One Nano Step For Man, One Giant Leap For Implant Dentistry...
The Bone Bonding® NanoTite™ Implant
Nano In Size, Profound In Effect

*The interlocking of the newly formed cement line matrix of bone with the implant surface.
The Revolutionary NanoTite™ Implant – A Bone Bonding® Surface

- Microtopography Of The OSSEOTITE® Implant Combined With A Nanometer-scale Discrete Crystalline Deposition (DCD™) Of Calcium Phosphate (CaP) Creates A More Complex Surface Topography. This Renders The NanoTite Implant A Bone Bonding Surface By The Interlocking Of The Newly Formed Cement Line Matrix Of Bone With The Implant Surface1, 16

- Preclinical Studies Demonstrate A Substantial Improvement On The Rate And Extent Of Osseointegration For The NanoTite Implant Versus The OSSEOTITE Implant Leading To Implant Stability12

- NanoTite Implants May Be Used For Immediate Function On Single Tooth And/Or Multiple Tooth Applications When Good Primary Stability Is Achieved, With Appropriate Occlusal Loading, In Order To Restore Chewing Function

Interface Of Cement Line Matrix And DCD Treated Implant Surface

Photo Courtesy Of: John E. Davies, BDS, PHd, DSc, FSBE
Why NanoTite™?

BIOMET 3i’s OSSEOTITE® Surface has more than a decade of clinical use and evidence based research to support its efficacy, so why is another surface needed? As treatment protocols get more advanced and dental implants are placed in more challenging clinical scenarios, there could be a benefit to a surface that provides a greater rate and extent of osseointegration on a more predictable basis. Potential scenarios where such an implant might be beneficial to patient and practice might include the following:

- Immediate And Accelerated Loading Protocols
- Immediate Replacement in Extraction Sockets
- Simultaneous Grafted Sites And Implant Placement
- Aesthetic Areas Where Bone Preservation Is Critical
- Implant Placement in Poor-Quality Bone
- Locations Requiring Short Or Wide Implants

Implants typically demonstrate good primary stability at the time of placement – in principle, a mechanical phenomenon. As bone remodels in subsequent weeks, there can be a reduction in implant stability that might impact early or immediate loading protocols.*

Now with the next generation surface technology, the NanoTite Implant incorporates the complex architecture at the nano-scale, which renders it a Bone Bonding® Surface. Preclinical studies have shown that the surface on the NanoTite Implant results in significantly enhanced integration compared to OSSEOTITE Control Implants. This enhanced osseointegration is occurring at early time points. BIOMET 3i is actively investigating via resonance frequency analysis the ability for the NanoTite Implant to produce a more Steady State Stability™ Condition in the early phases of healing.

It All Starts With The Proven OSSEOTITE® Surface...

For more than 10 years, with documentation from numerous global multicenter clinical evaluations, the OSSEOTITE Surface has proven to be a predictable and well-researched surface. Clinical studies on the OSSEOTITE Surface continue to document the benefits of increased contact osteogenesis, especially in poor-quality bone.†
An Innovative Implant Surface Technology

The Unique Patented Process:
1. Nanometer-scale, ultra small particles of highly Crystalline Calcium Phosphate (CaP) are suspended in the solution
2. These particles are then prompted to “Self-Assemble” onto the implant titanium oxide surface
3. This results in discrete crystal deposits of 20-100 nanometers in length on the dual acid etched OSSEOTITE® Implant Surface. The shear strength of crystal attachment to the OSSEOTITE Surface exceeds the minimum shear strength value of 34.5 MPa set by the ASTM standard (F 1609-03) for attachment of traditional HA coatings to implant surfaces.
**Using The Best Of Both Worlds**

The NanoTite™ Implant builds on the success of the OSSEOTITE® Surface by creating a more complex surface topography and maximizing the potential biological benefits of calcium phosphates (CaP).

Traditionally, CaP has been plasma sprayed on the implant surface, creating a coating thickness typically in the range of 50-100 microns. The nature of plasma sprayed coatings makes them susceptible to events such as delamination or dissolution of the amorphous content of the coating.* Hence the positive attributes of CaP may be offset by certain risk factors.

The NanoTite Implant is different. The CaP is not applied via a plasma sprayed process but rather a solution based form of self-assembly. It is not a continuous coating but consists of actual deposits of discrete crystals that occupy approximately 50% of the OSSEOTITE® Surface. The total amount of CaP material on a NanoTite Implant is so small that it weighs less than 20 micrograms (or about one-third the weight of one grain of ordinary table salt). This is in contrast to the 20,000 micrograms of CaP on the typical plasma sprayed surface — a one thousand fold difference.

The dissolution of DCD™ on a NanoTite Implant is extremely low in physiologically neutral pH given the highly crystalline nature of the CaP crystals. This provides implants with a more consistent and stable phase of CaP, allowing the implant site to capitalize on the positive attributes of this biomaterial. In addition, the DCD Process increases the micro-surface area by 200%, providing greater microcomplexity.

The NanoTite™ Implant builds on the success of the OSSEOTITE® Surface by creating a more complex surface topography and maximizing the potential biological benefits of calcium phosphates (CaP).

<table>
<thead>
<tr>
<th>NanoTite Implant vs. HA Plasma Sprayed Implant</th>
<th>APPLICATION METHOD</th>
<th>ADHESION STRENGTH</th>
<th>CRYSTALLINITY</th>
<th>IMPLANT COVERAGE</th>
<th>SURFACE AREA INCREASE OVER OSSEOTITE</th>
<th>AMOUNT OF CaP</th>
</tr>
</thead>
<tbody>
<tr>
<td>NanoTite Implant</td>
<td>Nano crystal self assembly</td>
<td>&gt;40x ASTM standard</td>
<td>&gt;95% pure crystalline HA</td>
<td>50% of the OSSEOTITE Surface</td>
<td>200% greater surface area</td>
<td>3.6-22.8μg</td>
</tr>
<tr>
<td>HA Plasma Sprayed Implant</td>
<td>Plasma sprayed</td>
<td>ASTM standard of 34.5 MPa</td>
<td>Variable crystallinity: typical amorphous content</td>
<td>100% on Grit-blasted Surface</td>
<td>N/A</td>
<td>20,000μg</td>
</tr>
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</table>

**Researchers Are Seeing Impressive Results**

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**Benchtop Testing**

Both quantitative and qualitative benchtop performance tests demonstrate superior adhesion strength of the nano-scale crystals to the OSSEOTITE® Implant

<table>
<thead>
<tr>
<th>Study Center</th>
<th>Evaluations</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIOMET 3i</td>
<td>Quantitative Analysis of Nano-Scale Shear Strength/Stress</td>
<td>The average crystal-surface adhesion shear strength was three orders of magnitude greater than the average implant-bone shear stress¹¹</td>
</tr>
<tr>
<td>BIOMET 3i</td>
<td>Qualitative Analysis of Nano-Crystal Adhesion</td>
<td>Field Emission Scanning Electron Microscope imaging indicated that the nano-crystals did not become dislodged during implant placement and removal¹²</td>
</tr>
</tbody>
</table>

**Preclinical Studies**

A comprehensive series of animal studies were performed on the NanoTite™ Surface in various animal models. Further, these studies conclusively demonstrated that the NanoTite Surface results in a greater rate and extent of osseointegration as compared to the OSSEOTITE Surface alone. The micro-topography of the OSSEOTITE Surface combined with the nanometer-scale architecture created with the NanoTite Surface Treatment renders it a Bone Bonding® Surface by the interlocking of the newly formed cement line matrix of bone with the implant surface.

<table>
<thead>
<tr>
<th>Study Center</th>
<th>Evaluations</th>
<th>Comparisons With OSSEOTITE</th>
<th>Healing Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCLA</td>
<td>Rat Push-in</td>
<td>Up to 129% push-in force difference¹⁴</td>
<td>14 days</td>
</tr>
<tr>
<td>SkeleTech</td>
<td>Rabbit Pull-out</td>
<td>109% increase in pull-out force¹²</td>
<td>14 days</td>
</tr>
<tr>
<td>University of Toronto</td>
<td>T Plant Histology</td>
<td>160% increase in Bone-To-Implant-Contact (BIC)¹⁶</td>
<td>9 days</td>
</tr>
<tr>
<td>University of Toronto</td>
<td>Tensile 1</td>
<td>700% detachment force difference¹⁶</td>
<td>9 days</td>
</tr>
<tr>
<td>University of Toronto</td>
<td>Tensile 2</td>
<td>&gt;1,000% detachment force difference¹⁶</td>
<td>9 days</td>
</tr>
</tbody>
</table>

Bone that has undergone osteoclastic resorption demonstrates a unique surface complexity not all that dissimilar from the NanoTite Surface complexity. The nanoscale topography of the NanoTite Implant is thought to play a significant role in the osseointegration potential of this implant.

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Osteoclastic Resorption Image
Courtesy of J.E. Davies, BDS, PhD, DSc, FSBE University of Toronto

NanoTite Surface
at 20,000x magnification
Numerous prospective human trials have been initiated with the NanoTite™ Implant and global evaluation of the product has been in progress since June of 2006. These human protocols were specifically designed to assess the comparative performance of the NanoTite Implant in more challenging clinical indications to include immediate loading. Human histology has also been procured demonstrating a substantive increase in Bone-To-Implant-Contact (BIC) with the NanoTite Surface.

### Bone-To-Implant-Contact Outcome
**At Eight Weeks Of Healing**

Human histological sections have demonstrated an impressive amount of bone to implant contact around the NanoTite Surface, further supporting its unique potential for osseointegration.

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### Ongoing Preclinical And Clinical Studies

<table>
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<th>Study Center</th>
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<th>Healing Time</th>
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<tbody>
<tr>
<td>15 Study Centers</td>
<td>Immediate loading of single tooth restorations and short span bridge cases (Human)</td>
<td>Prospective study: One year follow-up, 343 implants placed; 95% cumulative success rate</td>
<td>Provisionalized in ≤48 hours</td>
</tr>
<tr>
<td>BIOMET 3i Clinical Registry</td>
<td>All evaluators provided early access to NanoTite Implants (Human)</td>
<td>Prospective study: At study close (Dec 2007), 1057 implants placed in 664 patients; 98.8% cumulative success rate</td>
<td>Varied</td>
</tr>
<tr>
<td>The Department of Stomatology and Oral Science at the University G. d’Annunzio, Chieti – Pescara</td>
<td>Trephined mini-implant (Human)</td>
<td>15 pairs NanoTite / OSSEOTITE; 70% increase in BIC. <em>J Periodontol</em> 2007;76:209-218.</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Dr. Ronnie J. Goené, Amsterdam Dr. Tiziano Testori, Como Dr. Paolo Trisi, Pescara</td>
<td>Trephined mini-implant (Human)</td>
<td>9 pairs NanoTite / OSSEOTITE - 197% increase in BIC at 4 weeks - 148% increase in BIC at 8 weeks. <em>Int J Periodontics Restorative Dent</em> 2007:27:211-219</td>
<td>4 and 8 weeks</td>
</tr>
<tr>
<td>The Sahlgrenska Academy at Göteborg University</td>
<td>Soft and Hard Tissue (Animal)</td>
<td>In-life phase complete – under histological analysis</td>
<td>2/4 weeks</td>
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<tr>
<td>Universidad Complutense de Madrid</td>
<td>Soft and Hard Tissue (Animal)</td>
<td>In-life phase complete – under histological analysis</td>
<td>4 hours and 1, 2, 4, 8 weeks</td>
</tr>
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*Int J Periodontics Restorative Dent, 2007;27:211-219*
Surface And Design Technology
That’s Out Of This World

• The NanoTite™ PREVAIL® Implant incorporates integrated platform switching and an internal connection with the OSSEOTITE® Surface and nano-scale crystals to the top of the collar, creating a continuous bone-loading surface

• The NanoTite Straight Collar PREVAIL Implant provides users the benefits of the PREVAIL Implant in a straight collar design to allow for flexibility in tight interdental spaces or where ridge width is limited

• The NanoTite Tapered PREVAIL Implant includes benefits of the PREVAIL Implant in a tapered design for indications where a natural tooth root shape is preferred and early stability is desired

• The NanoTite Tapered Implant closely approximates the shape of a natural tooth root with the OSSEOTITE Surface and nano-scale crystals to the base of the implant collar

• The NanoTite Certain® Implant provides an internal connection and has coverage of both the OSSEOTITE Surface and nano-scale crystals to the base of the implant collar

• The NanoTite External Connection Implant has coverage of both the OSSEOTITE Surface and nano-scale crystals to the base of the implant collar
What Your Peers Are Saying About The NanoTite™ Implant

Dennis Tarnow, DDS, New York, NY

“It’s very exciting to us as clinicians and as academicians because this discrete deposited nano technology allows for the best of both worlds. Without having a full coating on the implant, you now have a surface that will integrate that’s the regular OSSEOTITE®...combined with something that acts as an attractor to the bone and in fact might allow for actual deposition of bone on the electron microscope level.”

Robert Emery, DDS, Washington, D.C.

“We try to stay at the cutting edge of oral and maxillofacial surgery and especially implant dentistry because we do such a large amount of implant surgery. To stay at the cutting edge you have to evaluate new products and see if they improve patient care. This “DCD” Technology or the Nano Calcium Phosphate is probably the biggest improvement that’s hit implant dentistry in the past few years. It’s a big step forward.”

Markus Hürzeler, DMD, PhD, Munich, Germany

“We have already treated patients in one day. We placed implants and we immediately placed some teeth on those implants and we had a pretty good success rate. But now, with this new technology, I am pretty sure that in the future, we will have an even better success rate with this approach and if you have the opportunity to give the patient...that you come in the morning to the office and get implants...you get the teeth right away...in the same day...this I think is a big advantage and a big effect for the patient.”

J. E. Davies, BDS, PhD, DSc, FSBE, Toronto, Canada

“Certainly these results are incredible. I don’t think it’s because we’ve discovered a new phenomenon in biology, but certainly the interface which has been created between bone and this particular implant surface is quite different from anything ever seen before.”

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References


Nano Fact:
The planet earth is approximately one billion times larger than a soccer ball—the same correlation of a meter to a nanometer.
**NanoTite™ Implant Ordering Information**

### NanoTite Certain® PREVAIL®

<table>
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<tr>
<th>Length</th>
<th>3.25mm(D)</th>
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</tbody>
</table>

**D = Diameter**  
**P = Rastorative Platform**

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