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Oral implants – the future

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ABSTRACT

The current and future application of implants to support intra- and extra-oral prostheses is a function not primarily of a current or eventual future, e.g., implant surface configuration, treatment procedure or loading protocol. In contrast, it must be understood by a more complex conceptualization of the practical application of the osseointegration phenomenon. This review will attempt to address the future use of oral implants based on current cutting edge research within the fundamentals that constitute the practical applications of the osseointegration concept.

Key words: Dental implantation, dental prosthesis, implant dentistry, prosthodontics.

Abbreviation: BMP = bone morphogenetic proteins.

INTRODUCTION

Writing about the future of oral implants is a challenging and risky task because ongoing research can rapidly change its direction. One belief is that our current metallic dental implants should be regarded only as a first generation of tissue engineering devices and that they will disappear in the very near future and be replaced by genomic and proteomic applications that will be able to offer improved biosynthetic solutions. Given the current enormous investments of capital on medical devices research globally this scenario may not be completely utopian. Other pathways are easier to predict because they reflect the current cutting-edge osseointegration and oral implants research activities presented in scientific meetings.[1]

What are the current ''hottest'' implant research topics?

One important research field is on understanding and improving the implant-bone interface by applying new knowledge from nano-technology research, by chemically modifying the titanium surface and/or by incorporating osseoinductive substances in the surface.

A second research field is on ceramic implants, which has been revived with the introduction of Zirconia, also known as zirconium-oxide. No adequate clinical data are available though.

The third research avenue is a corollary of the enormous advances made in developing innovative recombinant-DNA techniques which enables scientists to manufacture extra-cellular matrix proteins, e.g., bone morphogenetic proteins (BMP). Although their exact role in the healing process cascade is currently not fully understood, it is probable that these substances eventually will have an important therapeutic usefulness.

However, we must not forget that scientific research in itself is not a goal and that the ultimate objective of research on oral implants is to improve the technology to enable better and affordable care for all. In this perspective, what do we really know about this technology termed ''implant therapy''?

- Does the technology work? (i.e., a question of effectiveness);
- How does the technology work? (i.e., a question of process of intervention or delivery);
- Does it matter to patients? (i.e., a question of salience);
- Will it do more good than harm? (i.e., a question of safety);
- Will the patient accept the new intervention? (i.e., a question of acceptability);
- Is it worth paying for the intervention? (i.e., a question of cost effectiveness);
- Is this the right intervention for particular patients? (i.e., a question of appropriateness); and
- Are users, providers and other stakeholders satisfied with the interventions? (i.e., a question of satisfaction with the intervention).

These very essential questions have so far received less attention, issues that could be very appropriately addressed in dental practice-based research networks

rather than in academic institutions. Several initiatives worldwide to establish such practice networks lately may possibly target this important research field in the near future.

How many implant brands do we really need?

The growth of new implants and implant systems today is explosive. In a review paper from 2003 an investigator team identified 225 different implant brands from 78 producers.[2] In the period since this publication an additional 160 implant brands have entered the international market. According to anecdotal information, China has a rapidly growing implant industry that also supplies the more well known and established implant companies. During this same period, at least 90 implant brands have disappeared from the market. The question of who should identify and/or repair these implants when mechanical defects are bound to develop remains unanswered.

This explosion of products and components could have been predicted and we can expect that this will continue to proliferate under the current lax global regulatory situation. What we are seeing is history repeating itself. Retrace the situation of oral implant research and treatment practices to the era immediately before PI Brånemark and his team in Gothenburg, Sweden presented their revolutionary results in the mid 1970s. The implant field was mostly empirical, perhaps even bordering on the unscientific. One of the most comprehensive reviews of the status on oral implantology at the time authored by the American Dental Association (ADA)[3] presented some rather depressing facts of what a few dentists prescribed under the pretext of ''helping'' their edentulous patients. As late as 1978, the official stance of the ADA, at the Harvard conference about dental implants benefits and risk, was that ''The council still believes that dental endosseous implants formed from all types of material should be considered in the new-technique phase and in need of continuing scientific review to obtain additional longitudinal evaluations''.[4]

It was with full awareness of this formidable resistance towards dental implants that Brånemark and his research and development team in Gothenburg, Sweden, after many years of basic research, animal experiments and pilot clinical studies, first dared to present their comprehensive results to a global audience.[5] Several other episodes from the period illustrate how dedicated Brånemark was to find solutions to overcome the negative reputation and antipathy against the use of dental implants. The production of the new implants was licensed to the company Bofors in 1978 (subsequently changed to Bofors Nobelpharma in 1981, then to Nobelpharma and later to Nobel Biocare in 1999). In spite of being one of the most advanced high-tech companies in Sweden at the time, Brånemark insisted and secured the rights that he had to approve personally all the stages of the production process in a newly-built production facility. It was after investments of the order of USD$60 million and many crises between the developer and different industrial leaders that the two parts came to some form of agreement, and it was first in 1989 that Nobelpharma could report a financial surplus – 10 years after they obtained the production license.[6] Moreover, Brånemark mandated that all potential users of the new implants had to demonstrate satisfactory training at a Nobelpharma-approved institution, and thereby become licensed. Even the terminology was changed to avoid the negatively conceived word ''implant'', so the term ''fixture'' was used consistently in all promotional material at the time. Even today, many dentists and other implant companies still use this term without knowing its original etymology. It is not unknown to many that all these initiatives that were implemented to assure an extraordinary level of quality assurance of the production, handling and clinical application already from day one were challenged, ridiculed and deemed as ''anti-competitive''.

Unfortunately, the regulatory agencies worldwide did not use the golden moment of opportunity in the mid 1980s to raise the bar and set new standards for minimum requirements for approval of dental implants. The consequence is today the ''jungle'' of products and devices, often founded on nothing more than a drawing board and a few theoretical ideas.

Are the regulatory agencies doing their job?

Is it logical that ''somebody'' ought to regulate this ''jungle'' of implants? The common denominator being, they are meant to be placed in a human body, and remain there for a lifetime. What makes such regulations difficult is that we still don't know all aspects of the osseointegration phenomenon. One may be able to avoid some dubious implants, but may also run the risk of blocking or delaying innovative products. What needs to be emphasized for all potential purchasers of implants is that there are no independent institutions or organizations anywhere in the world that verifies that new implants fulfill any minimum qualitative or quantitative clinical criteria. In contrast, the health regulatory agencies in North America and Europe have chosen a rather pragmatic risk-benefit evaluation by having defined oral implants as so-called Class 2 medical devices. That an oral implant is not defined as a medical device where possible defects are life threatening (Class 3 device) is understandable. It is, however, strange that the same rules for clinical documentation and risk evaluation apply for maxillofacial implants (Class 2b) as for restorative materials

(Class 2a). While the latter can be removed or replaced easily, the biological consequences of a defective implant both on a short and long perspective are far more serious. It is not improbable that we will see a reclassification of oral implants in the near future once disastrous news hits the media, as was done for TMJ joint implants less than a decade ago.

This means in practice that producers who intend to introduce a medical device into commercial distribution in Europe or the USA only have to provide evidence that the product is appropriate for use as intended (as it is practised in Europe), or in the USA, that the product is equivalent to an already existing implant product registered before 1976 (according to the so-called 510K rule). In fact, the current regulations do not require any clinical studies at all: "In accordance with the least burdensome provisions of the FDA Modernization Act of 1997, the agency will rely on well-designed bench and/or animal testing rather than requiring clinical studies for new devices unless there is a specific justification for asking for clinical information to support a determination of substantial equivalence."[7] A critical question is of course how it can be that the bureaucrats in the FDA are more able to determine substantial equivalence than dental clinician researchers, who generally do not believe in extrapolating preclinical experiment data to clinical realities? Perhaps the realization that laboratory tests cannot replace clinical studies will come about in the future and hopefully limit the proliferation of new devices?

How reliable are experimental data for predicting clinical outcomes?

Preclinical evaluations of new implants with new modified surfaces and/or structures are difficult to extrapolate to clinical realities. Examples of experimental variables that affect histological and biomechanical results are: implant length; diameter, design and material; the surface topography; the animal model; the implantation time and site; biomechanical loading speed and functional loading conditions; the analysed length; and the orientation and thickness of the histological sections.[8] If one is to follow results from experimental animal models where the amount of bone is measured we should use only pure titanium and not titanium alloy implants. However, we observe that many implants made from titanium alloys work well clinically. Another example is the use of wide-bodied implants that should have worked well according to finite element computer simulations and even functioned well in animal models, while the clinical realities are different. Real confusion sets in when we can now read from a renowned researcher that implants made from a gold alloy also osseointegrate in the jaws of beagle dogs, albeit not equally well as when made from titanium.[9] If it hadn't been for the prohibitive price of precious metals would we perhaps already have had commercially available gold alloy implants?

Does the surface topography really make a difference?

The surface topography and chemical inertness of titanium implants can be modified in several ways, although there is no general consensus about nomenclature, or appropriate way of measuring differences in surface topographies.[10] It is therefore unclear how differences between surfaces should be defined and even interpreted in terms of clinical adaptability.[11] One variation is to describe the surfaces according to Table 1. What is hoped to be achieved with the many surface modifications is to induce osseoconduction; -genesis and -induction. Earlier terms such as "bioactive" (or "bioreactive") and "biopassive" are also used to describe the appropriateness as biocompatible materials. However, the situation is complex, because osseointegration between bone and implants must be regarded as a physical-biological phenomenon over several layers. The first layer is between the metal and its metal-oxide, the next between the oxide-layer and different extracellular biomolecules, and the third is the interaction between these biomolecules and preosteogenic and osteogenic cellular activities (adhesion, differentiation, proliferation and motility). The research activity within the field is extensive, and it appears that the time required between extrapolated results based on a laboratory experiment to a new commercial product or feature becomes shorter and shorter – even amongst the large manufacturers.

An example of how little we know about basic biological mechanisms of osseointegration can be illustrated by a series of book chapters and papers in the 1980s condemning the implant "Swede-Vent" (produced by Core-Vent, USA) because the surface was "contaminated" with 5–10% fluorine. Apparently, the implants were at that time cleaned with hydrofluoric acid. Twenty years later, one particular global implant company promotes an implant that has been exposed to almost identical surface treatment as being far superior to others – allegedly because of trace amounts of fluorine on its surface. Perhaps not surprisingly, the clinical data to support the claim remains to be published.

What are the relevant morphological differences between implants?

Implants are apparently dissimilar, but does it mean that they are unique and which differences are relevant? Is it of any relevance to state that two implants are different if they are made from the exact same metal, dimensions and surface treatment, but one has a right

Table 1. Surface topography of dental implants (sorted according to μm roughness)

Roughness	Machining process	Resulting surface topography	Example
> 2.0 μm "rough"	Hydroxyapatite coated surface	In general, a rather rough and isotropic surface	Sustain® (Lifecore Biomedical Inc, Chaska, USA)
> 2.0 μm "rough"	Titanium Plasma Sprayed (TPS) surface	A relatively rough isotropic surface	ITI® TPS (Institute Straumann AG, Waldenburg, Switzerland)
1.0–2.0 μm "moderately rough"	Blasted surface (the surface is blasted with hard particles)	An isotropic surface	TiO_2 particles (Tioblast®, Astra Tech AB, Mölndal, Sweden)
1.0–2.0 μm "moderately rough"	Blasted + acid etched surface (the surface is first blasted and then acid etched)	An isotropic surface	1. Large size Al_2O_3 particles & HCl & H_2SO_4 (SLA®, Institute Straumann AG, Waldenburg, Switzerland); 2. Tricalcium phosphate & HF & NO_3 (MTX®, Centerpulse Dental, Carlsbad, USA)
1.0–2.0 μm "moderately rough"	Oxidized surface (increased thickness of the oxidized layer)	Isotropic surface with the presence of craterous structures	TiUnite® (Nobel Biocare AB, Göteborg, Sweden)
0.5–1.0 μm "minimally rough"	Acid etched surface (the surface is usually etched in a two-step procedure)	Isotropic surface with high frequency irregularities	HCl/H_2SO_4 (Osseotite®, 3i Implant innovations, Palm Beach Gardens, USA)
0.5–1.0 μm "minimally rough"	Turned surface	Cutting marks produce an oriented, anisotropic surface	Brånemark System® MKIII (Nobel Biocare, Göteborg, Sweden)

pitch thread and the other a left pitch? Of course not – neither from a biological nor a clinical perspective. What makes a difference clinically should be the criterion for describing implant differences. Unfortunately, this knowledge basis is still largely unknown. We are therefore still uncertain how we can describe "differences" apart from perhaps the actual metal used. One may find good support in the literature to suggest that an object made in titanium following careful osteotomy will osseointegrate as long as its surface is not contaminated. Perhaps it is therefore only academic to discuss the purity of the titanium or its surface morphology. Regrettably, there is little information in the literature to state that eventual differences have any clinical relevance.[2] The problem is even compounded by the lack of consensus of the terminology to describe detailed aspects of oral implants. For example, where does an implant collar begin and end, and is this different from the implant neck which is then perhaps identical with the implant flange? We will in the future need to establish a universal nomenclature or perhaps implement the nomenclature introduced in 2007.[12]

Perhaps creating an implant register is a good idea?

The idea of introducing registers of oral implants to hopefully identify the good and the bad products is reasonable. Many attempts have been made, the first one as early as in 1974 by the American Academy of Implant Dentistry in the USA and the most recent one by the FDI World Dental Federation. Efforts have also been made in several countries to develop national registers, but the only country in the world that has maintained some form of quality control over several years is Finland. The intentions have been the best, but a combination of indifference by the profession and industry, inadequate financing and deficient monitoring and updating have made the registers obsolete or completely phased out. There is, however, rising interest to embark on developing a register of oral implants in at least one professional organization, i.e., the Academy of Osseointegration.

Have the principles recommended by Brånemark in the mid 1970s since seriously been challenged?

Dentistry's contribution to the Brånemark team's development of titanium implants was near non-existent and very little of what had been written about dental implants in the dental literature at the time was validated by the Brånemark group. The developmental research, as it has been described later in literature about PI Brånemark, was built methodologically, piece by piece on their own experiments.[6] The revolutionary was principally the new material, at the time the "purest kind of titanium available", which was machined using a turning process that made oriented cutting marks creating an oriented, anisotropic surface. Many different screw designs were attempted, but when the first commercial product was placed on the market only three designs were used. One may find on page 28 in Brånemark and co-workers' original publication from 1977[5] different screw designs with both internal and external connections, different flange morphologies, different thread forms and pitch, surface structures and variations of relative dimensions.

Also, the procedures for installing the implants were solely limited to their own experiments. In contrast, with contemporary practices of placing the implant immediately after post-extraction, one of the principles was to wait three to four months for healing. Another

principle was to always use a two-step surgical operation to allow a more predictable osseointegration, again in contrast with others who at the time advocated that immediate loading could work well. Based on a biomechanical rationale, it was advised to place six implants, symmetrically to the midline to avoid "overloading", and a screw retained fixed prosthesis. Moreover, relatively tall transgingival components were used to minimize potential plaque-induced peri-implant mucositis or perhaps even bone loss. It should in this context be acknowledged that there is no evidence in the literature to date to suggest that the clinical success of these early Brånemark standard implants decline 35–40 years after having been placed intra-orally.

Today, many consider some of these principles as too rigorous and over-precautious and perhaps even unnecessary. However, the current evidence-basis for replacing these principles is weak and at best show equivalence or minor superiority.[13-15] Moreover, the principles recommended by the Brånemark team were established on a new and higher standard of the quality of the research than what was the case at the time. In fact, this level of research quality is what we would expect should be conducted to support the introduction of new implants or surgical interventions, which unfortunately is not the situation today.

CONCLUSIONS

Judging from past history and the current situation it seems that dental implants are regarded more as a commodity rather than medical devices meant to last for a lifetime. Whether we will change this view when the market is saturated with 400, 1000 or 6000 different implant brands remains to be seen. However, it should be food for thought that since there seems apparently to be a thriving commercial opportunity for more and more implant companies, there must be enough customers to create this mushrooming industry. Are the companies speculating perhaps that there may be other motives than the purely scientific that determines which implant system dentists choose to begin using in their practices? It is up to the profession, then, to demonstrate that this is not the situation.

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