Biomimetic Dental Implants — New Ways to Enhance Osseointegration

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© J Can Dent Assoc 2002; 68(5):286-8

Endosseous dental implants are currently the most innovative and exciting treatment modality in dentistry. They are being widely used for a variety of indications, and most of the various techniques in use are evidence-based and predictable. However, in many cases, the intended implant site is compromised because of poor bone quality (i.e., low bone density, in the case of highly cancellous bone, or low vascularity, in the case of primarily cortical bone) or insufficient quantity of bone (in terms of the width or height of the alveolar ridge). Lack of sufficient alveolar ridge height is often related to the proximity of the implant site to other anatomical structures (i.e., the maxillary sinus or the mandibular canal). In these situations separate preparatory procedures may be required to augment the available volume of bone before placement of the implant, which may result in extra morbidity, longer treatment time, greater risk of complications and higher costs. Surgical procedures that have been developed to deal with the problems of insufficient alveolar ridge width or height include ridge augmentation with block grafts or particulate graft materials and protective barriers (a procedure known as guided bone regeneration), splitting of the alveolar ridge, direct or indirect sinus grafting or elevation, repositioning of the alveolar nerve bundle and distraction osteogenesis. Alternatively, orthodontic procedures have been used to extrude and eventually extract "hopeless" teeth or to move salvageable teeth into adjacent edentulous sites. Ultimately, this approach leads to regeneration of lost bone and enables implant placement in the vacated site.

With most surgical approaches, the bone graft of choice has been autogenous (e.g., grafts taken from the chin, the ramus of the mandible, the maxillary tuberosity or the iliac crest of the same patient). However, as effective as these procedures may be, the risks of complications are greater than for single site procedures, and greater morbidity is associated with the existence of a second operative site.[1] Among the complications occurring at the donor site are infection, pain, sensory loss and hematoma formation. In addition, a donor site with sufficient quantity of bone is not always available. Allografts (i.e., bone taken from a different person and processed and managed by a tissue bank or commercial supplier) have often been substituted, but this method also has limitations, including inconsistent osteoinductive activity, unfavourable host immune responses,[2] delayed resorption, and risk of prion and virus transmission.[3,4]

An ideal bone graft for use in implant dentistry should have the following properties: it should be biomimetic, having the ability to induce differentiation of the appropriate cells (i.e., endothelial and osteoblastic cells) for the formation of new bone; it should be easily synthesized or produced, rather than having to be extracted from allograft materials (to eliminate all risks of disease transmission); it should be easily and quickly resorbed as the osteogenic response occurs; it should have no immune-provoking properties; it should be easily transported and stored; and it should be reasonably cost-effective. The consensus at present is that the future of such materials lies in the so-called recombinant bone morphogenetic proteins (BMPs), which are produced by genetic engineering. These proteins have been shown to induce bone formation at compromised sites in a variety of experimental and clinical situations, and are currently being reviewed for safety by the U.S. Food and Drug Administration.

Urist[5] was the first to report (in the mid-1960s) on the group of proteins that, because of their demonstrated osteoinductive potential, came to be known as the BMPs. These proteins act on undifferentiated, primarily mesenchymal cells, inducing them to differentiate into osteoblasts and, in some situations, chondroblasts. *De novo* bone formation can be achieved anywhere that these proteins are implanted, including extra-osseous sites such as muscle or subcutaneous tissue. This property of BMPs has

been shown experimentally to be highly effective in the management of compromised sites intended for future implants. Using osteoinductive substances either as actual graft materials or as biomimetic coatings on the surface of dental implants holds great promise for controlling and optimizing the cascade of biological events that result in the bone formation appropriate for securing a dental implant.

Biomimetic dental implants may be the next development in the field. A variety of biomimetic coatings may prove helpful for application in individual patients. For example, coating implants with factors known to induce endothelial cell differentiation and proliferation may promote greater vascularity in highly cortical bone, thereby improving conditions for early and long-term (in response to functional loading) bone remodelling. Coating implants with pharmacological agents such as bisphosphonates[6] may be a way of locally improving bone density in highly cancellous bone. Coating implants with BMPs may also accelerate initial healing times during integration of the dental implant, thereby reducing overall treatment times and improving implant success rates. Experimental investigations with a BMP known as recombinant human BMP-2 (rhBMP-2) in animal models have shown that it promotes initial integration of dental implants[7,8] and "rescues" implants affected by experimentally induced peri-implant bone loss.[9,10]

The work to date has raised the question of which implant surface(s) should be coated with biomimetic factors to obtain optimal results. One criterion for successful osseointegration is direct contact between the bone and the implant surface. Subsequent bone formation will be influenced by both the chemical composition and the surface geometry or "topography" of the implant. It may be that degradation of an implant surface coating will help to promote *de novo* bone formation, as a result of either enhanced osteoconductivity due to the resulting changes in surface topography or enhanced osteogenesis due to local release of calcium or other elements that may promote bone formation.

A variety of implant surface textures are currently available for clinical use. Some of these have the ability to enhance and direct the growth of bone and achieve osseointegration when implanted in osseous sites.[11]

Modifying the surface characteristics of the implant can promote migration of mesenchymal cells to the implant surface, enhance attachment and proliferation of these cells, and, in some instances, stimulate osteoblastic differentiation.[12] Some reports have suggested that in designing a biomimetic implant one should choose a surface texture of high roughness (presumably with some optimum value) and ensure a high surface area, to optimize the ability of the implant to act as a "carrier" for the planned biomimetic coating(s). Such a design might also enhance osteoconductivity (the directed migration of osteoblast precursor cells) and osteogenesis, and thereby improve long-term fixation of the implant through more effective mechanical interlock at the bone-to-implant interface after osseointegration.

Transforming an implant with this preferred geometry into a biomimetic implant requires adding a coating of the growth factor (e.g., one of the BMPs) or pharmacological agent of choice. This layer should preferably be thin enough not to alter the underlying surface topography. The addition of such coatings may require precoating of the implant with an appropriate delivery vehicle for attachment and release of the active agent. Biodegradable ultra-thin layers of calcium phosphate have also been proposed as potential carriers.[13]

At present, no biomimetic implant system is available commercially, primarily because of the need to ensure the absence of undesired host–tissue reactions. Research and development in this field will require attention to 3 main aspects: selecting the appropriate surface texture, developing efficient carrier vehicles or surface precoating agents for initial retention of the biomimetic substances and their subsequent controlled release, and identifying the appropriate biomimetic agents for achieving the desired outcome in a particular clinical scenario (e.g., better vascularization, better osteoinduction, accelerated healing time or enhanced bone density). Combining the concepts of biomimetics and dental implants may change the world of implant dentistry as we know it today. Patients with challenging situations, such as poor bone quality and quantity, will benefit from an improved, predictable treatment modality, shorter initial healing times and better long-term performance of the dental implant. Understanding implant geometry, chemistry and bioactivity and the interactions between these factors is the key to future improvements in implant design and to ensuring progress in this exciting and rewarding field of dentistry. ◆

Acknowledgments: The authors wish to thank Dr. Douglas Deporter and Dr. Robert Pilliar for their helpful comments on this manuscript.

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The views expressed are those of the authors and do not necessarily reflect the opinion or official policies of the Canadian Dental Association.

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