Title: AUGMENTATION AND TREATMENT OF GINGIVAL DEFECTS

Abstract: The present invention relates to non-surgical methods for the rapid and effective augmentation of gingival tissues and treatment of defects in gingival tissues by the injection of a dermal filler or injectable material approved for soft tissue augmentation. In particular the present invention provides non-surgical methods to correct loss of gingival architecture and contour using an available dermal filler or other injectable material approved for soft tissue augmentation, to shorten patient discomfort and wait time by providing effective supportive foundation when the use of dentures is needed, accommodating fit and function of dentures and dental prostheses.
AUGMENTATION AND TREATMENT OF GINGIVAL DEFECTS

FIELD OF INVENTION

The present invention relates to methods for the rapid and effective functional augmentation of the gingiva including the alveolar ridge and treatment of deficiencies in gingival tissues by the injection of dermal fillers and other injectable materials approved for non-surgical soft tissue augmentation. The methods are useful for treatment of gingival deficiencies such as occurs with tooth loss, increase in age, periodontal disease and disorders, and periodontal trauma. In particular, the present invention provides methods of accommodating fit of dentures by injecting gingiva with dermal fillers for soft tissue augmentation.

BACKGROUND OF INVENTION

Periodontal disease

Periodontal disease is a generic name used to describe inflammatory disease of the periodontium, the tissue surrounding and securing teeth to the jawbone. The periodontium consists of the cementum, periodontal ligaments and the gingiva (gum), which includes the alveolar bone and the soft tissue covering it. Periodontal disease is the leading cause of tooth loss in the adult population [Anderson's Pathology, p.2000, John M. Kissane ed., 9th ed. (1992)].

Loss of gingival soft tissue and bone

Gingivitis is an accumulation of bacterial plaque in the gap between the gingiva and the tooth. As the disease progresses, a periodontal pocket is established below the gingival margin, thus prolonging and promoting the inflammatory process. Successive inflammatory reactions result in the progressive erosion of the tooth-supporting tissues, i.e., the collagenous fibers making up the periodontal ligament and the bone pocket in which the tooth sits. [Reviewed in Anderson's Pathology, pp. 1999-2000, John M. Kissane ed., 9th ed. (1992); Shafer et al, A Textbook of Oral Pathology, 4th ed. (1983)]. As the disease progresses, the pockets deepen and more gum tissue and bone are destroyed. Eventually, teeth can become loose and may have to be removed.
In addition to dental disease associated with periodontal diseases and tooth decay, tooth developmental defects caused by severe malnutrition, genetic defects such as Dentinogenesis imperfecta, trauma or drugs use can all lead to tooth loss. Dental prostheses are used in patients who have partially or entirely lost their teeth.

Edentulous bone, namely alveolar bone without teeth embedded, progressively loses its volume, since no stress is transferred to the bone, as there is no tooth root or implant to transfer the forces of mastication to the bone. As a result of the diminishing volume the contour and architecture of the alveolar ridge changes. The same happens with dentures, and the phenomenon of bone resorption is even more pronounced if dentures are used, and this is the reason why the dentures gradually lose their fit.

**Dental Prostheses**

Dental prostheses are restorative, replacement devices designed as therapeutic aids for functional, as well as esthetic/cosmetic reasons. These devices serve as artificial replacements for one or more natural teeth and/or associated structures. Types of dental prostheses include, but are not limited to, full dentures, over dentures, partial dentures, and dental bridges.

The concomitant loss of teeth and supportive gum and bone leads to a situation where the patient is in need of dentures but the mouth lacks a supportive foundation upon which the dentures will rest. The application of dentures under these circumstances may result in improper fit and function of the dentures, caused by the diminishing height and volume of the alveolar ridge secondary to the gradual bone resorption.

Healthy gum tissue and bone form the supportive foundation of each tooth. The alveolar bone, cemenrum, periodontal ligament and gingiva provide the supportive foundation and beneficial environment for teeth in a healthy mouth. The alveolar ridges are the maxillary and mandibular jawbone ridges that contain the sockets (alveoli) of the teeth. Use of dentures often involves augmentation of the alveolar ridges and surrounding soft tissue for proper fit and function of these devices.

The main goals to achieve when dental restoration is attempted are to provide stable soft and hard tissues upon which dentures or implants can be placed and the deepening of the flange area so that increased resistance to displacement forces is provided.
A great deal of research has been directed to methods of regenerating gingival soft tissue and bone loss. Efforts have focused on surgical approaches that fill the defects with a variety of materials, such as bone chips or tissue grafts, and on the use of guided tissue regeneration by introduction of cells and growth stimulators such as growth factors or morphogenic bone proteins.

Augmentation and/or repair of gingival soft tissue and bone

There are three general groups of soft tissue procedures or combination of soft and bone tissues applications. 1) Mucogingival surgery uses periodontal flaps from tissue obtained primarily from the gingival zone of the palate. Flaps, connective tissue grafts or more recently, hydroxyapatite implants, are used for alveolar ridge augmentation; 2) Maxilllary or Mandibular soft tissue procedures are mainly used for the adaptation of complete/partial dentures in the edentulous atrophic ridge. Anterior vestibuloplasty (plastic surgery of the mouth), for example, utilize free mucosal graft (from palate, labial, cheek mucosa) and are considered in cases of deficiency of facial mucosa, due to trauma or ablative surgery; 3) Mandibular or maxillary augmentation with simultaneous vestibuloplasty (several types), is used for patients with simultaneous bone loss. These procedures use either hydroxyapatite particles or bone grafts (autogenous, allogenic, or composite). (Cohen E. S., Atlas of Periodontal Surgery. Lea & Febinger, Philadelphia, 1988; Fonseca and Davis, Reconstructive Preprosthetic Oral and Maxillofacial Surgery. W.B. Saunders, Philadelphia, 1995).

These surgical techniques and procedures have several disadvantages and complications: In any type of graft there are two operative sites, potential infection complications, scar formation at the donor site, discomfort, danger of compromised blood supply for the graft site and subsequent necrosis, reabsorption or retention of the graft, potential hemostasis problems, and poor aesthetic results (color and texture differences). Moreover many procedures require several weeks to months before the soft tissues are ready for dental prostheses causing great discomfort to the patient. Thus, there is a need for the development of non-invasive techniques for the effective and satisfactory treatment of tissue loss and defects due to periodontal diseases and to edentulous alveolar bone resorption particularly with regards to the augmentation of gingival and oral mucosal tissue applicable in the fit and function of dental prostheses.

A variety of materials are available and have been used for bone augmentation by grafting and regeneration: Autogolous bone is bone material taken from other parts
of a patient's body. The primary shortcomings in the use of autogenous bone are the need for a second operative site, the attendant patient morbidity and the possibility of being unable to obtain sufficient material. An additional problem associated with the use of autografts is that in some cases fresh grafts may be associated with root resorption. [Jeffcoat, M. K. et al., J. Am. Dent. Assoc. 128:713-724 (1997)]. The use of allografts raises the issue of immunogenicity and pathogens and concern as successful grafting may depend upon the health history of the donor. Whereas use of allografts taken from cadavers (that may be frozen, freeze-dried, demineralized freeze-dried and irradiated) is met with patient reluctance Freeze-dried, demineralized bone has been used as an allograft and shown to promote bone formation. However, the predictability and the amount of bone fill achieved vary. [Jeffcoat, M. K. et al., J. Am. Dent. Assoc, 128:713-724 (1997)]. Synthetic bone materials include plaster, calcium carbonates, and ceramics such as hydroxyapatite. Clinical trials have demonstrated that the use of synthetic grafts has resulted in improvements in probing depth and attachment level. Histologic findings, however, indicate that, in general, synthetic grafts act primarily as space fillers, with little if any regeneration. [Jeffcoat, M. K. et al., J. Am. Dent. Assoc, 128:713-724 (1997)].

Augmentation of soft tissue and bone by guided tissue regeneration

In an attempt to overcome the disadvantages and complications of surgical techniques used to augment and/or repair gingival soft tissues or bone, injection of composite materials comprising cells and/or growth stimulators, such as growth factors or morphogenic bone proteins, and/or bone particles mixed with 3-D matrices and fillers has been described. US patent 6,991,652 and US Patent Applications 20060039896, and 20070207131 teach the compositions of cell-matrix-filler composite formulations and disclose methodologies for injection of said cell bearing composites for the augmentation and/or repair of soft tissue, including periodontal tissues. Injection of biocompatible composites is a non-surgical procedure disclosed to augment and/or repair periodontal soft tissues. Composite formulations are mixtures of human cells or tissues, with or without additional growth factors, and three-dimensional matrix carriers and fillers. However, use of cell-matrix compositions methodology suffers from inherent limitations. Specifically, these methodologies are limited by the composites used and the components thereof, in particular the inclusion of live...
autologous cells which requires the taking of a biopsy specimen, cell culturing under appropriate culture conditions and requirements, tissue culture expansion several weeks prior to the treatment and the removal of immunogenic proteins (xenogeneic serum components) prior to treatment. In the case where non-autologous cells are used, cells are collected from donors, fetal tissue or embryos. Then, in vitro tissue culture methodologies are used to expand and extensively prepare cells, minimally over the course of 3-4 weeks. Independent of cell source, isolated cells are combined with carrier materials prior to injection. In addition to subjecting patients to biopsies and time constrains, methods using autologous cells are limited by tissue resorption, while methods using cells from non-autologous sources are subject to potential dangers of eliciting an immune response and the transfer of pathogens to the patient.

Thus, the limitations of using live cells include patient safety, success of the procedure, long wait times while cells are prepared, and long wait times for cellular regeneration to occur after injection prolonging patient discomfort. Similarly, injection of growth stimulators suffers from limited success and long wait times for cellular regeneration or cellular migration to the sites of interest to occur.

US Patent 6,991,652 and US Patent Applications 20060039896, and 20070207131 teach the use of porous three dimensional constructs suitable for supporting cell growth comprising biodegradable, injectable filler material, as part of the composite materials injected. US Patent Application 20070134342 discloses a method whereby injectable composite formulations are used to deliver osteogenic proteins for augmentation and rehabilitation of the alveolar ridge and other, unspecified periodontal defects. The composition comprises osteogenic proteins (bone morphogenetic proteins-BMPs) and hyaluronic acid esters. This method is limited by the complexity of bone repair. Unlike regenerative therapies that use single regenerative factors, the natural processes of bone formation and repair require the coordinated expression of many molecules, including growth factors, BMPs, and specific transcription factors. The optimal BMPs to be used in different clinical applications have not been elucidated, and a comprehensive evaluation of the relative osteogenic activity of different bone morphogenetic proteins is lacking (Cheng et al., The Journal of Bone and Joint Surgery. 85:1544-1552,2003). US patent 4,820,306 teaches a method of augmenting alveolar ridges in an edentulous patient using hydroxyapatite.
US Patents 7,304,030 and 7,423,013 disclose the use of amelogenins, also known as enamel matrix derivatives for treatment of periodontal defects and dentin defects. The preferred delivery vehicle is propylene glycol alginate.

Nowhere in the background art is it taught or suggested that injection of dermal fillers, devoid of cells and/or growth stimulators, such as BMPs, is efficacious in providing a supportive foundation needed for proper function of dentures.

Nowhere in the background art is it taught or suggested that injection of fillers, devoid of cells and/or growth stimulators, is efficacious for accommodating the fit of dentures.

Dermal fillers

There have been efforts to develop and use compositions to correct defects in skin, such as scars and wrinkles, or to augment the tissue of a subject in order to improve the appearance of the skin, particularly facial skin. The principal method employed to correct such defects involves injecting a filler composition into the dermal layer of the skin proximate to the defect or desired tissue augmentation.

Numerous types of biodegradable, injectable filler materials used for either dermal or other soft tissue augmentation are currently available and have utility in the present invention.

Currently, dozens of dermal filling agents exist and include autologous implantable materials, allogeneic products, xenogeneic products and synthetically derived products. Some of the available products include, among others: injectable bovine collagen, injectable porcine collagen, recombinant collagen, hyaluronic acid and hyaluronic acid derivatives, dried acellular particulate dermal matrix (a micronized injectable form of human skin), poly-L-lactic acid, polyacrylamide gel, polymethyl methacrylate, tri-calcium phosphate, alkyl-imide gel, carboxymethylcellulose, polyethylene oxide, dextran molecules, autologous fat, gelatin matrices and autologous human collagen.

US patent 6,991,652 and US Patent Applications 20060039896, and 20070207131 teach the use of composites consisting of biodegradable filler material of collagen or hyaluronic acid mixed with autologous cells.

The dermal filler Radiesse®, a composite of calcium hydroxyapatite microspheres and filler, has been used to correct a variety of oral and maxillofacial conditions including periodontal and cystic defects, ridge augmentation, extraction
sites, craniofacial augmentation and sinus lifts. Radiesse® is designed to serve as a lattice upon which the body forms a scaffold for new bone growth and tissue infiltration.

Nowhere in the background art is it taught or suggested that inert injectable non-particulate acellular dermal fillers, are efficacious for providing a supportive foundation needed for accommodating the fit and for proper function of dentures.

SUMMARY OF THE INVENTION

The present invention overcomes the deficiencies of the background art by providing methods for rapid and effective functional augmentation of the gingiva and treatment of deficiencies and defects in gingival architecture and contour by non-surgical means. The methods of the invention are minimally-invasive and achieve gingival augmentation by the injection of dermal fillers and other injectable materials approved for soft tissue augmentation. The methods of the invention are suitable for treatment of gingival deficiencies such as occur with tooth loss, increase in age, periodontal disease and disorders, periodontal trauma and after tooth implants. The present invention provides methods for augmentation of defects in gingival architecture and contour by injection of dermal fillers into gingival tissues at or adjacent to the sites of loss of gingival soft tissue and bone. In particular, the present invention provides methods for the rapid and functional augmentation of the gingival tissues in order to correct specific defects that lead to loss of supportive foundation for dental prosthetics such as dentures, or partial dentures, by injection of dermal fillers for the enhancement of fit and function of the dentures.

The present invention thus provides a simple, non-surgical, and effective method for gingival soft tissue augmentation. Among the numerous advantages of the present invention are the rapid results, the decrease in trauma compared to surgical intervention and the reduced costs compared to replacing dentures. The skilled artisan will appreciate that the methods of the present invention do not replace the need for good denture design, it is a complementary procedure intended to immediately overcome the loss of good fit of the existing dentures due to the progressive diminishing of volume and contour changes of the edentulous alveolar ridge, and to provide improved denture support and seal.

This invention is based in part on the unexpected discovery that dermal fillers, injected into gingival soft tissues at sites lacking a supportive foundation for dentures
in human patients, enhanced the stability and function of dentures used by these patients. Unexpectedly, the use of dermal fillers was particularly successful at improving the fit of the dentures because it created a malleable surface at the interface of the gingival ridge with the dentures.

A particular benefit is the fact that there is no time delay to achieve the desired outcome. On the contrary, the patient is required to use the prosthetic device immediately following the tissue augmentation in order to allow correct contouring of the gingiva, as long as the filler is still in a malleable state.

According to the principles of the present invention the fillers that are useful in the methods of the invention are dermal fillers as are commonly used in the field of cosmetic applications. Specifically, the preferred dermal fillers are devoid of cells, devoid of biopharmaceuticals such as growth stimulators, and devoid of particulate matter such as calcium hydroxyapatite microspheres.

According to a first aspect, the present invention provides methods for the injection of an effective amount of dermal filler or other injectable materials approved for soft tissue augmentation at sites of tissue defect or deficiency so that the gingival architecture and contour is augmented. According to some embodiments, typical defects of gingival architecture and contour which can be corrected by the injection of dermal fillers, or other injectable materials designed for soft tissue augmentation, include gum and mucosal layer restoration, preprosthetic techniques for partial or complete dentures and mucogingival or alveolar ridge problems which precede the application and/or fit of dental prosthetic such as partial or complete dentures.

According to an exemplary embodiment, defects of gingival architecture and contour caused by bone resorption and leading to the improper support and foundation for dentures can be corrected by injection of dermal fillers or other injectable materials approved for soft tissue augmentation. The injectable fillers can also contribute to functional and esthetic restoration of the soft tissue around bridges, crowns, crowns on implants and peri-implant defects of the gingiva including the alveolar bone.

According to an alternative embodiment, peri-implantitis, i.e. an infection around a dental implant which causes local chronic inflammatory conditions that may lead to peri-implant bone resorption and subsequent implant loss, can be treated by injection of dermal fillers or optionally further comprising antiseptic or antibiotic materials, following mechanical debridement of the infected tissue.
The present invention provides a simple, non-surgical, and effective method for gingival soft tissue augmentation. In another aspect of this invention non-surgical methods are provided for pre-dental prostheses augmentation, comprising the step of administering to an individual in need thereof, an effective amount of a dermal filler or other injectable materials designed for soft tissue augmentation, at sites of gingival ridge (including the alveolar bone) degeneration and loss. A preferred method of delivery is by injection. According to some embodiments the dermal filler or other injectable materials designed for soft tissue augmentation, can be readily injected into a target area of the body of a subject to fill a void or cavity comprising but not limited to, the gingival tissue adjacent to the area of degeneration or into tissue subadjacent to a defect in the oral mucosa, or into the tissue of the palate of a human subject. According to exemplary embodiments the dermal filler or other injectable materials approved for soft tissue augmentation, is injected into the buccal and lingual ridge area.

According to an additional aspect, the present invention provides methods comprising the step of administering by injection to an individual in need thereof, an effective amount of dermal filler or other injectable materials approved for soft tissue augmentation, at sites of gingival degeneration and loss so that the gingival architecture and contour are augmented. The scope of the invention encompasses all inert nontoxic non-migratory materials approved for use in soft tissue augmentation. It is to be understood explicitly that the present invention is not directed to use of these materials as carriers for cells, growth factor, bone stimulatory materials or particulate matter, but rather to compositions that fulfill the need for tissue augmentation in a rapid and cost effective manner using commercially available known fillers or their generic equivalents. Excluded from the scope of the present invention are dermal filler compositions that include cells and/or growth stimulators such as growth factors or morphogenic bone proteins and/or particulate material such as calcium hydroxyapatite microspheres and the like.

According to an exemplary embodiment, dermal filler compositions used in these methods comprise those with collagen as a major constituent. According to some embodiments the compositions for use in methods of the present invention consist essentially of collagen in an acceptable carrier. According to an additional exemplary embodiment, dermal filler compositions used in these methods comprise those with hyaluronic acid as a major constituent. According to some embodiments
the compositions for use in methods of the present invention consist essentially of
hyaluronic acid in an acceptable carrier. It will be understood by the skilled artisan
that such compositions will often contain preservatives and inactive excipients. Often
the compositions will be conveniently packaged in sterile prefilled syringes.

According to an additional aspect, the present invention provides the use of
dermal fillers or other injectable materials approved for soft tissue augmentation, at
sites of deficiencies and defects in gingival architecture and contour and bony tissue
defects such as occurs with teeth loss, increase in age, periodontal disease and
disorders, periodontal trauma and after tooth implants, for the enhancement of fit and
function of dental prosthetics including but not limited to implants, crowns, bridges,
partial or complete dentures. According to an exemplary embodiment, dermal filler
compositions used in the present invention comprise those with collagen as a major
constituent. According to an additional exemplary embodiment, dermal filler
compositions used in the present invention comprise those with hyaluronic acid as a
major constituent.

According to an additional aspect, the present invention provides methods
comprising the step of administering by injection to an individual in need thereof, an
effective amount of dermal filler, or other injectable materials approved for soft tissue
augmentation, at sites of specific deficiencies and defects in gingival architecture and
contour and bony tissue defects such as occurs with teeth loss, increase in age,
periodontal disease and disorders, periodontal trauma and after tooth implants, for the
enhancement of fit and function of dental prosthetics including but not limited to
implants, crowns, bridges, partial or complete dentures.

According to certain embodiments, the present invention provides methods
comprising the step of administering by injection to an individual in need thereof, an
effective amount of dermal filler, or other injectable materials approved for soft tissue
augmentation, at sites of gingival soft tissue degeneration and loss, including but not
limited to the periodontal pocket, peri-implant pocket, and/or the gingival tissue
adjacent to the area of degeneration or into tissue subadjacent to a defect in the oral
mucosa, into the tissue of the palate of a human subject, or to the buccal and lingual
alveolar ridge area for the enhancement of fit and function of dental prosthetics
including but not limited to implants, crowns, bridges, partial or complete dentures.

According to additional embodiments, the present invention provides methods
comprising the step of administering by injection to an individual in need thereof, an
effective amount of dermal filler compounds, or other injectable materials approved for soft tissue augmentation, comprising biocompatible, inert materials. Inert materials will preferably mean non-antigenic, non-carcinogenic, non-teratogenic, and non-migratory. Preferably the compositions for use in the methods of the present invention will be cost effective dermal or soft tissue fillers approved by the US Food and Drug administration, including but not limited to fillers comprising structural proteins, polysaccharides or synthetic polymers. Exemplary embodiments include collagen, such as reconstituted bovine collagen products including, but not limited to, ZYDERM I®; ZYDERM II® and ZYPLAST® of Collagen Corporation; reconstituted porcine collagen EVOLENCE™ of ColBar LifeScience; natural human collagen COSMODERM™ and COSMOPLAST™ manufactured by INAMED; and endogenous collagen from the subject, AUTOLOGEN® produced by Collagenesis. Additional examples of dermal filler compositions may be selected from those with hyaluronic acid, including but not limited to such products as HYLAFORM® gel manufactured by INAMED and Genzyme Corporations, derived from the rooster combs of domestic fowl; and RESTYLANE® manufactured by Medicis, a hyaluronic acid derivative derived from streptococcal bacterial fermentation. Hyaluronic acid includes both non-cross-linked and/or cross-linked hyaluronic acid derivatives as are well known in the art.

Excluded from the present invention are dermal filler compositions that include cells and/or growth stimulators such as protein growth factors or morphogenetic bone proteins and/or particulate matter such as calcium hydroxyapatite microspheres. According to exemplary embodiments, dermal filler compositions used in these methods comprise collagen or hyaluronic acid as a major constituent for the enhancement of fit and function of dental prosthetics including but not limited to implants, crowns, bridges, partial or complete dentures. According to additional exemplary embodiments, dermal filler compositions used in these methods consist essentially of collagen or hyaluronic acid as a major constituent for the enhancement of fit and function of dental prosthetics including but not limited to implants, crowns, bridges, partial or complete dentures.

According to another aspect the present invention provides a pharmaceutical composition comprising a dermal filler for treatment of gingival deficiencies such as occur with tooth loss, increase in age, periodontal disease and disorders, periodontal trauma and after tooth implants. According to some embodiments the pharmaceutical...
compositions comprising dermal fillers are for rapid and effective functional augmentation of the gingiva and treatment of deficiencies and defects in gingival architecture and contour by non-surgical means.

According to some embodiments the dermal filler compositions are provided in the form of prefilled disposable syringes. According to other embodiments the dermal filler compositions are provided as ampoules or cartridges or caxpules adapted for use with a reusable dental syringe. The use of dental syringes and dental ampoules also referred to herein as dental carpules are well known to dental surgeons and oral health care professionals and particularly convenient for the applications disclosed herein.

According to exemplary embodiments, the present invention provides methods comprising the step of administering by injection into the gingival soft tissue, to an individual in need thereof, an effective amount of dermal filler for the enhancement of fit and function of dentures, including increased stability of dentures, decreased food penetration under dentures, decreased movement of dentures during mastication, and decreased pain associated with fit and wearing of dentures.

These and additional benefits and features of the invention will be better understood by those skilled in the art with reference to the following detailed description taken in conjunction with the figures, non-limiting examples and claims that follow.

**BRIEF DESCRIPTION OF FIGURES**

Figure 1A-IB. Shows CT scans of the Mandible of patient No. 1.

The CT scans show edentulous mandible with two dental implants situated at the frontal segment of the mandible, with very significant bone resorption throughout. The small reserve of bone stock is not sufficient for implant-based prosthetics. The implant supported dentures, the patient has been using, are unstable due to the irregular architecture and contour of the supporting tissue (gingiva - including alveolar ridge).

Figure 2A-2D. Shows patient No. 2
Figure 2A Shows the partially edentulous mandible, with extreme decrease in alveolar ridge volume, with striking narrowing and lowering of the alveolar crest.

Figure 2B-D Show the administration of an injectable dermal filler into the buccal aspect of the gingiva, demonstrating the expansion of the soft tissue.

DETAILED DESCRIPTION OF INVENTION

The present invention provides methods for the rapid functional augmentation of gingival architecture and contour defects and alveolar ridge defects that lead to loss of a supportive foundation for dentures. Specifically, the invention provides methods whereby injection of dermal fillers into gingival soft tissue provides the supportive foundation needed for the enhancement of fit and function of dentures. The methods of the present invention are useful for the rapid and effective augmentation of defects in gingival architecture and contour and bony tissue defects such as occurs with teeth loss, increase in age, periodontal disease and disorders, periodontal trauma and after tooth implants. The methods of the present invention are also useful for the rapid and effective inter-dental papilla augmentation: augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under dental bridgework.

The present invention is based, in part, on the recognition that commercially available dermal fillers, or other injectable materials approved for soft tissue augmentation, provide an ideal material, immediately available and safe, to augment the gingival soft tissue in order to provide a supportive foundation for dentures.

The currently available surgical or non-surgical treatments are designed to augment, or claim to augment, the bony tissue. With the exception of gingival grafting, the augmentation and/or repair of the gingival contour is contributed by the increase in bone volume. The volume and quality of the soft tissue of the gingiva is unaffected. These methods do not provide an answer for the need of early and sound fit of dentures to allow correct function, comfort of use and esthetic outcome.

It would be advantageous to develop non-surgical methods to correct loss of gingival architecture and contour using readily available dermal fillers or other commercially available injectable materials designed for soft tissue augmentation, that
are devoid of cells, particulate material and/or biopharmaceuticals such as growth stimulators, in order to shorten patient discomfort and wait time by providing effective supportive foundation when the use of dentures is needed. In addition, it would be advantageous to develop injection methodologies using available dermal fillers which do not elicit an immune response, are not rapidly resorbed by the body, and do not risk introduction of foreign pathogens.

The human subject is provided two sets of teeth, which make their appearance at different periods of life. The first set, the temporary, deciduous, or milk teeth, appears in childhood. The second set is permanent, composed of thirty-two teeth: four incisors, two canines, four bicuspids, and six molars in each jaw. In general, each tooth consists of three portions: the crown or body - projecting above the gum; the root - entirely concealed within the alveolus; and the neck - constricted portion lying between the crown and the root.

The neck and root of the tooth are in intimate contact with the surrounding soft tissues. The soft tissue or gum, which is a reflection of the mucous membrane from the lips (anterior) and the cheeks (lateral), covers the upper and lower alveolar arches composed by the spaces in the mandibular and maxillar bones, into which the teeth are anchored. The gingiva or gums, is a stratified epithelium over a layer of connective tissue known as the lamina propria of the gingiva. Surrounding the roots of the tooth there is an extra layer of connective tissue separating the solid portion of the roots from the soft tissues, called the periodontium or alveolar periostium.

To facilitate an understanding of the present invention, a number of terms and phrases are defined below.

Definitions

The term "gingiva" or gums as used herein refers to the mucosal tissue that overlays the jaws with the gingival epithelium referred herein as the "gingival soft tissue".

As used herein the term "augmentation" refers to the process whereby a tissue's volume is supplemented by the exogenously added material.

"Periodontal disease" or "periodontal disorder" is used herein to describe inflammatory disease of the periodontium, the tissue surrounding and securing teeth to the jawbone. The condition is characterized by inflammatory and degenerative
processes that develop at the gingival margin (gingivitis) and lead to a progressive breakdown and resorption of the periodontal ligament and bone (periodontitis), oftentimes resulting in severe diminution of the periodontium and the progressive erosion of the tooth-supporting tissues securing the tooth to the alveolar bone and resulting in loss of teeth and supportive gum and bone tissues and the need for dental prostheses. Examples of periodontal disease that result in gingival soft tissue and bone degeneration include, but are not limited to, periodontal degeneration, gingivitis, recurrent aphthous stomatitis, non-healing wounds of the palatal mucosa or gingival mucosa, bone degeneration, or trauma to the oral mucosa or bones (e.g. tooth extraction).

As used herein the term "periodontal defect" or "gingival defects" used interchangeably refers to the loss of gingival architecture and contour often associated with bone loss due to tooth loss or periodontal disease or disorder or deformities associated with loss of gingival soft tissue and bone including but not limited to trauma from foreign objects associated with implants, oral cancer and tumor resections, physical trauma or reconstructive procedures for congenital cleft palate/lip, mucogingival or alveolar ridge problems that require the use of dental prostheses and preprosthetic techniques. As used herein the term "dental prostheses" or "dental prosthetics" refers to the use of prosthetic devices including but not limited to dental implants, crowns, bridges, partial and complete dentures including but not limited to implant dentures, interim or provisional dentures, overlay dentures, removable or fixed partial dentures, or transitional dentures.

As used herein the term "dermal fillers" refers to agents and compositions for soft tissue augmentation injected at or proximate to the site of defect or desired tissue augmentation, including but not limited to proteins, polysaccharides and synthetic polymers. Specific examples of suitable injectable materials include reconstituted bovine or porcine collagen, non-particulate gelatin matrices, autologous human collagen, hyaluronic acid and hyaluronic acid derivatives, dextran molecules, recombinant collagen, and synthetic polymers including Poly-L-Lactic acid, Polyacrylamide, Polymethyl methacrylate, Carboxymethylcellulose, and Polyethylene oxide; dermal fillers include but are not limited to those which are commercially available, biocompatible, non-antigenic, non-carcinogenic, non-teratogenic, non-migratory, approved by the US Food and Drug administration for use in the treatment of an individual or patient, example of which are listed herein below. Excluded from
the scope of the invention are dermal filler compositions that include cells and/or growth stimulators, such as growth factors or morphogenic bone proteins, and/or particulate matter such as calcium hydroxyapatite microspheres.

As used herein an "individual" or "patient" for purposes of treatment includes any subject affected by any condition, disease, disorder, defect or trauma where augmentation of gingival soft tissues using an effective amount of a dermal filler has beneficial therapeutic or functional or cosmetic effect. According to some embodiments the desired beneficial effect is on the fit and function of dentures. In additional embodiments the subject is any human or non-human mammal affected by defects in gingival architecture and contour such as occurs with tooth loss, increase in age, tooth implants, or any subject requiring interdental papillary augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under bridgework. Alternative embodiments will include treatment of peri-implantitis.

The term "effective amount" as used herein refers to an amount of dermal filler, or other injectable material approved for soft tissue augmentation, effective to alleviate or ameliorate gingival architecture and contour defects, or periodontal defects in a subject being treated. More specifically, an "effective amount" means the injection of an amount of dermal filler, or other injectable material approved for soft tissue augmentation, used in the methods of the present invention to provide a supportive foundation for dentures, and to provide soft tissue approximation to prosthetic devices and natural teeth in place of gingiva and bone that has degenerated in a patient to improve function and esthetics.

The present invention provides methods for the rapid and effective augmentation of defects in gingival architecture and contour as may be associated with bony tissue defects such as occurs with teeth loss, increase in age, periodontal disease and disorders, periodontal trauma and after tooth implants. The present invention also provides methods for the rapid and effective inter-dental papilla augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under dental bridgework, by injection of dermal fillers or other injectable materials approved for soft tissue augmentation. An additional
embodiment will include treatment of peri-implantitis, by injection of dermal fillers or other injectable materials approved for soft tissue augmentation, either alone or in conjunction with antibiotic or antimicrobial treatment. The present invention further provides methods for rapid and effective augmentation of defects in gingival architecture and contour by injection of dermal fillers into gingival tissues at or adjacent to the site(s) of the defect. In particular, the present invention provides methods for the rapid and effective augmentation of specific defects that lead to loss of a supportive foundation for dental prosthetics, such as dentures, by injection of dermal fillers for the enhancement of fit and function of dentures and to provide soft tissue approximation to prosthetic devices and natural teeth in place of gingiva and bone that has degenerated in a patient to improve function and esthetics...

According to some embodiments the dermal filler compositions are provided in the form of prefilled syringes. Commercially available dermal fillers are typically supplied in the form of prefilled disposable sterile syringes.

According to other embodiments the dermal filler compositions are provided as ampoules or cartridges or carpules adapted for use with a reusable dental syringe. The use of dental syringes and dental carpules are well known to dental surgeons and oral health care professionals and particularly convenient for the applications disclosed herein.

According to one embodiment the present invention provides methods for the injection of an effective amount of dermal filler at sites of gingival soft tissue and bone degeneration and loss so that the gingival tissue is augmented. According to another embodiment, defects of gingival soft tissue and bone to be corrected by the injection of dermal fillers are selected from gum and mucosal layer restoration, preprosthetic techniques for partial or complete dentures and mucogingival or alveolar ridge problems or defects which precede the application and/or fit of dental prosthetic such as partial or complete dentures. Periodontal diseases, disorders or defects that result in gingival soft tissue and bone degeneration are selected from a group comprising periodontal degeneration, bone and tissue resorption, gingivitis, recurrent aphthous stomatitis, infection, non-healing wounds of the palatal mucosa or gingival mucosa, bone degeneration, or trauma to the oral mucosa or bones (e.g. tooth extraction), trauma from foreign objects associated with implants, oral cancer and tumor resections, physical trauma or reconstructive procedures for congenital cleft
palate/lip, and mucogingival or alveolar ridge problems. According to particular embodiments, the defects of gingival architecture and contour, which can be corrected by injection of dermal fillers are due to bone resorption leading to the formation of improper support and foundation for dentures or implants or alveolar ridge problems prohibiting, or complicating, implant-based oral restoration and proper support for dentures.

The methods of the present invention provide a rapid and effective treatment that can either replace or defer surgical intervention designed to treat gingival dimensions, architecture or contour, or bone loss. Furthermore the methods of the invention are more cost effective and less traumatic than currently used surgical interventions.

A common surgical procedure has been widely used to treat bone loss caused by periodontal disease. In this procedure the gingiva is incised and reflected back to expose the tooth root and bone. Irregular shaped bone is removed the site is cleaned and a bone regeneration material is placed into the osseous defects that remain in the bone and the gingiva is sutured around the tooth. Guided tissue regeneration barriers are placed over bone regeneration material in deeper osseous defects. While this procedure has been effective, incisions in the gingiva cause patient discomfort, pain, swelling, gingival recession, sensitive teeth, a long healing time, and increase the possibility of infection as well as cosmetic difficulties that result from the loss of the interdental gingiva and creates dark spaces between the teeth. Other surgical procedures and approaches entail filling of defects with a variety of materials (bone grafting) or use of guided tissue regeneration using compositions of cell-matrix-filler composite formulations that include cells, growth stimulators such as growth factors or morphogenic bone proteins and/or hydroxy apatite microspheres. The use of these methodologies is limited by the composites used and components thereof, in particular the inclusion of live cells which requires biopsy, cell culturing, and culture expansion several weeks prior to the treatment of the degenerative disease or defect and the removal of immunogenic proteins (xenogeneic serum components) prior to treatment; thus prolonging patient discomfort. In addition to subjecting patients to biopsies and time constrains, methods using cells are limited by tissue resorption, and methods using cells from non-autologous sources are subject to potential dangers of eliciting an immune response and the transfer of pathogens to the patient. Similarly,
injection of growth stimulators suffers from limited success and long wait times for cellular regeneration or cellular migration to the sites of interest to occur.

According to another embodiment the present invention provides a simple, non-surgical, and effective method for gingival soft tissue augmentation. In yet another embodiment the present invention non-surgical methods are provided for pre-dental prostheses augmentation, comprising the step of administering to an individual in need thereof, an effective amount of a dermal filler at sites of gingival architecture and contour degeneration and bone loss. A preferred method of delivery is by injection. According to some embodiments the dermal filler can be readily injected into a target area of the body of a subject to augment the gingival contour and/or the gingival tissue proximal to the area of degeneration or into tissue subadjacent to a defect in the oral mucosa, the tissue of the palate, the maxillary or mandibular alveolar ridges, the sulcus, the mucogingival junction, and the gingival epithelium of the gingiva. According to other embodiments the dermal fillers are injected into the buccal and lingual areas of the alveolar ridge.

The term "proximal" as to the site at which a composition of the invention is placed to carry out the inventive method is used herein to mean near but not exactly at the site of the defect to be repaired or the augmentation to be carried out. Thus, adjacent, subjacent or above and nearby are included within the term "proximal".

According to other embodiments the present invention provides methods comprising the step of administering by injection to an individual in need thereof, an effective amount of dermal filler at sites of gingival architecture and contour degeneration and bone loss so that the gingival tissue is augmented. The determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. The exact formulation, route of administration, and dosage can be chosen by the individual physician in view of the patient's condition. (See, e.g., Fingl, E. et al. 1975 "The Pharmacological Basis of Therapeutics," Ch. I.S,p.l.). Depending on the severity and responsiveness of the condition to be treated, dosing can be of a single or a plurality of administrations, with course of treatment lasting from several days to several weeks, or until cure is effected or diminution of the defect is achieved. The amount of a composition to be administered will, of course, be dependent on the subject being treated, the severity of the affliction, the manner of administration, the judgment of the prescribing physician, etc. Excluded from all embodiments are
dermal filler compositions that include cells and/or growth stimulators such as growth factors or morphogenic bone proteins and/or calcium hydroxy apatite microspheres.

According to additional embodiments, the present invention provides the use of dermal fillers at sites of defects in gingival architecture and contour and bony tissue defects such as occurs with tooth loss, increase in age, periodontal disease and disorders, periodontal trauma, and after tooth implants, for the enhancement of fit and function of dental prostheses or implants comprising crowns, bridge, partial or complete dentures comprising implant denture, interim or provisional denture, overlay denture, removable or fixed partial denture, or transitional denture, and for interdental papilla augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under bridgework. According to another embodiment the methods may be used for treatment of peri-implantitis.

According to other embodiments, the present invention provides methods comprising the step of administering by injection to an individual in need thereof, an effective amount of dermal filler at sites of defects in gingival contour and bony tissue defects such as occurs with tooth loss, increase in age, periodontal disease and disorders, periodontal trauma, and after tooth implants, for the enhancement of fit and function of dental prostheses or implants comprising crowns, bridges, partial or complete dentures comprising implant denture, interim or provisional denture, overlay denture, removable or fixed partial denture, or transitional denture, and for interdental papilla augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under a bridge pontic, hi another embodiment the methods may be used for treatment of peri-implantitis.

According to certain embodiments, the present invention provides methods comprising the step of administering by injection to an individual in need thereof, an effective amount of dermal filler at sites of gingival soft tissue and bone degeneration and loss, comprising the gingival tissue proximal to the area of degeneration or into tissue subadjacent to a defect in the oral mucosa, the tissue of the palate, the maxillary or mandibular alveolar ridges, the sulcus, the mucogingival junction, and the gingival epithelium of the gingival for the enhancement of fit and function of dental prostheses or implants comprising crowns, bridge, partial or complete dentures comprising
implant denture, interim or provisional denture, overlay denture, removable or fixed partial denture, or transitional denture. According to particular embodiments the dermal filler are injected into the buccal and lingual areas of the alveolar ridge to accommodate the fit and function of dental prostheses such as dentures.

According to particular embodiments dermal filler compositions, or other injectable material approved for soft tissue augmentation, used in the present invention comprise those that are biocompatible, inert materials. Inert materials will preferably mean non-antigenic, non-carcinogenic, non-teratogenic, and non-migratory. Preferably the compositions for use in the methods of the present invention will be cost effective dermal or soft tissue fillers approved by the US Food and Drug administration, including but not limited to fillers comprising structural proteins, polysaccharides or synthetic polymers. According to a particular embodiment, dermal filler compositions used in these methods comprise those with collagen as a major constituent, such commercially available compositions are well known in the art. Examples of such products are exogenous proteins such as reconstituted bovine collagen products commercially available including, but not limited to, ZYDERM I®, ZYDERM II® and ZYPLAST® of Collagen Corporation which comprises reconstituted bovine collagen fibers cross-linked with glutaraldehyde; reconstituted porcine collagen EVOLENCE™ of ColBar LifeScience derived from pig tendons; natural human collagen COSMODERM™ and COSMOPLAST™ manufactured by INAMED consisting of natural human collagen. Other examples comprise endogenous proteins, such as any type of collagen from the subject. An example of such a filler is autologous collagen from the subject, AUTOLOGEN® produced by Collagenesis, Inc. AUTOLOGEN®™ is a dispersion of autologous dermal collagen fibers from the subject, and should not elicit an immune response. In order to obtain AUTOLOGEN® for the subject, a specimen of tissue is obtained from the subject and forwarded to Collagenesis, Inc., where it is turned into AUTOLOGEN®.

According to an additional particular embodiment, dermal filler compositions used in these methods comprise those with hyaluronic acid as a major constituent. Hylauronic acid includes both non-cross-linked and/or cross-linked hyaluronic acid derivatives as are well known in the art. Such commercially available compositions are well known in the art. Examples of such products are HYLAFORM® gel manufactured by INAMED and Genzyme Corporations, derived from the rooster combs of domestic fowl and reported to be less immunogenic and longer lasting than
bovine collagen; and RESTYLANE® manufactured by Medicis, an FDA-approved non-animal-stabilized hyaluronic acid derivative used for soft tissue augmentation, derived from streptococcal bacterial fermentation.

According to specific embodiments, the present invention provides methods comprising the step of administering by injection into the gingival soft tissue, to an individual in need thereof, an effective amount of dermal filler for the enhancement of fit and function of dentures, including increased stability of dentures, decreased food penetration under dentures, decreased movement of dentures during mastification, and decreased pain associated with fit and wearing of dentures.

The methodologies of the present invention can be used to correct defects in tissue of a subject, such as, for example, defects in the palatal mucosa, gingival mucosa, for the enhancement of fit and function of dental prostheses and the formation of supportive foundation for dental prostheses such as dentures. Such methodologies can be used as preprosthetic techniques, for example, for wear and use of dental prostheses such as crowns, bridges, partial or complete dentures, and for inter-dental papilla augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under bridge pontic. According to another embodiment the methods can be used for treatment of peri-implantitis.

The methods and procedures of the present invention may be performed under general, local, topical, monitored, or with no anesthesia, depending upon patient compliance and tolerance, the amount of injected or placed material, and the type of injection or engraftment performed in accordance with the skilled artisan or physician discretion using any suitable type of anesthesia or analgesics known in the art.

To repair, contour or augment gingival tissue, several treatment techniques available for the connective tissue are well known in the art and have applications in the present invention. In the presence of a periodontal or gingival defect, the dermal filler material can be injected under local anesthesia by means of the use of a fine needle gauge 23 to 30, positioned perpendicular to the neck of the tooth if present, and advancing the needle by positioning it sub-epithelial, into the lamina propria region of the gingiva and injecting the filler material. Injections of filler material are also used when the presence of mucogingival or alveolar ridge problems are present as well as for inter-dental papilla augmentation, augmentation of papillae between crowns...
mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under bridge pontic. According to other embodiment the filler material may be used for treatment of peri-implantitis, either alone or with antibiotics. In a particular exemplary embodiment the injectable fillers are used to improve the fit and formation of supportive foundation for dental prostheses such as dentures by means of gingival augmentation.

Examples

Administration of the dermal filler pharmaceutical compositions

Dermal filler pharmaceutical compositions can be used for the enhancement of fit and function of dental prostheses, or for inter-dental papilla augmentation, augmentation of papillae between crowns mounted on natural teeth or implants, augmentation of papillae between crowns and natural teeth, augmentation of the contour of the gingiva under bridge pontic by use of the several techniques. If the tissue to be injected contains defects in the palate or gums of the subject, the tissue to be injected with a filler composition is subadjacent to the defect. After the tissue to be injected has been prepped, a syringe filled with a suitable dermal filler composition is fitted with a 23-30 gauge needle. The needle is inserted into the tissue; the orientation of the bevel is not critical to the success of this method of the present invention. The injection of the filler composition is made by gentle pressure until a slight blanch is seen in the injected tissue and proper augmentation is achieved. Multiple serial injections are made.

Example 1 - Enhanced fit and function of dentures

Patient No. 1:

A 74 year old Caucasian female suffering from hypercholesterolemia, reactive psychotic depression, osteoarthritis of the knee, and essential hypertension.

Dental status:

Upper jaw (maxilla): No teeth, restored by removable upper denture.

Lower jaw (mandible): treatment history: up to 4 years ago- teeth No. 31, 32, 33, 41, 42 restored by ceramic/metal bridge and a posterior bi-lateral removable partial denture. 4 years ago- restoration failure, existing teeth removed, 3 implants inserted
for denture support, bone resorption prohibited instillation of additional implants for a
fixed restoration. 2 years ago- implant at tooth No.44 rejected, patient left with
support of only two implants, increased bone resorption observed at prostheses area.
Patient complained of instability, imbalance and dysfunction of lower prostheses
(denture) function, mainly food penetration under denture during mastification
leading to denture displacement, padding attempts of denture foundation showed no
improvement.

Treatment: Gingival soft tissue augmentation was preformed to enhance the fit of the
tissue to the prostheses. Injection of 0.5 cc of "EVOLENCE™" reconstituted porcine
collagen at the buccal and lingual area of the alveolar ridge at the right segment was
preformed under local anesthesia with "TEVACAINE®". Treatment monitoring 3, 18
and 39 day post treatment showed enhancement of fit and function of denture,
increased stability of denture, no food penetration under denture, and markedly
decreased movement of denture. An "EVOLENCE™" injection of 0.5 cc was
preformed 4 months post initial treatment at the buccal and lingual area of the alveolar
ridge at the left segment for treatment completion under local anesthesia with
"TEVACAINE®". Treatment monitoring 7 days after 2nd injection showed painless
recovery and restoration, no food penetration under denture, and proper fit and
function of denture.

Patient No. 2:
A 65 years old Caucasian female of general good health.

Dental status:
Lower jaw (mandible): major lack of teeth, existing teeth- No. 31, 32, 41, 48 and root
of tooth No. 33 retained for maintenance of bone volume. A removable partial denture
is supported by soft tissue and teeth No. 32, 42 and 48. The patient had both left and
right segment very constricted alveolar ridge, distal to existing teeth prohibiting
implant-based oral restoration. Patient complained of instability of lower prostheses,
and food penetration under denture during mastification.

Treatment: Gingival soft tissue augmentation was preformed to enhance the fit of the
tissue to the prostheses. Injection of 1 cc "RESTYLANE®" hyaluronic acid
derivative at the right and left segments of the buccal and lingual area of the alveolar
ridge distally from tooth No. 32, and from Tooth No. 42 distally to tooth No. 48, was
preformed under local anesthesia with "TEVACAINE®". The patient reported no
pain after procedure, and reported a significant enhancement of denture stability, and markedly decreased food penetration under denture to the point of no disturbance or inconvenience.

While the present invention has been particularly described, persons skilled in the art will appreciate that many variations and modifications can be made. Therefore, the invention is not to be construed as restricted to the particularly described embodiments, rather the scope, spirit and concept of the invention will be more readily understood by reference to the claims which follow.
CLAIMS

1. A method of enhancing the fit and function of dental prostheses in a subject comprising injecting a dermal filler composition to augment gingival tissues of the subject.

2. The method of claim 1, wherein the dermal filler composition comprises an inert, biocompatible, acellular, non-particulate composition.

3. The method of claim 1 wherein the dermal filler composition is selected from injectable reconstituted bovine or porcine collagen, gelatin matrices, autologous human collagen, hyaluronic acid and hyaluronic acid derivatives of animal and non-animal sources.

4. The method of claim 1, wherein the dermal filler composition comprises collagen as a major constituent.

5. The method of claim 1, wherein the dermal filler composition comprises hyaluronic acid or derivatives thereof as a major constituent.

6. The method of claim 1, wherein the dermal filler is injected to fill voids or cavities at or proximal to the site of gingival soft tissue degeneration or loss.

7. A method of augmenting gingival tissue comprising the step of administering by injection to an individual in need thereof, an effective amount of an injectable material for soft tissue augmentation, at sites of gingival degeneration and loss so that the gingival architecture and contour are augmented.

8. The method of claim 7 wherein gingival augmentation is for achieving functional and esthetic restoration of the soft tissue around bridges, crowns, crowns on implants and peri-implant defects of the gingiva including the alveolar bone.
9. A method of augmentation and treatment of oral tissue defect or degeneration in a subject in need thereof, wherein the method comprises:
   a) identifying a site of oral tissue degeneration or defect in the subject,
   b) providing a pharmaceutical composition comprising a dermal filler,
   c) injecting an effective amount of the dermal filler into the site or adjacent to the site and,
   d) achieving augmentation of the oral tissue.

10. The method of claim 9, wherein the oral tissue is gingival soft tissue.

11. The method of claim 10, wherein the dermal filler composition comprises inert, biocompatible, acellular, non-antigenic, non-carcinogenic, non-teratogenic, non-migratory compositions.

12. The method of claim 10 wherein the dermal filler composition is selected from injectable reconstituted bovine or porcine collagen, gelatin matrices, autologous human collagen, hyaluronic acid or hyaluronic acid derivatives of animal and non-animal sources.

13. The method of claim 11, wherein the dermal filler composition comprise collagen as a major constituent.

14. The method of claim 11, wherein the dermal filler composition comprise hyaluronic acid or derivatives thereof as a major constituent.

15. The method of claim 13, wherein the dermal filler is injected to fill voids or cavities at or proximal to the site of gingival soft tissue degeneration or loss.

16. Use of a dermal filler composition for preparation of a medicament for preprosthetic augmentation of gingival architecture or contour for the enhancement of the function of a dental prosthesis or implant.
17. Use of a dermal filler composition for preparation of a medicament for enhancement of the fit and function of dentures, increased stability of dentures, decreased food penetration under dentures, decreased movement of dentures during mastication, and decreased pain associated with fit, wear and use of dentures.

18. The use according to claim 16 or 17, wherein the dermal filler composition comprises inert, biocompatible, acellular non-antigenic, non-carcinogenic, non-teratogenic, non-migratory compositions.

19. The use according to claim 18 wherein the dermal filler comprises injectable reconstituted bovine or porcine collagen, gelatin matrices, autologous human collagen, hyaluronic acid or hyaluronic acid derivatives of animal and non-animal source.

20. The use according claim 18, wherein the dermal filler composition comprises collagen as a major constituent.

21. The use according to claim 18, wherein the dermal filler composition comprises hyaluronic acid or derivatives thereof as a major constituent.

22. The use according to claim 18, wherein the dental prosthesis or implant is selected from a crown, bridge, partial or complete dentures.

23. The use according to claim 22, wherein the partial or complete dentures are selected from an implant denture, interim or provisional denture, overlay denture, removable or fixed partial denture, or transitional denture.

24. A method for enhancing fit of a dental prosthetic comprising administering to a gingival soft tissue in an area of an alveolar defect of an individual, a composition comprising an effective amount of a biocompatible acellular dermal filler devoid of growth stimulators and ceramic and bone-derived materials, thereby augmenting the gingival soft tissue for enhancing the fit of the dental prosthetic.
25. The method of claim 24, wherein the dermal filler composition comprises collagen as a major constituent.

26. The method of claims 24, wherein the dermal filler composition comprise hyaluronic acid or derivatives thereof as a major constituent.

27. The method of claim 24-, wherein the dental prosthesis or implant is selected from a crown, bridge, partial or complete dentures.

28. The method of claim 27, wherein the partial or complete dentures is selected from an implant denture, interim or provisional denture, overlay denture, removable or fixed partial denture, or transitional denture.

29. The method of claim 24, wherein the dermal filler is injected at or proximal to the site of gingival soft tissue augmentation.

30. The method of claim 24, wherein enhancement of the fit and function of dentures comprises at least one of increased stability of dentures, decreased food penetration under dentures, decreased movement of dentures during mastication, and decreased pain associated with fit, wear and use of dentures.


32. The dermal filler of claim 31 in a form selected from an ampoule, a cartridge or a carpule.
International application No
PCT/IL 09/00421

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61 F 13/00 (2009 01)
USPC - 424/422

According to International Patent Classification (IPC) or to both national classification and IPC

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC 424/422

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC 424/422, 423, 424, 433/5
See Search Terms Below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
pubWEST(PGPB,USPT,EPAB,JPAB), USPTO, Google Web
Search Terms Used inert, biocompatible, acellular, no-particulate, dermal, dental, inject$, filler, implant, prosthe$, fit, stab$, soft tissue, denture

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<td>Y</td>
<td>US 2006/0039896 A1 (KLEINSEK et al) 23 February 2006 (23 02 2006) para [0066], [0072], [0127]</td>
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