Acid-etched microtexture for enhancement of bone growth into porous-coated implants

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We designed an *in vivo* study to determine if the superimposition of a microtexture on the surface of sintered titanium beads affected the extent of bone ingrowth. Cylindrical titanium intramedullary implants were coated with titanium beads to form a porous finish using commercial sintering techniques. A control group of implants was left in the as-sintered condition. The test group was etched in a boiling acidic solution to create an irregular surface over the entire porous coating. Six experimental dogs underwent simultaneous bilateral femoral intramedullary implantation of a control implant and an acid etched implant. At 12 weeks, the implants were harvested *in situ* and the femora processed for undecalcified, histological examination. Eight transverse serial sections for each implant were analysed by backscattered electron microscopy and the extent of bone ingrowth was quantified by computer-aided image analysis. The extent of bone ingrowth into the control implants was 15.8% while the extent of bone ingrowth into the etched implants was 25.3%, a difference of 60% that was statistically significant.

These results are consistent with other research that documents the positive effect of microtextured surfaces on bone formation at an implant surface. The acid etching process developed for this study represents a simple method for enhancing the potential of commonly available porous coatings for biological fixation.

J Bone Joint Surg [Br] 2003;85-B:1182-9.

Received 5 February 2003, Accepted 16 June 2003

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doi:10.1302/0301-620X.85B8.14233 \$2.00

There has been over 20 years of experience with a wide variety of porous materials being used in joint replacement.¹⁻⁶ During this time, porous-coated implants have become increasingly popular worldwide, especially for younger, more active patients.⁷⁻⁹ Despite their general clinical success, there is a lack of consistency in the literature concerning the extent of bone growth within the implant porosity.^{4,10-13}

In this regard, various approaches have been investigated to stimulate new bone formation and increase the likelihood of implant fixation by bone ingrowth. Successful methods include non-invasive, low-intensity ultrasound, administration of pharmaceutical agents, and the addition of growth factors or calcium phosphate materials to the implant substrate.^{4,12,14-23}

An entirely different approach to enhancing bone-forming activity is the manipulation of implant surface topography. Surface topography is commonly described by the parameter R_a , the average of the absolute values of the deviations from the mean centreline roughness. In studies directly related to peri-implant bone formation, comparisons of identical titanium (Ti) surfaces, differing only in roughness (R_a), have demonstrated significantly different effects on osteoblast activity *in vitro* and *in vivo*. Numerous *in vitro* studies have shown that smooth surfaces ($R_a < 0.5 \mu\text{m}$) do not stimulate osteoblastic activity characteristic of bone formation. Osteoblasts, however, are responsive to rough irregular surfaces (such as those created by blasting Ti with small particles of aluminium oxide) with an R_a ranging from about 1 to 7 μm .²⁴⁻²⁹ Osteoblasts cultured on microtextured surfaces demonstrate increased adherence, induction of metabolic activity and the release of potent osteo-inductive extracellular factors such as prostaglandin E_2 and transforming growth factor $\beta 1$.²⁸⁻³⁰

These *in vitro* studies have been corroborated by numerous *in vivo* and clinical studies demonstrating that new bone forms on textured implant surfaces with R_a values ranging from 1.0 to 6.7 μm , while stable implants with R_a of less than 0.4 μm are generally apposed by fibrous tissue.³¹⁻³⁹ Above the 0.5 μm R_a threshold, surface microtexture stimulates a response that culminates in some degree of osteoblastic activity. In addition, the magnitude of surface roughness can modulate the rate of new bone formation. Some studies have shown that finer textured surfaces

Fig. 1

The as-sintered control (top) and the acid-etched (bottom) femoral intramedullary implants used in this study.

(R_a , 1 to 2 μm) develop greater bone coverage more rapidly when compared to rougher textures (R_a , 4 to 5 μm).³⁹⁻⁴¹ Based on this evidence, finer surface textures may be advantageous for stimulating new bone development into porous materials.

Porous coatings fabricated from materials, such as sintered beads and fibre metal, possess surface features with an R_a that is typically less than 0.5 μm . Therefore, from the standpoint of microtexture, these coatings may not be optimised for stimulating new bone formation. We are unaware of prior studies that have investigated the osteoconductive effect of an irregular microtexture superimposed on a standard porous coating, such as those produced by the sintering of beads or fibre metal. The purpose of our study was, therefore, to determine whether the positive bone response, observed with microtextured implant surfaces, could modify the biological fixation of a porous coating in a canine implant model. The study hypothesis was that the addition of a fine surface texture to sintered beads would increase the extent of bone ingrowth.

Materials and Methods

Femoral intramedullary implants. We designed a cylindrical implant 90 mm long and 9 mm in diameter for surgical placement within the femoral intramedullary canal of experimental dogs (Fig. 1). Each implant consisted of a 3 mm diameter solid central core of a Ti, aluminium, vanadium (Ti-6Al-4V) alloy to which a 3 mm thick coating of commercially pure Ti beads was sintered using commercial grade sintering techniques (Implex Corp, Allendale, New Jersey). The bead size ranged from 100 to 300 μm in diameter and the 3 mm thick porous coating comprised approximately 12 to 15 bead layers. The average pore size of the coating, as determined by the linear intercept method, was 230 μm . Two different implant groups were prepared according to surface treatment. Six implants were left in the as-sintered condition and served as controls. Six text implants underwent chemical etching. All implants were

cleaned using ultrasonically, passivated techniques and sterilised by gamma irradiation.

Chemical etching (microtexturing) process. The porous-coated implants were placed in a boiling solution of hydrochloric acid for a period of 20 minutes. Immediately after etching, the implants were rinsed three times in distilled water and soaked in distilled water for a period of 24 hours. Then, both control and chemically-etched implants were passivated in a 30% solution of nitric acid at room temperature for 30 minutes, and again rinsed three times and soaked in distilled water for 24 hours, with occasional sonication by ultrasound.

Characterisation of implant surfaces. Scanning electron micrographs of implant surfaces were obtained to provide a qualitative impression of surface topography. In addition, topography was quantified using a Wyko TN 2000 (Veeco, Rochester, New York) non-contact optical profiler. Three regions from each of three implants of each type were analysed.

Surface chemical analysis was by X-ray photo-electron spectroscopy. For all measurements we used a dual-anode source in a VG Escalab MKII instrument (Thermo VG Scientific, Beverly, Massachusetts) with non-monochromatised Mg K radiation ($h\nu$, 1253.6 eV) operated at 20 mA and 15 kV. Survey spectra were obtained at 90° from the sample surface using a pass energy of 100 eV, 1.0 eV stps, and a 15 x 6 mm slit-width, which resulted in an analysed surface area of 3 x 2 mm. When present, specimen-charging effects were compensated by adjusting the binding energy of the survey spectra so that the binding energy of the hydrocarbon peak was at 285.0 eV. The concentration of each element was determined from the X-ray photo-electron spectroscopy signal area and the corresponding X-ray photo-electron spectroscopy atomic sensitivity factor relative to Fluorine 1s electron. The sensitivity of the technique was 0.1 at 100%. With this technique, measurements below 0.2% are considered contaminant levels.

Canine intramedullary model. A simple canine femoral intramedullary implant model was devised for examining the tissue response to non-load-bearing implants in an environment similar to that of a porous-coated femoral stem. As prior studies have shown that a mature osseous response develops within 12 weeks of surgery, we chose this for our *in vivo* studies.^{42,43} A control implant was inserted into the femur of six dogs and an acid-etched implant inserted on the contralateral side. This model enabled paired analysis of bone ingrowth data from the implants in each animal.

The surgical procedure involved a small, lateral incision over the greater trochanter, creation of a pilot hole in the piriformis fossa, progressive reaming of the intramedullary canal up to 9 mm, and tapping of an implant into position. The procedure was repeated on the contralateral side at the same surgical sitting. Both the implant and dog sizes (30 to 35 kg) were selected to ensure a relatively loose fit of the rods within the intramedullary canal. All dogs returned to normal weight-bearing shortly after implantation.

Fig. 2

Scanning electron micrograph of A) the as-sintered control and B) the acid-etched beads. The acid-etched beads possessed an irregular surface texture (R_a , $1.12 \pm 0.72 \mu\text{m}$) that was significantly different from the as-sintered beads (R_a , $0.09 \pm 0.02 \mu\text{m}$) ($\times 210$).

Histological analysis. Implants were harvested *in situ* and prepared for examination by uncalcified, thin-section histology. The bone-implant specimens were stripped of soft tissue, fixed in 10% buffered formalin, photographed using high-resolution film and radiographed in multiple views using Faxitron X-ray apparatus (Hewlett-Packard, Boise, Idaho). Specimens were then dehydrated in ascending solutions of ethanol, defatted in ether and acetone, vacuum infiltrated with polymethylmethacrylate monomer, and cured at room temperature into a hard acrylic block. Undecalcified

sections 2 mm thick were cut at 10 mm intervals with a low-speed, low-deformation, diamond-bladed cut-off machine (Buehler Corp, Markham, Canada). High-resolution radiographs of the sections were obtained prior to further analysis.

The sections were prepared for backscattered scanning electron microscope (BSEM) imaging to produce a high resolution image of several μm of the uppermost bone-implant surface. This involved progressively polishing the surface down to $0.5 \mu\text{m}$ alumina grit, ultrasonically clean-

Fig. 3

Surface topography of the A) as-sintered control and B) the acid-etched sintered beads as imaged and quantified by the non-contact optical profilometer.

ing, drying and mounting on a stage, and sputter coating with gold-palladium. Using computer-aided image analysis based on grey-scale discrimination, the extent of bone ingrowth was determined. This was defined as the amount of new bone within the pores divided by the area porosity of the porous coating. Since there were differences between the area porosity of the control and acid-etched porous coatings, for acid-etched implants bone ingrowth was normalised for the difference (normalised extent of bone ingrowth_{etched} = [average porosity_{etched}/average porosity_{control}] × extent bone ingrowth_{etched}). Differences in bone ingrowth between implant types were tested for statistical significance using paired Student's *t*-tests, with *p* < 0.05 being significant.

Results

Characterisation of implant surfaces. Scanning electron micrographs of the implant surfaces are shown in Figure 2 and optical profilometry images in Figure 3. The surface roughness of the control sintered beads, $R_a 0.09 \pm 0.02 \mu\text{m}$, was significantly different (*p* < 0.001) to that of the acid-etched beads, $R_a 1.12 \pm 0.72 \mu\text{m}$.

Fig. 4

Chemical composition of the as-sintered control and acid-etched implants. There were no significant differences between the two surfaces.

Fig. 5

Representative AP radiograph of A) the as-sintered control and B) the acid-etched femoral implants. No notable differences are apparent at the bone-implant interfaces.

Comparison of the X-ray photo-electron spectroscopy results between the control and acid-etched implants showed that there was no significant difference between the surface chemistries (Fig. 4).

Fig. 6

Eight paired serial transverse sections from one animal of A) the as-sintered control and B) the acid-etched implants. No complete radiolucencies were apparent in any section. Substantial new bone formation adjacent to both the control and acid-etched implants was evident in all sections.

Fig. 7

Back-scattered scanning electron micrographs of control (left) and acid-etched (right) sections. Implant is white, bone is grey and other material is black. New bone formation within the porous coating is visible in both sections (x 7).

Fig. 8

Graphical representation of the mean extent of bone ingrowth for the as-sintered control implants and acid-etched implants. The 60% relative difference was statistically significant.

Radiographic and histological findings. After harvest and soft-tissue cleaning, the contact radiographs of the femora revealed no obvious differences between the bone-implant interfaces of the control and acid-etched implants (Fig. 5). Radiographs of the transverse serial sections (Fig. 6) revealed similar findings. There were no complete radiolucencies around any of the implants. BSEM revealed that new bone had formed to some extent within the porous coating of both control and acid-etched implants in all histological sections (Fig. 7).

Quantification of bone ingrowth. Analysis of 96 histological sections for area porosity of the porous coating showed that the mean value of the acid-etched implants, 39.6%, was significantly greater than that of the control implants, 34.7% ($p < 0.001$). Considering all of the BSEM images from all 96 sections, bone growth into the control implants averaged $15.8\% \pm 12.3\%$, while bone growth into the acid-etched implants averaged $25.3\% \pm 16.5\%$ (Fig. 8). In relative terms, this represented a 60% enhancement of bone ingrowth with the acid-etched implants. Paired analysis indicated this difference was statistically significant ($p = 0.001$).

Discussion

Long-term, asymptomatic survival of porous-coated joint replacement implants depends largely on biological fixation by bone ingrowth. This enhances mechanical stability, decreases pain that can result from micromovement and

potentially decreases migration of wear particles into the peri-implant space.⁴⁴⁻⁴⁶ Histological retrieval analyses have clearly shown that the extent of bone growth into a porous coating varies widely and never completely fills the porosity, often averaging 10% to 13% of the available space for ingrowth.^{13,46,47} In osteoporotic bone, revision cases, or patients with systemic disease, the challenge of establishing effective bone ingrowth is greater, and significant benefits could be gained if the rate and/or extent of ingrowth could be enhanced.⁴⁸ Our study demonstrated that the simple superimposition of an acid-etched microtexture to sintered Ti beads used for conventional porous coatings increased the extent of bone ingrowth by 60% compared with control surfaces.

Acid etching has also been used as a method to texture the surfaces of dental implants.^{49,50} Here, the etching process is generally secondary to a coarser surface texturing such as grit-blasting or machining of the implant screw threads. Numerous reports indicate that the secondary acid etching of the implant surface generally results in a 10% to 40% increase in bone contact and a significant increase (up to twofold) in pull-out and torque strength.^{49,51,52}

There have been many prior demonstrations of the positive effect of a rough irregular surface texture (R_a , 1 to 7 μm) on bone formation.^{31,32,39,40,53-55} Of relevance in this context are the experimental and clinical studies of implants with calcium phosphate coatings, particularly the plasma-sprayed type of hydroxyapatite (HA) coating, which report significant enhancement of bone attachment by the addition of an HA coating to textured or porous surfaces.^{20,56-59} It is interesting to note that plasma-sprayed HA coatings possess an irregular topography (R_a 5 to 8 μm) in addition to being effective for osseointegration. While the positive effect of HA coatings is usually attributed to their chemical composition, Hacking et al⁴² recently reported the results of an animal model in which about 80% of the bone apposition to HA coatings was due to the stimulatory effect of their microtexture alone, without contribution from calcium and phosphorus chemistry.

The increase in bone ingrowth by the acid etching technique is less than that recently reported by other techniques, such as ultrasound therapy or use of bisphosphonates. With ultrasound stimulation, Tanzer et al¹⁵ reported a 119% mean increase in bone growth into porous tantalum rods in the canine ulna. Using the same model, Bobyn et al⁶⁰ showed that systemic administration of zoledronate enhanced bone ingrowth by a mean of 108%. The acid-etch process described in our study, however, possesses several attributes. Since it is not a line-of-sight method, it can effectively texture the entire porous coating and thus evoke a complete topographical stimulus; this could be important to the creation of an enhanced biological seal against the migration of polyethylene debris from the joint surface.^{17,45,46,61} Acid etching is also a relatively simple and inexpensive manufacturing process and, from a practical viewpoint, existing implants would not need to be rede-

signed to take advantage of its benefits. Finally, since the acid-etched texture is contiguous with the porous coating there is no possibility of debonding or dissolution, thus avoiding concerns with third-body-wear particles or long-term fixation.^{62,63}

The acid-etch process remains to be optimised for clinical application. The effect on bone growth into porous coatings should ideally be evaluated at different time periods and perhaps with different porous coatings in other animal models. We also need to assess the effect of acid etching on the static and fatigue strengths of the porous coating itself and the metallurgical bond to the implant substrate. In a broader context, the acid-etching process would also have to be optimised for specific porous coatings, both in terms of geometry and material. Notwithstanding the indication for additional studies, it is clear from the results of this preliminary experiment that an acid-etched microtexture superimposed on to a porous coating enhances the bone ingrowth response.

Funding for this study was provided by the Canadian Institute of Health Research.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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