Good Manufacturing Practices of AVANA® implant system

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Since basic and clinical predictability of osseointegrated endosseous implant were proved by several researchers including Brånemark in 1980s, it is established as an innovative and attractive treatment modality overcoming limitations of conventional prosthetic options due to continual efforts made by researchers and clinicians. 20 years has passed since implant was introduced in South Korea, active clinical practice of implant started about 10 years ago and this tendency is expected to increase rapidly. Since at the early days related basic science was immature and clinical experience was not accumulated sufficiently, imported implant brands that were supported by long-term research and development and recognized on global dental community were mainly used. Thus the cost of imported implant brands was burden to the patients who cannot afford. To release the cost burden, the need of development of simple and economic implant is pointed out. Since 1998, economic hardship of South Korea made emergence of domestic implant manufacturers trying not to imitate imported brand implant and develop original world-market competitive quality implant. With the grant from Ministry of industry & resource, Government of South Korea, ADIS Lab(Ajou Dental Implant System Laboratory, Ajou University) collaborated with Ossetem Inc. (South Korea) for qulaity improvement, research and development, and clinical study of implant materials for 3 years since 1999. Due to the collaboration, recognition of FDA, USA was achieved. A part of research activities are introduced in this article.

Experimental study on the effect of surface treatment upon osseointegration of dental implant in canine mandibles.

INTRODUCTION

Osseointegrated implant introduced by Brånemark was developed for complete edentulous patient first and accomplished successful outcomes. Since the number of complete edentulous patient decreases, modern implant dentistry shifts its focus to partial edentulous patients. Even though Brånemark implant also provide predictable outcome for partial edentulous patients, complete edentulism is different from partial edentulism biomechanically, microbiologically, and anatomically. In addition, with the increase of clinical application of implant, various patients status such as bone graft need for site of improper bone quality should be considered. Abreksson suggested that 6 factors such as implant material, design, surface characteristics, bone quality, and surgical procedure, loading condition are very important. Recently to meet with these clinical tendency, instead of machined conventional Brånemark implant, rough surface implant is developed to increase surface area, increase early stability for immediate loading or improvement of improper bone quality, and facilitate new bone formation due to easy attachment of undifferentiated cell. Surface treatment of implant include acid etching, titanium plasma spray(TPS), hydroxyapatite coating, various particle layer(e.g., oxide alumium or bioglass). Biocompatibility, early bone formation, and mechanical binding capability advantage hydroxyapatite. In the long-term, however, loss of hydroxyapatite coating, fracture, and resorption are problematic. Based on these past studies, the purpose of this study is to quantitatively assess the effect of surface treatment such as blasting and etching.

MATERIALS AND METHODS

Healthy 15kg 1 year old 6 adult dogs were used. 2.0mm in deiameter and 8.5mm in length experimental titanium implant was made. Blasting with hydroxyapatite and 45% nitric acid(HNO_3) after blasting with hydroxyapatite were performed on the experimental implant.

Surface roughness measurement

TopScan 3D UBM lightscope profiler was used. Parameters of 2D surface roughness including Ra(average roughness), Rq(squared average roughness), and average roughness from arbitrary chosen 3 locations of screw (1.3 µm) were measured using Gaussian filter.

For general anesthesia, 1ml/kg Ketalar(Yu-Han Yanghaeng, South Korea) was injected via vein. To increase reliability of experiement and simulate real alveolar bone situation by excluding variety of wound healing process after implant placement, mandible alveolar bone was chosen (Fig 1). 2 implant were placed on right and left side of a mandible and so 24 implants were placed collectively(Fig 2). To prevent infection, 50mg/Kg Cefamezin(Dong-A Pharmaceuticals, South Korea) was injected daily intramuscularly for 7 days. All 6 adult dogs were divided into two equal size groups. The 3 were sacrificed using paraformaldehyde diffusion on the 6 week, and the other 3 on the 12 week. Tissue block section was pefromed on the implant and adjacent bone tissue of the sacrificed adult dogs. 30µm section observed using BX51 microscopy (Olympus, Japan). Distance between bone and implant was expressed as percentage of ratio of entire length of screw to bone implant contact length of screw (Fig 3). Surface measurement was expressed as percentage of ratio of surface of screw and surface of bone (Fig 4). Analysis was conducted using KAPPA program (Acusoft).

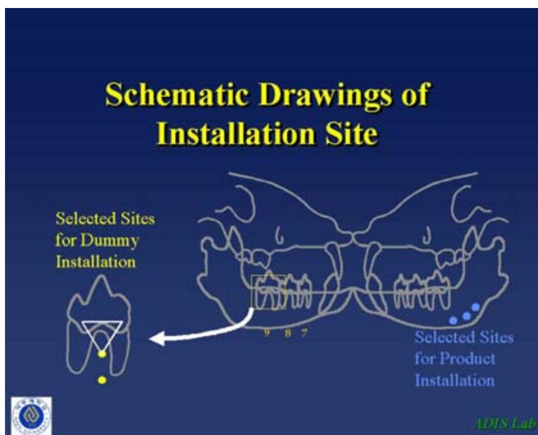

Fig 1. Schematic drawing of installation site

Fig 2. The 2 most eminent points of #9 canine was regarded as apex of triangle. 5mm distant two points were selected as implant site. Root of canine and inferior alveolar nerve was considered

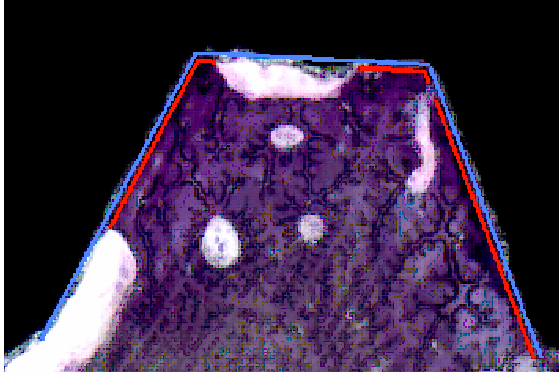

Fig 3. Bone-to-Implant Surface

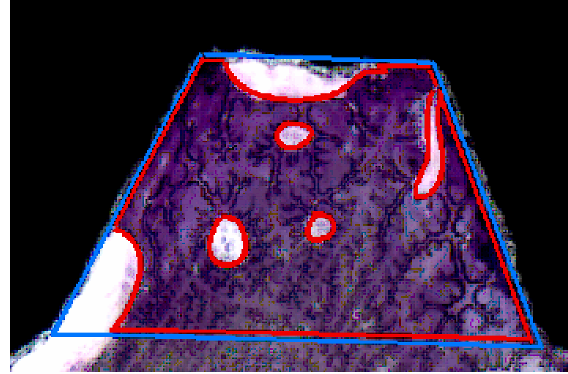

Fig4. Bone density

Result

From the 6 week sacrificed animal's block section, histomorphometric observation was made. Length measurement found 53.92% for machined implant, 64.39% for blasted implant, and 72.65% for 45% nitric acid etched and blasted implant (Fig 5). In average, hydroxyapatite blasted implant and nitric acid etched and blasted implant show the best osseointegration ($p<0.05$). In surface measurement, 75.33 for machined implant, 75.88% for blasted implant, and 81.74% for 45% nitric acid etched and blasted implant. Difference between machined implant and blasted implant was not statistical significant ($p>0.05$). Fig 6 represents that nitric acid etched and blasted implant show the best($p<0.05$).

From the 12 week sacrificed animal's block section, length measurement found 84.55% for machined implant, 73.10% for blasted implant, and 88.68% for 45% nitric acid etched and blasted implant ($p<0.05$). In surface measurement, 70.94 for machined implant, 78.31% for blasted implant, and 82.43% for 45% nitric acid etched and blasted implant. As shown on Fig 7, nitric acid etched and blasted implant show the best ($p<0.05$).

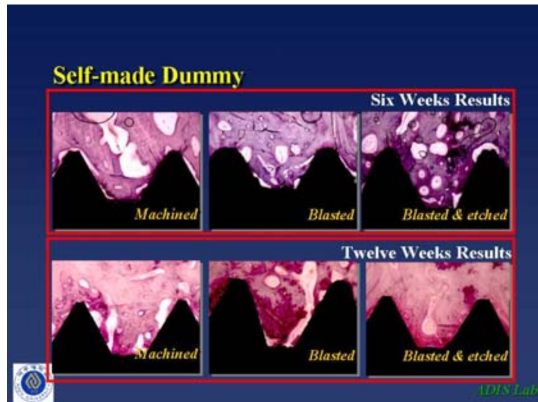

Fig 5. Microscopic images after 6 weeks

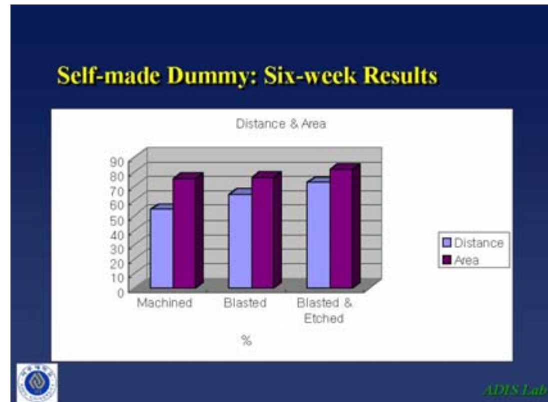

Fig 6. After 6 weeks

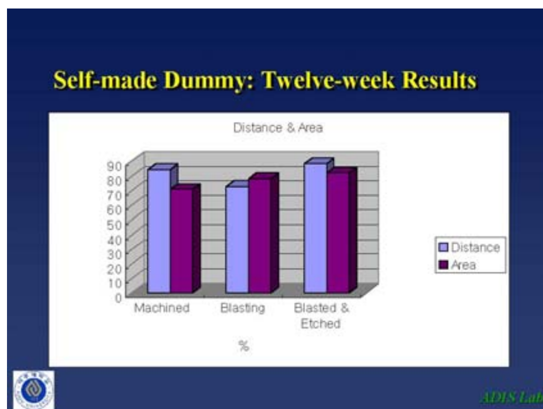

Fig 7. After 12 weeks

DISCUSSIONS

In early studies of Brånemark et al, (1) biocompatible material such as commercially pure titanium (2) not invasive surgical procedure(3) submerged process(4)wound healing of 3~6 months without loading were essential conditions for functionally and mechanically permanent integration between bone tissue and implant interface. However, reevaluation of these conditions is occurring. For example, one stage process introduced by International Team of Oral Implantology(ITI) showed satisfactory clinical outcomes after

more than 20 years of observation. A few studies found that immediate loading during healing period did not affect success. Schnitman et al reported that Brånemark implant placed on complete edentulous patients and immediate loading increased failure. Tarnow et al and Salama et al argued that several implant should be connected together to increase immediate loading implant. Corso et al reported that 39 out of 40 hydroxyapatite coated implant and titanium plasam sprayed implants for single unit succeeded. Surface characteristics of implant plays an important role in bone healing when subtle mobility exists. Increase of surface roughness advantages osseointegration by increasing interface between bone and implant when bone quality is improper. This facilitates migration of undifferentiated cells and new bone formation. Acid etching includes HNO_3, HF, HCL, H_2SO_4 and mixture of aforementioned acid. Heat provided on titanium makes Titanium plasma surface. Titanium Plasma Spray makes rough surface having 6 times surface area by hitting particles on the titanium plasma surface. Hydroxyapatite coating is frequently used in industry too. Hydroxyapatite ceramic has biocompatibility and shows increase of roughness similar to Titanium Plasma Spray. In addition, a few studies reporting increase of bone formation at the early healing stage exists. Hydroxyapatite coating increases implant stability when bone is improper. Thus, for Type IV (according to Lekholm and Zarb's classification) bone to achieve bone formation during early healing period and for immediate implant placement right after extraction of tooth to induce bone tissue regeneration, hydroxyapatite coated implant is recommended on purpose. However, hydroxyapatite particles have inferior dynamical characteristics (e.g., higher hardness and lower fracture endurance than bone), resorption in the body, and lower combining force between coated metal and coating hydroxyapatite. Recently, to reduce cost of surface treatment, use of inferior biocompatible material such as oxide alumium tend to increase. Impure materials are cleansed through several processes. This cleansing process removes surface roughness of implant additionally and the role of blasting to increase surface roughness does not work. Thus, excessive cleansing should be avoided. Animal studies regarding osseointegration by surface treatment has been conducted on femurs or extraction sockets. In contrast, this current study avoided extraction socket formation and excluded the influence of healing process. Machined implant, hydroxyapatite blasted implant, and 45% nitric acid etched and hydroxyapatite blasted implant were compared with respect to osseointegraion and bone density in the current study. 45% nitric acid

etched and blasted implant shows the 45% nitric acid etched and hydroxyapatite blasted implant has the best osseointegraion and bone density.

COCLUSION

Machined implant, hydroxyapatite blasted implant, and 45% nitric acid etched and hydroxyapatite blasted implant were compared with respect to osseointegraion and bone density in the current study. 45% nitric acid etched and blasted implant shows the 45% nitric acid etched and hydroxyapatite blasted implant has the best osseointegraion and bone density.

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