The purpose of the current study was to ascertain the relative contributions of surface chemistry and topography to the osseointegration of hydroxyapatite-coated implants. A canine femoral intramedullary implant model was used to compare the osseous response to commercially pure titanium implants that were either polished, grit-blasted, plasma-sprayed with hydroxyapatite, or plasma-sprayed with hydroxyapatite and masked with a very thin layer of titanium using physical vapor deposition (titanium mask). The titanium mask isolated the chemistry of the underlying hydroxyapatite layer without functionally changing its surface topography and mor-

phologic features. At 12 weeks, the bone-implant specimens were prepared for undecalcified thin section histologic evaluation and serial transverse sections were quantified with backscattered scanning electron microscopy for the percentage of bone apposition to the implant surface. Bone apposition averaged 3% for the polished implants and 23% for the grit-blasted implants. Bone apposition to the hydroxyapatite-coated implants averaged 74% whereas bone apposition to the titanium mask implants averaged 59%. Although there was significantly greater osseointegration with the hydroxyapatite-coated implants, 80% of the maximum bone forming response to the implant surfaces developed with the titanium mask implants. This simple, controlled experiment revealed that topography is the dominant factor governing bone apposition to hydroxyapatite-coated implants.

List of Abbreviations Used

- PGE$_2$ prostaglandin E$_2$
- TGF-β transforming growth factor-beta
During the past 2 decades, advances in the development of noncemented hip implants and surgical techniques have rendered noncemented total hip arthroplasty a highly successful procedure.\textsuperscript{2,7,17,30,40} However, there is persistent research focus on the reliability or rate and extent of osseointegration (defined as the direct apposition of bone, resolved at the light microscope level) because the results are not always reproducible and stable fixation of the implant is not always achieved.\textsuperscript{8,9} This particularly is true in revision surgery where bone stock and healing potential often are compromised. Fixation failure often may be related to issues such as the general implant design, the surgical technique, initial implant stability, and the disease process.\textsuperscript{18,21,32,48} However, it also may be attributable to the interaction between bone and implant at a very local, microscopic level. Implant surface chemistry and topography are crucial to implant design yet their precise influence on tissue response and implant fixation is not fully understood.

One approach to increase the likelihood of osseointegration has been to coat implant surfaces with various calcium phosphate formulations.\textsuperscript{1,12,16,24,52} These coatings typically are either of hydroxyapatite or tricalcium phosphate or a combination of both. Because of their finite dissolution rate, they often are described as being bioactive by providing a supplementary source of Ca and P for incorporation into ossifying bone in the immediate periimplant environment.\textsuperscript{16,23–25,35,47,52} The compositional or chemical similarity of hydroxyapatite to bone generally is accepted as the most suitable explanation for its biocompatibility and osteoconductive properties.\textsuperscript{16,23–25,52,59} However, notwithstanding inferences to bioactivity and the possibility of chemical bonding, the exact nature of the interaction between calcium phosphate coatings and bone is not completely known.\textsuperscript{14}

A different approach relies on surface topography (microtexture) instead of chemistry to encourage bone apposition. Unlike hydroxyapatite-coated implants, microtextured Ti implants present a chemically stable bioinert surface of titanium oxide to the perimplant environment. Implants with microtextured surfaces, such as those created by corundumization or grit blasting, possess irregular surface features on the order of only several micrometers and as such are different from porous implant coatings with pore openings of several hundred micrometers.\textsuperscript{17,21} Despite their limited potential for mechanical interlock with new bone compared with porous coatings designed for bone ingrowth, these microtextured implants have been shown experimentally and clinically (under the right conditions of stability) to become osseointegrated and rigidly fixed by bone apposition or ongrowth.\textsuperscript{20,43,54,58,60,61,63,64}

Interestingly, with functional and nonfunctional implants, the bone response to grit-blasted Ti surfaces can be remarkably similar to that which occurs with hydroxyapatite-coated implants.\textsuperscript{13,33,38,52,53,55} Although the topographies of these metallic and ceramic surfaces can be similar, the surface chemistries are different. Both surfaces can enhance osteoconduction along the implant surface in the form of a thin neocortex and promote the filling of substantial gaps between implant and bone.\textsuperscript{52,53,55} This raises the provocative question of which factor, surface chemistry or surface topography, is more important for the stimulation and regulation of bone formation at the hydroxyapatite-bone interface? This question is prompted by two observations.

The first observation is that the surface roughness of grit-blasted Ti implants and hydroxyapatite plasma-sprayed coatings is similar. Surface texture can be expressed by parameters such as $R_p$ (mean size of the five highest peaks) but is most commonly quantified and expressed in terms of the parameter $R_a$, the average departure from the centerline between the surface peaks and valleys (Fig 1). Plasma-sprayed hydroxyapatite coatings generally possess a surface roughness of $R_a = 3$ to 8 $\mu$m and grit-blasted Ti implants used in total hip arthroplasty generally possess an $R_a$ in the range of 3 to 5 $\mu$m.\textsuperscript{15,29,40,49,64} The second observation is the positive or osteoconductive tissue response that has been described in the context...
of grit-blasted Ti implants and plasma-sprayed hydroxyapatite coatings. Interestingly, several studies have been unable to show a difference in response to microtextured implant surfaces with and without hydroxyapatite coating.\(^\text{19,51,62}\) In an 8-year study of 1202 implants, Wheeler\(^\text{62}\) found no statistically significant differences in survival rates between dental implants that had either hydroxyapatite or grit-blasted Ti surfaces. Similarly, Evans et al\(^\text{19}\) found no significant difference in the clinical, histologic, and radiographic outcomes of load-bearing dental implants with or without hydroxyapatite coatings. In a matched pair analysis of hydroxyapatite-coated and Ti plasma-sprayed cementless femoral stems, Rothman et al\(^\text{51}\) found no clinical or radiographic advantage to the use of hydroxyapatite in primary total hip arthroplasty.

Also of interest is the evidence that surface topography alone has a profound effect on osteoblast behavior. Much of the basic experimental work involving grit-blasted Ti implant surfaces has involved cell culture studies. Studies of a range of surface roughnesses have determined that a broad range of cell types show activity that is specific to substrate topography.\(^\text{3,6,31,41,56}\) In vitro studies have shown that smooth surfaces (Ra < 0.5 \(\mu m\)) do not stimulate osteoblastic activity characteristic of bone formation; however, osteoblasts are responsive to surfaces with an Ra ranging from approximately 1 to 7 \(\mu m\).\(^\text{10,44}\) Osteoblasts cultured on surfaces with an Ra ranging from 1 to 7 \(\mu m\) have increased adherence, induction of metabolic activity, and the release of potent osteoinductive extracellular factors such as PG-E\(_2\) and TGF-\(\beta\).\(^\text{40,46}\) Grossner-Schreiber and Tuan\(^\text{27}\) showed that avian osteoblasts formed calcified nodules on grit-blasted Ti surfaces with an Ra of approximately 1.5 \(\mu m\) and not on polished surfaces with an Ra of approximately 0.30 \(\mu m\). Perhaps the most convincing demonstration of the effect of surface topography versus surface chemistry on cell behavior is the work of Curtis and Wilkinson\(^\text{11}\) who showed that on surfaces with chemical and

**Fig 1A–B.** Schematic representations of (A) Ra and (B) Rz are shown. Ra is the mean absolute value of the deviations from the mean roughness (dotted line) to the surface peaks and valleys (solid line) along a surface length L. Rz is the mean value of the five largest peaks or valleys.
topographic patterns opposed to each other at 90°, nanometer-sized topographic patterns overrode cellular influences arising from the chemical patterning. They coined the term topographic reaction to describe these events.

These in vitro studies have been corroborated by numerous in vivo and clinical studies showing that new bone forms on implant surfaces with an $R_a$ of 2.8 to 6.7 $\mu$m. When placed in an osseous environment, stable implants with an $R_a$ less than 0.4 $\mu$m generally are apposed by fibrous tissue that results in a less rigid and therefore less optimal outcome in joint replacement. However, above this 0.5 $\mu$m threshold, surface microtexture stimulates a response that culminates in some degree of osseointegration. Surface topography also has been shown to modulate the rate and pattern of bone formation. Wong et al,63 Feighan et al,20 and Wennenberg et al61 all have shown that the rate of bone apposition to finer textured surfaces is greater for early periods when compared with that for rougher textures. In a canine total hip arthroplasty model, Hacking et al28 showed that surface texture influences the pattern (mean length of individual contact regions) of bone formation at the implant surface.

The use of joint replacement implants with hydroxyapatite-coated or grit-blasted Ti surfaces is prevalent worldwide; however, there has been little work that reconciles their generally accepted but presumably different mechanisms of osseointegration. It is essential to the process of implant design to resolve the relative contributions of surface chemistry and topography to the osseointegration of hydroxyapatite-coated implants. There also are practical arguments for clearly distinguishing between these design parameters. Surface microtexturing generally does not involve heat treatments for bonding a coating to the substrate, thereby eliminating issues related to local or bulk deleterious effects of heat treating on the implant. Because microtextured surface treatments are not additions to the substrate, there is no risk of particle debonding or coating dissolution that could cause loss of implant fixation or loose bodies that could damage the articulating surfaces and accelerate wear. Given the increasingly cost-conscious climate of today’s healthcare system, it also is notable that microtextured implants generally can be manufactured at reduced cost compared with porous-coated or hydroxyapatite-coated devices.

Although there are many studies that attest to the positive effect of hydroxyapatite coatings on osseointegration, this effect is invariably described and conclusions are made without an appropriate control surface that was normalized for surface topography and morphologic features. Given these fundamental and practical considerations, the purpose of the current study was to ascertain the relative contributions of surface chemistry and topography to the bone forming tissue response to hydroxyapatite-coated implants using an in vivo canine implant model. The study hypothesis was that surface topography is the dominant factor influencing bone formation at an implant surface.

**MATERIALS AND METHODS**

**Physical Vapor Deposition of Ultra Thin Titanium Film (Titanium Mask)**

Because of differences in manufacturing and material properties it only has been possible to approximate the surface topography of hydroxyapatite-coated implants with grit-blasted Ti implants. Because subtle differences in surface topography and morphologic features can have a significant effect on cell behavior, this inability to precisely match surface topography has been the prime confounding variable in comparisons of the effects of hydroxyapatite and nonhydroxyapatite surfaces on periimplant cell differentiation and tissue formation. A key element in the current approach to determining the relative influence of surface chemistry and topography was the development of a new technique for isolating (masking) implant surface chemistry without altering topography. This was accomplished by applying at the atomic level, a dense, homogeneous, and extremely thin film ($< 100$ nm) of commercially pure Ti to the hydroxyapatite substrate (Fig 2) by physical vapor deposition. The physical vapor deposition process com-
monly is used for the production and deposition of thin films in the electronics industry and films produced in this manner are hard and resistant to abrasion and chemical attack.\textsuperscript{34,42,50}

**Femoral Intramedullary Implants**

Twenty commercially pure Ti cylindrical implants 9 cm long and 0.9 cm in diameter were manufactured (Implex Corp, Allendale, NJ) for surgical placement within the femoral intramedullary canal of experimental mongrel dogs (Fig 3). Four different implant groups were prepared according to surface treatment. Four of the intramedullary rods were polished after machining (polished). Four rods were microtextured using industry standard alumina-oxide grit blasting techniques (grit-blasted Ti). Six rods were grit-blasted and subsequently plasma-sprayed with a layer of hydroxyapatite using industry standard techniques (hydroxyapatite). A final group of six rods was grit-blasted, hydroxyapatite-coated, and then chemically masked with a thin physical vapor deposition film of commercially pure Ti as described above (titanium mask).

The in vivo studies were used to assess the tissue responses to surfaces of identical topography and morphologic features that exposed either hydroxyapatite or commercially pure Ti (titanium mask group) to the bone environment. In addition, the polished and grit-blasted Ti groups served as controls for comparisons of tissue response. All implants were sterilized by gamma irradiation.

**Fig 2A–B.** (A) A schematic representation (not to scale) shows an osteoblast on a Ti mask hydroxyapatite surface. The Ti mask (black) intimately follows the surface contours and isolates the underlying hydroxyapatite. (B) A scanning electron micrograph shows a polished (Pol) Ti surface with an ultrathin Ti film applied by plasma vapor deposition (PVD). The arrow delineates the junction between the coated and noncoated regions. The thinness of the coating and the persistence of original surface scratches from the polishing process can be seen.

**Fig 3A–D.** This photograph shows the (A) polished, (B) grit-blasted Ti, (C) hydroxyapatite, and (D) Ti mask, canine femoral intramedullary rods.
Canine Intramedullary Model

A simple canine femoral intramedullary implant model was devised for examining the tissue response to nonload bearing implants in an environment similar to that of a cementless femoral stem. Prior studies with such intramedullary implants possessing microtextured surfaces have shown that a mature osseous response develops within 12 weeks of surgery. This period therefore was selected for the in vivo studies. There were two surgical groups of dogs. In the test group, one hydroxyapatite rod and one Ti mask rod were inserted bilaterally into the femurs of six dogs. In the control group, one polished Ti rod and one grit-blasted Ti rod were inserted bilaterally into the femurs of four dogs.

A small lateral incision was made over the greater trochanter, a pilot hole was created in the piriformis fossa, the intramedullary canal was reamed progressively as much as 9 mm, and the implant was tapped into position. The implant and dog sizes (30–35 kg) were selected to ensure a relatively loose fit of the rods within the intramedullary canal. Bilateral implantations were done at the same surgical setting (Fig 4). All dogs returned to normal weightbearing shortly after implantation.

Characterization of Implant Surfaces

Implant Topography

Scanning electron micrographs of all implant surfaces were obtained to provide a qualitative impression of surface topography. In addition, topography was quantified using a Wyko NT 2000 (Veeco, Rochester, NY) noncontact optical profiler. Three regions from each of three implants of each type were analyzed.

Surface Chemistry

Surface chemical analysis was done using x-ray photoelectron spectroscopy. All measurements done using a dual-anode source in a VG Escalab MKII instrument (Thermo VG Scientific, Beverly, MA) with nonmonochromatized Mg Kα radiation (hv = 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 steps, and a 15 mm × 6 mm slit-width, which result in an analyzed surface area of 3 mm × 2 mm. When present, specimen-charging effects were compensated by adjusting the binding energy of the survey spectra to fix the binding energy of the hydrocarbon peak at 285.0 eV. The concentration of each element was determined from the x-ray photoelectron spectroscopy signal area and the corresponding x-ray photoelectron spectroscopy atomic sensitivity factor relative to Fluorine 1s electron. The sensitivity of the technique was 0.1 at 100% and measurements below 0.2% were considered contaminant levels.

Hydroxyapatite Coating

Hydroxyapatite implants were coated using commercial grade plasma spray techniques (Implex Corp, Allendale, NJ). The process resulted in a 60-μm thick hydroxyapatite coating that was 98% hydroxyapatite and 64% crystalline with a density of 99% and a Ca:P ratio of 1.67.

Physical Vapor Deposition Titanium Mask Film

Multiple surface regions on three Ti mask rods were analyzed by x-ray photoelectron spectroscopy to determine whether the underlying hydroxyapatite Ca and P chemistry could be detected. In addition, hydroxyapatite rods (for the Ca and P profile) and commercially pure Ti rods (for the profile of a commercially pure Ti surface) and Ti mask commercially pure Ti rods were analyzed to provide control profiles.

Also, the resistance to dissolution of the Ti mask film used in this experiment was determined by immersing three hydroxyapatite and three Ti mask rods in 500 mL of Ringer’s lactate (Baxter Corp,
Toronto, Ontario) for 90 days at 37°C. Aliquots were obtained at Days 0, 30, 60, and 90. Aliquots were analyzed by sequential inductively coupled plasma spectrometer (Trace Scan, Jarrell-Ash Corp, Franklin, MA). Certified commercial standards (1000 ppm) were used and subsequently were diluted with deionized water. Standard concentrations bracketed the test samples. Two-level standardization was used and Ca, P, and Ti compounds were used in the standard preparation. Detection limits for Ca and Ti by this system were in the range of 5 parts per billion.

**Histologic Analysis**

Implants were harvested in situ and prepared for undecalcified thin section histologic evaluation. The bone-implant specimens were stripped of soft tissue, fixed in 10% buffered formalin, photographed, and radiographed in multiple views using high-resolution film and a Faxitron x-ray apparatus (Hewlett-Packard, Boise, ID). Specimens were dehydrated in ascending solutions of ethanol, defatted in ether and acetone, vacuum infiltrated in polymethylmethacrylate monomer, and cured at room temperature into a hard acrylic block. Undecalcified thin sections approximately 1 mm thick were made at 1-cm intervals with a low-speed, low-deformation, diamond-bladed cut-off machine (Buehler Corp, Markham, Ontario). High-resolution radiographs of the thin sections were obtained before additional analysis.

The thin sections were prepared for backscattered electron microscope imaging. This involved progressively polishing the bone-implant surface down to 0.5 μm alumina grit, ultrasonically cleaning, drying and mounting on a stage, sputter coating with gold-palladium, and imaging in back-scattered electron mode to produce a high resolution image of the uppermost several microns of the bone-implant interface. Using computer-aided image analysis, regions of bone in direct contact with the implant surface were measured, summed, and expressed as a percentage of the implant perimeter. One hundred sixty histologic sections were analyzed for bone apposition. Differences in bone apposition between implant types were tested for statistical significance using paired and unpaired Student’s t tests, with p < 0.05.

**RESULTS**

**Characterization of Implant Surfaces**

Scanning electron micrographs of the implant surfaces are shown in Figure 5 and optical profilometry images are shown in Figure 6. The Ra and Rz values for the different implant surfaces are shown in Table 1. The surface roughness of the polished Ti rods was Ra = 0.09 ± 0.02 μm. The grit-blasted Ti rods had a surface roughness of Rz = 3.64 ± 0.72 μm. These surface topographies were significantly different (p < 0.001). Surface roughness measurements of hydroxyapatite rods and Ti mask rods yielded identical values of Ra = 5.58 ± 1.1 μm. This confirmed that the Ti mask did not alter the implant topography and enabled an equitable comparison of the tissue responses to the hydroxyapatite and Ti mask surface chemistries (Fig 6). The Rz (mean of five highest peaks or valleys) measurements revealed a very low value for the polished surface (1.5 μm), a relatively high value for the grit-blasted Ti surface (42.9 μm) and identical values for the hydroxyapatite and Ti mask surfaces (50.2 μm). The Rz values were approximately an order of magnitude greater than the Ra values.

**Effectiveness of the Titanium Mask**

The surface chemistry of the physical vapor deposition Ti mask film was not significantly different from that of an uncoated commercially pure grit-blasted Ti surface, a polished Ti surface or a Ti mask grit-blasted Ti surface. For the hydroxyapatite surfaces, O was detected at the highest level followed by C, Ca, and P (Fig 7). After analysis of multiple locations on different implants, only trace amounts of Ca at contaminant levels (0.2%) were detected on the polished Ti rods. No Ca or P was detected on the grit-blasted Ti or Ti mask rods.

There was no detectable amount of Ti or increase in Ca or P concentration in solution from the Ti mask rods that were immersed in Ringer’s lactate at either 30, 60, or 90 days. The detection limit for Ti, Ca, and P was 5 parts per billion.

**Radiographic and Histologic Findings**

After specimen harvest and soft tissue cleaning, the contact radiographs of the femurs revealed no obvious differences between the bone-implant interfaces of the hydroxyapatite and Ti mask implants. Intramedullary bone around the
hydroxyapatite and Ti mask implants generally appeared more extensive and more dense than around the grit-blasted Ti implants (Fig 4). Radiographs of the transverse serial sections and backscattered scanning electron microscope images revealed similar findings but with progressively more detail (Figs 8, 9). There were no complete radiolucencies around any of the grit-blasted Ti, hydroxyapatite, or Ti mask implants. Two grit-blasted Ti implants had regions of incomplete radiolucencies on several of the transverse sections. New bone formation and/or densification of existing bone was clearly apparent adjacent to the surfaces of the grit-blasted Ti, hydroxyapatite, and Ti mask implants in approximately all histologic sections and backscattered scanning electron microscope images.

### TABLE 1. Surface Topography Measurements of Femoral Implants

<table>
<thead>
<tr>
<th>Implant Type</th>
<th>$R_a \pm$ Standard Deviation ($\mu$m)</th>
<th>$R_z \pm$ Standard Deviation ($\mu$m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polished titanium</td>
<td>0.09 ± 0.02</td>
<td>1.54 ± 0.40</td>
</tr>
<tr>
<td>Grit-blasted titanium</td>
<td>3.64 ± 0.72</td>
<td>42.88 ± 9.06</td>
</tr>
<tr>
<td>Hydroxyapatite-coated</td>
<td>5.58 ± 1.08</td>
<td>50.18 ± 5.69</td>
</tr>
<tr>
<td>Titanium mask</td>
<td>5.58 ± 1.10</td>
<td>50.18 ± 5.76</td>
</tr>
</tbody>
</table>

Fig 5A–D. Scanning electron micrographs show the (A) polished, (B) grit-blasted Ti, (C) hydroxyapatite, and (D) Ti mask implant surfaces. There is apparent similarity between the hydroxyapatite and Ti mask surfaces.
Fig 6A–D. Surface topography of the (A) polished, (B) grit-blasted Ti, (C) hydroxyapatite, and (D) Ti mask implants as imaged and quantified by the noncontact optical profilometer are shown. The differences in $R_a$ between the polished and grit-blasted Ti surfaces and the similarities in $R_a$ and morphologic features of the surface between the hydroxyapatite and Ti mask surfaces are evident.

Fig 7. The chemical composition is shown of a polished (Pol) Ti and a grit-blasted (GB) Ti implant (controls), a hydroxyapatite-coated implant, and a Ti mask implant. There are no significant differences between the polished Ti, grit-blasted Ti, and Ti mask surfaces. The Ti mask completely isolated the underlying chemistry of the hydroxyapatite substrate.
**Fig 8A–D.** Serial transverse sections show (A) polished, (B) grit-blasted Ti, (C) hydroxyapatite, and (D) Ti mask matched implant pairs. The complete radiolucencies around many of the polished implant sections can be seen. Varying degrees of new intramedullary bone formation adjacent to most sections of the grit-blasted Ti, hydroxyapatite, and Ti mask implants can be seen.

**Fig 9A–D.** Backscattered scanning electron micrographs of representative transverse sections of (A) polished, (B) grit-blasted Ti, (C) hydroxyapatite, and (D) Ti mask implants show the typical osseous response and bone apposition.
In contrast to these findings, a thin radiolucent line was visible adjacent to all polished Ti implants that was readily apparent in transverse serial sections and backscattered scanning electron microscope images (Figs 8, 9). This radiolucency extended around virtually the entire implant in every case.

Quantification of Bone Apposition
Considering all of the backscattered scanning electron microscope images from the transverse histologic sections, bone apposition to the hydroxyapatite rods averaged 73.6% ± 22.7% whereas bone apposition to the Ti mask rods averaged 59.1% ± 26.2% (Fig 10). Paired analysis indicated this difference was statistically significant (p = 0.002). Bone apposition to the grit blasted Ti rods averaged 23.0% ± 11.0%, statistically significantly less than apposition to the hydroxyapatite (p < 0.0001) and titanium-mask rods (p < 0.0001). Bone apposition to the polished Ti rods averaged 2.8% ± 2.0%, a statistically lower value than measured for the hydroxyapatite (p < 0.0001), Ti mask (p < 0.0001), and grit-blasted Ti rods (p < 0.0001, paired analysis).

DISCUSSION
The essence of the current study was the use of a novel, ultrathin physical vapor deposition Ti film that effectively masked or isolated the underlying hydroxyapatite chemistry without functionally altering its topography. The Ti mask technique enabled the first direct and equitable comparison of surface chemistry and surface topography and the discovery of their respective contributions to implant osseointegration. On average, the hydroxyapatite implants showed statistically significantly more bone apposition than the Ti mask implants, but the mean difference was not very large. Approximately 80% of the maximum bone appositional response to the intramedullary implants (59/74 × 100%) was attributable to the surface topography of bioinert Ti, without influence from the bioactive hydroxyapatite chemistry. This represents new and compelling information about the fundamental parameters governing osseointegration, derived from a simple experiment that was strictly controlled for all variables but that of surface chemistry.

No Ca or P was detected on the Ti mask implant surfaces with numerous xray photoelectron spectroscopy surface scans of the upper 10 nm of the Ti mask film. This confirmed that the Ti mask effectively isolated the hydroxyapatite chemistry from the surrounding environment. The durability and protective nature of the Ti mask also was shown by a lack of detectable Ti dissolution or escape of Ca or P in a simulated in vivo environment as long as 90 days. In addition, the Ti mask surface chemistry was not significantly different from that of a polished Ti implant, grit-blasted Ti implant, or a Ti mask implant. The results from the topographic analysis of the hydroxyapatite and Ti mask samples also confirmed that the physical vapor deposition Ti film did not alter the surface topography in any significant manner.

The control data derived from the comparison between the polished and grit-blasted Ti surfaces also were instructive. They confirmed that very smooth implant surfaces generally...
are not apposed by osseous tissue and that grit-blasted surfaces are conducive to substantial bone formation and apposition. These are not new findings but were important to show in the context of the same experimental model used for the hydroxyapatite and Ti mask implants. Interestingly, there was approximately a threefold difference in bone apposition between grit-blasted and hydroxyapatite implants (23% versus 74%, respectively) in this study. The most likely explanation for this was the difference in surface topography between grit-blasted Ti ($R_a = 3.6 \mu m$) and hydroxyapatite ($R_a = 5.6 \mu m$) surfaces. In most prior studies comparing implants with grit-blasted and hydroxyapatite surfaces, substantially more bone formation also was documented adjacent to the hydroxyapatite surfaces.4,19,24,25,39,52,55,57 However, because plasma-sprayed hydroxyapatite implants generally have a rougher surface and different morphologic features than grit-blasted implants, not controlling for surface topography has confounded prior conclusions regarding the effect of hydroxyapatite chemistry on osseointegration.25,26,39,52 The finding of increased bone apposition to hydroxyapatite surfaces in uncontrolled experiments, repeated over time in numerous studies, has led to a widely accepted premise about the importance of hydroxyapatite chemistry for osseointegration.4,19,25,26,39,52,55,57 The results of the current study clearly indicate that this premise is somewhat exaggerated. It is worth noting, separate from the principal finding of this study, that the plasma spray technique used for the hydroxyapatite coatings resulted in a surface topography and morphologic features that were highly effective for osseointegration, much more so than obtained with grit blasting (59% versus 23% bone apposition, comparing Ti mask with grit-blasted Ti surfaces).

Some comparisons of hydroxyapatite and nonhydroxyapatite surfaces that have been reasonably matched for topography have reported equivocal bone apposition results. This is apparent in the study of Carlsson et al5 who compared nonload-bearing hydroxyapatite-coated implants and microtextured Ti implants, approximately matched for surface roughness, in the human knee with arthritis. They found no significant difference in the tissue reaction and fixation strength to the topographically related but chemically different surfaces. The results led them to postulate that surface topography may be more important for osseointegration than surface chemistry.

In a comparison of uncoated and hydroxyapatite-coated grit-blasted Ti implants in the medial condyle of the canine knee where controlled micromotion was introduced, Søballe et al53 reported that there was significantly more fibrous tissue and less bone adjacent to the grit-blasted Ti than the hydroxyapatite implants. The implants were approximately matched for surface topography (grit-blasted Ti $R_a = 4.1 \mu m$, hydroxyapatite $R_a = 4.7 \mu m$). However, when micromotion ceased, fibrous tissue was replaced by bone for both implants and no significant differences in either bone apposition or fixation strength subsequently were measured.

A final note concerning implant surface features is that standard methods of quantifying topography may not be sufficient for describing the parameters that are important, and more specifically, optimal for stimulating osteoblastic activity. It is clear from a preponderance of literature that osteoblasts and their precursor cells are exquisitely sensitive to subtle changes in surface architecture.3,6,10,11,27,28,31,36,40,44,46,61,63 It may be that the morphologic features of the surface, that is, not just the sizes of the peaks and valleys, but as yet undefined characteristics of individual features such as their spatial distribution or radii or curvature is just as important as the sizing parameters. This clearly is an important area for future research and understanding.

The current study quantified the relative contributions of surface chemistry and topography to the osseointegration of hydroxyapatite-coated implants. The results clearly support the study hypothesis, namely that topography is the dominant factor governing new bone apposition. This is not to suggest that hydroxyapatite chemistry is inconsequential to the os-
seous response, but that it may be of much less benefit than previously thought. Using the Ti mask technique it will be helpful to evaluate this finding in the context of other models that incorporate different periods, different calcium phosphate coating chemistries and topographies, bone-implant gaps, and bone-implant micromotion.

The implications of this finding are wide ranging. It means that many previous experimental and clinical studies citing the positive effects of hydroxyapatite coatings have to be critically reviewed and reconsidered with a new perspective. It also means that future studies of this type have to maintain absolute control over topography and morphologic features if implant chemistry is to be evaluated for its bone response in an implant model or surgical application. It will no longer suffice to approximately match surfaces for topography; this variable now must be eliminated in study design, not just casually addressed. In addition to these considerations are the practical issues relating to the manufacturing techniques of different implant surfaces and their relative cost, reliability, and benefit to osseointegration. Advantage may be gained in the future by more deeply exploring and developing simple and cost-effective methods for surface texturing of orthopaedic implants that use the principles elucidated in this study.

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