Zeev DAVIDOVITCH, *et al.*

Electro-Orthodontics

Science News **121 : 330 (15 May 1980)**

Shifting Teeth Faster Electrically

Wearing braces to move and straighten teeth can be a lengthy, painful experience. Now, two University of Pennsylvania researchers believe electrical stimulation of the gum may cut in half the time braces must be worn. The researchers are just beginning a 3-year clinical study with 60 female patients to test the mehtod.

Othrodontist Zeev Davidovitch, who began the work in 1975 with materials scientist Edward Korostoff, says orthodontists have conventionally used mechan ical force to shift teeth. Mechanical devices that push or pull a tooth apply force to a tooth's crown. The force is transmitted downward to the root. there the bone tneds to dissolve or resorb ahead of the moving tooth's root where the pressure is high and to build up behind the root where the pressure is low. the problem, says Davidovitch, is that tissue remodeling doen'st happen overnight. "What we're doing with electricity is simply enhancing the rate of tissue remodeling", he says. Although braces are still necessary, they are needed for a shorter time.

The electricity source is approximately the size and shape of two nickels stuck together. It consists of a transistor and several resisors and batteries, encased in epoxy and dental acrylic plastic. The device provides a constant current of between 15 and 20 microamperes at about 1.5 volts. Korostoff says the easily installed movable circular unit attaches to the bracket already installed for orthodontic wires and lies against the gum, between the gum and the check. One major effort during the first year of the clinical trials will be to reduce the size of the device, Korostoff says. A graduate student researcher, who has worn the device for a short time, says its presence is noticeable, but it is not uncomfortable compared with the normal discomfort people suffer when they wear orthodontic braces. He says he did not feel the electric current at all.

Although the method was tested successfully on cats, Davidovitch admits that testing it on humans is a new field. "We don't know what will happen", he says. "There are many questions we haven't answered yet". Initially, patients will weat the device for about 8 to 10 hours at night. "We may find that it's not sufficient", says Davidovitch, "but this is why we plan to conduct these experiments, to get the bugs out of the system".

Both Korostoff and Davidovitch are optimistic that their method will work on humans as well as it did on cats, and they are very excited about their work. Through the university of Pennsylvania, they hold a patent on the method and device now being tested at the university's School of Dental Medicine.

***Moneysworth*, mid-1980s**

Effect of Electric Braces Shocking

Philadelphia -- Electric braces, which could take a big bite out of the amount of time usually needed to straighten teeth, have been developed by researchers at the University of Pennsylvania School of Dental Medicine.

Dr Zeev Davidovitch, orthodontics professor and dead of the research team, says miniature batteries, transistors and resistors produce and regulate the low-level electric current in the device.

The electrical-mechanical device, used with conventional orthodontics braces, has been successfully tested on animals. Davidovitch says it could straighten teeth twice as fast as regular breaces and be no more inconvenient. He hopes to begin a 3-year study on humans soon. "The bulkiness of this power pack resembles the bulkiness of an extension screw, [often] used to expand palates", he says.

"It can be easily taken in and out and should pose no dicomfort to the patient. he can weat it only at night, and he can't throw it out of adjustment unless he steps on it or breaks it with a hammer."

In initial tests, sandard braces were placed on one side of a cat's mouth, the device on teh other. An electrode was placed on either side of a tooth and a small amount of electricity was generated.

Weeks later, the researchers sound that where there was electrical stimulation tooth movement was twice as fast. The scientists also found that because cell stimulation occurs a few minutes after electricity is intriduced, the device does not have to be worn 24 hours a day.

"When you try to move teeth, you apply forces -- the wires, srings and elastic bands -- to the teeth. The force is transmitted to the surrounding tissue," Davidovitch explains.

"We thought if we could get more cells involved in the surrounding tissue, we would get rapid tooth movement."

It has been estimated that only 5 to 10 percent of those who need orthodontia receive it, Davidovitch says. If treatment time, which often runs into years, can be halved, more patients will be willing to undergo treatment, he predicts.

US4153060

Method and Apparatus for Electrically Enhanced Bone Growth and Tooth Movement

1979-05-08
KOROSTOFF EDWARD; DAVIDOVITCH ZEEV
Classification: - international: A61C7/00; A61N1/05; A61N1/32; A61C7/00; A61N1/05; A61N1/32; (IPC1-7): A61N1/36
Abstract -- Disclosed is a method and apparatus for electrically stimulating bone growth and tooth movement in the mouths of mammals. A positive electrode is placed on the gum surface adjacent the bone structure which is to be resorbed. A negative electrode is placed on the gum surface adjacent the bone tissue which is to be accreted or built up. A current source is connected, such that a small current flows between the electrodes, which has the effect of stimulating bone growth in a specific direction. In a preferred embodiment, the electrodes are placed on the gum surface adjacent a tooth, the positive electrode on the side towards which the tooth should move, and the negative on the side from which the tooth will move. Application of a small current to the electrodes will enhance the repositioning of the tooth in conjuction with normal orthodontic practices.

BACKGROUND OF THE INVENTION

The present invention relates to orthodontic techniques in general, and the reduction in time required for specific tooth movement in particular.

Orthodontic tooth movement presently is accomplished by the application of mechanical forces to teeth. An apparatus is connected inside the mouth of a patient which applies, through the use of springs, rubber bands, or other means, a mechanical force in the direction of desired tooth movement. These forces cause the bone to resorb (be moved) in the direction of force and cause the bone to grow on the other side of the tooth.

This process of orthodontic force application enables teeth to move in the mouth within the boundaries of the neighboring tissues. The tooth movement is clarified by Wolff's Law which states, in effect, that bone under mechanical stress is remodeled to accomodate or reduce the stress. The unfortunate practical aspect to known techniques of orthodontic movement is that the mechanical apparatus, or "braces", must be worn by the patient for extended periods of time, often several years or more.

U.S. Pat. No. 3,842,841 teaches the application of a direct current to aid healing of bone fractures in the human body, but requires surgical implantation. A negative electrode (cathode) is surgically inserted into the site of a fracture, and a positive electrode (anode) is taped to the skin elsewhere. Although the precise biological process is not understood, the current flowing through the factured bone increases the healing rate of the damaged bone tissue.

However, to date, there have been no substantial improvements in enhancing tooth movement to reduce the total amount of time over which an orthodontic appliance must be used in order to accomplish a given amount of tooth movement or repositioning.

SUMMARY OF THE INVENTION

Therefore, in view of the foregoing, it is an object of the present invention to reposition teeth in a patient's mouth by applying an electrical potential to the patient's gums in the immediate vicinity.

It is a further object of the present invention to increase the rate of movement of teeth undergoing mechanical stress in accordance with known orthodontic practices.

It is a still further object of the present invention to provide an electronic circuit capable of being retained in conjunction with an existing orthodontic appliance for providing a constant current output to electrodes located adjacent to a tooth to be repositioned.

It is an additional object of the present invention to provide a method and apparatus for stimulating and controlling bone growth in a patient's mouth in order to correct alveolar bone defects, close cleft palates, or maintain the alveolar ridge in edentulous patients (those who have lost their teeth).

In accordance with the above, the other objects, a method and apparatus for the initiation and enhancement of tooth movement comprises the disposition of an anodic electrode in the direction of applied force and a cathodic electronic on the opposite side of the tooth to be moved. A current source is connected to the two electrodes which causes the tooth to be repositioned either solely or in combination with an existing orthodontic appliance.

The application of a small current, through appropriate surface electrodes in the mouth, also can be utilized to stimulate bone accretion in the vicinity of a cathodic electrode and bone resorption in the vicinity of an anodic electrode.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and the attendant advantages thereof will be more clearly understood by reference to the following drawings wherein:

FIG. 1 is a bottom view of an orthodontic appliance showing the location of the apparatus in relation to the orthodontic springs;

FIG. 1

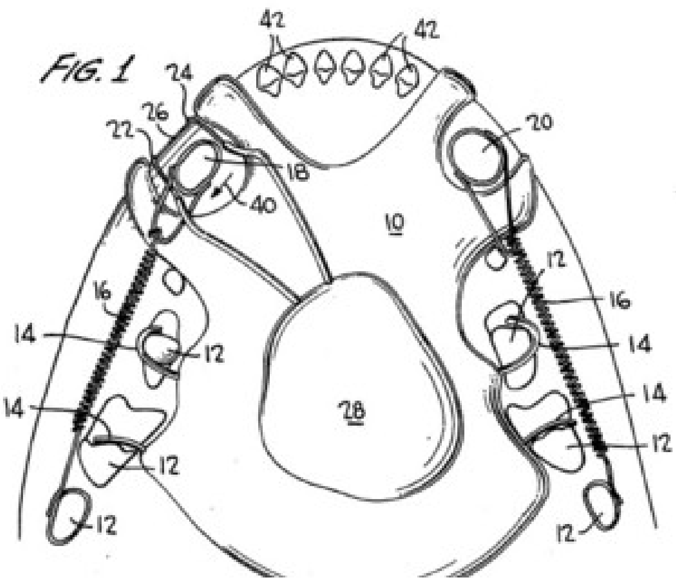


FIG. 2 is a side view showing the placement of the electrodes according to a preferred embodiment;

FIG. 2

FIG. 3

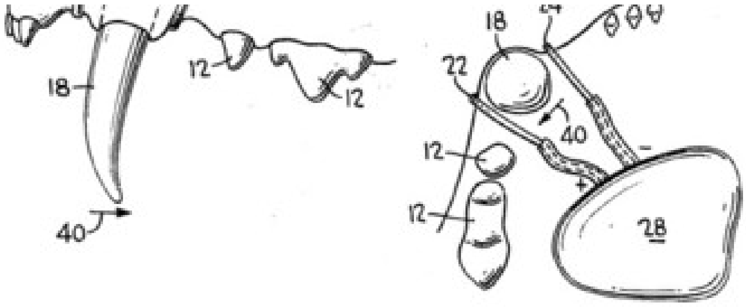


FIG. 3 is a bottom view showing a preferred embodiment of the anode and cathode electrodes;

FIG. 4 is an electrical schematic of a preferred embodiment of a constant current circuit;

FIG. 4

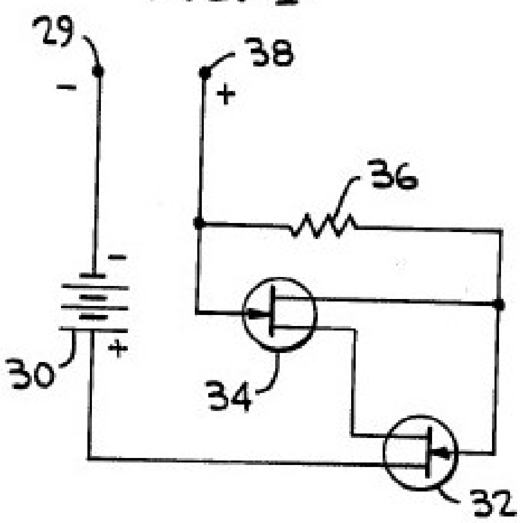


FIG. 5 is a perspective view showing the placement of the cathode electrode to correct aveolar bone defects;

FIG. 5

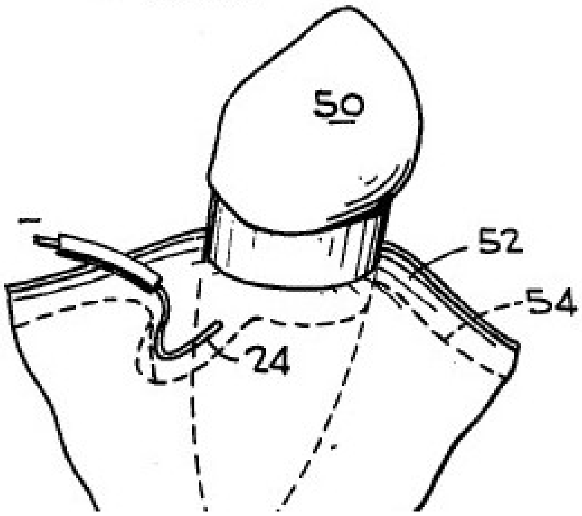


FIG. 6 is a bottom view of the placement of cathode electrodes for the correction of a cleft palate; and

FIG. 6

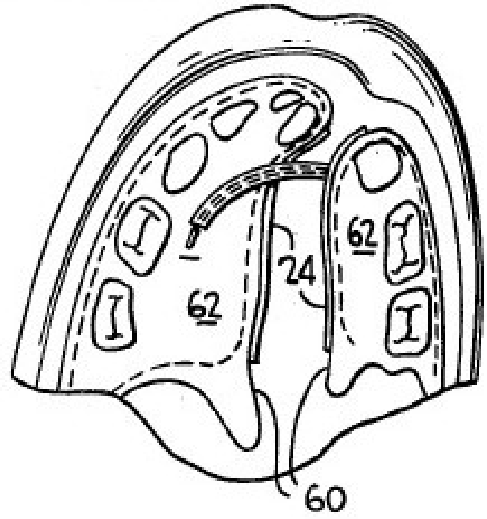
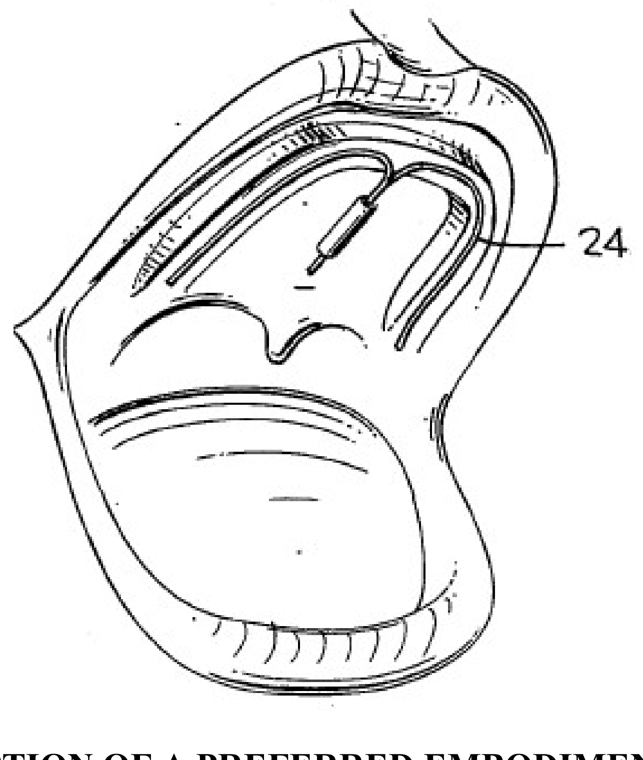


FIG. 7 is a perspective view showing the placement of the cathode electrode in an edentulous patient.

FIG. 7



DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

Referring now to the drawings wherein like reference characters designate like parts throughout the several views, FIG. 1 is a bottom view of an orthodontic appliance along with the present invention fitted to a cat's mouth in accordance with known techniques. Although the present application was reduced to practice and demonstrated on a cat tooth, the anatomy and histology of the cat canine and its surrounding tissues is similar to one-rooted human teeth. Although the present description will be of the application of the present invention to the test animals, the invention is clearly of use in the human application, which would provide no unobvious difficulties. A base plate 10 is located in the roof of the patient's mouth and fixed to the premolar teeth 12 by conventional clamps 14. Orthodontic springs 16 are connected to the rearmost premolar teeth 12 and the teeth to be repositioned, in this instance, canine teeth 18 and 20.

An anode electrode 22 and a cathode electrode 24 are placed such that they are in contact with the gingival tissue 26. The anode 22 is placed adjacent the tooth in the direction of desired movement, in this instance, towards spring 16. The cathode 24 is placed on the opposite side of tooth 18. The anode 22 and cathode 24 are connected to positive and negative leads from power pack 28 contained in base plate 10.

The details of the power pack's internal features can be seen by reference to FIG. 4. The negative terminal 29 is connected to the negative side of battery 30, with the positive side of the battery 30 connected to transistor 32. Transistor 32 is interconnected with transistor 34 and resistor 36 and, then, to the positive terminal 38. In this preferred embodiment, a constant current of approximately 20 microamperes is provided over a range of tissue impedances, such that the changing impedance between the anode and cathode does not substantially affect the amount of current flowing therebetween.

FIGS. 2 and 3 are side and bottom views, respectively, of a preferred electrode placement, with the direction of desired movement shown by arrow 40. Although the mechanical force generating system comprising orthodontic springs 16, shown in FIG. 1, are not included in FIGS. 2 and 3, they could clearly be added to further enhance the movement of tooth 18 in direction 40. However, tooth movement can be accomplished solely by means of the electrical stimulation shown in FIGS. 2 and 3, and this remains one embodiment.

However, the preferred embodiment of the present invention is the use of the electrodes to increase the rate of movement of teeth undergoing orthodontic treatment.

In a test of the FIG. 1 apparatus, five female cats (Group A) had both canine teeth tipped in the direction of arrow 40 by coil springs generating 80 grams of force for a period of 14 days. Five additional female cats (Group B) had both canines tipped in the same direction. However, Group B cats also had a stainless steel cathode 24 and a gold anode 22 connected to the electrical circuit of FIG. 4, with the electrode placement shown in FIG. 1. Both electrodes were in contact with the gingival tissues at, and partially surrounding, the area of the alveolar bone crest. Dummy electrodes (not shown) were also placed in contact with the gingival tissues surrounding canine tooth 20, but were not connected to power pack 28.

In the Group A animals, the rate of canine tooth movement was similar on both sides. In Group B, however, the rate was unequal with the activated electrode side doving canine tooth 18 twice as much as electrically unactivated canine tooth 20. For instance, the distance between incisors 42 and unactivated canine tooth 20 increased by 0.29 mm after seven days, and an additional 0.17 mm after fourteen days. The distance between the incisors 42 and the electrically activated canine 18 after seven days had increased 0.58 mm, and after fourteen days an additional 0.61 mm. Because both canine teeth 18 and 20 had identical mechanical forces applied thereto (by springs 16), the increased rate of movement of canine tooth 18 is attributable to the application of electric current to the surrounding gum tissues.

Because the present invention essentially doubles the rate of movement, the length of time necessary to achieve a repositioning of a tooth would be cut in half. Although human tests have not yet been conducted, it is believed the results will be similar to those shown in the cat studies, because of the similarity of cat canine teeth and their surrounding tissues to single root human teeth. Thus, the applicability to the human orthodontic patient is believed obvious in view of the above teachings. The application to the human patient may require current levels different from the 21 microamps applied in the cat embodiment.

Similarly, different combinations of implanted and surface electrodes will be obvious to those of ordinary skill in the art in view of the applicants' teachings. Although, a constant current supply source was utilized in a preferred embodiment, constant voltage with a variable current source may be used with slightly different results. Additionally, an alternating current with a D.C. impressed thereon would also work. The only requirement being that one electrode be substantially anodic and the other substantially cathodic, i.e., the total current (AC and DC combined) is more in one direction than the other.

The current supply means utilized in the cat tests delivered a constant current of 21.+-. 4 .mu. amps. It is believed that some variation may be necessary for individual patients, but that current ranges of between 5 and 100 microamps will be useful in obtaining similar results in humans. Additionally, where, as will be seen, extended electrodes are utilized, as in FIGS. 6 and 7, the total current applied to the extended electrode (or a series of button electrodes) must be increased in order to maintain a current density at the gum tissue, sufficient to cause bone accretion or resorption.

The present embodiments indicate the placement of electrodes on the soft gingival tissue adjacent, but not in contact with, the bone in order to produce the desired effect, although there is no indication that placement of the electrodes on the bone itself would have a deleterious effect. A preferred circuit for a constant current power supply is shown in FIG. 4, although many compact intra-oral power supplies will become apparent to those skilled in the art in view of the applicants' invention.

The application of surface electrodes to stimulate controlled bone growth can also supply the solution for non-surgical correction of alveolar bone defects, and cleft palates. FIG. 5 depicts a tooth 50, gum 52, with the alveolar bone ridge 54. A defect in the alveolar bone ridge is indicated at 56. The placement of a cathodic surface electrode 24 on the gum in the region of the defect 56 could stimulate bone growth so as to eliminate the defect. The anodic surface electrode (not shown) would be located elsewhere in the patient's mouth.

A similar application of the surface electrode could be utilized in conjunction with a cleft palate, as shown in FIG. 6. The region of the cleft 60 would be gradually filled by bone due to the electrical stimulation of cathodic electrodes 24 placed on the surface of tissues covering the bony palate 62. As in FIG. 5, the anodic electrode would be located elsewhere in the patient's mouth. As in all depictions of the use of surface electrodes, only in the region where bone growth is to be stimulated, or the bone is to be resorbed, is the electrode in contact with the gum, or gingival tissues. Elsewhere, the wires connecting the surface electrodes to the power supply would be insulated so as to restrict bone accretion, or resorption, to the desired area. It has been proposed that over an extended period of time, the bone accretion to the bony palate in the vicinity of electrodes 24 would result in a buildup, and eventual closure, of the cleft region 60 in the victim of a cleft palate.

It has been found that the bone has piezoelectric properties: that is to say, when a force is applied to the tooth, the resulting force on the bone generates very small, but measurable, electrical currents. It is believed that the application of these minute currents stimulate, and maintain, the alveolar bone ridge, which serve as the base for anchoring of human teeth. However, edentulous patients suffer from a gradual resorption of the alveolar bone ridge in the mouth, which makes it more and more difficult to anchor false teeth in the patient's mouth. It is believed that the absence of real teeth in the edentulous patient causes the termination of the minor stimulation currents necessary for the maintenance of the alveolar bone ridge and, consequently, the ridge resorbs into the roof of the mouth.

FIG. 7 depicts an arrangement of cathodic electrode 24, wherein it would be placed adjacent the alveolar bone ridge in a patient's mouth. The application of a suitable current supply with the anode (not shown) located elsewhere in the mouth may provide sufficient stimulation to the alveolar bone ridge, such that it is maintained, or even reformed, in the edentulous patient. Obviously, the power supply, and appropriate electrodes, could be located in the bridge work of false teeth, and would be applicable both to the upper and lower bond ridges.

Although the invention has been described relative to a specific embodiment thereof, it is not so limited and many modifications and variations thereof will be readily apparent to those skilled in the art in light of the above teachings. It is, therefore, to be understood that, within the scope of the appended claims, the invention may be practiced otherwise than as specifically described.

Biocompatible electrode and use in orthodontic electroosteogenesis

US Patent # 4854865

Abstract: An improved method of orthondontic electroosteogenesis comprises providing a biocompatible anode having a noble metal portion in engagement with an electrolytic gel portion comprising agarose and an electrolyte, where the anode gel portion is in engagement with epithelial gingiva at an area of osteoclastic or osteoblastic activity, and a biocompatible cathode having a noble metal portion in engagement with an electrolytic gel portion comprising agarose, an electrolyte, and a weak, biocompatible acid, where the cathode gel portion is in engagement with epithelial gingiva at an area of osteoblastic or osteoclastic activity. Electric current is then applied across the anode and cathode to stimulate osteogenesis. The invention also comprises biocompatible electrodes for electric stimulation of tissue.

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http://cro.sagepub.com/cgi/content/abstract/2/4/411

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DOI: 10.1177/10454411910020040101

Tooth Movement

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This article reviews the evolution of concepts regarding the biological foundation of force-induced tooth movement. Nineteenth century hypotheses proposed two mechanisms: application of pressure and tension to the periodontal ligament (PDL), and bending of the alveolar bone. Histologic investigations in the early and middle years of the 20th century

revealed that both phenomena actually occur concomitantly, and that cells, as well as extracellular components of the PDL and alveolar bone, participate in the response to applied mechanical forces, which ultimately results in remodeling activities.

Experiments with isolated cells in culture demonstrated that shape distortion might lead to cellular activation, either by opening plasma membrane ion channels, or by crystallizing cytoskeletal filaments. Mechanical distortion of collagenous matrices, mineralized or non-mineralized, may, on the other hand, evoke the development of bioelectric phenomena (stress-generated potentials and streaming potentials) that are capable of stimulating cells by altering the electric charge on their membrane or their fluid envelope. In intact animals, mechanical perturbations on the order of about 1 min/d are apparently sufficient to cause profound osteogenic responses, perhaps due to matrix proteoglycan-related "strain memory".

Enzymatically isolated human PDL cells respond biochemically to mechanical and chemical signals. The latter include endocrines, autocrines, and paracrines. Histochemical and immunohistochemical studies showed that during the early places of tooth movement, PDL fluids are shifted, and cells and matrix are distorted. Vasoactive neurotransmitters are released from periodontal nerve terminals, causing leukocytes to migrate out of adjacent capillaries. Cytokines and growth factors are secreted by these cells, stimulating PDL cells and alveolar bone lining cells to remodel their related matrices. This remodeling activity facilitates movement of teeth into areas in which bone had been resorbed.

This emerging information suggests that in the living mammal, many cell types are involved in the biological response to applied mechanical stress to teeth, and thereby to bone. Essentially, cells of the nervous, immune, and endocrine systems become involved in the activation and response of PDL and alveolar bone cells to applied stresses. This fact implies that research in the area of the biological response to force application to teeth should be sufficiently broad to include explorations of possible associations between physical, cellular, and molecular phenomena. The goals of this investigative field should continue to expound on fundamental principles, particularly on extrapolating new findings to the clinical environment, where millions of patients are subjected annually to applications of mechanical forces to their teeth for long periods of time in an effort to improve their position in the oral cavity. Recently developed research tools such as cell culture techniques and immunologic probes, are the best hope for enhancing this development.

USP 4570637
Electrode

Robert L. Gomes // Joseph P. Maffione

Abstract -- An improved medical electrode is particularly adapted for transmitting DC currents. The electrode includes (1) an electrically conductive substrate electrically connected to a stud member and chemically inert with respect to the electrically and ionically conductive material, such as a gel, coupling the electrode to the skin of the user, and (2) a predetermined amount of an electrically-conductive material, preferably silver, disposed on the substrate in spaced relationship to the stud member and interfacing with the electrically and ionically conductive material.

USP 4757804
Device for Electromagnetic Treatment of Living Tissue

July 19, 1988
Griffith, et al.

Other References: "Fracture Healing in the Rabbit Fibula When Subjected to Various Capacitively Coupled Electrical Fields" by Brighton et al, Journal ofOrthopedic Research, vol. 3, No. 3, 1985..
"Electrical Stimulation of Hard and Soft Tissues in Animal Models" by Jonathan Black, Ph.D., Clinics in Plastic Surgery, vol. 12, No. 2, Apr. 1985..
"Bioelectric Stimulation of Bone Formation: Methods, Models, and Mechanisms" by Spadaro, Journal of Bioelectricity, vol. 1, No. 1, 1982..
"A Review of Electromagnetically Enhanced Soft Tissue Healing" by Cyril B. Frank, M.D. and Andrew Y. J. Szeto, Ph.D..
"Treatment of Osteonecrosis of the Hip with Specific, Pulsed Electromagnetic Fields (PEMFs): A Preliminary Clinical Report" by C. A. L. Bassett et al, Journal of Bone Circulation..

Abstract: A solenoid device for treatment of body tissue such as bones or other regions with pulsed signals comprises a flexible flat belt for encircling a body part or cast surrounding a body part containing tissue to be treated. The belt has a plurality of parallel conductors extending along its length and has its opposite ends offset by one or more conductor spacings. The resultant aligned conductor ends are connected together to form at least one continuous coil, with the resultant unconnected outer conductor ends at opposite sides of the belt comprising inputs across which a suitable electrical signal can be connected. An adjustment device or buckle is mounted on the belt to allow the diameter of the belt to be adjusted. The buckle traps a doubled over portion of the belt circumference which is adjustable in length to change the diameter of the device to closely fit the underlying body part or cast.

Relaxins

US Patent 6984128
Methods for Enabling and Stabilizing Tooth Movement

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates generally to medical apparatus and methods. More particularly, the present invention relates to methods and systems for facilitating, accelerating, and stabilizing tooth movement before, during and after orthodontic procedures.

Orthodontic procedures suffer from four major problems. First, the braces or other appliances which effect the tooth movement must be worn for long periods of time. Second, even after a successful orthodontic treatment, the teeth often relapse towards their original positions once the braces or other treatment appliances are removed. Third, the mechanically induced movement of teeth can cause significant discomfort to the patient. Fourth, the wearing of braces is esthetically displeasing, uncomfortable, and compromises oral hygiene. While recently introduced clear plastic visible "aligners" largely overcome the latter problems, such aligners are not suitable for all patients. Moreover, the aligners do not reduce treatment time, do not reduce the risk of relapse, and do not lessen the pain associated with tooth movement in the jaw.

For these reasons, it would be desirable to provide improved orthodontic technologies for moving teeth which overcome at least some of the problems noted above. In particular, it would be desirable to provide orthodontic methods and systems which can reduce the time necessary to effect a desired tooth movement, which can reduce the pain associated with tooth movement, which can reduce the tendency of teeth to relapse to their original positions after the orthodontic treatment is stopped, and/or which can reduce the time in which unsightly braces need to be worn.

2. Description of Background Art

Nicozisis et al. (2000) Clin. Orthod. Res. 3:192-201, describes experiments which demonstrate the presence of endogenous relaxin in cranial tissue of mice and speculates that relaxin may be used as an adjunct to orthodontic or surgical therapy to promote manipulation of sutural tissues or affect stability. The application of electrical current to stimulate bone growth and remodeling in orthodontic procedures is described in U.S. Pat. Nos. 4,854,865; 4,519,779; and 4,153,060. Appliances for local and systematic drug delivery to the gingival tissues are described in U.S. Pat. Nos. 6,159,498, 5,633,000; 5,616,315; 5,575,655; 5,447,725; 5,294,004; 4,959,220; 4,933,183; 4,892,736; 4,685,883; and Re. 34,656. Polymeric shell appliances for repositioning teeth are described in U.S. Pat. No. 5,975,893. The full disclosures of each of the above U.S. patents are incorporated herein by reference.

BRIEF SUMMARY OF THE INVENTION

The present invention provides improved methods and systems for repositioning teeth in patients. In addition, the present invention provides improved methods and systems for stabilizing teeth which have already been repositioned in order to reduce or eliminate the tendency of the repositioned teeth to relapse, i.e., move back toward their prior positions. The methods for repositioning teeth comprise applying force to at least one tooth, and typically to more than one tooth and/or to different teeth over time, in the jaw of the patient. For both repositioning or stabilizing, tissue remodeling and/or an angiogenic substance(s) is administered to the patient to promote remodeling of periodontal tissue surrounding the root(s) of the tooth or teeth to be moved. Preferred substance(s) will bind to and activate the relaxin receptor in the tissues which anchor the teeth or other craniofacial structures. Most preferred is relaxin or an analog or mimetic thereof which combines tissue remodeling activity with angiogenic activity. Analogs include peptides, oligomers, fragments, etc. which comprise the active region of native relaxin and mimetics include small molecule drugs, typically below 2 kD, designed to mimic the activity of native relaxin. Alternatively, substance(s) with predominantly angiogenic activity could be selected, such as VEGF, bFGF, estrogen, nitrous oxide, naltrexone, or the like. Further alternatively, collagenases or other tissue-softening enzymes could be utilized to promote periodontal tissue remodeling according to the present invention. In some instances, it may be desirable to combine two or more tissue remodeling and/or angiogenic substance(s) having differing activities. In other instances it may be desirable to deliver different tissue remodeling and/or angiogenic substance(s) at different times during the orthodontic treatment and/or to different regions of the periodontal tissue.

The term "relaxin" means human relaxin, including intact full length relaxin or a portion of the relaxin molecule that retains biological activity [as described in U.S. Pat. No. 5,023,321, preferably recombinant human relaxin (H2)] and other active agents with relaxin-like activity, such as Relaxin and portions that retain biological activity Like Factor (as described in U.S. Pat. No. 5,911,997 at SEQ ID NOS: 3 and 4, and column 5, line 27-column 6, line 4), relaxin analogs and portions that retain biological activity (as described in U.S. Pat. No. 5,811,395 at SEQ ID NOS: 1 and 2, and column 3, lines 16-40), and agents that competitively displace bound relaxin from a receptor. Relaxin can be made by any method known to those skilled in the art, for example, as described in any of U.S. Pat. Nos. 5,759,807; 4,835,251 and co-pending U.S. Ser. No. 07/908,766 (PCT US90/02085) and Ser. No. 08/080,354 (PCT US94/0699).

The tissue remodeling and/or angiogenic substance(s) will be delivered at a delivery rate and a total dosage which are selected to facilitate tooth repositioning and tissue remodeling. Typically, the dosage rates will be in the range from 1 ng to 500 ?g per day, usually from 10 ng/day to 20 ?g/day, preferably from 20 ng/day to 10 ?g/day. The dosage and other aspects of the delivery may be adjusted from time-to-time in response to the effectiveness of treatment, such as the resistance of a particular tooth or group of teeth, where the dosage might be increased if resistance is not sufficiently reduced in response to an initial dosage.

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WO/2004/041106
METHODS AND SYSTEMS FOR ENABLING AND STABILIZING TOOTH MOVEMENT

BACKGROUND OF THE INVENTION

[0001] 1. Field of the Invention. The present invention relates generally to medical apparatus and methods. More particularly, the present invention relates to methods and systems for facilitating, accelerating, and stabilizing tooth movement before, during and after orthodontic procedures.

[0002] Orthodontic procedures suffer from four major problems. First, the braces or other appliances which effect the tooth movement must be worn for long periods of time. Second, even after a successful orthodontic treatment, the teeth often relapse towards their original positions once the braces or other treatment appliances are removed. Third, the mechanically induced movement of teeth can cause significant discomfort to the patient. Fourth, the wearing of braces is esthetically displeasing, uncomfortable, and compromises oral hygiene.

While recently introduced clear plastic visible"aligners"largely overcome the latter problems, such aligners are not suitable for all patients. Moreover, the aligners do not reduce treatment time, do not reduce the risk of relapse, and do not lessen the pain associated with tooth movement in the jaw.

[0003] For these reasons, it would be desirable to provide improved orthodontic technologies for moving teeth which overcome at least some of the problems noted above. In particular, it would be desirable to provide orthodontic methods and systems which can reduce the time necessary to effect a desired tooth movement, which can reduce the pain associated with tooth movement, which can reduce the tendency of teeth to relapse to their original positions after the orthodontic treatment is stopped, and/or which can reduce the time in which unsightly braces need to be worn.

[0004] 2. Description of Background Art.

Nicozisis et al. (2000) Clin. Orthod. Res. 3: 192-201, describes experiments which demonstrate the presence of endogenous relaxin in cranial tissue of mice and speculates that relaxin may be used as an adjunct to orthodontic or surgical therapy to promote manipulation of sutural tissues or affect stability. The application of electrical current to stimulate bone growth and remodeling in orthodontic procedures is described in U. S. Patent Nos. 4,854, 865; 4,519, 779; and 4,153, 060. Appliances for local and systematic drug delivery to the gingival tissues are described in U. S. Patent Nos. 6,159, 498, 5,633, 000; 5,616, 315; 5,575, 655; 5,447, 725; 5,294, 004; 4,959, 220; 4,933, 183; 4,892, 736; 4,685, 883; and Re. 34,656. Polymeric shell appliances for repositioning teeth are described in U. S. Patent No. 5,975, 893. The full disclosures of each of the above U. S. Patents are incorporated herein by reference.

BRIEF SUMMARY OF THE INVENTION [0005]

The present invention provides improved methods and systems for repositioning teeth in patients. In addition, the present invention provides improved methods and systems for stabilizing teeth which have already been repositioned in order to reduce or eliminate the tendency of the repositioned teeth to relapse, i. e. , move back toward their prior positions.

The methods for repositioning teeth comprise applying force to at least one tooth, and typically to more than one tooth and/or to different teeth over time, in the jaw of the patient.

For both repositioning or stabilizing, tissue remodeling and/or an angiogenic substance (s) is administered to the patient to promote remodeling of periodontal tissue surrounding the root (s) of the tooth or teeth to be moved. Preferred substance (s) will bind to and activate the relaxin receptor in the tissues which anchor the teeth or other craniofacial structures. Most preferred is relaxin or an analog or mimetic thereof which combines tissue remodeling activity with angiogenic activity. Analogs include peptides, oligomers, fragments, etc. which comprise the active region of native relaxin and mimetics include small molecule drugs, typically below 2 kD, designed to mimic the activity of native relaxin. Alternatively, substance (s) with predominantly angiogenic activity could be selected, such as VEGF, bFGF, estrogen, nitrous oxide, naltrexone, or the like. Further alternatively, collagenases or other tissue-softening enzymes could be utilized to promote periodontal tissue remodeling according to the present invention. In some instances, it may be desirable to combine two or more tissue remodeling and/or angiogenic substance (s) having differing activities. In other instances it may be desirable to deliver different tissue remodeling and/or angiogenic substance (s) at different times during the orthodontic treatment and/or to different regions of the periodontal tissue.

[0006] The term"relaxin"means human relaxin, including intact full length relaxin or a portion of the relaxin molecule that retains biological activity [as described in U. S. Pat.

No. 5,023, 321, preferably recombinant human relaxin (H2)] and other active agents with relaxin-like activity, such as Relaxin and portions that retain biological activity Like Factor (as described in U. S. Pat. No. 5, 911, 997 at SEQ ID NOS: 3 and 4, and column 5, line 27-

column 6, line 4), relaxin analogs and portions that retain biological activity (as described in U. S. Pat. No. 5,811, 395 at SEQ ID NOS: 1 and 2, and column 3, lines 16-40), and agents that competitively displace bound relaxin from a receptor. Relaxin can be made by any method known to those skilled in the art, for example, as described in any of U. S. Pat. Nos. 5,759, 807; 4,835, 251 and co-pending U. S. Ser. Nos. 07/908, 766 (PCT US90/02085) and 08/080, 354 (PCT US94/0699).

[0007] The tissue remodeling and/or angiogenic substance (s) will be delivered at a delivery rate and a total dosage which are selected to facilitate tooth repositioning and tissue remodeling. Typically, the dosage rates will be in the range from 1 ng to 500 ug per day, usually from 10 ng/day to 20 ug/day, preferably from 20 ng/day to 10 ug/day. The dosage and other aspects of the delivery may be adjusted from time-to-time in response to the effectiveness of treatment, such as the resistance of a particular tooth or group of teeth, where the dosage might be increased if resistance is not sufficiently reduced in response to an initial dosage.

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