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Review Article

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Dental Implant Supported Semi-implanted Platform and its Applications for Long-term Painless Drug Delivery and Blood Monitoring

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Abstract

With the mature of Internet, wireless communication, and complementary metal-oxide semiconductor (COMS) technology, the intelligent portable and wearing devices have become popular in the beginning of the 21st century. Various applications rapidly develop by the smart phone, related apps, and the connected outer devices. However, the medical applications are highly limited due to the restrictions of non-invasive monitoring, such as heart rate, walking steps, oxygen saturation, etc. Such limitations restrict the devices in further medical applications. The dental implant supported drug delivery and biosensor platform may provide a chance for relative painless, long-term and continuous molecular releasing and bio-sensing by directly contact to the upper jaw bone marrow and reach the inside blood pool. We review the current medical procedures and discuss the concept of dental implant along with the principles to avoid painful sensations in this article. Then we also discuss the advantages, special considerations and challenges of such intra-oral device in the medical, dental and engineering aspects. The device may perform long-term and continuous drug releasing and bio-sensing, which may significantly improve life quality and allow more participations for the intelligent portable device in medical applications. However, development of such device is just beginning, and further improvements are urgently required. Fortunately, most of the challenges seem to be achievable with modern technologies of electrical, chemical and mechanical engineering. Finally, the intra-oral module should be regarded as a medical device and the applications should follow the standard medical and dental principles to avoid further risks of complications.

Keywords

Complementary metal-oxide semiconductor (COMS); Dental implant; Drug delivery; Biosensor

Current Situations of Intelligent Portable and Wearable Devices

The history of the intelligent device development, also known as a computer, or a programmable electronic device that can store, retrieve and process data, can be traced from the mid-20th century. Then the technique becomes mature with VLDL improvement in the 1990's, and the portability has become one of the important concerns during its improvement [1]. Later the personal digital assistances (PDAs) become popular in the beginning of the 21st century, leading the portable device into a new advancement. Currently the portable device development is carried out to another high level with the external supplements, apps promotions, wireless module improvements, and Internet maturations since the first iPhone launched by Apple Inc. in 2007 [2]. As the result, Smartphone has become the most important portable device today due to its popularity [3].

Based on the portability, the Smartphone may provide multiple functions to meet personal demands as the following lists:

a) Basic assistances: Including functions provided without Internet, such as calendars, clocks, memos, etc.

b) Internet and global position-finding system (GPS) supported: These functions include maps/navigations, news, mobile learning, and searches, such as society/communication, banking/finance, dinning/restaurant, etc.

c) Internal device supplements including cameras, 3-dimensional accelerometer, microphone, and so on: These kinds of functions provide various entertainments including photography, video/movies, music, recording, games, etc.

d) External device supplements: Here the Smartphones become the mediator and provide as the intelligent controller for further professional applications, such as various self-monitoring and distant controllers.

All of the above Smartphone functions may be broadly divided into two kinds of applications including customers really need and they want. According to Nielsen's market survey in September 2010, 61% of the total downloaded apps belong to games [4]. And only 14% belong to health care. However, it does not mean that medical applications are neglected in the portable device development. Basically Smartphone supported medical applications may have chances to become the customer needed types, but they need more external device supplements and show some restrictions in current situations, which will be presented more in detail as following.

Also with the maturation of internet, sensor technology and wireless connections including Wi-Fi, radio frequency identification (RFID), Bluetooth, and near field communication (NFC) since 2010, wearable devices developed rapidly in five major applications including (1) home and automotive applications, (2) health and wellness, (3) home, security and automations, (4) games and entertainment, and (5) sports and fitness. In the above applications, glasses and watches are highly relative to the health and wellness, which belong to a part of the homecare system. Therefore we will perform the discussions about current medical procedures applied in hospitals to figure out the potential applications for portability at daily homecare.

Current Medical Procedures

To figure out the valuable thinking process toward a newly portable intelligent device for medical applications, we will perform a brief review of the current medical procedures at first. Dr. Lawrence

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L. Weed suggested the problem-oriented medical record based on the individual patients in the 1960's [5,6], and such procedure may provide us a brief review of current medical managements. According to the standard principle, patients will follow the below steps to complete the admission when they go to the hospital for help, and the physicians will also finish the medical records according to the same principle.

Subjective

After admission, patients will describe their major sufferings and abnormal symptoms noticed by them. Physicians will figure out the valuable parts from the information and arrange further exam according to their symptoms.

Objective

That means data collection by scientific procedures including primary physical examinations and further clinical analysis. Here the clinical analysis including (A) fluid analysis and (B) image exam. Both of these terms may be divided into the invasive and non-invasive procedures, which are presented in Figure 1. Obviously blood-monitoring procedures belong to invasive procedures, which may bring tendency of pain and damages to surrounding tissues.

Assessment

After primary analysis, physicians may obtain some hints for primary differential diagnosis. Then following managements will design according to the primary impression.

Plan

As we know, the medical procedures are mainly divided into two parts including (A) Surgery and (B) Administrations with non-surgical pathways. Here according to the properties, non-invasive procedures only includes oral tablet, skin patches, sublingual and intra-anal absorptions, etc. Otherwise the injections may also bring irritations by passing through the skin barrier.

The above steps and the relative procedures are presented in figure 1, and the arrow denotes the block in deeper color corresponding to the invasive monitoring, which is mainly from blood sampling. We will focus on the objective procedure in order to perform more valuable information for further assessment and managements. Actually homecare improvement is critical and important in modern geriatrics since it may provide more advantages for further medical managements. However, due to the safety concern, the invasive blood monitoring is highly limited in current homecare applications, even if it may provide plenty of useful information for further managements.

The development of the intelligent device may also face the same limitation as current homecare systems. Currently the wearable devices including glasses, cardiac monitors, smart watches, and wearable fitness sensors may bring lots of bio-monitoring functions. However, most of them provide relative non-invasive monitoring, such as heart rate (HR), the number of walking steps, electrocardiogram (ECG), the degree of oxygen saturation, respiratory rate (RR), etc. Based on the safety concerns, these wearable devices all belong to the non-invasive monitoring currently, and that lead these devices to become for just healthcare, sports, figure control, or even entertainment purposes. Therefore we proposed a dental implant support platform with semi-implanted properties that may achieve long-term painless, continuous drug releasing and bio-sensing as following below to provide more medical and homecare applications.

Basic Design of the Dental Implant Supported Semi-Implanted Platform

Dental implant has been regarded as a mature tooth reconstructive technique since Dr. Branemark introduce in the 1970's [7]. In general, the implant structure contains two components including the outside prosthetic abutment (A) with replaceable properties, and the inside pure titanium implant fixture (B) directly contact to the surrounding bone marrow within rich blood supply which presents in the immobile properties. Both of the two components are shown in Figure 2.

After the patients suffering from teeth loss due to various origins including dental caries, traumatic fracture or progressive periodontitis, the ridge becomes edentulous and allows dental implant placement with proper surgical procedures under local anesthesia, which is shown in Figure 2. During the above procedures, the pain origin over primary natural teeth including the inside pulp structures and the outside periodontal ligaments (PDL) are both removed. Therefore the artificial dental implant create a painless pathway that may directly achieve the inside jaw bone marrow and contact to the surrounding blood pool [8,9], as the arrow denotes from the outside prosthetic abutment (A) to the inside implant fixture (B).

By the above anatomic facts, we proposed the dental implant supported platform as shown in Figure 2. The drug delivery (1) and bio-sensing modules (2) belong to the prosthetic abutment (A) with replaceable properties placed above the immobile implant fixture. The drug delivery module (1) contains drug chamber, piezoelectric micro-pump, and power supply inside to allow drug releasing passing through the below outlet. While the bio-sensing module (2) has the integrated circuit (IC) part, the set of electrodes including working, counter, and reference ones, the Bluetooth component, and power supply inside [10]. Compared to other commercial and non-invasive oral detectors including occlusal loading by piezoelectric sensors [11], oral cancer and pre-cancer lesions by the photoelectric modules [12,13], and tooth structures by tomography [14], our proposed intra-oral module may directly contact to the blood pool inside the jaw bone marrow, which may lead to both advantages in blood monitoring, and other risks in further infection status that should be under control.

Figure 3 presents the highly correlated relationships between the glucose concentration and the voltage changes in the biosensor preliminary evaluations. Here we should notice that the sensor function is not merely limited in the specific types of bio-molecular monitoring, and multiple molecular monitoring is also possible with proper IC design, which will be discussed later. Other preliminary studies and experiments have also been published [10], and further improvements are currently undergoing.

Discussions

Basically this newly intra-oral portable design is highly supported by the clinical and dental technology, and therefore it should be regarded as a medical device and work under established medical principles for further maintenance and disinfection while drug reloading or sensor replacement. However, it may bring benefits and show some advantages as following:

Drug delivery module

Due to the size and anatomic restrictions, the total amount of the releasing drug is around 1ml. Therefore the main application

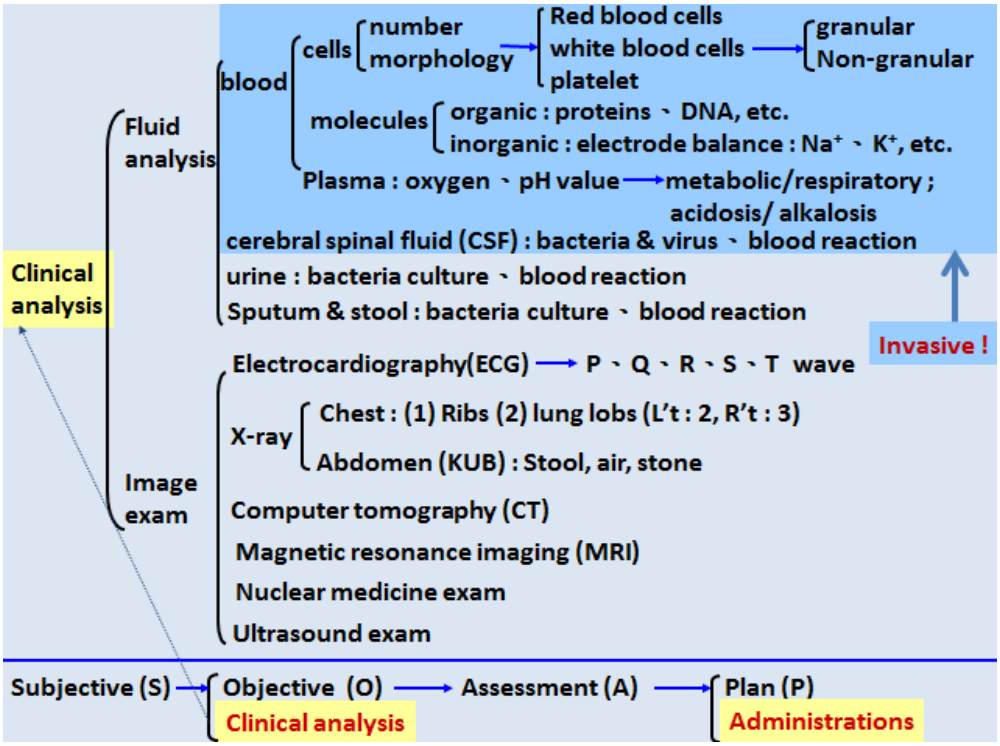

Figure 1: The brief review of the medical procedure after patients' admission in hospital, including the four steps of subjective, objective, assessment, and the plan. Basically the clinical analysis includes (1) fluid analysis and (2) image exam. Notice that the arrow denotes the block belongs to the invasive procedures due to blood sampling.

will be focus on the slow releasing of functional biomolecule, which is impossible to design as oral medicine and pass through the gastrointestinal (GI) tract directly. For example, patients suffering from diabetes in the later stage will need to receive insulin therapy regularly [15]. In addition, the newly drug delivery pathway may be powerful in neurodegenerative disease (ND) applications, such as Alzheimer's disease (AD), Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. Currently the functional peptide administration including coenzyme Q10 and targeting Tau biomolecules have shown benefits in reducing disease progressions [16-19]. However, loading the above drugs will result in frequently invasive procedure, which may be unacceptable by patients with such chronic disease without life threatening concerns. Here the intra-oral device provides another chance for long-term and continuous macromolecules releasing, such as protein peptides, or even for the bigger bio-polymers [20]. It may also be responsible for some specific molecular releasing which is not easy absorbed in GI tract, sub-lingual tabs and skin patches including heme and nonheme irons.

Biosensor module

Compared to other wearable or portable devices, the intra-oral platform may provide the specific data from blood, which is traditionally obtained from the inevitably invasive procedures. Such information may be much powerful in further medical differential diagnosis and directly lead to the relative managements. For example, continuous blood sugar monitoring may affect the further insulin releasing dosage decision. Furthermore, the rapid value elevation of Creatine kinase (CK), Cardiac Troponin I is the important sign of acute myocardiac infraction (AMI), which needs further clinical management immediately [21].

In addition, the intra-oral device presents in semi-implanted property, which means the above module is replaceable without further invasive procedures while drug reloading, sensor replacement and battery exchange. The titanium implant fixture is immobile inside the jaw bone marrow and that may avoid from the risk of device loosening and internal bleeding. The surrounding bone structure within the blood pool may also prevent from further risks of thrombosis and related stroke syndrome. The drug-refilled procedure is recommended to complete by the dentists in the clinic or hospital to prevent from further infection risks. With current technology, the optimal volume for the drug delivery may sufficient for about 1-2 week of administrations, and about 1 month for continuous blood monitoring within every 5 minute's sampling. That means the patient should have the dental appointment every week to prevent from the daily invasive procedures. Furthermore, since long-term drug delivery and continuous blood monitoring is the main purpose of such newly device, we can expect that most users may belong to the elderly. For the above reason, geriatric concerns such as health care may take into considerations. Actually elderly health care is a critical issue in Geriatric developments. Multiple pathogenic origins with severe pharmacokinetic side effects may also worsen the situations. Fortunately modern dentistry has the mature experiences to deal with such geriatric problems since a large percentage of the dental patients belong to the elderly in Prosthodontics, Implantology, and Periodontics. The most important point is that the above non-dental applications should only preform under the healthy periodontal conditions without infection status.

From mechanical points of view, the intra-oral device also has the advantages to prevent from stolen, lost or forgotten due to its fixed property inside our oral cavity, and that may reduce the stress when using it. Compared to other wearable devices, it presents much

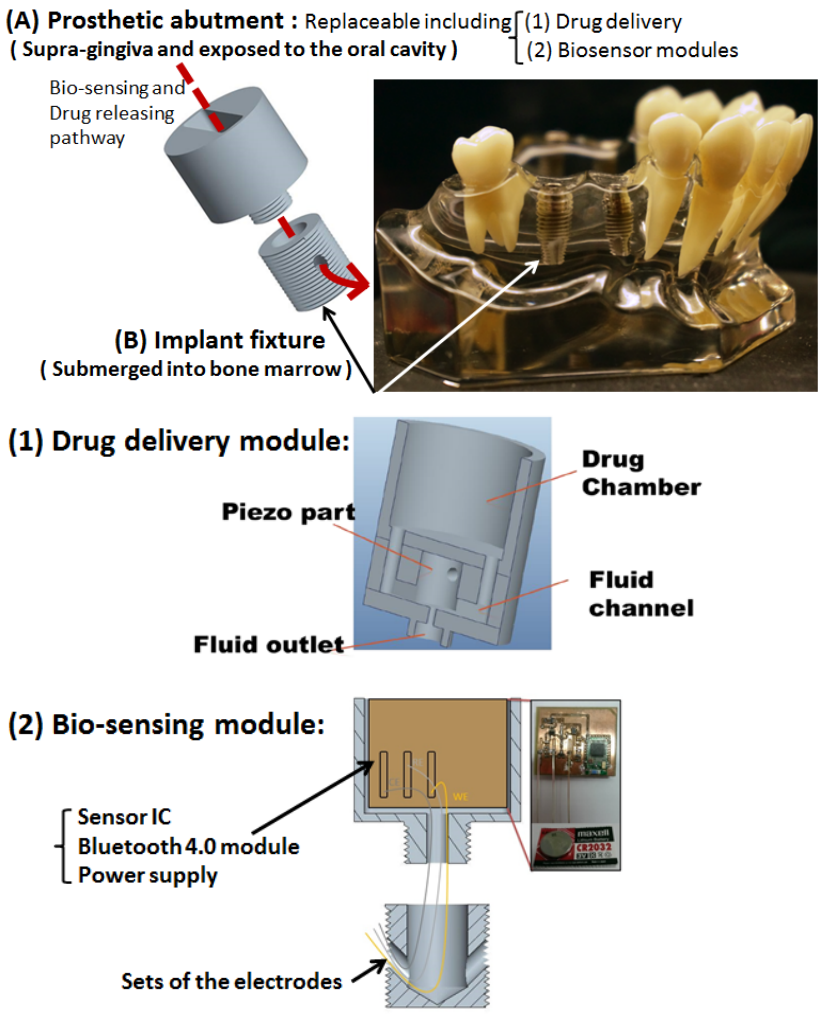

Figure 2: The basic design of dental implant supported drug delivery (1) and biosensor (2) platform. Both of these modules belong to the replaceable prosthetic abutment (A) and placed above the immobile titanium implant fixture (B) **[10].**

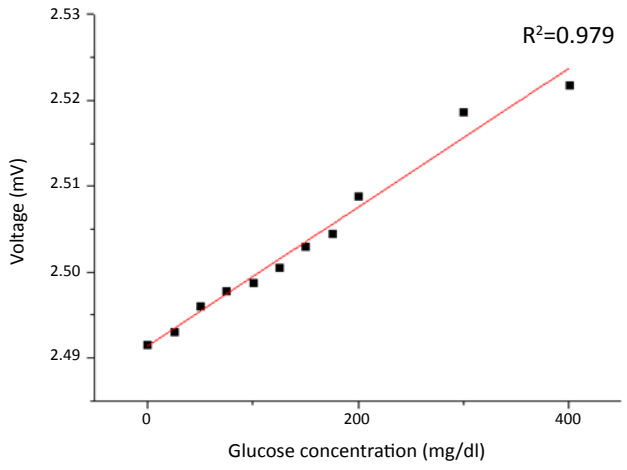

Figure 3: The relationships between the glucose concentration and the voltage changes shows highly correlated in the in-vitro implant supported biosensor study.

more powerful in medical applications for various blood monitoring and continuous molecular releasing. However, development of such intra-oral device is still undergoing and has not been mature yet currently. Fortunately, most challenges belong to electronic, chemical and mechanical problems, which may be achievable by modern technology and therefore allow more participation for these experts. These challenges are list as following:

Blood sugar presents in a relative higher concentration and reaches to the degree around 100 mg/dl basically, and thus the sensor design for blood sugar monitoring is much easier. However, most of the functional peptide concentration may be around 10-100 μg/dl, which shows much higher demand in the sensor accuracy. Therefore further improvements to enhance the signal-to-noise ratio (SNR) either by the software Algorithm, IC design or electrode modifications are emergently required. That will also allow more participation for computer, electronic and mechanical engineers.

Power supply should be carefully considered due to the safety concerns about the moist environment inside the oral cavity and the related pain-arousing tendency. In contrast, the sufficient electricity will reduce the clinical appointment frequency.

Privacy and safety concern are also important including wireless bio-information transferring and the relative drug releasing control procedures.

Module size reduction is important in both drug delivery and bio-sensing to minimize the risk of infection, which may be achieved by current complementary metal-oxide semiconductor (COMS) and microelectromechanical system (MEMS) processing techniques.

The intra-oral intelligent device for continuous molecular releasing and blood monitoring may bring more benefits and convenience with proper apps, wireless modules and portable device supports. The development of such device is just beginning and presents much possibility in both powerful applications and engineering participations. However, the medical and dental procedure establishment for safety concern is also important due to directly contact inside the human body throughout the circulation system.

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