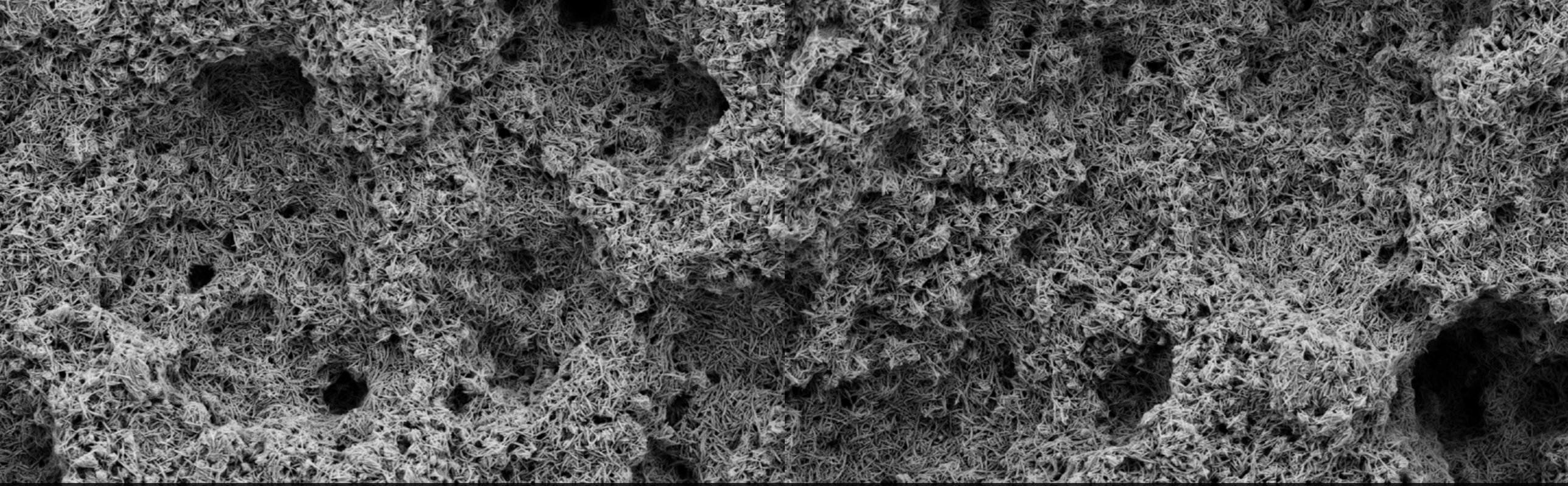
MAKING IMPLANTS INTEGRATE

HA*nano* Surface



The HA*nano* Surface is a 20 nanometer thin implant surface made of crystalline hydroxyapatite (HA) which through size, shape, and structure mimics living bone tissue. It has been proven to significantly accelerate and enhance osseointegration of implants, and can be used on all commercial implants regardless of material and geometry.

An Osteoconductive Coating for All Implants

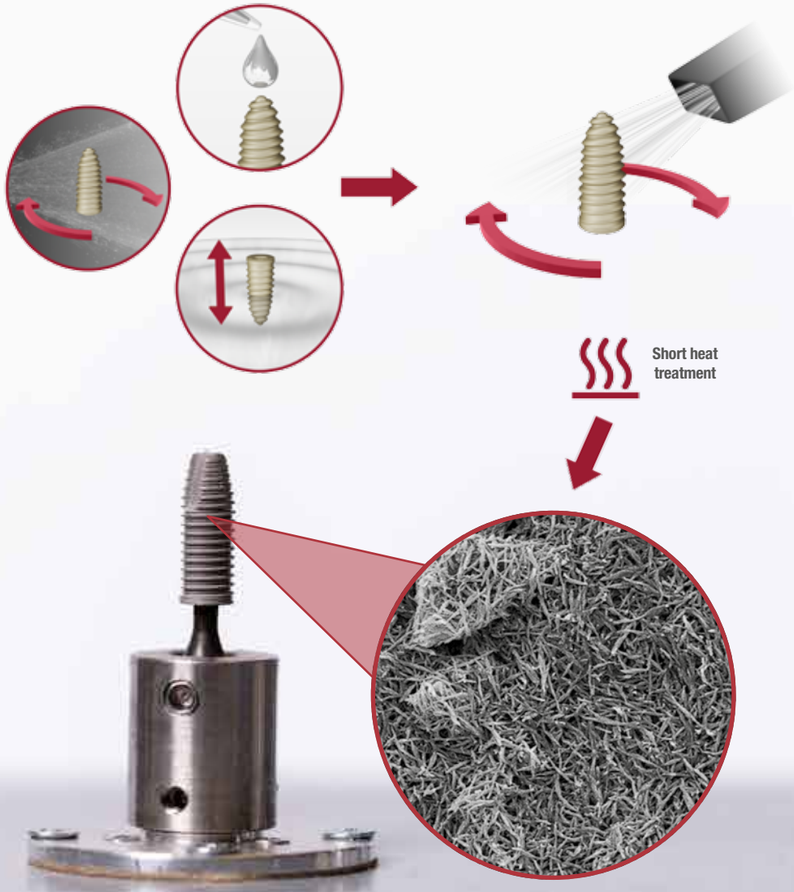
Unique Process for Nano-Thin Coating

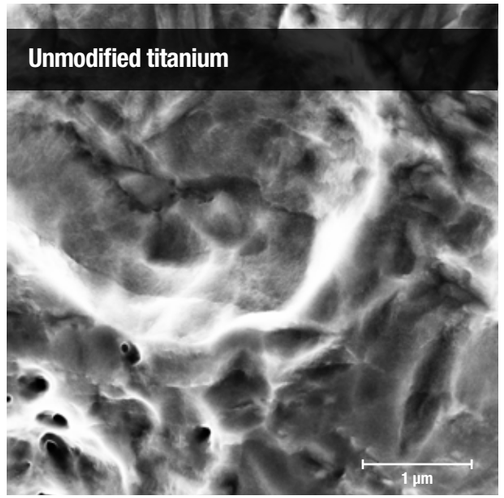
The HA*nano* Surface has excellent compatibility with all implant materials, including ceramics, metals, pyrocarbon, and PEEK. The unique coating process also allows the HA*nano* Surface to be applied to any implant geometry, including complex and porous implants without compromising the porosity of the surface.

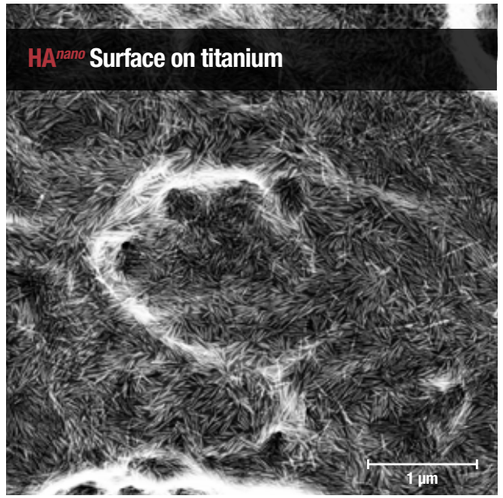
The HA*nano* Surface coating process is based on off-the-shelf equipment and does not require line-of-sight. It is easy to adapt to any commercial implant, and renders a homogenous coverage of nanometer-sized HA throughout the implant surface.

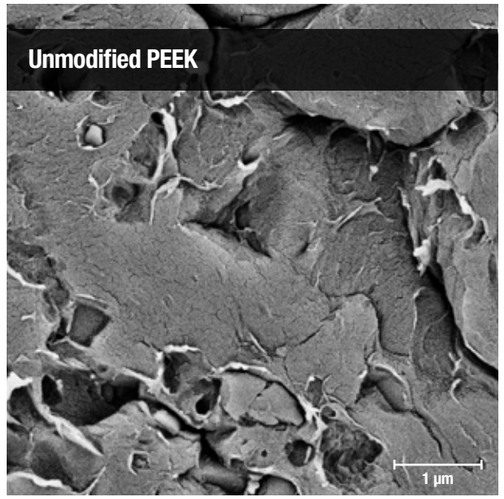
The unique coating process is based on wet chemistry. The HA crystals are formed in a coating liquid and applied to the implant by drop-wise addition, spraying or dipping the implant. Excess coating solution is removed, for example by spinning and using pressurized gas. The final step of the process is a short heat treatment, which does not affect the mechanical properties of the bulk material of the implant. The result is an extremely thin coating of synthetic bone that will enhance the bone growth and create stronger anchoring of the implant.

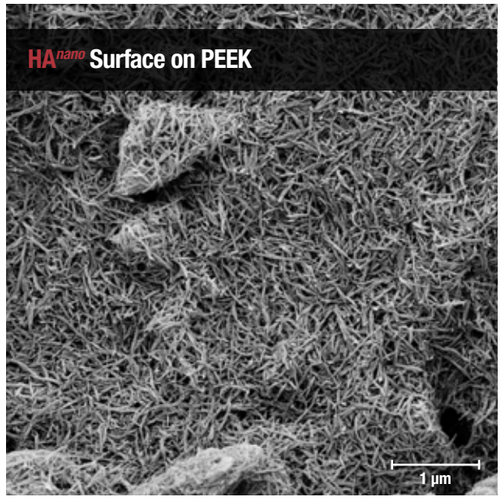
The HA*nano* Surface has been cleared by the FDA for a generic dental implant (510(k) no. K101225) and has a Device Master File submitted for PEEK.









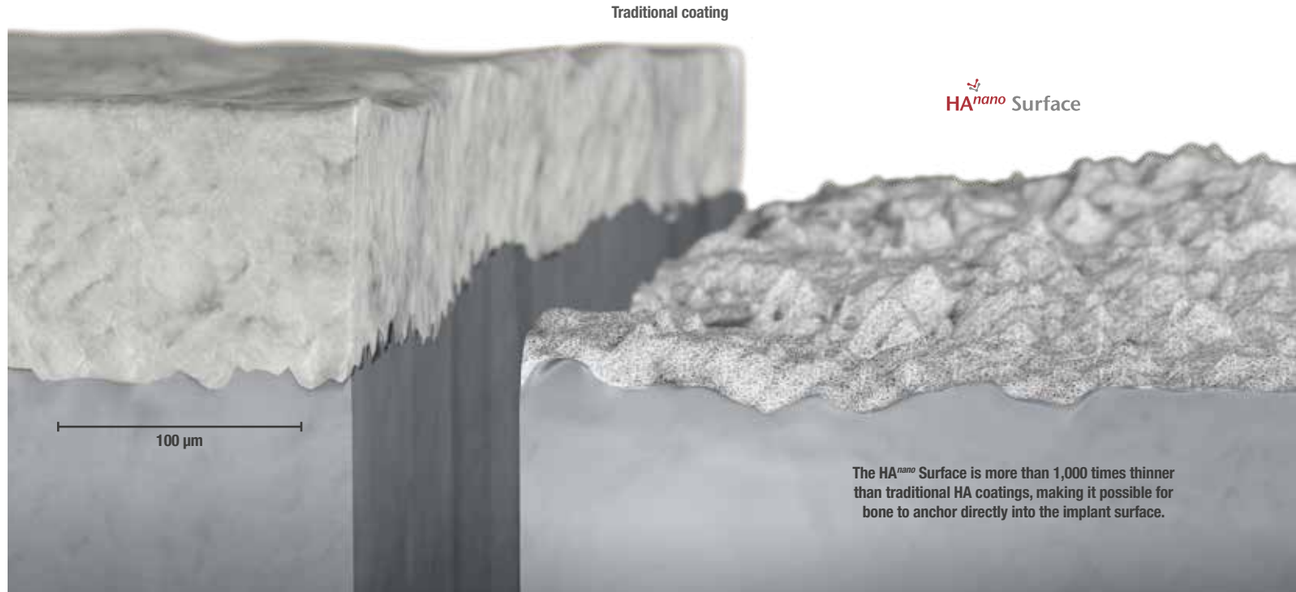


New Size Regime for Better Integration

Integration in the Nanometer Range

The HA*nano* Surface introduces a completely new size regime for implant coatings. Its thinness enables newly formed bone to grow directly into the micrometer topography (i.e. roughness) of the implant surface, thereby providing a mechanical stability independent of the coating itself.

The HA*nano* Surface will never act as an interface separating bone from the implant, which is the opposite of traditional coatings where bone will anchor into the coating itself. The thinness of the HA*nano* Surface also means that there is no risk for cracking or flaking of the coating, and the flexibility of the implant material is retained. In addition, since the dimensions of the implant are unchanged, there is no need for new implant designs or instruments during surgery.



The HA*nano* Surface is more than 1,000 times thinner than traditional HA coatings, making it possible for bone to anchor directly into the implant surface.

Rapid Pathway to Product Launch

From Concept to Market in 12 Months

Promimic assists you through the process from idea to market.

1 Concept Evaluation
Promimic helps you evaluate the HA^{nano} Surface on your products:

- Technology adaption: coating of customer samples and validation of results by Promimic and/or customer
- Advisory services in regulatory processes and production set-up, process and indicative cost

2 Development Phase
Promimic assists your preparations for market launch:

- Continued/extended coating services
- Optimization of coating process and design of equipment
- Regulatory filings, and *in vitro* and *in vivo* studies (optional)

3 Production Preparation
Promimic supports your coating process:

- Small series production performed by Promimic
- Establishment of coating process on-site or with CMO, ramp-up of production volumes

4 Commercial Phase
Promimic supports you throughout the product life cycle:

- Coating process at customer or CMO production plant
- Promimic provides coating liquid for production
- QC, training and technical support

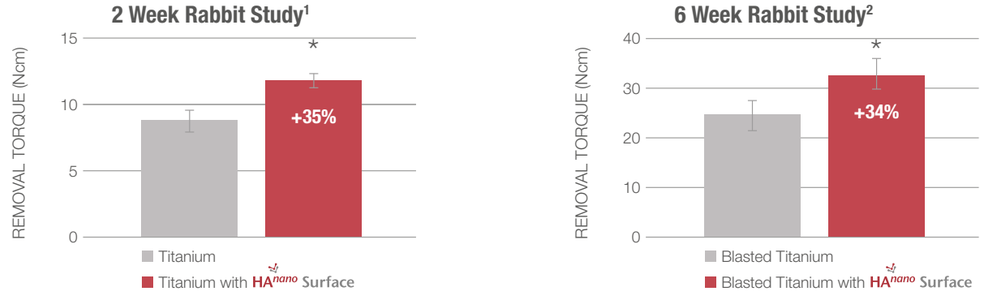
Enhanced and Accelerated Bone Growth

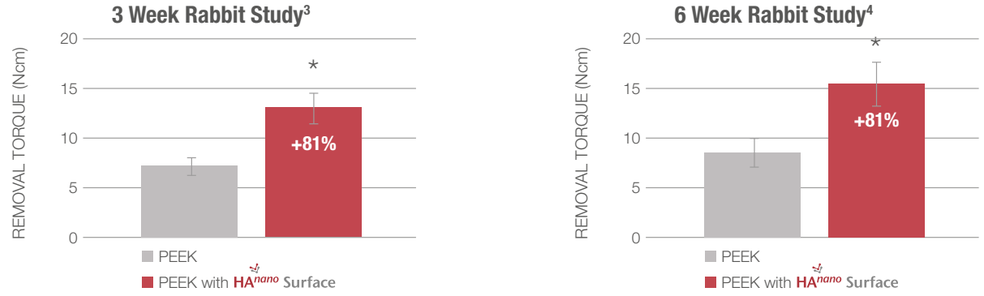
Catalyzing the Biological Response

Coating of implants with the HA*nano* Surface catalyzes the biological response. The coating has proven to accelerate the initial bone growth and to increase the anchoring strength of implants in more than 20 pre-clinical *in vivo* studies. The nano-thin coating has shown to increase the anchoring of titanium implants by up to 35% and by over 80% for PEEK implants during the first critical time of healing.

Applying the HA*nano* Surface to your implant significantly improves the hydrophilicity of the implant material. This facilitates the absorption of body fluids into small pores and cavities of the implant surface. As a result, the nanometer-sized hydroxyapatite particles enable increased attachment of bone cells to the implant and accelerate bone growth.

The HA*nano* Surface changes the material's wettability from hydrophobic (left) to hydrophilic (right), enabling a more close interaction with bone tissue.





Error bars represent standard error, p<0.05

1 Jimbo et al. (2011), 'Genetic Responses to Nanostructured Calcium-phosphate-coated Implants', J Dent Res, Dec;90(12):1422-7.

2 Jimbo et al. (2012), 'The biological response to three different nanostructures applied on smooth implant surfaces', Clin Oral Implants Res, Jun;23(6):706-12.

3 Johansson et al. (2014), 'Biomechanical evaluation and surface characterization of a nano-modified surface on PEEK implants: a study in the rabbit tibia', Int J Nanomedicine, Aug;9:3903-11.

4 Barkarmo et al (2014), 'Enhanced bone healing around nanohydroxyapatite-coated polyetheretherketone implants: An experimental study in rabbit bone', J Biomater Appl, Nov;29(5):737-47.

Making Implants Integrate

Promimic is an innovative biomaterial partner developing and marketing nano-thin coatings for all implant materials. Promimic is specialized in nanotechnology and production of HA. Promimic fulfills the requirements of SS-EN ISO 13485:2003 with respect to development, production and sales of synthetic bone material for surface applications.

Nano-Thin Coating for All Implants

- Coating thickness of only 20 nm
- Optimal adhesion on PEEK, metals, pyrocarbon and ceramics
- Accelerates osseointegration
- Increases anchoring strength
- Produces a super-hydrophilic implant surface

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