soft tissue scaffold represents a suitable environment for fibroblast migration and soft tissue formation and closely adheres/binds to the product that has been applied to the natural tooth or dental substrate.

The application of the product to the dental substrate modifies the surface of the dental substrate and fosters the attachment of gingival tissue and fibers to the dental substrate.

A sixth aspect of the present disclosure is a dental substrate coated with a polymer coating, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers, pH responsive polymers, and mixtures thereof.

Examples of thermoresponsive polymer are provided in U.S Patent US 9,453,197 B2 and include poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate). Mixtures of these polymers may also be comprised in the polymer coating.

Examples of pH responsive polymers are provided in U.S Patent US 9,453,197 B2 and include copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate. Mixtures of these polymers may also be comprised in the polymer coating.

The polymer coating may therefore comprise one or more polymers selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate), copolymers of acrylic acid and dimethylamino-ethylacrylate hydroxyethylacrylate.

The polymer coating may further comprise at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses and autologous fat.

In one embodiment, the filler may be selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In a further embodiment the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the polymer coating may be present in an amount from 2 to 90 wt. %, preferably 5 to 75 wt.%, more preferably 10 to 60 wt.%, most preferably 30 to 50 wt.% based on the total weight of the polymer coating.

In a seventh aspect of the present disclosure, is provided a dental substrate according to the sixth aspect of the present disclosure for use in a method of treating or preventing peri-

implantitis or periodontitis in a subject. Specifically, a dental substrate coated with a polymer coating, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers, pH responsive polymers, and mixtures thereof, may be used in a method of treating or preventing peri-implantitis or periodontitis in a subject. The thermoresponsive polymers and pH responsive polymers include those polymers mentioned above.

The application of a polymer coating on a dental substrate modifies the surface of the dental substrate and fosters the attachment of gingival tissue and fibers to the dental substrate.

An eighth aspect of the present disclosure is the use of a polymer coating for coating a dental substrate *ex vivo*, wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and a pH responsive polymer.

Examples of thermoresponsive polymer are provided in U.S Patent US 9,453,197 B2 and include poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate). Mixtures of these polymers may also be comprised in the polymer coating.

Examples of pH responsive polymers are provided in U.S Patent US 9,453,197 B2 and include copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate. Mixtures of these polymers may also be comprised in the polymer coating.

The polymer coating may therefore comprise one or more polymers selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate), copolymers of acrylic acid and dimethylamino-ethylacrylate hydroxyethylacrylate.

The polymer coating may further comprise at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses and autologous fat.

In one embodiment, the filler may be selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In a further embodiment the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the polymer coating may be present in an amount from 2 to 90 wt. %, preferably 5 to 75 wt.%, more preferably 10 to 60 wt.%, most preferably 30 to 50 wt.% based on the total weight of the polymer coating.

The polymer coating of the sixth aspect of the present disclosure is preferably coated on the surface of the dental substrate to which gingiva tissue attaches.

A ninth aspect of the present disclosure is a polymer coating for use in a method of treating or preventing peri-implantitis or periodontitis in a subject, wherein the polymer coating is applied on a natural tooth or a dental substrate in the oral cavity;
wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and pH responsive polymers.

Examples of thermoresponsive polymer are provided in U.S Patent US 9,453,197 B2 and include poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate). Mixtures of these polymers may also be comprised in the polymer coating.

Examples of pH responsive polymers are provided in U.S Patent US 9,453,197 B2 and include copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate. Mixtures of these polymers may also be comprised in the polymer coating.

The polymer coating may therefore comprise one or more polymers selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate), copolymers of acrylic acid and dimethylamino-ethylacrylate hydroxyethylacrylate.

The polymer coating may further comprise at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites bioglasses and autologous fat.

In one embodiment, the filler may be selected from the group consisting of hyaluronic acid, alginates, chitosan and mixtures thereof. In another embodiment, the filler is selected from the group consisting of poly(lactic-co-glycolic acid), hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene and mixtures thereof. In a further embodiment, the filler is selected from hydroxylapatite, beta-tricalcium phosphate, salt particles, microspheres, zeolites, bioglasses and mixtures thereof.

In a further embodiment the filler is selected from hyaluronic acid and alginates. In another embodiment, the filler is selected from poly(lactic-co-glycolic acid), polytetrafluoroethylene and expanded polytetrafluoroethylene. In a further embodiment, the filler is selected from hydroxylapatite and beta-tricalcium phosphate. In an alternative embodiment, the filler is selected from salt particles, microspheres, zeolites and bioglasses.

The filler compound present in the polymer coating may be present in an amount from 2 to 90 wt. %, preferably 5 to 75 wt.%, more preferably 10 to 60 wt.%, most preferably 30 to 50 wt.% based on the total weight of the polymer coating.

The polymer coating of the eighth aspect of the present disclosure is preferably coated on the surface of the dental substrate to which gingiva tissue attaches.

A tenth aspect of the present disclosure is a dental substrate having an outer surface to which a polymer film is attached, wherein the dental substrate is selected from the group consisting

of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

The polymer film preferably comprises at least one polymer selected from polyethylene terephtalate, polystyrene, polycarbonate, polyamide, polyurethane, olefin polymers, dextran, silicone and polyacrylate.

The polymer film of the tenth aspect of the present disclosure is preferably coated on the surface of the dental substrate to which gingiva tissue attaches. The polymer film may be attached to the dental substrate by one or more layers of adhesives or by thermal shrinking.

The adhesive preferably comprises at least one resin selected from epoxy-based resin, polyurethane-based resin, acrylate-based resin and silane terminated polymers. In a preferred embodiment, the resin is acrylate-based resin.

The one or more relief features of the polymer film refer to indentations or protrusions that are introduced onto the polymer film. Details of the relief features and the methods for their creation are described in U.S Patent US 9,453,197 B2. Relief features include ridges, posts, domed protrusions, beads, or combinations thereof. Each of the relief features may be present on the polymer film alone or in combination with other relief features to form a regular or irregular pattern, of relief features.

The more or more relief features can also be introduced on the polymer by embossing or micro-embossing. During the process of micro-embossing, a polymer film is treated with a heated engraved roll to emboss a pattern on the film. The resulting polymer films have

increased surface area and the relief features provide sites for mechanical anchoring. Such sites include pillars, mushroom shaped structures and cavities.

An eleventh aspect of the present disclosure is a dental substrate according to the tenth aspect of the present disclosure for use in a method of treating or preventing peri-implantitis or periodontitis in a subject.

The relief features present on the polymer attached to a dental substrate modify the surface of the dental substrate and foster the attachment of gingival tissue and fibers to the dental substrate.

A twelfth aspect of the present disclosure is a polymer film for use in a method of treating or preventing peri-implantitis or periodontitis, wherein the polymer film is applied on a natural tooth or a dental substrate in the oral cavity;
wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

A thirteenth aspect of the present disclosure is the use of a polymer film for application on a dental substrate *ex vivo*, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

A fourteenth aspect of the present disclosure is a method of making the dental substrate according to the tenth aspect of the present disclosure, comprising the steps of:

a) forming one or more relief features on a polymer film by embossing the film; and

b) attaching the polymer film to the outer surface of the dental substrate by one or more layers of adhesives or by thermal shrinking.

Specifically, the fourteenth aspect of the present disclosure concerns a method of making a dental substrate having an outer surface to which a polymer film is attached comprising the steps of:

a) forming one or more relief features on a polymer film by embossing the film to form a polymer film having one or more relief features on at least a portion of the film; and

b) attaching the polymer film to the outer surface of the dental substrate by one or more layers of adhesives or by thermal shrinking;

wherein the dental substrate is selected from the group consisting of an implantable device such as a dental implant, an implant abutment, a personalized implant abutment, a fixation screw, a CAD/CAM personalized implant abutment, a manually customizable abutment assembly, a healing abutment, a healing cap, a cover screw and any other dental component; a prosthetic component such as a crown or a bridge; and combinations thereof.

The present invention can also be illustrated by reference to the following exemplary embodiments:

Item 1: A method of applying a product to a dental substrate or a natural tooth in vivo or ex vivo, wherein the product comprises:

a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones,

polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;

and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

Item 2: The method according to item 1, wherein the product is applied to a dental substrate ex vivo.

Item 3: Use of a product for coating a dental substrate ex vivo, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat;
and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof.

Item 4: A product for use in a method of treating or preventing peri-implantitis or periodontitis in a subject in need thereof, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat.

Item 5: The product as defined in any one of items 1 to 4, wherein

(i) the first composition and the second composition are combined to form a single composition; or

(ii) wherein the first composition is present in a first layer and the second composition is present in a second layer.

Item 6: The product according to item (ii) of item 5, further comprising one or more layers between the first layer and the second layer, and wherein one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

Item 7: A dental substrate coated with a polymer coating, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and pH responsive polymers.

Item 8: The dental substrate according to item 7, wherein the thermoresponsive polymer is selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate) and mixtures thereof; and the pH responsive polymer is selected from the group consisting of copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate and mixtures thereof.

Item 9: The dental substrate according to item 7 or 8, wherein the polymer coating further comprises at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses and autologous fat.

Item 10: A use of a polymer coating for coating a dental substrate ex vivo, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and a pH responsive polymer.

Item 11: The use according to item 10, wherein the thermoresponsive polymer is selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate) and mixtures thereof; and the pH responsive polymer is selected from the group consisting of copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate and mixtures thereof.

Item 12: A dental substrate having an outer surface to which a polymer film is attached, wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer film has one or more relief features on at least a portion of the film.

Item 13: The dental substrate according to item 12, wherein the polymer film comprises at least one polymer selected from the group consisting of polyethylene terephlalate, polystyrene, polycarbonate, polyamide, polyurethane, olefin polymers, dextran, silicone and polyacrylate.

Item 14: The dental substrate according to any one of items 7, 8, 9, 12 or 13 for use in a method of treating or preventing peri-implantitis or periodontitis in a subject.

Item 15: A method of making the dental substrate according to item 12 or 13, comprising the steps of:

a) forming one or more relief features on a polymer film by embossing the film; and

b) attaching the polymer film to the outer surface of the dental substrate by one or more layers of adhesives or by thermal shrinking.

Claims

1. A product for use in a method of treating peri-implantitis in a subject in need thereof, wherein the product comprises:
a first composition comprising at least one resin selected from the group consisting of epoxy-based resin, polyurethane-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers; and

a second composition comprising at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat.

2. The product for use according to claim 1, wherein the method comprises applying the product to a dental substrate.

3. The product for use according to claim 1 or 2, wherein
(i) the first composition and the second composition are combined to form a single composition; or
(ii) wherein the first composition is present in a first layer and the second composition is present in a second layer.

4. The product according to item (ii) of claim 3, further comprising one or more layers between the first layer and the second layer, and wherein one or more layers comprise a component selected from a polymer, a tackifier resin, a filler, a stabilizing additive and a rheology modifying additive.

5. The product for use according to any one of claims 1-4, wherein the first composition comprises at least one resin selected from the group consisting of epoxy-based resin, vinyl-based resins such as acrylate-based resin and silane terminated polymers.

6. The product for use according to any one of claims 1-5, wherein the second composition comprises at least one filler selected from the group consisting of hyaluronic acid, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses, and autologous fat.

7. A polymer coating for use in a method of treating peri-implantitis in a subject, wherein the polymer coating is applied on a dental substrate in the oral cavity and wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; wherein the polymer coating comprises at least one polymer selected from the group consisting of thermoresponsive polymers and pH responsive polymers; and wherein the polymer coating comprises at least one filler selected from the group consisting of hyaluronic acid, hydroxylapatite, beta-tricalcium phosphate, poly(lactic-co-glycolic acid), alginates, salt particles, chitosan, microsphere, hydrogel polymers, silicones, polytetrafluoroethylene, expanded polytetrafluoroethylene, zeolites, bioglasses and autologous fat.

8. The dental substrate according to claim 7, wherein the thermoresponsive polymer is selected from the group consisting of poly(N-isopropylacrylamide), poly(di(ethyleneglycol)methylether methacrylate) and mixtures thereof; and the pH responsive polymer is selected from the group consisting of copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate and mixtures thereof.

9. The dental substrate according to claim 8, wherein the thermoresponsive polymer is poly(di(ethyleneglycol)methylether methacrylate); and the pH responsive polymer is selected from the group consisting of copolymers of acrylic acid, dimethylamino-ethylacrylate hydroxyethylacrylate and mixtures thereof.

10. A polymer film for use in a method of treating peri-implantitis, wherein the polymer film is applied on a dental substrate in the oral cavity; wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; wherein the polymer film has one or more relief features on at least a portion of the film; and wherein the polymer film comprises at least one polymer selected from the group consisting of polyethylene terephlalate, polystyrene, polycarbonate, polyamide, polyurethane, olefin polymers, dextran, silicone and polyacrylate.

11. A method of making a dental substrate having an outer surface to which a polymer film is attached, comprising the steps of:

a) forming one or more relief features on a polymer film by embossing the film; and

b) attaching the polymer film to the outer surface of the dental substrate by one or more layers of adhesives or by thermal shrinking;

wherein the dental substrate is selected from the group consisting of an implantable device, a prosthetic component and combinations thereof; and wherein the polymer film comprises at least one polymer selected from the group consisting of polyethylene terephlalate, polystyrene, polycarbonate, polyamide, polyurethane, olefin polymers, dextran, silicone and polyacrylate.

Figures

Fig. 1

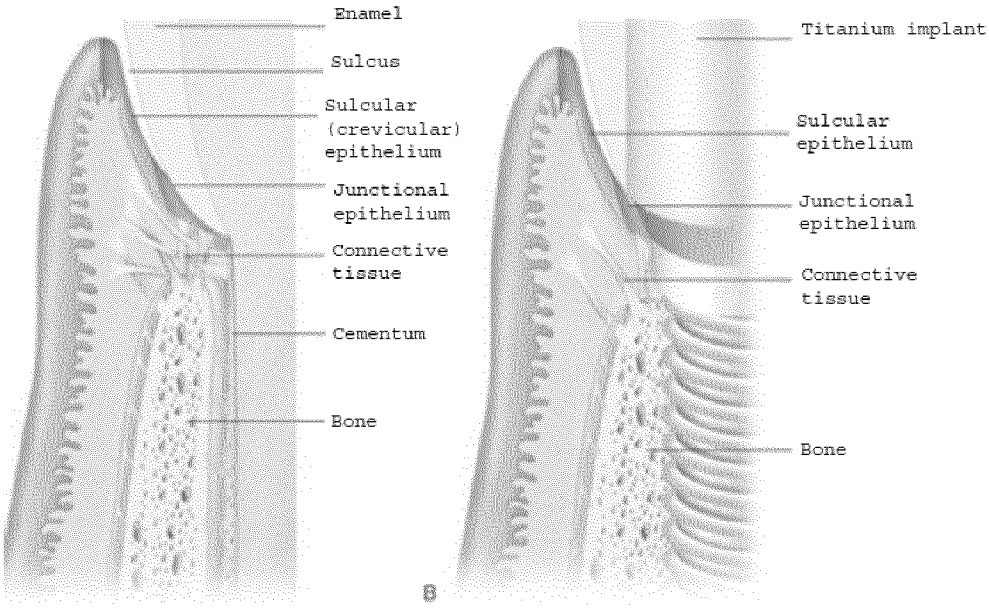
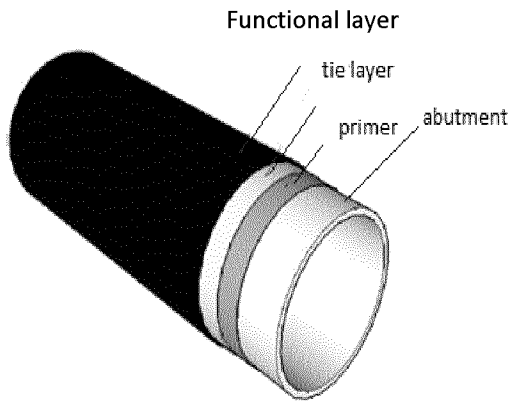


Fig. 2



1

Fig. 3

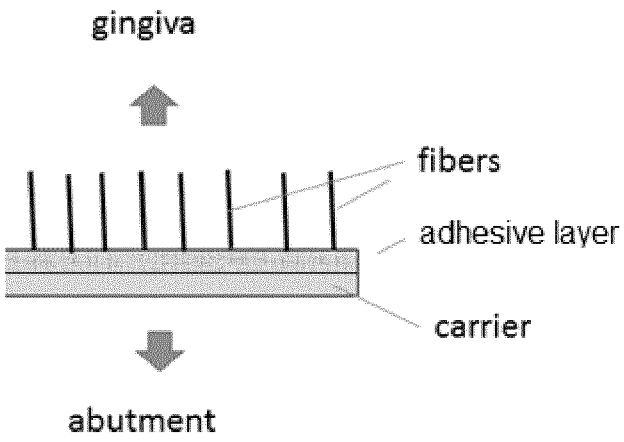


Fig. 4

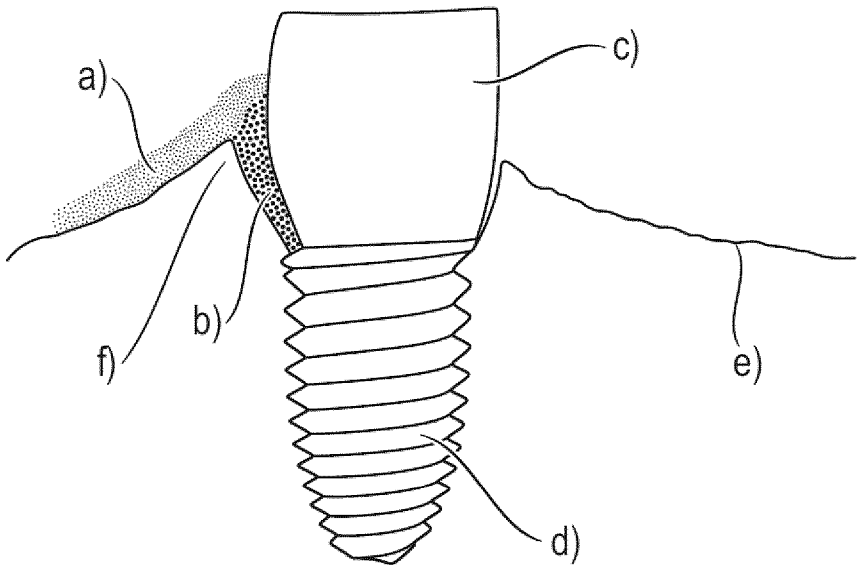


Fig. 5

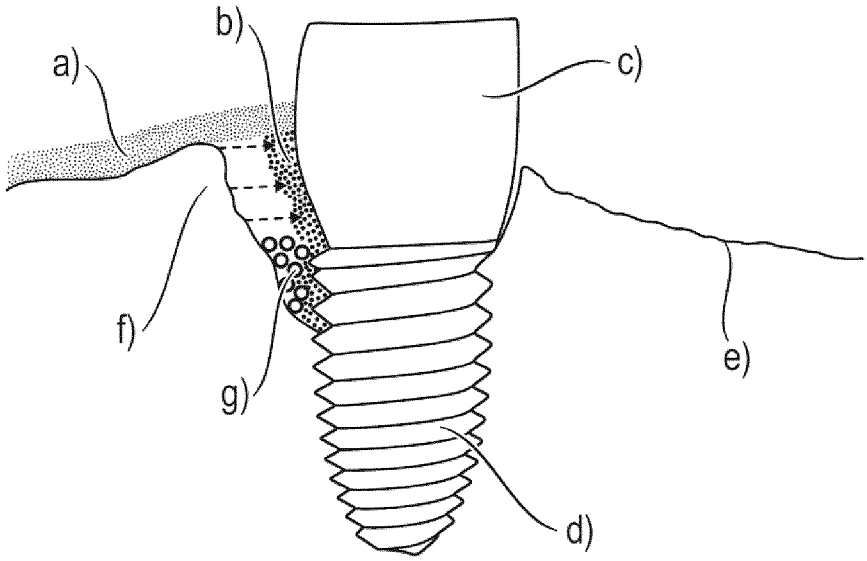


Fig. 6