Implant Surfaces beyond Micron Roughness. Experimental and Clinical Knowledge of Surface Topography and Surface Chemistry

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Surface texture has long been considered important in osseointegration of implants, and the finer detail of surface texture and its effect on bone response can guide implant development and surgery.

Implant surface topography at the micrometer level of resolution ("microtopography") has been regarded as the most important factor for successful implant treatment during the last decade. Allegedly, shorter healing periods and greater implant success will result from the use of moderately roughened surfaces. However, there is a dearth of clinical documentary evidence for such statements. In addition, it is difficult to control implant surface topography at the micrometer level without altering the surface at the nanometer level ("nanotopographies"). The available clinical documentation mainly refers to topographical changes at the micrometer level of resolution.

Furthermore, even with the best of approaches, altering surface topography will most often result in a changed surface chemistry as well, indicating the need to consider different aspects of surface quality rather than topography alone. Hence, attempted surface enlargement at the micrometer level may change nanotopography and surface chemistry as well; the latter surface alterations accidental rather than planned in many cases.

Even with great awareness of the complicated series of events that may follow surface microenlargement, as in the OsseoSpeed™ surface (Ellingsen, 1995; Ellingsen et al., 2004), it may prove difficult to explain the strong bone response. There is indeed evidence that microtopography alone cannot explain the enhanced integration of OsseoSpeed™ implants (Ellingsen et al., 2004). Is the incorporation of OsseoSpeed™ supported by its modified nanotopography or by the surface being bioactive (Figure 1)? A bioactive surface is capable of establishing chemical bonds across the interface, resulting in a rapidly achieved bony anchorage. The aim of this paper is to summarize *in vivo* experimental and clinical evidence of surface modifications with particular reference to the OsseoSpeed™ implant.

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Figure 1: OsseoSpeed™ implant, Astra Tech. A design including micro threads and a moderately rough surface topography.

Experimental tissue reactions and surface topography in the mIcrometer range

Based on our current knowledge, implant roughness is defined as follows: smooth implants are those with a S_a roughness of less than 0.5 µm; in oral implants found solely on abutments generally varying between 0.1 and 0.3 µm roughness. Minimally rough implants have a roughness (S_a) of between 0.5 to 1.0 µm and are represented by turned Brånemark and Astra Tech implants and by acid etched 3I implants. Moderately roughened surfaces vary between 1.0 and 2 .0 µm and include almost all modern implants, such as the Astra Tech TiOblast™ and OsseoSpeed™ surfaces, Nobel TiUnite, Straumann SLA and Dentsply Cellplus designs. Finally, rough implants are those with S_a above 2.0 µm and are exemplified by plasma sprayed devices and, among implants of today, the Dentsply Frialit implant (Albrektsson and Wennerberg, 2004a; Albrektsson and Wennerberg, 2004b).

Some *in vitro* studies have demonstrated increased osteoblast proliferation on moderately roughened surfaces (Mustafa et al., 1998; Derhami et al., 2000; et al., 2001; Soskolne et al., 2002). Furthermore, cell differentiation has proven to be influenced by surface roughness (Boyan et al., 2001) and cell alignment by the surface orientation (Brunette et al., 1983; Chehroudi et al., 1990; et al., 1991). However, it is generally impossible to make direct comparisons between results obtained in cell cultures with clinical outcome or even with *in vivo* observations. The clinical and *in vivo* situations are complicated and depend on interactions between different types of cells, the presence of growth and other hormones as well as loading stimuli, to mention but a few differences from the dimensional *in vitro* scenario. For these reasons we will abstain from further comment on *in vitro* data here.

In a series of studies in rabbit bone, the present authors have demonstrated that a blasted implant surface with an average height deviation of about 1.5 µm, an average wavelength of about 11 µm and a surface developed ratio of 1.5 seems optimal for a firm bone integration (Wennerberg et al., 2004). rough or very rough surfaces showed less robust bone responses than moderately roughened specimens. Other factors such as surface orientation seem to be of little practical importance (Hallgren et al., 2001; Göransson and Wennerberg, 2005). It is not fully understood why rough surfaces demonstrate weaker bone response than moderately rough surfaces. Suggested explanations such as impaired stability or increased ionic leakage do not seem convincing (Wennerberg et al.,1998; Wennerberg et al., 2004). One potential problem associated with rough surfaces is an increased incidence of mucositis and peri-implantitis (Åstrand et al., 2000; Becker et al., 2000). However, this problem does not seem to exist with moderately roughened surfaces (Kemppainen et al., 1997; Batenburg et al., 1998; Astrand et al., 1999; Meijer et al., 2000; van Steenberghe et al., 2000; Moberg et al., 2001; Tawse-Smith et al., 2001; Engquist et al., 2002 ; Geurs, 2002; Graf et al., 2002 ; Tawse-Smith et al., 2002 ; Jeffcoat et al., 2003).

Clinical knowledge of micron level surface roughness

Even if it seems obvious that the strongest bone response is seen with moderately rough surfaces, clinical evidence of the superiority of such implants is less convincing. Ignoring many comparisons between well-defined moderately rough implants and poorly defined so-called machined implants, we have found a number of well controlled, randomised clinical studies comparing the clinical success of turned and moderately roughened implants (Astrand et al., 1999; Puchades-Roman et al., 2000; van Steenberghe et al., 2000; Gotfredsen and Karlsson, 2001; Engquist et al., 2002; Åstrand et al., 2004; Wennstrom et al., 2004). These studies generally found no significant differences between minimally and moderately roughened implants, even if there was a trend towards better results for the moderately roughened implants. This outcome is strange considering the strongly significant improvement in bone response seen to the moderately roughened implants. Possible explanations may include;

(1) many comparisons were undertaken in good bone - the differences would have been greater in poor bone,

(2) experienced surgeons - i.e. those who write papers - see good results with any implants, hence differences would have been greater with inexperienced surgeons,

(3) the magnitude of the bone response is irrelevant; what matters is that a certain minimal percentage of bone anchorage (60% bone to implant contact, (Albrektsson et al., 1993) is seen.

Nanometer surface topography

The importance of nanometer sized surface irregularities has been frequently discussed in biomaterials science recently. However, to our knowledge there is no *in vivo* or clinical data documenting the importance of nanosurfaces. From a historic aspect, it is noteworthy that so called micropits, once patented by P-I Brånemark, were regarded as essential for proper osseointegration. Brånemark's micropits were below 1 µm in size, i.e. at the nanometer level of resolution. At our laboratories current *in vivo* projects are aimed at separately investigating the tissue response to nanometer sized indentations. These include attempts to filter out larger micro-irregularities so as to separately depict the nanometer indentations (Figure 2a, 2b, 2c). However, our results as well as *in vivo* results from other centres are still in the stage of

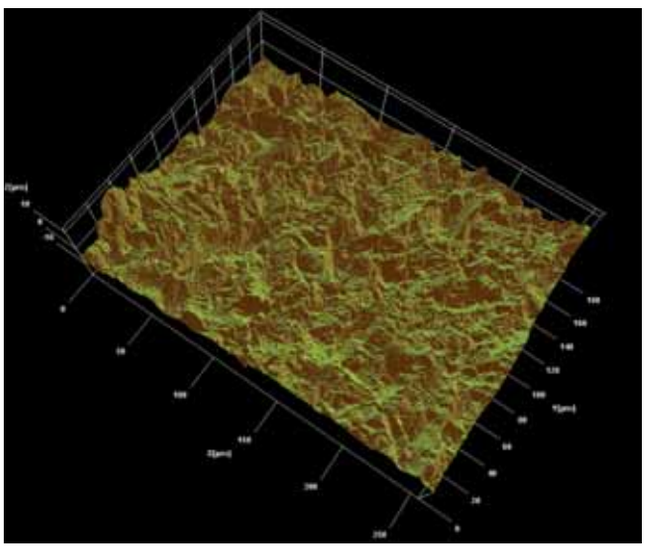

Figure 2a: Digital image from a surface roughness measurement of an OsseoSpeed™ flank area, 200 x 264 µm. The surface has S_a approximately 1.5 µm and Sdr 50%; a roughness found to be optimal for bone anchorage in previous experimental studies.

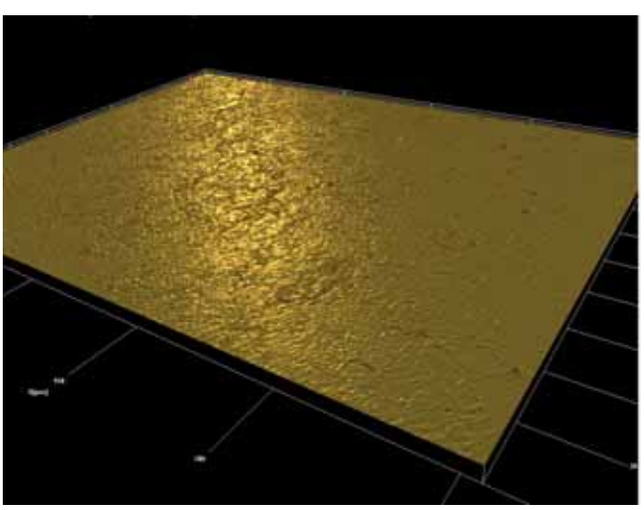

Figure 2b: The nanometer roughness of the OsseoSpeed™ surface; S_a of 22 nm and Sdr of 1 %. The nanometer roughness may be important for early protein adhesion and consequent enhanced bone formation around the implant.

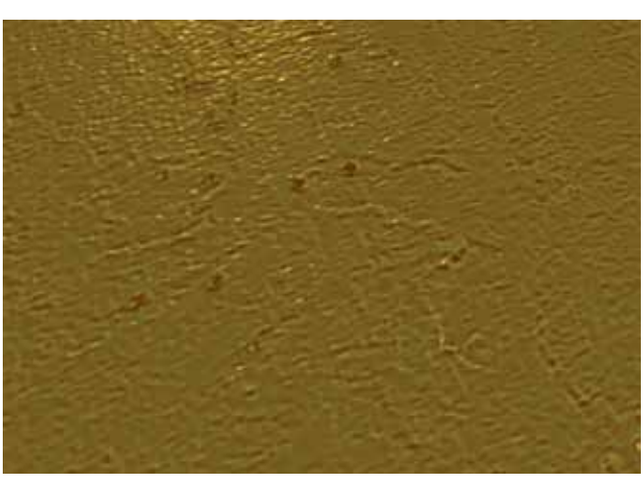

Figure 2c: A close-up of the nanometer sized structure. Shallow pits and scattered pores are clearly visible.

experimental working. Our conclusion regarding nanosurfaces is that they may influence tissue response, but that this remains unproven.

Physicochemical Modifications of surface characteristics

Hydrophilic surfaces have a high surface energy in contrast to hydrophobic surfaces. Hydrophilic properties have been regarded as a necessary condition for tissue integration in biomaterials science, but several modern oral implants such as the TiUnite and SLA implants (Buser et al., 2004) are in fact hydrophobic.

At our centre we performed experimental and clinical investigations of implants with a high surface energy (Carlsson et al., 1989) or hydrophilic properties (Suketa et al., 2005), without finding any advantages with such surfaces. One factor that may have influenced our lack of success with high surface energy surfaces was hypothesized to be an inevitable *in vivo* biological neutralization of the energy state at implant insertion due to, for instance, coverage with blood that will lower the initially elevated surface energy.

However, we have not investigated the commercially available hydrophilic SL-A implant but observed that these implants demonstrated a stronger bone response than explained by their microtopography alone (Buser et al., 2004). Having said this, at the time of writing, the potential contribution to clinical success of hydrophilic implants remains unknown.

Reference is commonly made to bioactivity, defined as "the characteristic of an implant material which allows it to form a bond with living tissues" (Hench, 1990). The theoretical advantage with bioactive implants is that the resulting biochemical anchorage is rapid, i.e. it functions at a time when proper biomechanical interlocking through hard tissue invasion of micro-irregularities has not been established. Just as differentiating surface topography between the micrometer or nanometer level of resolution is difficult, separating "bioactivity" from "high surface energy" may be awkward. Notwithstanding, whereas ordinary titanium implants are considered non-bioactive, titanium may be rendered bioactive through chemical treatment (Nishiguchi et al., 1999; Sul et al., 2002a) or by coating with calcium phosphates (Jarcho et al., 1977).

Experimental work by several groups (Ellingsen, 1995; Sul et al., 2002a; Sul et al., 2002b; Sul et al., 2002c; Buser et al., 2004; Ellingsen et al., 2004) has clearly demonstrated that modified physical characteristics, with surface microtopography controlled, result in a stronger bone response to the modified implants. However, whether this strong bone response really depends on hydrophilic properties, high surface energy,

bioactivity or other as yet unknown surface physical characteristics remains insufficiently investigated.

If commonly used oral implants are considered, there is as yet no evidence that TiUnite oxidised surfaces and SLA implants have any effects beyond their moderate surface roughness in contrast to SL-Active implants (Buser et al., 2004) and Astra Tech OsseoSpeed™ (Ellingsen et al., 2004) implants, with which factors other than microroughness must play a significant role in implant performance. From a clinical perspective there is some evidence of potential benefits from changing surface chemistry that cannot be explained by surface topography alone (Jeffcoat et al., 2003; Carlsson et al., 2006a; et al., 2006b). Jeffcoat and colleagues saw the best clinical results with potentially bioactive HA-coated implants compared to non-coated titanium, whereas and co-authors found evidence of significantly better results in hip arthroplasties for OsseoSpeed™ surfaces than conventional, moderately roughened surfaces.

Concluding remarks

We believe that the focus with new types of oral implants will shift from moderate surface roughness towards nanosurfaces or changed physical characteristics of oral implants. The anchorage of the OsseoSpeed™ implant may be explained by a combination of moderate surface micro-and particular surface nano-topography and bioactivity, without separately assessing the individual importance of the latter two factors.

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