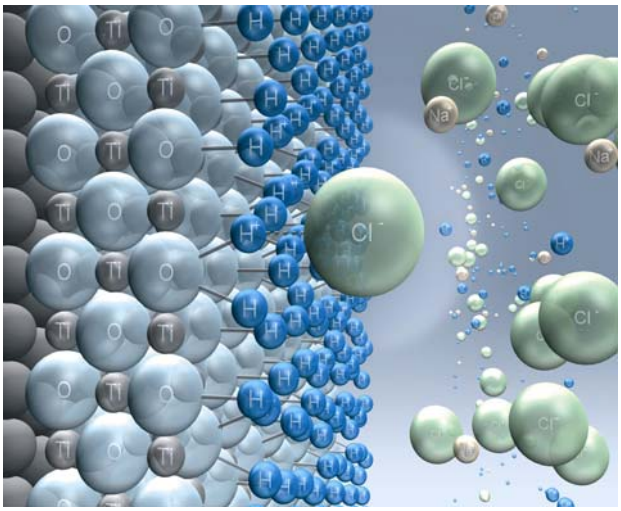
Backgrounder: SLActive®

SLActive® – the third generation in implant surface technology



The molecular surface structure of SLActive

A new dental implant surface technology, which has proven to cut healing times in half to just 3-4 weeks[1], was launched in Europe, North America and initial markets in Asia in 2006. Marketed under the trade name 'SLActive', the new technology has been pioneered by Straumann, a global leader in implant and restorative dentistry and dental tissue regeneration, and is available on a broad range of the company's implant types.

An extensive ongoing international clinical trial in 19 centers has shown that SLActive generally achieves excellent results even when the implant is loaded immediately or sooner after placement than usual.[2] In addition to this benefit of shorter treatment protocols, SLActive could open the door to successful implant treatment in patients with poor bone quality or other challenging treatment situations such as patients with diabetes, osteoporosis, or patients who smoke.

The enhanced surface properties, activated tissue responses and rapid osseointegration with SLActive make it – in the words of Professor Axel Zöllner, University of Witten/ Herdecke, Germany "an evolutionary step towards a revolution in dentistry".[3] It thus promises to set a new standard in tooth replacement and patient care and was supported by more scientific studies than any other dental implant technology at market launch because it is based and builds on the scientific data supporting the renowned and well documented SLA surface.

These attributes won SLActive the 2005 Medical Device Technology of the Year Award in a poll of independent experts conducted by business consultants Frost and Sullivan.

Healing times halved to 3-4 weeks
When Straumann developed the forerunner of SLActive - the SLA surface - in 1994, it dramatically reduced healing times from 12 to 6 weeks. SLA consequently became the gold

standard in implant dentistry and has hitherto remained the scientifically proven benchmark. SLA received FDA clearance for immediate loading back in 1999*.

With SLActive, the next generation implant technology, Straumann has again cut healing times by half, bringing them down to 3 to 4 weeks. The implications of this are: shorter treatment protocols, higher predictability and increased confidence with earlier loading, resulting in better patient care. Like SLA, SLActive offers the options of immediate loading* and immediate function.

Preclinical evidence for greater and faster implant stability
SLActive uses the same initial manufacturing process as SLA, involving Sandblasting with Large grit followed by Acid etching to achieve an optimal topography for bone cells to attach themselves. SLActive is conditioned in nitrogen and immediately preserved in an isotonic saline solution. This maintains its high surface activity, which would otherwise be lost due to reaction with the atmosphere.

The importance of hydrophilicity
Conventional titanium surfaces are hydrophobic and thus repel fluids, whereas the chemical purity and retained surface energy of SLActive give it remarkable hydrophilic properties. This was demonstrated in four preclinical studies conducted at an early stage in development.[4,5,6,7] As a consequence, the surface quickly attracts blood and proteins, promoting faster osseointegration around the implant.

Further preclinical results demonstrate increased bone-to-implant contact with the SLActive surface compared to the SLA surface at early healing periods of 2-4 weeks.[8] This in turn results in earlier secondary implant stability in the critical early stage of healing.[9]

In vitro studies also demonstrated that early cell response to SLActive was enhanced by up to 15-fold.[6,10,11,12] At the same time, other preclinical studies demonstrated that SLActive achieved up to 60% more bone at 2 weeks after placement,[8] showed greater removal torque,[9] and demonstrated faster and more mature bone formation in comparison with Straumann's gold-standard SLA surface.[13] The latter study by Schwarz et al (2007) showed that bone grows from the SLActive surface to fill vertical defects. The same researchers also showed that SLActive enhances the soft tissue response, which may have interesting implications for esthetic parameters.[14] The positive effects on bone formation with SLActive were corroborated by findings from a multicenter clinical trial; analysis has shown good bone level maintenance 12 months after implant placement, despite aggressive treatment protocols, and in some cases bone gain was observed.[2]

Implants most at risk 2-4 weeks after placement
When dental implants are placed in the jawbone, their helical thread and rough surface provide them with a mechanical or 'primary' stability. However, as part of the body's bone-repair mechanism, the bone around the implant is initially resorbed and the primary stability of the implant erodes. New replacement bone is formed that integrates with the implant and gives it long-term secondary stability but there is a critical period when the latter process is not far enough advanced to compensate for the lost primary stability. This period, between 2 and 4 weeks after placement, is called the "stability dip"[15] and is the point at which the implant is at greatest risk to failure.

* With good primary stability and appropriate occlusal loading. Multiple tooth applications may be rigidly splinted. In edentulous cases, four or more implants must be used for immediate loading.

By reducing healing times by half to just 3 - 4 weeks SLActive effectively minimizes the stability dip and increases implant stability, especially in the critical early stage of healing[9]. The implications of this are shorter treatment protocols, higher predictability and reduced risk with earlier loading, resulting in better patient care and satisfaction.

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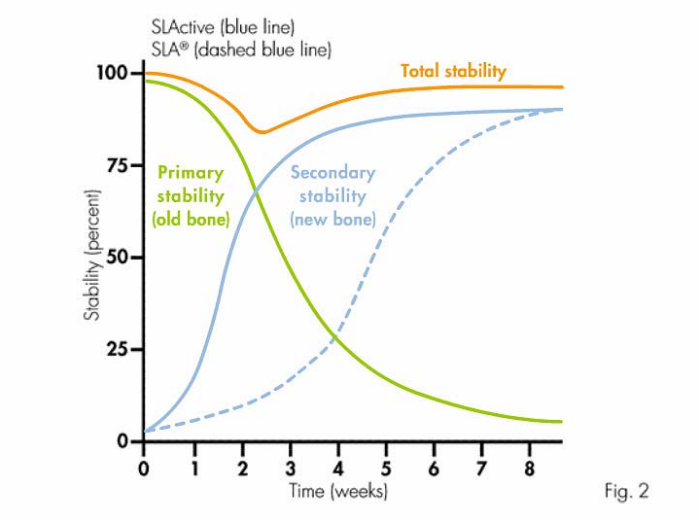

Fig. 2

Preclinical trial update

Current clinical results build on and confirm preclinical observations. Some of the impressive histological results observed in preclinical investigations, which have been published in peer-reviewed journals, are outlined here.

A pilot preclinical study, published in *Clinical Oral Implants Research*, conducted by Dr Frank Schwarz *et al* demonstrated the accelerated healing processes around SLActive implants[13]. Stable blood clot and rapid bone formation, with highly mineralized, organized bone and significantly increased proliferation of vascular structures and osteocalcin formation, was observed around SLActive implants compared to SLA implants. A second study, published in the *Journal of Clinical Periodontology*, demonstrated the promotion of bone regeneration around SLActive implants in dehiscence defects, with significantly greater and more mature bone and complete defect fill after 12 weeks, compared to SLA implants, where new bone formation was limited to only the most apical part of the defect. New bone height, percent linear fill, bone-to-implant contact and area of new bone fill were significantly increased around SLActive implants compared to around SLA implants.[16] These parameters were also shown to be significantly greater around SLActive in a similar study where SLActive and SLA implants were placed in a submerged or non-submerged procedure; submerged healing was also seen to improve outcomes.[17]

In another ongoing preclinical study, osteoblastic activity, and therefore bone production, was observed around SLActive implants at 1 week. After just 2 weeks, bone formation and production were much more advanced around SLActive than SLA. The effects of SLActive on soft tissue attachment have also been investigated, showing enhanced epithelial cell and fibroblast attachment and proliferation, leading to soft tissue attachment with well organized collagen fibers and blood vessels.[14] Another study has indicated that soft and hard tissue integration is more influenced by the surface hydrophilicity than the microtopgraphy.[18]

Clinical trials

Randomized, controlled, clinical trial shows earlier secondary implant stability during critical loading period

A dual-center, prospective, randomized, controlled, clinical trial performed in patients by a team led by Professor David Cochran has evaluated the comparative stability of SLActive and SLA in patients over the first 6 weeks of healing.[19] Cochran noted that the trial demonstrated "a highly significant difference in stability patterns between SLActive and SLA implants during the critical early treatment period between weeks 2 and 4". The change in stability pattern from decreasing primary stability to increasing secondary stability (break point) of the SLActive implant was twice as fast (2 weeks vs. 4 weeks; $p<0.0001$ for mandibular implants) relative to SLA, which is consistent with preclinical results. The findings prove in patients that SLActive offers accelerated healing and secondary implant stability in the early healing period of 2-4 weeks. Prof. Cochran concluded that "SLActive may therefore offer increased predictability". The study results were published in the *International Journal of Oral and Maxillofacial Implants*.

Immediate and early loading working well; high patient satisfaction

Results from a multicenter study conducted in 19 centers around the world have been published in *Clinical Oral Implants Research*. In the study, which focuses on the challenging indications of immediate or early loading with SLActive, patients were randomized to receive the provisional tooth restoration either on the day of implant placement (immediate) or 4 weeks later (early). To date, the immediate and early loading protocols show equivalent survival rates (98% and 97% for immediate and early loading, respectively), suggesting that SLActive achieves secondary implant stability sooner during the critical loading period between weeks 2 and 4, consistent with conclusions from preclinical studies.[2]

Early loading, three weeks after placement in patients

A clinical study is also being conducted by the Universities of Bern and Florida to investigate the effect of early loading (21/22 days) after placement of SLActive implants in 60 patients. The preliminary results suggest that aggressive early loading protocols and soft tissue healing are predictable after three weeks.

SLActive broadly available on multiple Straumann implant types

A recent review paper, reviewing the evidence for SLActive in preclinical and clinical studies, confirmed the potential of the SLActive surface to support tissue integration of dental implants.[20] SLActive has now become available on a broad range of Straumann implant types in Europe, North America and initial Asian markets and has been very well received.

References

1 Beagle J. Immediate and early loading clinical case reports with SLActive from the USA. 14th Annual Scientific Meeting of the European Association for Osseointegration, September 22-24, 2005, Munich, Germany.

[2] Ganeles J, Zöllner A, Jackowski J, ten Bruggenkate C, Beagle J, Guerra F. Immediate and early loading of Straumann implants with a chemically modified surface (SLActive) in the posterior mandible and maxilla: 1-year results from a prospective multicenter study. Clin Oral Implants Res 2008;19:1119-1128.

[3] Zöllner A. First clinical results from the SLActive multicenter study. 14th Annual Scientific Meeting of the European Association for Osseointegration, September 22-24, 2005, Munich, Germany.

4 De Wild M. Superhydrophilic SLActive implants. Straumann publication 151.527/d and 152.527/e.

5 Rupp F, Scheideler L, Olshanka N, de Wild M, Wieland M, Geis-Gerstorfer J. Enhancing surface free energy and hydrophilicity through chemical modification of microstructured titanium implant surfaces. J Biomed Mater Res A 2006;76:323-334.

6 Scheideler L, Rupp F, Wieland M, Geis-Gerstorfer J. Storage conditions of titanium implants influence molecular and cellular interactions. Poster #870, 83rd General Session and Exhibition of the International Association for Dental Research (IADR), March 9-12, 2005, Baltimore, MD, USA.

7 Seibl R, de Wild M, Lundberg E. *In vitro* protein adsorption tests on SLActive. STARGET 02.2005.

8 Buser D, Broggini N, Wieland M, Schenk RK, Denzer A, Cochran D, Hoffmann B, Lussi A, Steinemann SG. Enhanced bone apposition to a chemically modified SLA titanium surface. J Dent Res A 2004;83:529-533.

9 Ferguson SJ, Broggini N, Wieland M, de Wild M, Rupp F, Geis-Gerstorfer J, Cochran D, Buser D. Biomechanical evaluation of the interfacial strength of a chemically modified sandblasted and acid-etched titanium surface. J Biomed Mater Res A 2006;78:291-297.

10 Zhao G, Schwartz Z, Wieland M, Rupp F, Geis-Gerstorfer J, Cochran D, Boyan B. High surface energy of SLActive implants enhances cell response to titanium substrate microstructure. J Biomed Mater Res A 2005;74:49-58.

11 Rausch-Fan X, Zhe Q, Wieland M, Matejka M, Schedle A. The influence of hydrophilic versus hydrophobic Ti specimens with different topographical and roughness levels on contact guidance and cellular proliferation evaluated with time-lapse photography. *(In preparation)*.

12 Rausch-Fan X, Qu Z, Wieland M, Matejka M, Schedle A. Differentiation and cytokine synthesis of human alveolar osteoblasts compared to osteoblast-like cells (MG63) in response to titanium surfaces. Dent Mater 2008;24:102-110.

13 Schwarz F, Herten M, Sager M, Wieland M, Dard M, Becker J. Histological and immuno-histochemical analysis of initial and early osseous integration at chemically modified and conventional SLA titanium implants: preliminary results of a pilot study in dogs. Clin Oral Implants Res 2007;18:481-488.

14 Schwarz F, Herten M, Sager M, Wieland M, Dard M Becker J. Histological and immunohisto-chemical analysis of initial and early subepithelial connective tissue attachment at chemically modified and conventional SLA titanium implants. A pilot study in dogs. Clin Oral Investig 2007;11:245-255.

15 Raghavendra S, Wood MC, Taylor TD. Early wound healing adjacent to endosseous dental implants: A review of the literature. Int J Oral Maxillofac Implants 2005;20:425-431.

16 Schwarz F, Herten M, Sager M, Wieland M, Dard M, Becker J. Bone regeneration in dehiscence-type defects at chemically modified (SLActive) and conventional SLA titanium implants: a pilot study in dogs. J Clin Periodontol 2007;34:78-86.

17 Schwarz F, Sager M, Ferrari D, Herten M, Wieland M, Becker J. Bone regeneration in dehiscence-type defects at non-submerged and submerged chemically modified (SLActive) and conventional SLA titanium implants: an immunohistochemical study in dogs. J Clin Periodontol 2008;35:64-75.

[18] Schwarz F, Ferrari D, Hertan M, Milhatovic I, Wieland M, Sager M, Becker J. Effects of surface hydrophilicity and microtopography on early stages of soft and hard tissue integration at non-submerged titanium implants: an immunohistochemical study in dogs. J Periodontol 2007;78:2171-2184.

19 Oates TW, Valderrama P, Bischof M, Nedir R, Jones A, Simpson J, Toutenburg H, Cochran DL. Enhanced implant stability with a chemically modified SLA surface: a randomized pilot study. Int J Oral Maxillofac Implants 2007;22:755-760.

20 Schwarz F, Wieland M, Schwartz Z, Zhao G, Rupp F, Geis-Gerstorfer J, Schedle A, Broggini N, Bornstein MM, Buser D, Ferguson SJ, Becker J, Boyan BD, Cochran DL. Potential of chemically modified hydrophilic surface characteristics to support tissue integration of titanium dental implants. J Biomed Mater Res B Appl Biomater 2009;88:544-557.