Progression of human bone ingrowth into porous-coated implants

Rate of bone ingrowth in humans

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We report the measured progression of human cancellous bone ingrowth into load-bearing porous-coated titanium implants over 5 time periods (0, 3, 6, 9, and 12 months). There was a statistically significant progression of bone ingrowth into the implants over a 9-month period, but the 9- and 12-month data were not different. Investigators are advised to analyze time "0" implants in order to distinguish mechanical impaction of bone from the biological process of bone ingrowth.

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Early investigations of bone ingrowth using canine and baboon models (Galante et al. 1971, Bobyn et al. 1980), non-quantitative human implant retrievals (Collier et al. 1988) and other studies (Harris et al. 1983, Harris and Jasty 1985, Sumner and Galante 1990) suggest that bone ingrowth is a fracture healing event occurring within 4–12 weeks postoperatively.

More recent studies (Linder et al. 1988, Bloebaum et al. 1992, 1994, Hofmann et al. 1993, Carlsson et al. 1994) have suggested that the bone ingrowth process in human cancellous bone proceeds much slower. These studies found that the bone response at the interface had trivial amounts of callus type woven bone and limited endochondral bone formation, demonstrating that the newly formed cancellous bone in general grows appositionally from the bone fragments and host trabeculae to interdigitate initially with the outermost layer of the porous coating (Bloebaum et al. 1992, 1994).

We quantitatively and histologically documented the progression of human cancellous bone in a series of 36 commercially pure titanium porous-coated cylinders implanted into the load-bearing region of the human distal femoral condyles with arthrosis.

Material and methods

Implants

The implants were cylindrical in shape and had an inner core manufactured from titanium alloy (Ti6Al4V), with a commercially pure titanium porous coating. The implant measured 8 mm in length and 5 mm in diameter and had an average pore size of 400 μ (range 300–500 μ), with an average of 55% porosity (Intermedics Orthopedics, Inc., Austin, Texas).

Surgical implantation

The human model has been approved by the Institutional Review Board and has been previously reported (Hofmann et al. 1992). 36 patients, each with bilateral knee arthrosis, consented to participate in this study (Table). The ages of the patients averaged 67 (51–82) years.

Staged, bilateral total knee arthroplasties (TKA) are the prescribed treatment for patients in our community when both knees have severe arthrosis. During the first TKA surgery, and only after uncomplicated completion of the initial arthroplasty, the cylindrical implant was inserted percutaneously into the weight-bearing region of the contralateral medial femoral condyle flush with the articulating surface. With the knee flexed to 90 degrees, a 15–20 mm vertical incision was made on the medial aspect of the contralateral knee and carried down to the articular sur-

Demographics and time in situ of the 36 consenting patients. The percent porosity of each implant, host bone and bone ingrowth are shown for each patient. The mean and standard deviation (SD) for each group and category are shown at the bottom of each period

Group	Patient	Gender	Age years	In situ weeks	Implant %	Host bone %	Ingrowth %
Time 0	1	F	67	0	50	23	2
	2	M	51	0	47	8	1
	3	F	66	0	46	23	1
	4	F	68	0	49	37	2
	5	F	56	0	52	35	1
	6	F	72	0	56	34	1
	Mean (SD)		63 (8)	0 (0)	50 (4)	27 (11)	1 (1)
3 Months	7	F	82	6	49	35	6
	8	M	77	6	50	19	10
	9	M	73	7	51	32	7
	10	M	73	7	54	36	5
	11	M	69	7	56	48	16
	12	M	61	8	45	40	9
	13	F	64	8	54	46	11
	14	M	58	10	60	16	5
	15	M	77	11	51	55	13
	16	M	66	13	51	47	19
	Mean (SD)		70 (8)	8 (2)	52 (4)	37 (13)	10 (5)
6 Months	17	M	52	14	53	40	20
	18	M	69	14	54	45	16
	19	M	72	15	54	16	10
	20	M	54	15	59	25	6
	21	F	63	20	54	43	17
	22	F	68	21	57	47	9
	23	M	72	21	60	40	28
	Mean (SD)		64 (8)	17 (3)	56 (3)	37 (12)	15 (8)
9 Months	24	M	67	30	55	48	24
	25	M	75	30	57	54	19
	26	F	62	30	61	36	26
	27	M	76	35	55	68	37
	28	F	63	35	54	35	22
	Mean (SD)		69 (7)	32 (3)	56 (3)	48 (14)	26 (7)
1 Year	29	F	73	42	53	37	15
	30	M	64	42	55	57	19
	31	M	69	49	58	47	24
	32	M	72	52	53	44	29
	33	F	82	52	60	60	46
	34	M	76	59	58	51	19
	35	F	67	62	52	19	13
	36	M	52	131	50	57	27
	Mean (SD)		69 (9)	61 (29)	55 (3)	47 (14)	24 (10)
Overall	Mean (SD)		67 (8)	24 (26)	54 (4)	39 (14)	15 (11)

face. A 4.5 mm wide by 8 mm deep hole was drilled into the medial femoral condyle. Normal saline was used to flush out gently any loose debris left from the drilling process. Using a mallet, the implant was inserted into place. Additional operative time for insertion of the implants averaged 15 minutes.

Time 0 implants

In these 6 patients, the bone and implant specimens were obtained at the time of primary surgery.

Explantation of implants

The in vivo load-bearing implants averaged 36 (6–131) weeks in situ, depending on the clinical needs and wishes of each patient. During the second TKA surgery, the implants were retrieved en bloc along with the distal portion of the femoral condyle, which is normally resected and discarded at the time of TKA.

There were no complications with either the implantation or explantation of the implants. Intraoperative observations on the bearing surface of the tibia and gross photography of the explanted implants confirmed that the implants were placed appropriately. The burnished surfaces of the plugs and grooves in the opposing articulating surfaces of the tibial plateaus confirmed that load bearing on the implants had occurred. High resolution radiographs of the retrieved

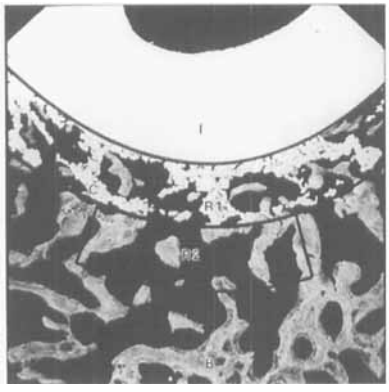

Figure 1. BSE photomicrograph of the implant (I), porous coating (C) and bone (B). R1 represents the region of the porous coating analyzed for bone ingrowth. R2 shows the periprosthetic region measured to determine the relationship of host tissue to bone ingrowth.

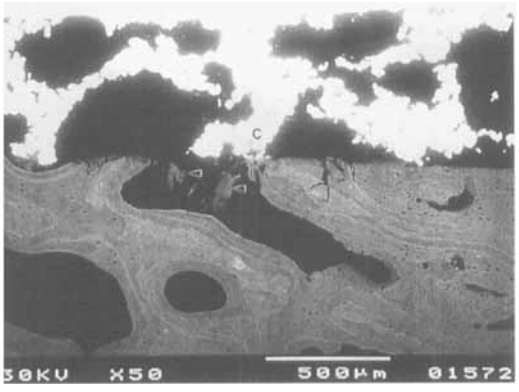

Figure 2. BSE image showing host bone (H), bone chips (arrows) and porous coating (C) at time '0' implantation. Note that there is no bone in the porous coating in this region of the implant. Black region: cells, bone marrow and soft tissue.

specimens demonstrated no radiolucencies or other radiographic signs of loosening of the implants.

Implant processing

Each explanted specimen was immediately fixed in 70% ethanol, dehydrated in graded alcohols to absolute, and cleared in xylene. Specimens were embedded in polymethylmethacrylate, using standard laboratory techniques (Emmanual et al. 1987).

The embedded specimens were sectioned perpendicular to the long axes of the cylindrical implants, using a water-cooled, high-speed, low-feed bone saw with a diamond-impregnated blade. 3 approximately equally thick sections of the porous coatings and surrounding bone were obtained. To remove any residual scratches, one face of each section was ground, using ascending grades of wet/dry grinding papers and polished to a high luster with 1 µ type alumina polishing suspension.

Bone ingrowth analysis

The polished faces of the specimens were sputter-coated with a thin layer of gold at 40 mTorr for 90 seconds in a Hummer VI sputter-coater (Anatech Ltd., Arlington, Virginia, USA). A scanning electron microscope equipped with backscatter electron (BSE) detector (JEOL BEI-35 scintillating detector, JEOL Technics Ltd., Tokyo, Japan) was used for imaging. At a magnification of 50×, 4 BSE photomicrographs of each section were taken around the perimeter of each section of the implant.

Following the BSE image analysis, the sections were stained with Villanueva or Rapid Bone Stain (Wasatch Scientific, Salt Lake City, Utah, USA) for histological analysis.

Data analysis

2 regions (Figure 1) of each photomicrograph were defined, using a transparent template: a region for bone ingrowth inside the porous coating and a region of surrounding periprosthetic bone outside the perimeter of the coating (Hofmann et al. 1992). Using an IBM-compatible computer, digitizing pad and custom software routines, the photomicrographs were digitized to determine the porosity of the implant, the volume fraction bone ingrowth into the porous coating and the volume fraction of the periprosthetic bone in the surrounding regions for each set of implant sections.

The data were not normally distributed and therefore, nonparametric statistical techniques were required. The Kruskal-Wallis test for nonparametric data was used to determine significant differences in the data, followed by a Kruskal-Wallis multiple comparison Z-value test. Statistical significance was established, using a p-value of less than 0.05 and a power of 0.80.

Results

Porosity and bone ingrowth analysis

The volume fraction of bone measured within the porous coating in the time "0" patients was 1 (1–2)% (Table). This represents the amount of bone impacted into the porous coating at the time of insertion (Figure 2). The 3-month patients had an average of 10 (5–19)% bone in the porous coating (Figure 3). This represented an early progression of bone ingrowth that was differed significantly from the time "0" implants ($p = 0.05$).

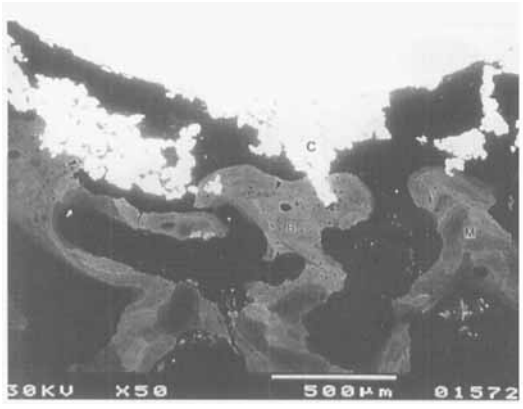

Figure 3. BSE image of bone (B) beginning to interdigitate and osseointegrate with the porous coating (C) at 3 months. Newly formed bone can be distinguished by the large circular lacunae (arrows) as compared to the small elliptical lacunae in the mature bone (M). Black region: cells, bone marrow and soft tissue.

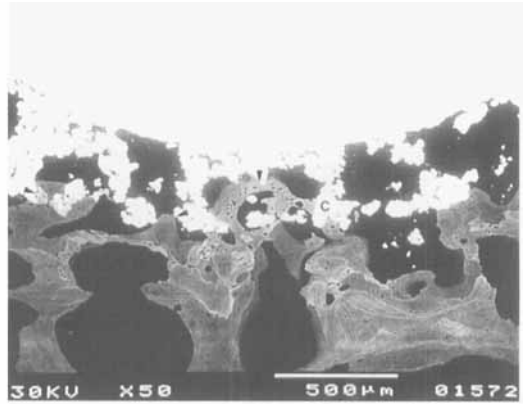

Figure 4. BSE image of 12-month retrieval showing mature lamellar type bone (B) within the porous coating (C). Bone penetrates (arrows) to osseointegrate with the substrate.

Bone ingrowth continued to progress into the porous coating at the 6- and 9-month time periods (Table). The 6-month implants had an average of 15 (6–28)% bone in the porous coating, while the 9-month group showed continued bone ingrowth, averaging 26 (19–37)% in the porous coating. The bone ingrowth in the 12-month group measured 24 (13–46)% (Figure 4). This did not differ ($p = 0.6$) from the 9-month group. When the data were organized graphically (Figure 5), it became evident that there was a continuous progression of bone ingrowth from the time "0" implantation, with the plateauing of the bone ingrowth occurring around 9 months.

The overall volume fraction of the "host" bone just outside the porous coating averaged 39 (8–68)%. The average volume fraction of the 3-month, 6-month, 9-month and 12-month groups (Table) were not measurably different ($p = 0.1$). However, the time "0" group had only two-thirds as much bone in the immediate periprosthetic region as the other three time groups ($p = 0.02$). This indicates that periprosthetic bone formation was stimulated by the implantation process and the resulting perturbation of the bone tissue.

Histology

The time "0" implants showed bone chips clustered along the interface having been displaced by the drilling and the process of inserting the implants. There were red blood cells and bone marrow mixed in with the bone chips. Within the porous coating, again a similar histological appearance to the interface, with the exception of a reduced number of bone chips seen in the porous coating, some areas of the porous coating being void of tissue.

Interface observations of the 3-month implants showed no observable endochondral bone, but they demonstrated new bone formation along the edges of the host bone and bone chips within the porous coating. Osteoblastic activity was apparent in the many epithelioid layers of osteoblasts observed along the surface of the osteoid interposed between the osteoblasts and host bone and bone chips at the interface. By 6 months, although the bone was obviously continuing to remodel, the presence of the epithelioid osteoblast layers and osteoid was reduced compared to than in the 3-month series.

By the 9- and 12-month periods, osteoid seams with osteoblasts were rarely seen morphologically, indicating the general quiescence of the bone remodel-

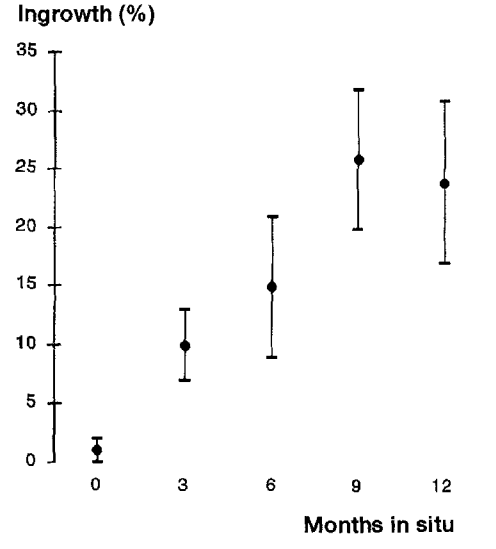

Figure 5. Mean bone ingrowth into porous-coated implants over 5 periods. Bars indicate 95% confidence limits.

ing. It should be noted that fibrous tissue and/or bone marrow were present in regions of the porous coating where bone did not completely fill the porous coating.

Discussion

Our findings demonstrate that human bone ingrowth plateaus around the 9-month postoperative period. These results in human cancellous bone conflict with previous qualitative investigations which reported bone ingrowth within 4–12 weeks (Galante et al. 1971, Bobyn et al. 1980, Harris et al. 1983, Harris and Jasty 1985). One of the reasons for the differences between our findings and others was that animal models were used. Charnley (Waugh 1990), Bloebaum et al. (1993) and Bobyn et al. (1981, 1990) have cautioned that bone remodeling and healing in animals may not be representative of bone healing in humans. This may explain why Bloebaum et al. (1994) and Carlsson and Linder (Linder et al. 1988, Carlsson et al. 1994) observed bone appositional healing in human cancellous bone, whereas advocates of the fracture healing model described their findings as similar to cortical bone healing properties after fracture.

There are other factors which may have contributed to the confusion in the literature. Many investigators did not conduct time "0" implantation which would be essential in interpreting the time frame for bone ingrowth. Spector et al. (1983) mentioned that they had deliberately under-broached the bone to allow for bone impaction. This has been a common practice in many bone ingrowth investigations. The absence of time "0" implantations in these types of investigations would make it impossible to isolate the biological event of bone ingrowth from the combination of bone impaction and bone ingrowth.

Another factor that must be considered is the type of porous coating. For example, if the coating protrudes beyond the substrate and if the bone preparation is undersized, then again, time "0" implants would be required to distinguish between initial bone impaction and/or bone ingrowth. The porous coating used in our investigation is flush with the substrate and does not protrude. This would explain the limited impaction seen in the time "0" implants.

We also found new bone formation in the periprosthetic bone at the interface as well as corresponding advancement of the bone into the porous coating over the 9-month period. The new bone was observed forming along the surface of the host trabeculae and the remnant bone chips caused by drilling of the hole prior to implant placement. These observations do not support the fracture healing model that is commonly reported, but not histologically quantitatively measured using histometric and fluorochrome labeling techniques.

A careful review of the literature now suggests that, to achieve reproducible skeletal attachment by human bone ingrowth into porous coatings, the coating should be within 50 μm of the human cancellous bone (Bloebaum et al. 1994). The implant should be inherently stable and should limit activity within the first 9 months after surgery. Bloebaum et al. (1994) demonstrated a regional acceleratory phenomenon at the interface of load-bearing implants, but human cancellous bone apposition remodeling was measured to repair slowly at approximately 1 μm/day, even when bioactive coatings such as hydroxyapatite are used in human bone (Hofmann et al. 1993). This helps to explain the relatively slow progression of bone ingrowth observed in this study on human cancellous bone and other studies on retrieved porous-coated tibial components from humans (Bloebaum et al. 1992).

In conclusion, our findings show that maximal bone ingrowth is achieved around 9 months post-implantation and that the progression of human cancellous bone ingrowth into the porous coating is slower than previously reported. These quantitative results conflict with previous animal and clinical studies that did not perform time "0" implants to determine the combination of the effects of bone impaction and bone ingrowth on the amount of bone observed in the porous-coated implants.

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