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Osseointegration in hip prostheses: experimental study in sheep

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Abstract Sixteen 2- to 3-year-old sheep were submitted to a hemiarthroplasty of the hip joint with a specially designed femoral component. The proximal two thirds of the stem had a circumferential, plasma-sprayed, porous coating with hydroxyapatite. The animals where killed a 15, 30, 60, 90, 120, 180, 200, 270, 360, and 540 days after surgery. Femurs were submitted to plain radiographs, computerised tomography (CT) scan, and dual energy X-ray absorptiometry (DEXA). Cross-sections were obtained at four different levels and studied using scanning electron microscopy. In the coated portion of the stem, apposition of woven immature bone was evident at 15–30 days and mature lamellar bone by 30 days. With time, the gap between the endosteum and the coated surface was filled by bridges of lamellar bone with a marked trabecular orientation. In the distal uncoated portion of the stem, the implant was initially surrounded by fibrous tissue that, with time, transformed into lamellar bone.

Résumé Seize moutons de 2–3 ans ont subis une hémiarthroplastie de la hanche avec un composant fémoral spécialement conçu. Les 2/3 proximaux de la tige avaient une couche poreuse circonférentielle de plasma vaporisé avec hydroxyapatite. Les animaux ont été sacrifiés aux jours 15, 30, 60, 90, 120, 180, 200, 270, 360 et 540 après chirurgie. Les fémurs ont été soumis à des radiographies ordinaires, une tomodensitométrie, une analyse DEXA. Des sections ont été obtenues à quatre niveaux différents et étudiées en utilisant la microscopie électronique. Dans la portion recouverte de la tige la présence d'os immature était évidente à 15–30 jours et celle d'os lamellaire mature à 30 jours. Avec le temps, l'intervalle entre l'endoste et la surface couverte, a été rempli par des ponts d'os lamellaire d'une orientation trabeculaire marquée. Dans la portion distale, non couverte, de la tige l'implant a été initialement entouré par un tissu fibreux qui avec le temps s'est transformé en os lamellaire.

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Introduction

Good results of the osteoconductive properties of hydroxyapatite (HA) have been reported in the literature [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. We studied osseointegration in hydroxyapatite-coated femoral stems, correlating scanning electron microscopy (SEM) findings with conventional radiography (CR), computerised tomography (CT), and dual energy X-ray absorptiometry (DEXA).

Materials and methods

Sixteen sheep 2–3 years old weighing 35–38 kg underwent unilateral hip arthroplasty with a specially designed femoral component made of a titanium alloy—Tilastan (Ti 6Al 4 V) according to the international standard qualifications ISO 5832/III and ASTM F 136-79, with a low modulus of elasticity (110.000 mN). The femoral stem was straight and cylindrical in design, with a collar and two longitudinal deep grooves in the diaphyseal portion and 11 transverse teeth each side. The cervical angle was 135°. The proximal two thirds of the stem had a porous structure obtained by a "material withdrawal process" (shelling with corundum) that allowed us to obtain pores 70 µm in diameter. The pores were 50–100 µm in diameter and 105–108 µm thick. A 22 mm CoCr alloy head was used with a 10–12 mm Morse taper.

Under endotracheal general anaesthesia an anterolateral approach to the hip joint was performed. After neck resection the proximal medullary canal was reamed to accurately fit the prosthetic component. We used three different stem sizes. During the operation an intravenous injection of cefazolin (20 mg/kg) was given. A second dose was administered 6 h later. A combination of streptomycin and penicillin (1.200.000 units) was administered subcutaneously for 7 days post-operatively.

The animals were allowed unrestricted weight bearing. They were killed by a barbiturate overdose after 30, 45, 45, 60, 60, 90, 120, 120, 180, 180, 200, 200, 270, 360, 540, and 540 days. Both

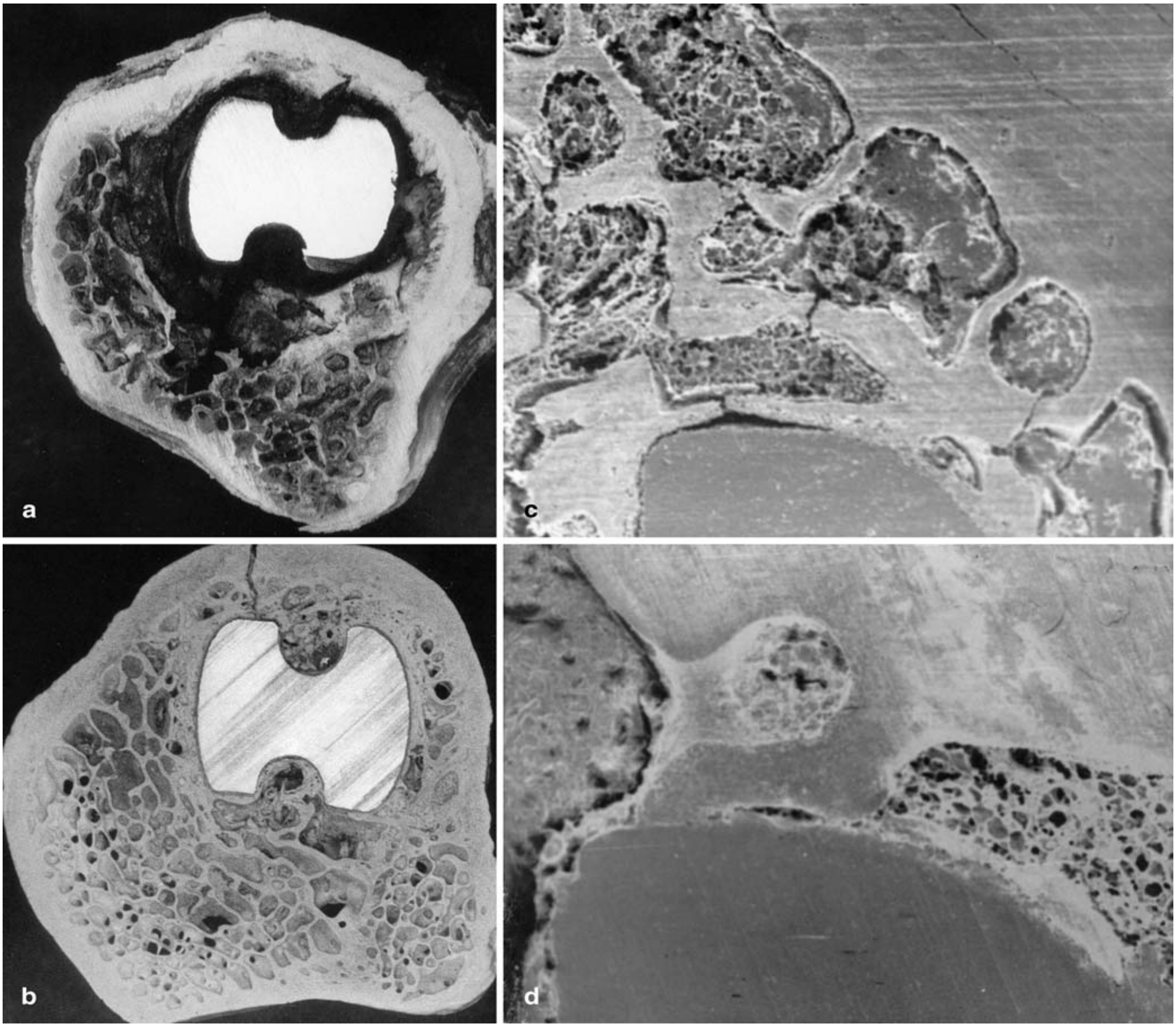

Fig. 1 Anatomic specimen (**a**). Osteogenesis at bone–implant interface led to apposition of osteoid at 30 days. At 540 days (**b**), the gap between the implant and the host bone was filled by mature lamellar bone, as confirmed by scanning electron microscopy (**c** 29×, **d** 50×)

femur and the pelvis were removed and the soft tissues ablated. All specimens were examined by CR using a micro-focus radiogenic tube with nominal 0.1 mm focal spot that allowed performing X-ray magnifications of the femoral stem. X-ray magnification was obtained by a focus film distance of 120 cm and a specimen film distance of 90 cm, realising geometric magnifications of 4×. CT was performed by SIEMENS Somaton Plus 4 (Siemens, New York, NY, USA) using 3-mm-thick sections from the prosthetic collar to the tip of the stem.

DEXA was performed by a LUNAR (Lunar, Madison, WI, USA) expert with a rotating C-shaped arm that allowed scanning on anteroposterior (AP) and latero-lateral (LL) plains. Seven zones were considered on AP plain according to Gruen [12], and another seven zones on LL according to Johnston [13]. DEXA detected the bone mineral content (BMC). All specimens were fixed in 10% buffered formalin. Cross-sections were obtained by a high-speed diamond saw (Exact cutting–grinding system, Bioptica (Norderstedt, Germany) in the proximal femur at four levels: intertrochanteric, upper, middle, and distal portion of the diaphysis filled by the stem. The sections were prepared for observation by the classic procedure of fixation in 2.5% glutaraldehyde, post-fixation in 1% Osmium tetroxide, dehydration in acetone, drying at the critical point in CO2, and metallised in gold, were observed under SEM (Zeiss DSM 962, Carl Zeiss, Oberkochen, Germany). The SEM field included periosteum, cortical bone, endosteum, bone implant interface, and implant.

Results

In the early phases (15–30 days) the HA coating maintained its original thickness and appeared strongly adherent to the metal surface. The gap, present at the HA–bone interface, was progressively filled by newly formed bone. Apposition of immature woven bone was evident at 2–3 weeks (Fig. 1a) followed by lamellar new bone with a marked trabecular orientation at 4–6 weeks. The greatest amount of bone ongrowth occurred in the

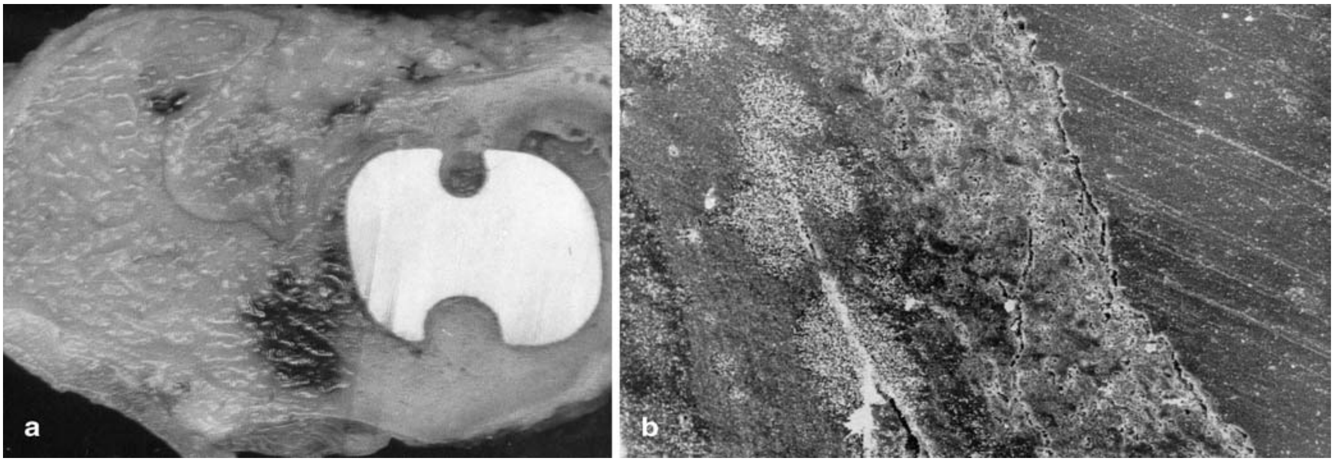

Fig. 2 Anatomic specimen (**a**) and scanning electron microscopy (200×) (**b**) of the metaphyseal hydroxyapatite-coated part at 200 days showing the absence of any gap at the bone–implant interface filled by newly formed bone

proximal and middle parts of the stem where HA coating was present. The new apposed trabeculae formed bridges in the gap between endosteum and HA coating, especially in the proximity of the transverse teeth.

The bone ongrowth increased with time. At 180–200 days we saw, especially on the metaphyseal level (Fig. 2a, b), a great condensation of widely remodelled bone trabeculae that appeared to become thicker, as shown by X-ray and CT scan.

In the diaphyseal HA-coated portion of the stem, we observed the same development in bone apposition as in the proximal metaphyseal portion. At 200 days the newly formed lamellar bone appeared enriched by residuals of amorphous HA crystals. With time the architecture of this newly formed bone became more similar to that of the host bone (Fig. 1b, c, d). In the distal, uncoated portion, the implant was surrounded by intervening fibrous tissue that subsequently transformed into lamellar bone.

The osteogenetic activity at the bone–implant interface is associated with evident changes of HA. The thickness of the hydroxyapatite coating was progressively reduced until its complete disappearance, observed about 200 days from surgery. The gap, previously filled by the HA, was replaced by lamellar bone, which was arranged differently in the various sections of the femur. The gradual replacement of HA by bone was proceeded by morphological and structural changes, already observable at 60 days, consisting in lacunae and cracks with variable orientation. After 90 days the confluence of crack lines led to micro-fragmentation of HA. After resorption was completed (270 days), amorphous residuals of HA mixed with a newly formed bone were seen. This bone was totally different from the host bone and bone formed in the early phases. The resorption of HA led to the appearance of a gap between the new bone and the exposed metal, which underwent progressive filling with time.

The adaptive bone remodelling from day 45 and onward led to thickening of the medial distal cortex (zones 6 and 5 of Gruen [12]) and a thinning of the lateral cortex, mainly in zone 2. Cortical changes were also evident beginning at 90 days in zone 7 under the medial collar, in zone 8 anteriorly, and in zones 12 and 13 of Johnston [13] posteriorly. Cancellous bone hypertrophy in zones 1 and 14 appeared progressively after 30 days and decreased again after 180 days, as shown by CT scan and DEXA.

In hydroxyapatite-coated regions of stem zones 1, 2, 6, and 7, the appearance of soft spot-welds were radiographically visible at 30 days (Fig. 3a) and became thicker after 45 days. Bone bridges became thicker between 90 and 180 days, mainly on the medial side, and increased in number and density, but thereafter decreased in thickness (Fig. 4a). In some zones CT showed a localised progressive increase of medullary canal density after 30–45 days; subsequently the progressive appearance of bone-like density structure filling the periprosthetic gap was observed until 540 days. This new bone formed bone bridges surrounding the stem and connected endosteal bone with the implant.

At 180 days, and more consistently up to 540 days, the bone bridges showed a characteristic triangular shape, with the apex towards the prosthetic surface and the base towards the endosteal bone. After 30 days an increase in bone density of the base of greater trochanter was seen both with CR and with CT and related to thickening of the bony trabeculae and continuing up till 90 days, followed by a progressive loss. In the uncoated portions of the stem (zones 3, 5, 10, and 12), no radiographic changes were observed at the bone–implant interface.

After 45 days a thinning of the cortex was observed by CR in zone 7. The thinning of the anterior cortex was more consistent in zone 8 and showed a uniform appearance up to 540 days. Cancellization of the calcar represented a peculiar finding at 180 days enhancing up to 540 days.

DEXA showed early loss of bone density in the trochanteric apex increasing until 90 days. From then on we observed a complete restoring of the previous density. In

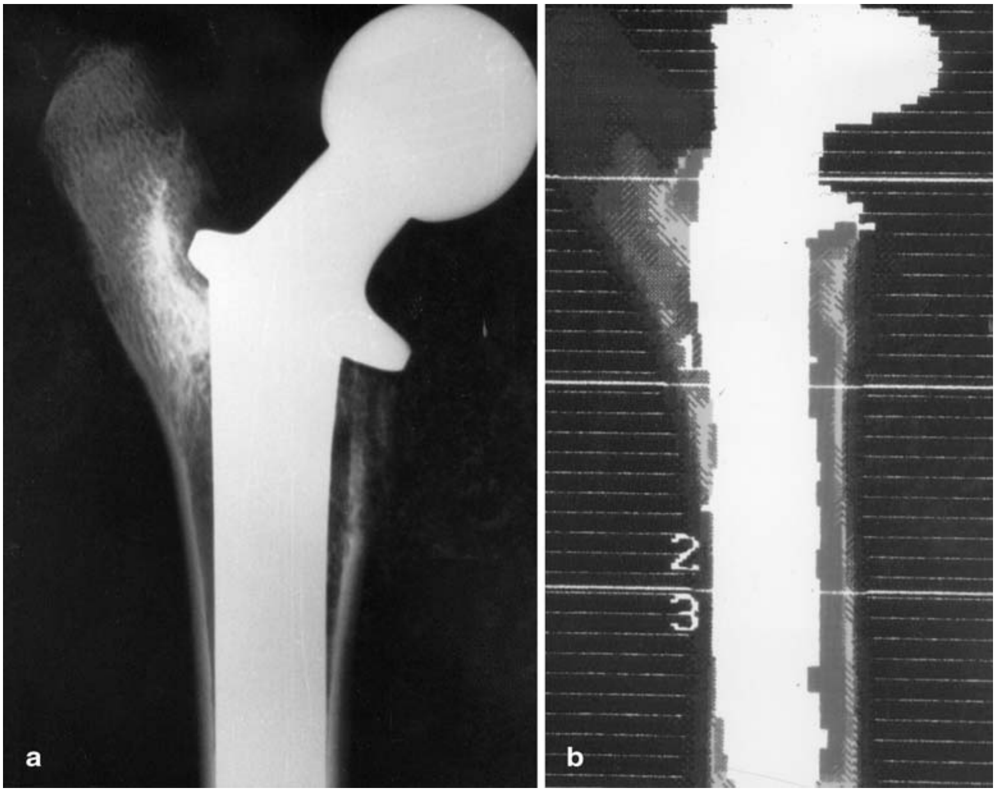

Fig. 3 Sectorial radiographic magnification (**a**) of hydroxyapatite-coated areas at 30 days. Appearance of soft spot-welds in zones 2, 6, and 7. On dual energy X-ray absorptiometry (DEXA) (**b**), in the AP view a precocious loss of density in the lateral cortex (zones 2 and 3), and densification of medial cortex at 30 days, is seen

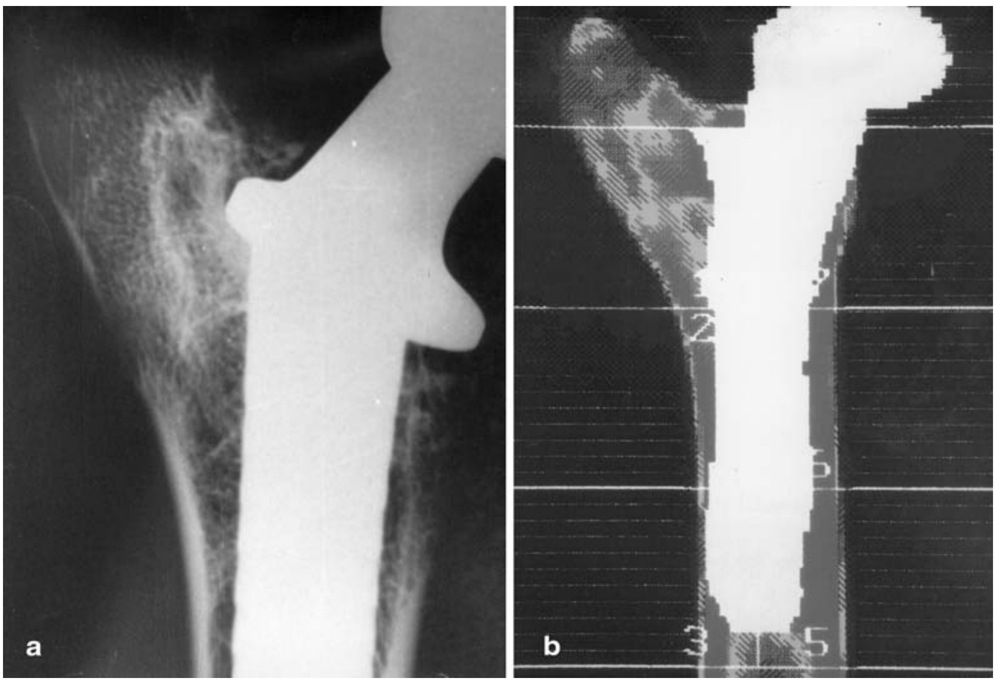

Fig. 4 Sectorial radiographic magnification (**a**) of hydroxyapatite coated areas at 540 days. Spot-welds increase in number and density but decrease in thickness in zones 6, 7, and 2. After a progressive loss of bone density from 30 to 180 days, at 540 days dual energy X-ray absorptiometry (DEXA) (**b**) shows a restoration of previous density

the base of the greater trochanter (zone 1) we found an increased bone density enhancing until 90 days. A density similar to the non-operated side was reached after 90–180 days and continued until 540 days.

In the AP view we observed a precocious progressive loss of bone density in the lateral cortex (zones 2 and 3) and densification of the medial cortex at 30 days (Fig. 3b). Thereafter the medial cortex became less dense, and the process continued until 180 days. Subsequently mineralization was restored up to 540 days when a marked hyperdensity of the periprosthetic bone was seen (Fig. 4b). In the lateral view a constant increase in the process of mineralization was evident at 90 days, both in zone 14 and on the anterior surface (zones 9 and 10).

Discussion

In our weight-bearing animal model, we obtained an adequate fixation of the uncemented hydroxyapatite-coated stems by bony ongrowth. The process of new bone formation was present at 30 days after implantation and was completed after 90 days, with apposition of mature lamellar bone trabeculae with bridges between the endosteal surface and the porous coating. The process was more evident at the level where the stems had a hydroxyapatite-coated surface. Remodelling of newly formed bone and host bone was evident throughout the experimental period. This process led to cancellous bone hypertrophy in the most proximal zone related to endosteal bone formation. Cortical cancellization was present in zones 7 and 8 under the collar, and in zones 12 and 13 posteriorly. A lateral cortical atrophy, mainly in zones 2 and 3, was related to a modified stress transfer. Bone resorption with spongious atrophy in the upper femur was an infrequent feature in this experiment, and a pedestal was never observed.

The tensile and fatigue properties of bioactive materials cannot compete with mechanical properties of surgical alloys. This was demonstrated by the numerous cracks in the coating that we observed by SEM. Thickness of the porous coating may influence the resistance to failure. Excessive coating will favour delamination and fragmentation, making an osseointegrated implant loosen, with breakdown within the coating itself [8, 14, 15]. Extensive contact between bone and implant and initial implant stability are prerequisites for a favourable evolution of the bone–implant interface. With time, the gap between endosteum and the porous-coated surface is filled by bridges of mature lamellar trabecular bone. This new bone formation is prevalent in the proximity of the teeth and on the posterior surface of the stem, and indicates a wide and early fixation of the stem by bone ingrowth, as confirmed by the SEM.

The insertion of a prosthetic stem into the proximal femur leads to redistribution of periprosthetic bone and adaptive bone remodelling. The proximal femoral remodelling leads to proximal spongious hypertrophy, with thickening of the distal cortex and thinning of the lateral cortex, and is related to design and stiffness of the prosthesis.

In the titanium alloy stem we used, the particular design and the presence of a collar were responsible for the reported femoral changes. Low implant stiffness and the presence of grooves significantly reduced the degree of "stress-shielding" [16]. Other factors, such as initial stability (percentage of canal fit and fill) and the location and extent of porous-coated surface, may also influence the adaptive bone remodelling.

The imaging techniques used in this study (CR, CT, and DEXA) confirmed the histological findings. CR enhanced by magnifying technique showed different phases of osseointegration with early formation of spot-welds and progressive formation of bone bridges. In fact, the radiographic magnification proved to be the most sensitive of all the imaging techniques in identifying osseointegration, while DEXA, in the same phase and zones, showed an apparent initial demineralisation, referring to the early process of cortical remodelling.

During the initial phases CT was less useful in showing osseointegration (spot-welds) while clear images confirmed the presence of bone bridges in the later phases. Besides, it showed the progressive and early transformation of the groove tissue into bone.

All techniques showed the changes at the base of the greater trochanter, the significant thickening of the spongious structure. These were not found after 540 days but only in the initial phase, due to stimulation of the collar on the calcar. The subsequent normalisation of the trabeculae structure after 180 days is tied to the definitive stabilisation of the prosthesis.

DEXA was superior to CR and CT to detect bone demineralisation, even in the presence of a normal radiographic thickness of the bone. However DEXA was not able to detect if differences in density were in the cancellous or the compact bone.

Apposition was more evident in the proximal two thirds of the stem where a hydroxyapatite-coated surface was present. In the distal one third, this phenomenon was absent. During new bone apposition around the implant, HA endured a progressive reduction of thickness until its complete disappearance within 200 days.

This study showed that hydroxyapatite coating enhanced ongrowth and attachment of bone, with reduction of fibrous tissue formation around the femoral implant. This may help to avoid aseptic loosening of uncemented components. Early fixation of the implants may also contribute to a reduced stress shielding.

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