BIOMET 3i - Clinical Research Department

NanoTite™ Implant Pre-Market Evaluation

The Appleseed Project

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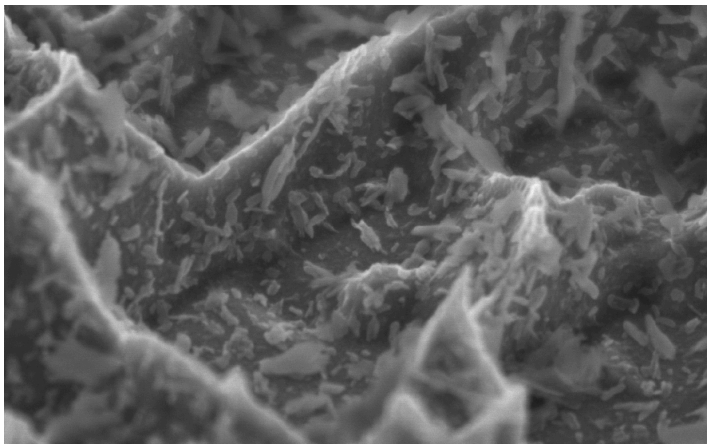
In March 2007, BIOMET ***3i*** commercially released the NanoTite Implant. Combining the novel application of nanotechnology with roughened acid etched dental implants, this implant once again established BIOMET ***3i*** as the leader in dental implant surface technology.

Historically, implant dentistry evolved from the use of machined surfaced implants (unloaded healing) requiring two surgeries in edentulous patients to roughened surfaced implants that have allowed clinicians to pursue single-staged surgeries and improved aesthetics. As a consequence of this development, long term Cumulative Survival Rates (CSRs) improved from the 85%–95%[1,2] seen with machined implants to the 95%–98%[3,4] range reported with the OSSEOTITE® Dual-Acid-Etched Implant Surface.

With such high CSRs, why continue to research and develop new advances in implant surface technology? Implants typically demonstrate good primary stability at the time of placement—in principle, a mechanical phenomenon. However, when bone remodels in the weeks following implant placement, primary implant stability can degrade which, in turn, might impact the ability to perform early or immediate loading protocols. This may lead to an increased potential for implant failure.

To meet the needs of clinicians in addressing these challenges, BIOMET ***3i*** applied nano-scale crystals of calcium phosphate (CaP) onto the OSSEOTITE Surface by using a Discrete Crystalline Deposition (DCD™) Process. This application of nanotechnology resulted in a new surface, which leverages the clinically proven OSSEOTITE Surface as the substrate while maximizing the known biologic benefits of calcium phosphate in bone formation and healing. The result: the NanoTite Implant, an implant with a more complex topography. The goal of this new implant surface is to enhance osseointegration at early time points.



Traditionally, CaP has been plasma sprayed onto the implant surface, creating a coating over the implant. The NanoTite Implant is very different. The calcium phosphate on the NanoTite Implant is not a coating. Rather, the NanoTite Implant consists of actual nano-scale deposits of discrete crystals that occupy approximately 50% of the OSSEOTITE Surface within its peaks and valleys. Further, the DCD Process actually increases the microsurface area by 200%. By creating an implant with greater microcomplexity at the nano-level, the implant surface is rendered a Bone Bonding® Surface by the interlocking of the cement line matrix of bone with the implant surface.[5]

For clinicians, this means that NanoTite Implants may be suitable for cases such as:

- Immediate and accelerated loading protocols
- Immediate implant placement in extraction sockets
- Simultaneous grafting and implant placement
- Aesthetic areas where bone preservation is critical
- Implant placement into poor quality bone
- Anatomic sites that require short or wide diameter implants

EVIDENCE-BASED RESEARCH AND PRODUCT EVALUATION

Prior to its commercial release, the NanoTite™ Implant underwent numerous bench tests, pre-clinical studies and initiation of various clinical studies. Among these studies was a pre-market evaluation of the implant by practicing clinicians. The following results complement preclinical and clinical studies demonstrating the implant's potential for achieving clinical success.

DEFINITIVE RESULTS FOR THE NANOTITE IMPLANT PRE-MARKET EVALUATION

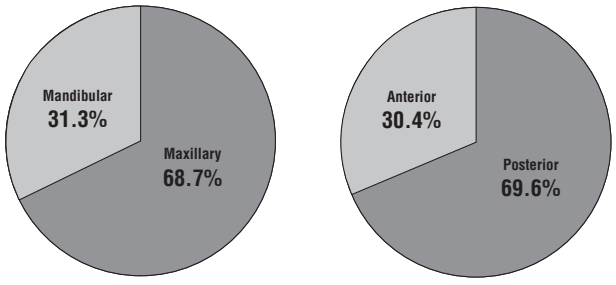
The initial product configurations included Certain® PREVAIL® and Certain Parallel Walled Designs using existing surgical instrumentation. At study close (Dec. 2007), 1057 NanoTite Implants had been placed and followed by 371 clinicians around the world. The implants were placed into 664 patients; mean age 54.7 years; range 17-90 years.

The following table summarizes the loading protocol pursued by the clinicians:

Loading Protocol	Patients	Implants (%)
Immediate Occlusal Loading	68	132 (12.5)
Early Loading (6-8 wks)	99	162 (15.3)
Delayed Loading (>8 wks)	488	752 (71.1)
Unspecified	9	11 (1.0)

There were 726 maxillary implants (68.7%) and 331 mandibular implants (31.3%). In anterior segments, 321 implants (30.4%) were placed while in the posterior, 736 (69.6%) implants were placed.

Implant Placement Locations



The majority of the implants were placed into normal bone – a qualitative assessment made by the clinicians at the time of implant placement. 896 of the implants were between 10mm and 13mm in length. Implants shorter than 8.5mm were not used.

Implants Placed

Implant Diameter (mm) \ Implant Length (mm)	8.5	10.0	11.5	13.0	15.0	Total
3.25	0	3	4	1	1	**9**
4.00	11	72	96	112	28	**319**
5.00	16	135	206	166	40	**563**
6.00	19	61	29	11	0	**120**
Total	**46**	**271**	**335**	**290**	**69**	***1011****

*The size of 46 implants was not captured; total 1011 + 46 = 1057

RESULTS

Thirteen (13) failures have been reported for the 1057 implants included in this survey for a CSR of 98.8%. Seven of the 13 failures were noted within 4 months of implant placement. The longest time frame noted for a failed implant was 7 months post placement.

SUMMARY

NanoTite Implants are derived from the proven OSSEOTITE® Implant. The application of nano-scale crystals of calcium phosphate results in a Bone Bonding® Implant Surface. Prior to its commercial introduction, this implant had been extensively researched by BIOMET ***3i***. In animal studies, NanoTite Implants have demonstrated a greater rate and extent of Bone to Implant Contact (BIC) as compared to OSSEOTITE Implants.[6] The outstanding results of this initial market evaluation have been further supported by human histology studies, which have been presented at meetings around the world and published in peer reviewed scientific journals.[7,8]

REFERENCES

1. Branemark PI, Hansson B, Adell R. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scand J Plast Reconstr Surg*. 1977; 16:1-132.
2. Adell R, Lekholm U, Rockler B, Branemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg*. 1981;10:387-416.
3. Lazzara R, Porter S, Testori T. A prospective multicenter evaluation loading of OSSEOTITE Implants two months after placement: one-year results. *J Esthet Dent*. 1998;10:280-289.
4. Testori T, Del Fabbro M, Feldman S, Vincenzi G, Sullivan D, Rossi, Jr, R, Anitua E, Bianchi F, Francetti L, Weinstein R. A multicenter prospective evaluation of 2-months loaded OSSEOTITE Implants placed in the posterior jaws: 3-year follow up results. *Clin Oral Implants Res*. 2002;13:154-161.
5. Mendes VC, Moineddin R, Davies JE. The effect of discrete calcium phosphate nanocrystals on bone-bonding to titanium surfaces. *Biomaterials. (2007), doi:10.1016/j. Biomaterials. 2007. 07. 020*.
6. Mendes VC, Davies JE. Discrete calcium phosphate nanocrystals enhance osteoconduction on titanium-based implant surfaces. *Institute of Biomaterials and Biomedical Engineering, Faculty of Dentistry, University of Toronto, Ontario, Canada*.
7. Orsini G, Piattelli M, Scarano A, Petrone G, Kenealy J, Piattelli A, Caputi S. Randomized-Controlled Histologic and Histomorphometric Evaluation of NanoTite™ and Control Site Evaluation Implants (SEI) in the Human Posterior Maxilla. *J Periodont*. 2007;78(2):209-18.
8. Goené RJ, Testori T, Trisi P. Influence of a nanometer-scale surface enhancement on de novo bone formation on titanium implants: a histomorphometric study in human maxillae. *Int J Periodontics Restorative Dent*. 2007;27(3):211-9.

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