Use of hydroxyapatite to fill cavities after excision of benign bone tumours

CLINICAL RESULTS

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We treated 75 patients with benign bone tumours by curettage and filling the defect with calcium hydroxyapatite (HA). There were 28 women and 47 men with a mean age of 27.7 years (3 to 80). The mean follow-up was for 41.3 months. Postoperative radiological assessment revealed that the implanted HA was well incorporated into the surrounding host bone in all patients. Two patients suffered fractures in the postoperative period. Two patients complained of pain associated with HA in the soft tissues, but this diminished within six months. No patient had local pain at the final follow-up. Recurrence of the tumour was seen in three cases. Histopathological study of the implanted area showed removal of the HA by histiocytes and multinucleated giant cells, and the formation of much appositional bone. We conclude that HA is an excellent bone-graft substitute in surgery for benign bone tumours.

Received 27 March 2000; Accepted after revision 14 June 2000

Much of the basic research on calcium hydroxyapatite (HA) has concerned its clinical use as a bone-graft substitute. Biological, histological and biomechanical surveys of its implantation into bone reveal that the material is safe and has excellent osteoconductive properties. It is often used as a coating for prostheses as well as to fill bone defects. There have, however, been few reports on the outcome of its clinical use in surgery for bone tumours. Since 1988, we have implanted HA for bone defects after resection of benign bone tumours.

Patients and Methods

We analysed the outcome in 75 patients with benign bone tumours. There were 28 women and 47 men, with a mean age of 27.7 years (3 to 80). All the lesions were imaged by plain radiography, CT and MRI. All patients had curettage of the tumour and filling of the resulting bone defect with HA, without autologous bone. Cortical fenestration was carried out using an osteotome and the intrasosseous tumours were removed by a curette. When sclerotic margins were present they were drilled to establish a connection to healthy bone marrow. After filling the bone defect with HA, the cortical window was replaced. No other adjuvant treatment such as phenol or cryotherapy was used after curettage. Internal fixation was not employed. External stabilisation with splints or slings was utilised postoperatively for patients judged to be at risk of pathological fracture.

The tumours were located in the femur (26 patients), phalanx or metacarpal (18), tibia (11), humerus (9), calcaneus (4), pelvis (3), radius or ulna (3) and fibula (1). Histological examination revealed that 21 were enchondromas, 18 fibrous dysplasias, 12 non-ossifying fibromas, eight solitary bone cysts, six Langerhans-cell histiocytes, three chondroblastomas, two giant-cell tumours of bone, one aneurysmal bone cyst, one osteofoveal dysplasia, one osteoid osteoma and one enostosis (bone island).

We used an HA compound (Ca\textsubscript{10}(PO\textsubscript{4})\textsubscript{6}(OH)\textsubscript{2}) with tricalcium phosphate (TCP) in a ratio of 70% HA to 30% TCP (Chugai Inc, Tokyo, Japan). The porosity was 3% to 55% and the pore size 1 to 15 μm. The sintering temperature ranged from 900° to 1300°C, and the bending strength from 50 to 800 kg/cm\textsuperscript{2}. Variously shaped pieces of HA were used in the operations, depending on the location and size of the tumour. The mass of implanted HA ranged from 3 to 55 g. After surgery radiographs were assessed according to the criteria of Uchida et al\textsuperscript{19} to determine changes in the radiolucent zone around the HA and the amount of incorporation and displacement of HA. Postoperative CT was carried out on some patients. The mean follow-up was 41 months (5 to 140).

Of the 30 patients with lesions of the upper limb, 24 were immobilised in a sling or a splint. All 18 patients with lesions in the phalanges and metacarpals had splints. The mean period of immobilisation was 3.5 weeks. Of the 42 patients with lesions in the lower limb, six were immobilised in splints. The mean period of immobilisation was 3.1 weeks.
Results

No patient developed a postoperative infection. At the final follow-up, radiography showed the implanted HA to be well incorporated into the surrounding host bone in all cases. Radiographs obtained immediately after surgery showed radiolucent zones between the implanted HA and the surrounding cancellous bone. Periodic assessments revealed that, over time, the radiolucent zones disappeared and new bone developed (Figs 1 and 2). The mean period required for the zones to disappear was 4.2 months. For patients aged 19 years or under, it was 3.2 months. As the radiolucent areas faded, radiographs showed increasing density of the material during the postoperative months, and the margins became indistinct. At the final follow-up, no degenerative changes were observed in nearby joints, even in the three chondroblastomas and two giant-cell tumours of bone in which the HA was implanted beneath the subchondral bone. No patient complained of local pain at the final follow-up. Three patients, with lesions in their
fingers had a slightly limited range of movement in joints adjacent to the lesions. No other patient had a restricted range of movement.

For patients with a femoral or tibial lesion of larger than half of the medullary cavity as measured by CT (20 cases), the mean period before full weight-bearing was 11.3 weeks. For patients with a lesion smaller than half the medullary cavity (17 cases), the mean period required before full weight-bearing was 7.4 weeks. CT at six months or more after surgery revealed satisfactory formation of new bone around the HA.

Postoperative fractures occurred in two patients. One, with a solitary bone cyst in the humerus, fell eight days after surgery, and the other, a patient with a non-ossifying fibroma in the distal tibia, sustained a fracture while playing football two weeks after operation. Two patients with enchondromas in the fingers complained of pain attributed to particles of HA in the soft tissues. The pain decreased within six months. In one patient, with a lesion in the femur, particles of HA became displaced during rehabilitation, but had disappeared at follow-up, whereas the HA in the bone was satisfactorily incorporated.

Recurrences of tumour were seen in three cases (1 giant-cell tumour of bone, 1 fibrous dysplasia and 1 Langerhans-cell histiocytoma). The patient with the recurrent giant-cell tumour of bone subsequently had further curettage and packing with methylmethacrylate. The patient with recurrent fibrous dysplasia required no further surgery. The patient with a recurrent Langerhans-cell histiocytoma had an open biopsy and reimplantation of HA six months after the initial surgery. Histopathological examination showed that part of the HA implanted into the bone marrow had been replaced by histiocytes and multinucleated giant cells, but a large amount of thick, newly-formed lamellar bone was attached to the surface of the HA (Fig. 3). Infiltration of the inflammatory cells, including plasma cells and lymphocytes, was very slight.

**Discussion**

Since the introduction of ceramics for the replacement of bone, numerous experimental and clinical studies have been undertaken. Many authors have shown bone ingrowth into HA implanted into bone marrow in animal experiments and in biopsy specimens from patients. Uchida et al found better bone ingrowth into HA with TCP than that with calcium aluminate. Holmes et al studied HA implanted into diaphyseal defects in dogs. They observed incorporation of the HA and bone ingrowth into the material with no sign of biodegradation. Sartoris et al assessed the radiological changes of HA used to fill defects after fractures. They showed excellent incorporation in most cases. They demonstrated that the intrinsic architecture of the HA was preserved on radiographs, but that the margins had become indistinct, suggesting partial biodegradation of the material.

HA has various applications in orthopaedic surgery such as in bone defects resulting from severe fractures, spinal surgery and arthroplasty. Holmes et al applied HA while treating 18 metaphyseal and diaphyseal fractures in 1984. Uniform healing was observed in all patients. The postoperative management was similar to that after autogenous bone grafting. In recent years, Itokazu et al packed HA into bone defects in fractures of the tibial plateau, and Ladd and Pliam used it in the treatment of distal radial fractures. It has been used in spinal fusion and laminoplasty. Bozic et al demonstrated that HA, used with electrical stimulation, increased the rate of lumbar spinal fusion. An HA spacer has been reported to be useful in laminoplasties. Many authors have reported that metal implants coated with HA achieve rapid surface bone apposition with good stability and HA has been packed into massive bone defects in revised total hip arthroplasties by Onishi et al. There have been few reports in the English literature on the clinical application of HA in surgery for bone tumours.

In our series, HA was well incorporated into the surrounding host bone in all cases within a mean period of 4.2 months. The radiological changes in the implanted HA were similar to those previously reported. After several months, they show an increased density with indistinct margins. These radiological findings coincided with the histological evidence in a specimen obtained from the patient with recurrent Langerhans-cell histiocytoma (Fig. 3). Histological examination showed that the HA was partially removed by histiocytes and multinucleated giant cells, with the formation of appositional, thick lamellar bone. The HA had not totally disappeared in any case at final follow-up. This suggests that although HA is biodegradable, it is only very slowly replaced by new bone.

We implanted HA into the cavities of one acetabular and four epiphyseal tumours. All the lesions lay beneath the subchondral bone plate. Although follow-up was short, degenerative changes were not observed in any joint.

![Fig. 3](https://via.placeholder.com/150)

Photomicrograph of a recurrent Langerhans-cell histiocytoma. The tissues were obtained from areas with recurrence of the tumour six months after the initial operation. The implanted HA was replaced by thick lamellar bone (haematoxylin and eosin ×70).
Before this study, we used autologous bone grafting for tumours adjacent to joints in order to support the articular cartilage. Our results indicate that HA is also effective in this situation.

Postoperative fractures occurred in two patients, both within two weeks of surgery. We believe that these incidents were not directly associated with the procedure; one was accidental and the other the result of not following instructions about bearing weight. No other patient sustained a fracture after full weight-bearing had begun. Piecuch et al.\(^1\) stated that once HA became incorporated, mechanical testing proved it to be as strong as normal bone. Hamson et al.\(^1\) found no significant difference between HA and autologous cortical bone in mechanical strength, six months after implantation. Vuola et al.\(^1\) reported that the compressive strength of HA was higher than bone marrow after 12 weeks. Full weight-bearing was, however, delayed as the radiological appearance of new bone in place of HA was slow to develop. Patients with lesions of the lower limb which were greater than half of the medullary cavity as measured by CT, required 11.3 weeks before they could safely bear full weight. The period of postoperative management is long.

Local recurrences of tumour were observed in three cases, which is similar to the recurrence rate for such tumours treated without implantation of HA and reflects the biological nature of each tumour.\(^2\) No patient complained of local pain at the final follow-up, but two, with enchondromas in the fingers, had pain attributed to HA in the soft tissues. This complication should be avoided by using a careful operative technique when packing HA into bone defects. HA in the soft tissues can be a source of mechanical irritation although only rarely does it cause a histological foreign-body reaction.\(^10\) The scattered HA disappeared within several months. It has been reported that extraskeletal implantation of HA does not lead to osteoinduction.\(^29\) We conclude that HA is an effective bone-graft substitute in surgery for benign bone tumours. Its implantation provides osseointegration with fewer complications and as a result we have abandoned autologous bone grafting in patients with these lesions.

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

### References


THE JOURNAL OF BONE AND JOINT SURGERY