

A powerful solution for better bone

AddBIO has developed the Zolidd® technology – a proprietary bioactive nanolayer with a bone strengthening drug

AS the population in the developed world ages and the baby boom generation enters old age, oral health issues such as periodontal disease and adult tooth loss are an increasing problem. Today, dental caries is one of the most common chronic diseases in the world, often leading to the need for tooth extraction if left untreated or treated improperly. Globally, as many as 90% of school children and up to 100% of adults suffer from some extent of primary or secondary caries. In addition, severe periodontal (gum) disease, which may result in tooth loss, is found in 15-20% of middle-aged (35-44 years) adults. Moreover, as indicated by the World Health Organization, globally about 30% of people aged 65-74 have no natural teeth.¹ In Europe edentulism (total or partial toothlessness) is less common than in the rest of the world, but tooth loss is still an important health issue.

Increasing use of dental implant forces innovations

Today dental implants have largely replaced dentures ("false teeth") as the go-to solution when treating edentulism. With a wealthier population, new dental technologies, methods and materials are introduced every year. The increasing use of dental implants is partially the result of a growing pool of potential patients. In the not too distant past dental implants were limited to a select group of patients. Today, implants are commonly used on a wider group of high-risk patients with compromised bone quality, such as smokers, patients with bruxism (teeth grinding and jaw clenching), diabetes, etc.

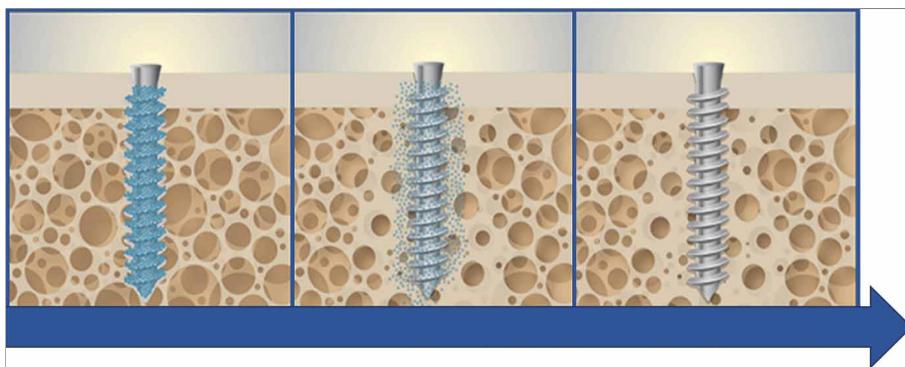


Fig. 1 The release of the drug from the implant to the surrounding in the bone

Implant manufacturers are constantly trying to outdo each other in their efforts to increase the success rate of the procedure in patients with unfavourable health conditions. Therefore, manufacturers develop various shapes and surfaces of implants to improve their functions. Current advancements in dental implant design has concentrated on the implant design; the length, width, amount of thread used and different implant surfaces in order to improve stability.

Unfortunately, the problem of poor implant fixation in high-risk patients remains. In addition, some of the trends in implant development have been shown to be counterproductive. For instance, the development of rougher surfaces has been shown to improve initial fixation. However, they have also been shown to harvest bacteria, causing infections (periimplantitis) and loss of bone around the implant long term. Another drawback of lowering the inclusion criteria for implantation is an increase in the required recovery time.

The more compromised the bone quality, the longer it takes to heal the bone and restore full load on the implanted tooth. At the same time, manufacturers seek methods that allow immediate implant loading and limit the post-surgical inconvenience to a minimum. As a result, cases of implant loosening or implant failure are quite frequent, causing pain, need for re-operation and generating additional costs for patients, dentists and healthcare systems.

In its efforts to provide a solution that addresses these problems, AddBIO has used an approach unlike any other dental implant manufacturer today. Rather than just another variation of an implant's geometry, surface type and material (which only improves implant stability), the company has created a unique method of adding a drug coating to virtually any given type of dental implant. As a result, AddBIO's technology is the world's first solution that improves bone stability.

Our solution: Zolidd®

The Zolidd technology uses a multilayer protein film of fibrinogen as a bonding agent between

the implant surface and drug particles. In its natural form, fibrinogen is a glycoprotein in vertebrates that helps the formation of blood clots. Blood proteins have long been regarded as key factors determining the *in vivo* acceptance of implants.

The Zolidd technology uses a biochemical treatment to create a multilayer layer of fibrinogen that is covalently bound to the metal surface of an implant and is able to absorb particles of other compounds. The drug used in AddBIO's coating is zoledronate (zoledronic acid) – a bisphosphonate commonly used to prevent osteoporotic loss of bone mass. The addition of bisphosphonate to the fibrinogen matrix creates a strong synergistic effect on bone regeneration, increasing the bone volume significantly.

By combining a fibrinogen multilayer with bisphosphonate and designing a manufacturing process of coating implants with this compound, AddBIO paves the way for a new standard in dental implantology. To date, dental implant manufacturers have avoided joining implants with pharmaceuticals, due to increased safety requirements imposed on drug/device medical products (e.g. need for clinical validation studies). AddBIO is, however, better placed to explore this sector of industry, as it offers scientific background and expertise in doing clinical validation studies – skills lacking in other dental implant manufacturers.

The Zolidd prototype has been evaluated in a five-year radiographic follow-up trial.² The study concluded that low doses of bisphosphonate, locally delivered from a fibrinogen matrix indeed improves early implant fixation with persistent effect after years of loading and that the coating has not imposed any complications. Hence, in contrast with other state-of-the-art implants, Zolidd coated implants allows for earlier implant loading, whilst decreasing the risk of post-surgical complications. Furthermore, Zolidd coated implants allow for smoother surface implants, that significantly reduce the rate of periimplantitis, enabling long-term implant retention both in the general public and amongst individuals with compromised bone quality (cancer patients, diabetics and smokers). The Zolidd-coated implants do not impact present surgical procedures.



Commercial and regulatory strategy

AddBIO is currently following a medical device pathway for CE marking and FDA approval. The Zolidd One ExHex is AddBIO's first product and a result of many years of research within the company. Zolidd One ExHex is currently evaluated in a clinical study required for CE marking of Class III Medical Devices.

The recruitment of patients for the clinical study has been completed and the outcome will be evaluated during 2018. AddBIO plan to commercialise a full dental platform with Zolidd-coated implants in 2019. The implants will be fully compatible with commonly used dental crowns, prosthodontics and dental technology.

Implants with the Zolidd technology is therefore expected to become a game changer for dentistry, disrupting the market for dental implants. The Zolidd coating has a proven local bone strengthening effect and enhances implant stability. Better implant stability will enable better implant function and reduce the risk of complications.

References

- 1 World Health Organization: Oral health, Information sheet, April 2012 http://www.who.int/oral_health/publications/factsheet/en/
- 2 Randomised trial of bisphosphonate-coated implant: Radiographic follow-up after 5 years of loading. Abtahi J *et al. Int J Oral Maxillofac Surg.* Dec 2016 ;45, (12), 1564–1569
- 3 A bisphosphonate-coating improves the fixation of metal implants in human bone. A randomized trial of dental implants. Abtahi J *et al. Bone.* 2012 May;50(5):1148-51

AddBIO was founded in 2008 with the aim to solve the central problem of the implant industry – weak bone. Professor Per Aspenberg, Linköping University, Sweden, had been working with bone healing for many years. Professor Pentti Tengvall, Gothenburg University, Sweden, was interested in biomaterials with special interest on surface modifications.

A collaboration between the two scientists led to the development of a technology to coat a titanium surface with a drug using a protein matrix. In 2012, Aspenberg and Tengvall published the first human clinical trial showing improved implant fixation using a coating with bone-strengthening drugs (bisphosphonates).³ Based on the technology developed by Aspenberg and Tengvall, AddBIO has established a platform technology designed for local availability of drugs from medical implants – Zolidd®.

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