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Cancellous impaction grafting in the human femur

Histological and radiographic observations in 6 autopsy femurs and 8 biopsies

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ABSTRACT – 6 whole postmortem femurs and 8 femoral biopsies were studied histologically, 3 months to 8 years after cancellous impaction grafting with a cemented stem for aseptic loosening. All stems were stable. Radiographs showed cortical healing in 5 cases, trabecular remodelling in 1 , and trabecular incorporation in 9. There was a radiolucent line in 1 case.

The histology varied. There was always a viable cortical shell around the grafted area. 1 patient showed complete bony restitution. The others still had varying amounts of remaining graft in the neo-medullary cavity, even after 8 years. The graft particles were usually embedded in dense fibrous tissue, thus forming a supporting composite tissue capable of carrying load. There was no time-dependent deterioration in the histological appearance.

Radiographically, cortical healing and trabecular remodeling corresponded to viable bone. The lack of a radiolucent line said little about the viability of the tissue closest to the cement. The radiographs did not detect thin soft tissue membranes.

Radiographic criteria used to assess primary total joint replacement do not necessarily apply to impaction grafting, and radiographic changes should be interpreted cautiously, especially as regards tissue viability.

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Revision hip arthroplasty with cancellous impaction grafting gives good functional results, favorable radiographic findings and a very low incidence of radiolucent lines (for review, see Tägil 2000). However, Leopold and Rosenberg (1999) pointed out that the biological interpretation of postoperative radiographic changes is inferred rather than known.

Experiments in goat femurs (Schreurs et al. 1994, 1996) have demonstrated advanced bony healing by 12 weeks. The first histological report in humans (Ling et al. 1993) showed a picture very like the histology after a successful primary THR, but subsequent reports, usually made up of single postmortem femora or limited numbers of biopsies (Nelissen et al. 1995, Ullmark and Linder 1998, Mikhail et al. 1999, Ullmark and Obrant 1999), have indicated that bony healing may be less predictable.

The present study is based on 6 impaction-grafted femurs retrieved postmortem and 8 femurs, from which biopsies were taken during reoperations. The aim is to present the histological observations made in these 14 patients and to correlate the histology with the findings on high-resolution radiographs.

Patients and methods

14 patients (aged 56–89 years) were revised with a cemented stem and impaction allografting in the femur, 3 months to 8 years prior to autopsy/biopsy (Table 1). The operations were carried out by several surgeons in Sweden, Norway and the U.K. No surgeon operated on more than 2 patients.

Table 1. Details about the 14 patients, procedures and radiographic features

Case	A	B	C	D	E	F	G	H	I	J	K
1	2	3	82	1	6	2	1		1+2	1/7, 3/5	1
2	1	1	72	1	12	1	2		2	all	
3	2	1	79	1	27	1	1		6	all	
4	1	1	72	1	42	1	1		1	2, 4	2
5	2	1	89	1	44	4	3		2	all	
6	2	1	73	1	99	1	1		3+5	all	
7	2	2	56	2	3	1	2	4	4	1, 2, 7,14	
8	2	1	76	2	4	2	2	1	4	3, 5, 12	
9	1	1	73	2	10	1	2	3	2	1, 2, 7	
10	2	1	71	2	19	3	2	5	2	2	
11	1	1	74	2	20	1	1	3	2	2, 6	
12	2	1	67	2	21	1	2	2	1+2	4	
13	1	1	78	2	28	1	2	1	1+2	2, 6	
14	1	1	78	2	72	1	2	1	1+2	2, 12,13	

A Gender
 1 Male
 2 Female
B Primary diagnosis
 1 Osteoarthrosis
 2 Rheumatoid arthritis
 3 Femoral neck fracture
C Age at revision, years
D 1 Autopsy
 2 Biopsy
E Follow-up after revision, months
F Type of stem
 1 Exeter
 2 Charnley
 3 CPT
 4 Exeter 240 mm
G Wire mesh
 1 Yes
 2 No
 3 Plate
H Reason for biopsy
 1 Femoral fracture
 2 Correction of malunited fracture
 3 Hematogenous infection
 4 Persistent infection around cup
 5 Trochanteric pain
I Radiographic finding
 1 Cortical healing
 2 Trabecular incorporation
 3 Trabecular remodeling zones 6+7
 4 No change
 5 Radiolucent line zones 2,3,4,5
 6 Not evaluable due to wire mesh
J Gruen zones examined histologically
K Notes
 1 Ullmark and Linder 1998
 2 Ling et al. 1993

The surgical technique has not always been described in detail; however, in all of the biopsy cases and in 2 of the autopsy cases, dedicated impaction instruments were used. Defatting of the graft by rinsing was not reported. The size of the allograft chips is unknown, but in all cases commercially available bone mills were used. Wire mesh was used in 4 of the autopsy cases to cover cortical defects. Postoperatively, the patients had restricted weight-bearing for 6–12 weeks.

All patients had clinically stable implants. The biopsies were not taken because of complications related to fixation but usually together with fixation of femoral fractures around the tip of the stem some time after surgery, or during extraction of the stem for hematogenous joint infection (Table 1). There was no suspicion of sepsis around the femoral component itself.

Processing for histology

All specimens were fixed in 10% formalin, the postmortem ones with the stems in situ. After high-resolution radiographs were taken using mammography film, the stems were removed. The cement mantles were filled with new bone cement and transverse sections, 5–8 mm in thickness and spaced 2–3 cm, were cut with a band saw. Contact radiographs were then taken of the bone slabs and all hardware (wires, mesh) removed.

The bone was kept in formalin for several weeks, after which the specimens were transferred to xylene and graded ethanols and embedded in methylmethacrylate without decalcification. During this process, the bone cement was dissolved out. Sections for histological examination were cut with a Jung Polycut-E microtome at 5 microns and stained according to Goldner. Other stains used were basic fuchsin-toluidine blue and htx-eosin.

Both transverse and coronal sections were prepared. The bone slabs were sectioned transversely and, in 3 autopsy cases, the intervening parts were sectioned coronally to correspond to the radiographic anteroposterior projection. The biopsies were oriented to make the graft-cement contact as long as possible.

Radiographic evaluation

In each patient, all available pre- and postrevision radiographs were employed to classify changes in the graft according to the nomenclature of Gie et al. (1993), using 4 main findings:

1. Cortical healing. A thinned-out cortex or a

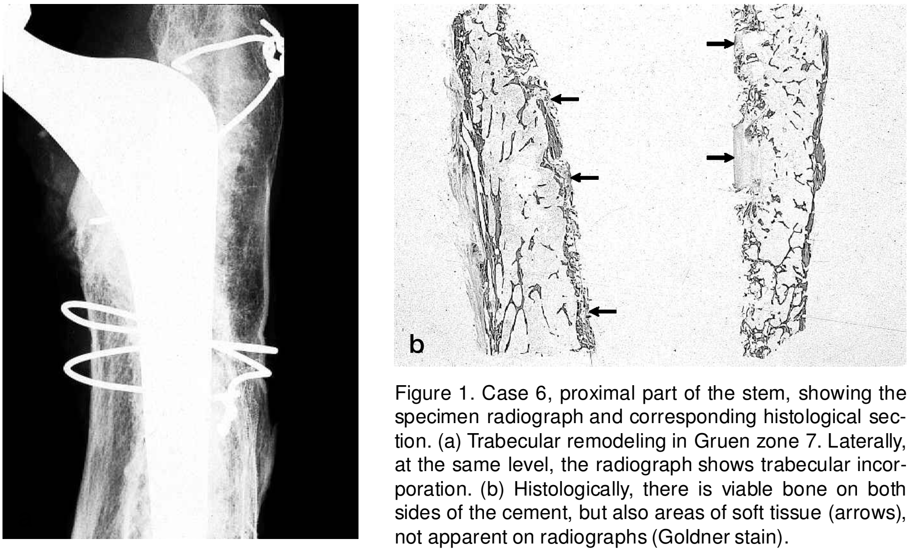

Figure 1. Case 6, proximal part of the stem, showing the specimen radiograph and corresponding histological section. (a) Trabecular remodeling in Gruen zone 7. Laterally, at the same level, the radiograph shows trabecular incorporation. (b) Histologically, there is viable bone on both sides of the cement, but also areas of soft tissue (arrows), not apparent on radiographs (Goldner stain).

cortex with localized endosteal erosions regaining a normal cortical structure and thickness for the region in question. Consequently, if the cortex is not affected by the loosening process, the term cortical healing is not applicable.

2. No change. Completely unchanged graft findings, compared to the first postoperative radiograph.

3. Trabecular remodeling. The graft has changed into a pattern within the medullary cavity of trabeculae running obliquely from the endosteal surface of the femur into the cement along the supposed lines of stress (Figure 1a).

4. Trabecular incorporation. Any change in the structure of the graft from the postoperative radiograph but not fulfilling the very strict criteria in (3) (Figure 1a).

The radiographic findings were classified for those Gruen zones (Gruen et al. 1979) in which the histological sections had been made (Table 1). Combinations of findings are possible, cortical healing describing only the reactions in the cortical bone, whereas trabecular remodeling and incorporation relate to the space between the endosteum and cement.

Results

Radiographic findings

Clinical radiographs. In the cortex, there was cortical healing in 5 patients. In the grafted medullary cavity, there was no change in 2, trabecular incorporation in 9 and trabecular remodeling in 1 patient. The radiographs in 1 patient were impossible to assess because of obstructing mesh. With one exception, there were no radiolucent lines.

In case 6, the stem had moved into varus shortly after the operation and then remained stable. Trabecular remodeling developed around the proximal part medially, whereas a radiolucency developed around the distal third of the stem (Figures 1a and 2a).

Contact radiographs. Except in case 4, the medullary contents looked more homogeneous and less structured than normal trabecular bone, appearing as a fuzzy mass of mineralized tissue surrounding the cement, completely or in patches (Figure 3a). In general, this tissue was thicker and more prevalent in the upper part of the femur (Gruen zones 1/7) than in the more distal areas (Table 2).

The contact radiographs showed radiolucencies in 2 cases: one was case 6, described above. The other was case 5, where a long-stemmed Exeter prosthesis was inserted to help fix a diaphyseal femoral fracture. The distal stem was not surrounded by cement, and a radiolucent line, not discernible in high-resolution radiographs, appeared on the contact radiograph as a circumferential lucency.

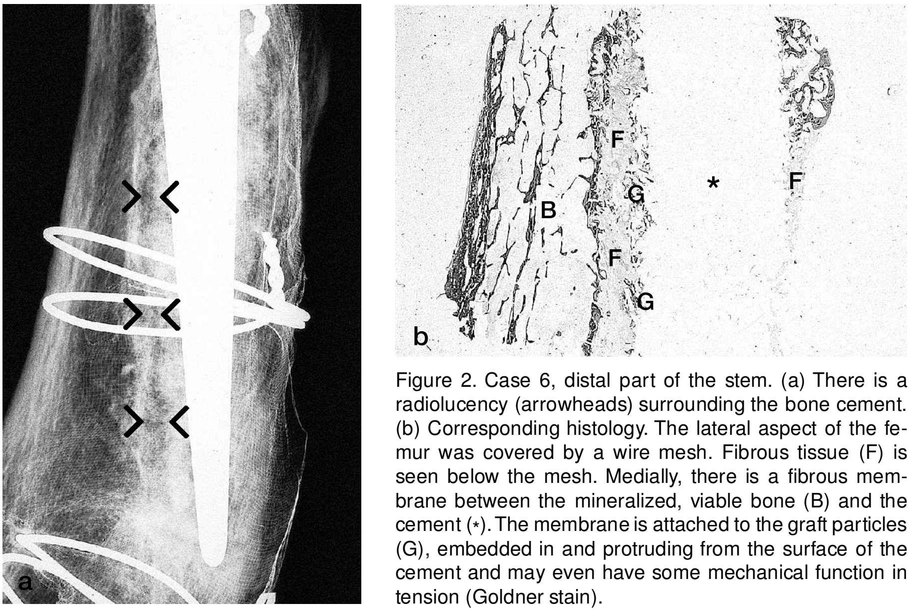

Figure 2. Case 6, distal part of the stem. (a) There is a radiolucency (arrowheads) surrounding the bone cement. (b) Corresponding histology. The lateral aspect of the femur was covered by a wire mesh. Fibrous tissue (F) is seen below the mesh. Medially, there is a fibrous membrane between the mineralized, viable bone (B) and the cement (*). The membrane is attached to the graft particles (G), embedded in and protruding from the surface of the cement and may even have some mechanical function in tension (Goldner stain).

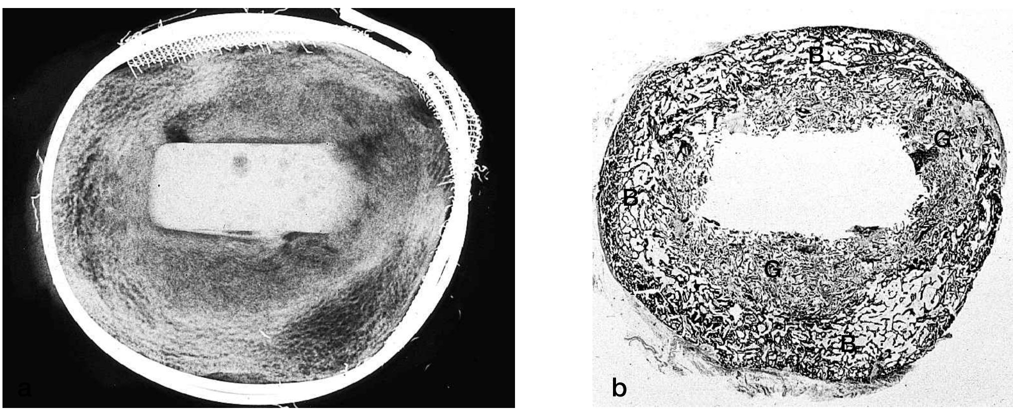

Figure 3. Case 3. Contact radiograph and corresponding histology from Gruen zone 2/6. (a) The radiograph shows non-structured mineralized tissue between the cement and normal trabecular bone. The trabecular bone is thicker in the area not underlying the mesh. (b) Histological examination shows the remaining graft (G), but no demarcation from the normal surrounding bone (B). This graft is partly infiltrated by fibrous tissue (Goldner stain).

Histology, biopsies

For practical reasons, the biopsies were taken from around the proximal part or around the tip of the stems. The histology of the biopsies generally supported the autopsy findings.

2 biopsies were taken 3 and 4 months postoperatively. In both, necrotic graft fragments were easily identified, embedded in either a blood clot or a cell-rich mesenchymal stroma. There were sparse signs of osteoid formation within the stroma at the surface of some of the bone particles, but never generalized bone formation.

In biopsies taken at later stages, the soft tissue stroma had organized into a dense fibrous tissue. There was not one instance in which this special form of tissue (see below) was not found, when looked for. Specimens, in which there was no doubt about the orientation, showed viable bone formed peripherally. There was never a direct contact between newly formed bone and the bone cement.

Histology, postmortem femurs

Cortex. The cortex showed complete reconstitu-

Table 2. Zonal analysis of the thickness (in mm) of the remaining graft in the cross-section of the postmortem femora

Gruen level	Location	Patient no. 1	2	3	4	5	6
1/7	Medial	m	m	6–8	x	0–2	0
1/7	Lateral	3	2	3	0	m	0–1
1/7	Anterior	1	1	4–8	x	0	3
1/7	Posterior	1	2–3	4	x	0–6	2
2/6	Medial	x	m	5–6	x	0–3	m
2/6	Lateral	x	1	1	0	0	0
2/6	Anterior	x	1	3–4	x	m	7
2/6	Posterior	x	1–3	0	x	0–6	0–3
3/5	Medial	1	na	5	x	0–1	m
3/5	Lateral	1	na	1	0	2–5	m
3/5	Anterior	0–1	1	5	x	0–1	7
3/5	Posterior	1	na	0	x	0–2	m

Interval minimum and maximum values,
0 close or established cement-osteoid/bone contact at some part(s) of interface,
m soft tissue membrane replacing graft,
na not applicable; no primary graft,
x not prepared for histological examination.

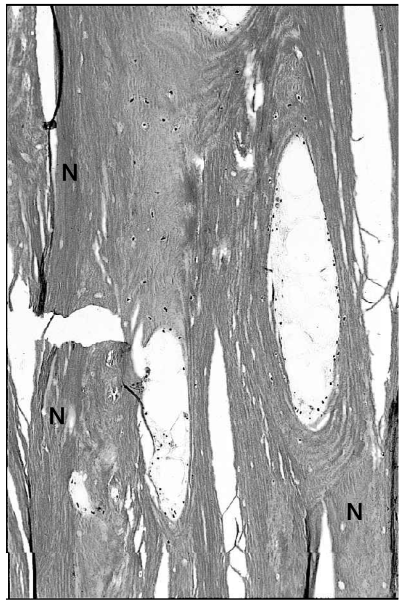

Figure 4. Case 3, demonstrating cortical healing. There are still remaining necrotic parts with empty osteocyte lacunae (N), but also newly formed osteons with normal-looking osteocytes and vascular channels (Goldner stain, ×250).

tion of viable lamellar cortical bone (case 4), or ongoing recvascularization of previously necrotic bone via cutting cones (Figure 4). Although the cortical bone was not always completely revascularized at the time of study, there was no sign of sequestration of any part of the bone. Clearly, the negative bone turnover caused by the loose prosthesis had been stopped and reversed into bone formation.

Medullary cavity. The findings showed a wide spectrum of tissues and stages of healing at various aspects of the interface, even in the same cross-section (Figure 5a). There was no obvious time-dependent maturation of the tissue after 6 months, nor was there any indication of a deterioration in the long-term specimens.

Since there was no demarcation line that separated the cortex from the medullary contents, it was impossible to locate the original border between host bone and impacted graft. Consequently, the distance of bony ingrowth could not be estimated.

The medullary contents consisted of the following principal tissue types from the periphery and inwards:

1. Viable trabecular bone
2. A composite of graft particles and fibrous tissue
3. Necrotic graft with no vascular invasion
4. Fibrous tissue membrane

It was obvious that the graft was first invaded by fibrovascular tissue from the periphery, and that this tissue eventually embedded the bone particles without a foreign body reaction (Figure 5b). However, the vascular front did not always reach the cement surface, and totally avascular impacted graft was also seen adjacent to the cement, sometimes in layers several mm thick (Figure 5c). Where the fibrous tissue reached the cement, foreign-body giant cells were seen on the surface of the tissue in contact with the cement. The composite of bone and fibrous tissue was seen at all time-intervals, even after 8 years. Only case 4 lacked this tissue.

It was equally obvious that new bone formation followed the vascular invasion. The front of bone formation was seen as a zone of intense remodeling, with osteoclastic resorption of the surface of graft granules and concomitant deposition of osteoid and bone (Figure 5b). Peripheral to this zone, the bone was always viable, consisting of

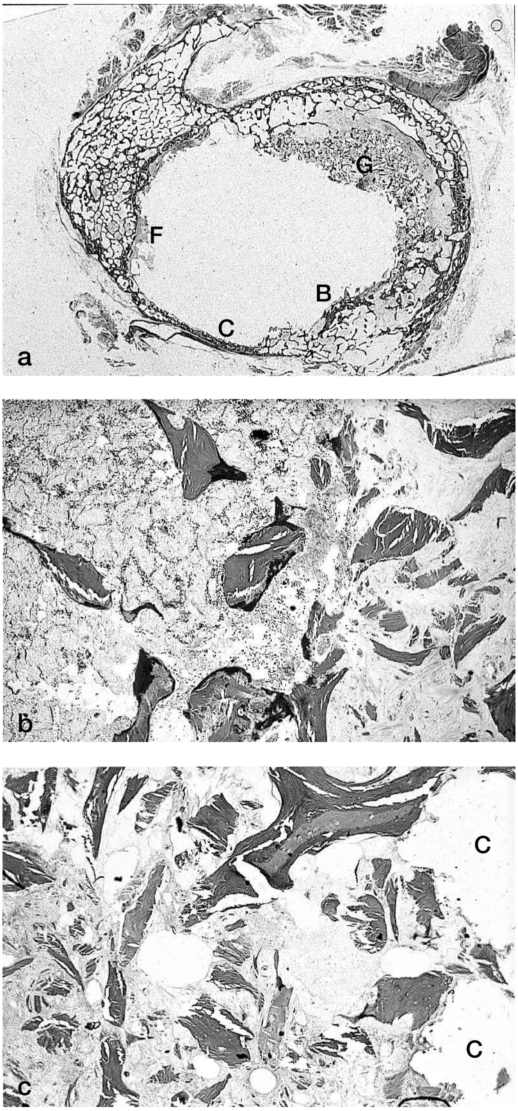

Figure 5. Case 5, Gruen zone 1/7. (a) Overview of cross-section showing that the tissue surrounding the cement can be highly variable, especially proximally in the femur (G remaining graft, F fibrous membrane, C contact between cortical bone and cement, B contact between regenerated trabecular bone and cement). (b) The front of bone formation is shown here. The left part shows normal trabecular bone and bone marrow, the right part necrotic graft embedded in a dense fibrous tissue stroma. The border is characterized by intense bone remodeling with osteoid formation (red) and bone resorption (Goldner stain, x100). (c) Necrotic graft without any tissue ingrowth bordering the cement (C) (Goldner stain, ×100).

cancellous bone and normal-looking bone marrow. Central to the zone of remodeling, there was no viable bone but either the composite tissue described above or necrotic graft. The distance between the bone formation front and the cement varied greatly (Table 2). In some cases, the front had reached the surface of the cement and osteoid made contact with the implant (Figure 6), in other instances the layer of remaining graft measured as much as 8 mm. Sometimes the layer of remaining graft was concentric (Figure 3b), in other cases it was more patchy. Generally, the metaphyseal level showed more remaining graft than the distal sections.

In 4 autopsy femora, a thin mesh had been used to reinforce a femoral window. In one case, the cortex showed remarkable, complete reconsititution, whereas in the other 3, bone formation inside the mesh appeared inhibited (Figures 3a and b). The dominating finding was fibrous tissue, remaining graft and sparse bone formation. On cross-section, the thickness of the remaining graft was greater along the aspect of the femur below the mesh.

A frank fibrous membrane was seen in a few cases, but only around parts of the interface (Table 2). The membrane was dense, and had no accumulations of macrophages and giant cells that would suggest a foreign body reaction. The membranes were not visible on the radiographs. Membranes were also found beneath the wire mesh in cases 1, 3 and 6 (Figures 2b and 3b).

In case 6, the distal 1/3 of the stem was surrounded by a 2 mm thick membrane, which was

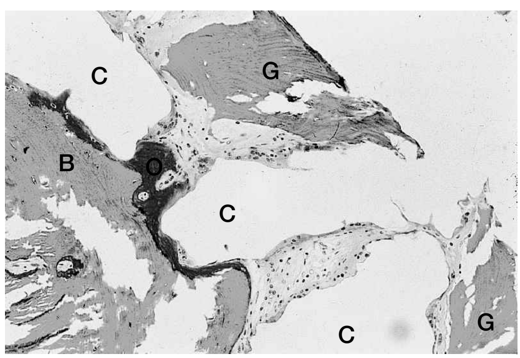

Figure 6. Case 6. Note the connection between the viable, mineralized bone (B) and the cement (C). The necrotic graft (G) is embedded in the cement and attached to the bone via osteoid (O) or soft tissue. Foreign body giant cells, typical adjacent to bone cement, line the soft tissue. These intact delicate tissue bridges show that there is no instability between the cement and the bone (Goldner stain, ×250).

obviously attached to the graft fragments protruding from the cement. It may therefore even have had some mechanical function in tension (Figure 2b). There was also a reaction-free fibrous membrane around the distal part of the long-stemmed Exeter prosthesis in case 5, where the cement mantle was absent.

Relation between radiography and histology

Cortical healing (5 cases). The general picture was one of repair with living bone, from ongoing repair at 28 months to full restitution at 42 months, supporting the assumption that radiographic restitution of the cortex corresponds to viable bone.

No change (2 cases). This was present in 2 biopsies with 3 and 4 months of observation and is to be expected when no ingrowth of mesenchymal tissue has taken place. It was also seen after a fibrous stroma had formed in the face of little graft resorption and little bone formation.

Trabecular incorporation (9 cases). This was the typical radiographic finding in both biopsy and autopsy cases. It also corresponded to the most varied histological appearance, encompassing viable bone, graft particles embedded in a fibrous stroma, necrotic graft without vascular invasion and thin fibrous membranes not detectable on clinical radiographs. The proportions of each tissue type could not be determined radiographically.

Trabecular remodeling (1 case). There was viable bone directly adjacent to the cement surface. However, some stretches of soft tissue also bordered the cement, and the picture was not so homogeneous as could be expected from the radiographs (Figure 1b).

Radiolucent line (1 case). The 2 mm radiolucency in case 6 corresponded to dense fibrous tissue (Figure 2b). Conversely, the absence of radio–lucent lines was no proof of viable tissue, but simply meant that no significant fibrous tissue layer had replaced the graft closest to the bone cement. In fact, the lack of a lucent line could equally well correspond to full bony restitution as to several mm of necrotic graft.

Discussion

Biology of impaction grafting: results in humans

Clinical success, early histological case reports of bone regeneration in human femurs (Ling et al. 1993, Nelissen et al. 1995) and almost complete bony regeneration within 3–6 months in goats (Schreurs et al. 1994, 1996) have supported the continued use of impaction allografting. Biopsies from the acetabulum in humans have suggested that bone regeneration may be completed within 15 months (Buma et al. 1996); other reports indicate a slower, but still complete incorporation by 7 years (Heekin et al. 1995). Taken together, however, these reports have led to the assumption that morsellized allograft will in time consistently become replaced by viable bone.

The present results with observation times of up to 8 years have shown that this assumption is by no means true of the femur, and that results obtained in animals are generally too optimistic vis à vis full bony restitution. The study has also shown the inherent danger of overinterpreting radiographs–e.g., by using similar criteria as in primary THR—since the same radiographic picture may hide unsuspected biological events.

It is unclear why the bony regeneration was so variable. There is no reason to believe that the present series was not representative of what was achieved with impaction grafting during the 1990s. The quality of impaction was beyond doubt in the vast majority of cases. However, the size of the allograft chips may not have been optimal; some patients were old, with reduced physical activity; the grafts were not always rinsed clean of marrow tissue; weight-bearing was postponed 6–12 weeks in all cases, factors which may be of importance, as shown in animal experiments (Thorén 1994, Tägil 2000).

The histological findings in the 6-month specimen and many of the longer-term specimens were similar, which indicates that the key biological events occur early. Clinical radiographs usually show little change after 2 years (Elting et al. 1995, Leopold et al. 1999, Nivbrant 1999), indicating that the stimulus to bone formation somehow ceases. The amount of remaining graft in long-term biopsies might therefore be related more to the extent of early ingrowth than to the actual length of follow-up. On the other hand, there was no time-dependent deterioration in the histological appearance.

Biology of impaction grafting: experiments in animals

Observations in the titanium chamber model in the rat strikingly resemble those in the present study (Thorén 1994, Wang 1996, Tägil 2000). Fibrovascular tissue penetrates the graft almost completely, while new bone formation is more limited. The addition of growth factor OP-1 to the impacted graft increased the bony ingrowth (Tägil 2000). This shows that biological factors are at work in impaction grafting, not least the state of the host bed and the bone-forming capacity of the host, but this aspect has not so far been considered in clinical practice.

Bone-fibrous tissue composite: biological and functional aspects

The composite of fibrous tissue and bone is a supporting tissue with biological and mechanical properties that are largely unknown. The ingrowth of fibrous tissue has been shown in the rat to double the compressive strength of the impacted graft (Tägil 2000). Indeed, macroscopically the tissue gave the impression of viable bone. As new bone formation was preceded by fibrous tissue invasion of the graft, it is reasonable to believe that at some stage after surgery all stems are supported by this composite tissue. Since it was seen in 13 of the 14 cases, it may obviously be replaced by bone in some persons, whereas in others it remains for many years, possibly indefinitely.

There was no indication that the prostheses were unstable in the bone bed. The necrotic graft entombed in and protruding from the cement surface made contact with the surrounding tissue through soft tissue bridges or sometimes osteoid (Figure 6). Had microinstability been present, such flimsy tissue bridges would not be intact. Obviously, the load-bearing capacity of the fibrous tissue-bone composite was adequate.

The graft particles in the fibrous stroma appeared as inert implants, and were not surrounded by inflammatory cells. There was no indication that the graft induced new bone, or that the graft was resorbed, but there seemed to be a peaceful co-existence of living and dead tissues. Since this appearance is compatible with excellent clinical results, a relevant question is whether it is possible to substitute the allograft with unresorbable particles of other materials. Although founded on other premises, such a principle has been used clinically since the 1980s with both hydroxyapatite granules in acetabular revisions (Oonishi et al. 1997) and titanium granules in primary uncemented THR (Bjursten et al. 1999), with reportedly good clinical results.

Wire mesh and graft incorporation

The use of a wire mesh requires some periosteal stripping and circumferential application of cerclage wires, which together ought to impair the cortical blood circulation, possibly making revacularization slower. Jazrawi et al. (1999) presented 2 cases of cantilever-type failure of the CPT stem, which they attributed to a proximal mesh inhibiting or delaying proximal bone ingrowth in the face of good distal fixation. The present results do not contradict this view.

While a well vascularized host bed is desirable in clinical practice, circumstances at times dictate that some form of external constraint to the graft is necessary to obtain a stable construct. It may therefore be that in such cases the risk of a retarded graft incorporation is the price that has to be paid for stability. The practical management of these patients is compounded by the fact that the bony reactions are difficult, at best, to assess on radiographs because of the obstructing mesh.

Graft tissue: mechanical aspects

Migration studies using radiostereometry (RSA) have shown that impaction-grafted stems migrate and then stabilize like primary stems, but the migration is larger (Kärrholm et al. 1999, Nivbrant et al. 1999). In primary THR, a permanent implant bed is formed by 6–12 months (Willert et al. 1974), consisting of viable bone and, usually, a thin fibrous membrane. This coincides with the cessation of prosthetic migration.

After impaction grafting, it is reasonable to assume that the initial migration is due to after-compaction of the graft, and that the gradual reduction in migration coincides with fibrous reinforcement of the graft. However, in the light of the present results, it seems highly questionable that the cessation of migration is due to a specific tissue type. Indeed, neither Nivbrant (1999) nor Kärrholm et al. (1999) were able find a relationship between cortical repair and migration, although cortical repair most probably is caused by restitution of living bone. Although RSA patterns in impaction grafting may mimick those of primary THR, there is still a difference of 2 orders of magnitude between the resolution of RSA and the histological findings. Correlative studies of RSA and histology have not been done.

Radiography

There is no consensus on the best way to classify the radiographic changes taking place after impaction grafting. The fact that the graft changes in appearance is obviously not sufficient to prove that restitution of viable bone has taken place, since radiographic overprojections may give false impressions. Clearly, there is a need for agreed-upon criteria if comparisons between studies and controlled modifications of surgical technique are considered, since radiographs are the cornerstone of outcome assessment. The radiographic changes most likely to be representative of viable bone are cortical healing and trabecular remodeling.

It is interesting to note that in uncemented revisions, using a long, distally-fixed stem, an initially thinned-out or deficient cortex is often reconstituted into normal-looking cortical bone, even without the use of bone grafts (Hartwig et al. 1996, Kolstad et al. 1996). This bone is no doubt viable. Whether in impaction grafting cortical repair occurs because of or in spite of the graft is an intriguing basic biological question that remains unanswered.

A very striking feature of impaction grafting is the low prevalence of radiolucent lines (Gie et al. 1993, Elting et al. 1995, Meding et al. 1997). It is generally agreed that after a primary or recemented revision joint replacement, a radiolucent line means that either fibrous tissue or fibrocartilage has resorbed and replaced the bone closest to the implant. This means that the soft tissue must be viable. Conversely, it also means that once the permanent implant bed forms (Willert et al. 1974), the absence of a lucent line is a positive feature.

Impaction grafting behaves in a fundamentally different way. The absence of a radiolucent line says little about the viability of the tissue closest to the cement. The lack of a radiolucent line can correspond to various tissue patterns, from a direct contact between cement and viable osseous tissue on the one extreme to a complete absence of tissue ingrowth on the other. The presence of a radiolucent line, on the other hand, signifies a viable soft tissue layer, but was seen in only 1 case in this material.

Future refinements

The clinical benefits of cancellous impaction grafting are beyond doubt, and the first steps towards creating an environment for true bony regeneration have been taken. The present results should therefore not be seen as critical of the technique, but rather as a background against which developments can be viewed. At least 3 principal lines of thought seem to be evolving already: (1) to accept the sometimes incomplete bone regeneration and concentrate on the mechanical stability of the construct, i.e., graft properties and impaction instruments; (2) to use bone- stimulating substances together with bone or bone substitutes in the hope of achieving a more complete and consistent bone regeneration; and (3) to use granules of unresorbable implant materials, expecting reinforcement with fibrous tissue or bone.

Regardless of strategy, it is obvious that a standardized method needs to be established for comparisons between these interventions.

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