Evaluating a Nanocrystalline Hydroxyapatite Bone Graft Substitute for the Treatment of Benign Bone Tumors

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Abstract

An increasingly popular method of treating benign bone tumors among orthopedic surgeons involves curettage and subsequent bone grafting. Synthetic bone grafts obviate some of the limitations of harvesting autograft and the use of allografts, and there are an increasing number of products available. A new bone graft using nanocrystalline hydroxyapatite (NanoBone® Bone Graft Substitute, Artoss GmbH, Rostock, Germany) was used in 98 patients treated for benign bone tumors. Patients were followed for a minimum of 6 months out to 2.5 years. Maturation of the bone graft with increasing difficulty of distinguishing the geographic border of the bone graft from the normal bone was observed in many cases as early as 4 weeks and in all patients by 12 weeks. Trabecular new bone formation growing through the bone graft indicating remodeling was also evident in all patients after 12 weeks. There were no cases of bone graft or bony resorption and repeat bone grafting was not required in any patients. Nanocrystalline hydroxyapatite provides for a simple and effective means of bone grafting and void filling of bone following curettage of benign bone tumors in the appendicular skeleton.

Introduction

Today many surgeons treat benign bony defects, particularly large defects in weight bearing areas with intraoperative filling of the lesions. Surgeons have used autogenous bone, allograft bone, synthetic bone grafts and bone cement (both PMMA or other synthetic curing compound).[1,2,3]

Limitations of autogenous bone include harvesting sufficient quantity and associated morbidity, allograft bone has a non-zero risk of disease transmission, along with a lack of any attributes other than osteoconductivity for the most part. Bone cement may well provide some immediate stability but makes subsequent bony healing more problematic.[2,3,4]

The nanocrystalline hydroxyapatite bone graft substitute used in this clinical series (NanoBone® Bone Graft Substitute, Artoss GmbH, Rostock, Germany) consists of a synthetic nanocrystalline

hydroxyapatite (50nm) embedded in a porous silica gel matrix used as a bone void filler and synthetic bone graft.[5,6] Animal studies have shown that nanocrystalline hydroxyapatite (NBS) has a high osteoinductive potential and demonstrates remodeling potential, with woven bone and lamellar bone being present followed by the remodeling with new bone formation based on mechanical stressors.[7] The key event initiating this process is the replacement of the silica matrix of NBS by a noncollagenase matrix similar to the extracellular matrix of bone in approximately fourteen days post-implantation.[8,9,10] Thus, the observed bone formation and subsequent remodeling process follows the same pattern of natural bone formation by osteoblasts, releasing a range of growth factors (IGF, FGF, TGF-beta, and BMPs), and mobilization of hydroxyapatite crystals.[6,11] Subsequently, mononuclear cells prepare the surface for new bone formation providing signals of osteoblastic differentiation and migration.[12]

METHODS

We evaluated the utilization of NBS in 98 patients who had undergone curettage and graft for benign bone tumors between August 1, 2018 and February 17, 2021. All patients had a minimum of 6 months follow-up with a mean follow-up of 2.5 years (range 6-36 months). The NBS was implanted into the cavities following removal of the tumor and coverage of the cavity opening with soft tissues. The distribution of tumor type is as indicated in Table 1:

Table 1

TUMOR TYPE	N
UNICAMERAL BONE CYST	22
ANEURYSMAL BONE CYST	15
NON-OSSIFYING FIBROMA/ FIBROUS CORTICAL DEFECT	19
ENCHONDROMA	13
GIANT CELL TUMOR OF BONE	12
FIBROUS DYSPLASIA	6
CHONDROBLASTOMA	3
OSTEOID OSTEOMA	8

The locations for implantation of the bone graft included the proximal humerus, distal radius, both ends of the femurs and tibias as well as hands and feet (Table 2).

Table 2

LOCATION:	**N**
PROXIMAL HUMERUS	38
DISTAL RADIUS	6
PROXIMAL FEMUR	7
DISTAL FEMUR	21
PROXIMAL TIBIA	8
DISTAL TIBIA	6
HANDS/FEET	12

All patients underwent curettage of the benign bone tumor with high-speed burring followed by repeat curettage and burring. In some patients the procedure was performed in a percutaneous fashion and a limited curettage was performed using a Jamshidi needle. In 36 patients with giant cell tumor, aneurysmal bone cyst, chondroblastoma, and some enchondromas, adjuvant margin enhancement was performed which included cryosurgery or the installation of liquid nitrogen into the cavity and cavity walls. It should be noted that the cryosurgical component of the procedure, the instillation of liquid nitrogen into the cavity following extraction of the tumor, does create a more hostile environment for bone growth to occur and does put the bone at risk for fracture.[13] In these patients, prophylactic internal fixation was utilized in the majority (23 of 36) of cryosurgical patients, consisting of either a carbon fiber or titanium plate and screws. The average volume of NBS used was 14 cc (range 1-25 cc).

Patient follow-up included physical examination, radiographic study and assessment of function strength and range of motion. Radiographic follow-up was by plain films in all cases, with plain films being performed immediately postoperative, then at 6 weeks, 12 weeks, 6 and 12 months, and biannually thereafter.

RESULTS

In all 98 patients successful extraction of the benign tumor and filling in of the entire void with the NBS product was achieved. There were no infections or other complications related to the bone graft or its technique of insertion. While fracture is a risk of cryosurgery, we demonstrated no fractures in any patients despite cryosurgery or the size of the cortical window in bone. The implants utilized for prophylactic internal fixation were all intact and well positioned at follow-up. The use of carbon fiber

plate allowed for much better radiographic visualization of the grafted site. The surgical time required for preparation of the NBS as well as its insertion was less then five minutes as the product is pre-packaged in its delivery container and require no additional formulation or preparation. The insertion into the cavity is delivery via syringe. Excess NanoBone overflowing into soft tissues caused no morbidity and resorbed within the soft tissues by 12 weeks and no evidence of heterotopic ossification was present.

Clinical and radiographic outcomes were determined based on pain reduction and functional outcomes such as full weight bearing and return to normal activity, incorporation of NBS was determined by radiographic evidence of the gradual diminishing and remodeling of the bone graft/host bone interface (Figure 1a,b,c). The time to healing ranged from 4 to 12 weeks. All patients demonstrated bony incorporation and initiation of remodeling by 12 weeks. At 12 weeks we observed new bone growth and reintroduction of trabecula into the bone grafted site. All patients were fully active and fully weightbearing by 12 weeks. Resorption and loss of bone graft was not noted or evident although in 3 patients, a lucency was evident at the margin of the bone grafted site. While these lucencies were initially concerning for local recurrence, upon thorough review the lucencies were present at the initial postop x-ray and remained stable and nonprogressive throughout the entire follow-up period. We hypothesized that the lucency represented retained fluid or blood in the cavity which persisted under hydraulic pressure as the bone graft was being placed into this closed cavity, which did not allow the bone graft to completely fill the entire cavity. This was deemed inconsequential to the patient's ultimate clinical outcome. There were no cases of bone graft or bony resorption and repeat bone grafting was not required in any patients.

In those cases where an adjuvant margin enhancer such as liquid nitrogen or cryosurgery was used, the NanoBone still incorporated at the same rate and quality based on radiographic examination as non "frozen" bone. The longer term follow up in these patients demonstrated equivalent remodeling based on radiographs as non-treated bone. There were no late fractures or infections.

DISCUSSION

NBS provides for a simple and effective means of bone grafting and void filling of bone following curettage of benign bone tumors in the appendicular skeleton. Even in a hostile environment such as following chemical or cryosurgical enhancement of margins thereby producing marginal osteonecrosis, bone graft incorporation was noted in all patients. It is a safe, non-disease transmitting option which allows for radiographic demonstration of healing and remodeling of bone. The osteoinductive nature of this product allows for successful use as a bone graft and large bony cavities.

Figure 1a: NBS in femoral head immediately post-op

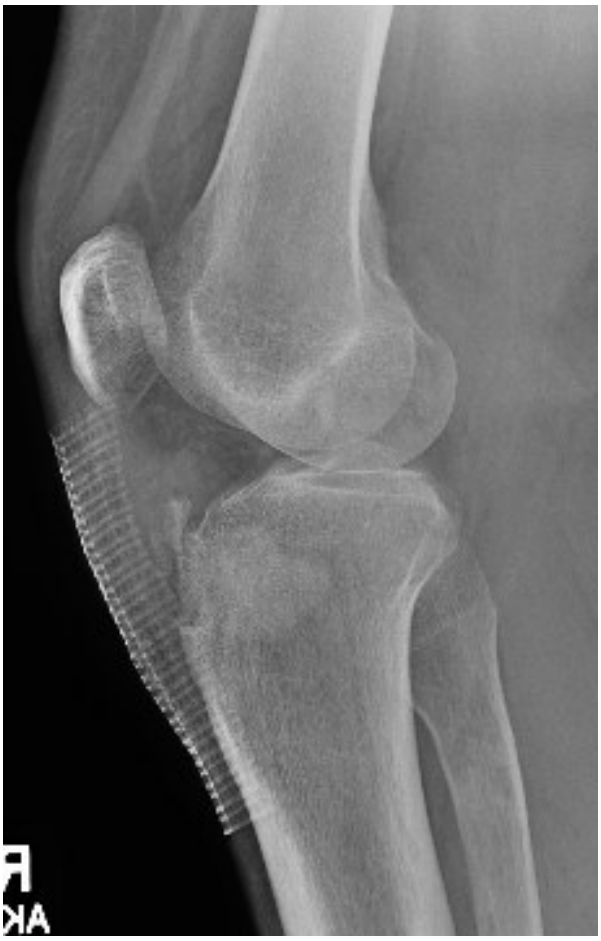


Figure 1b: NBS in head of humerus at 3 months post-op

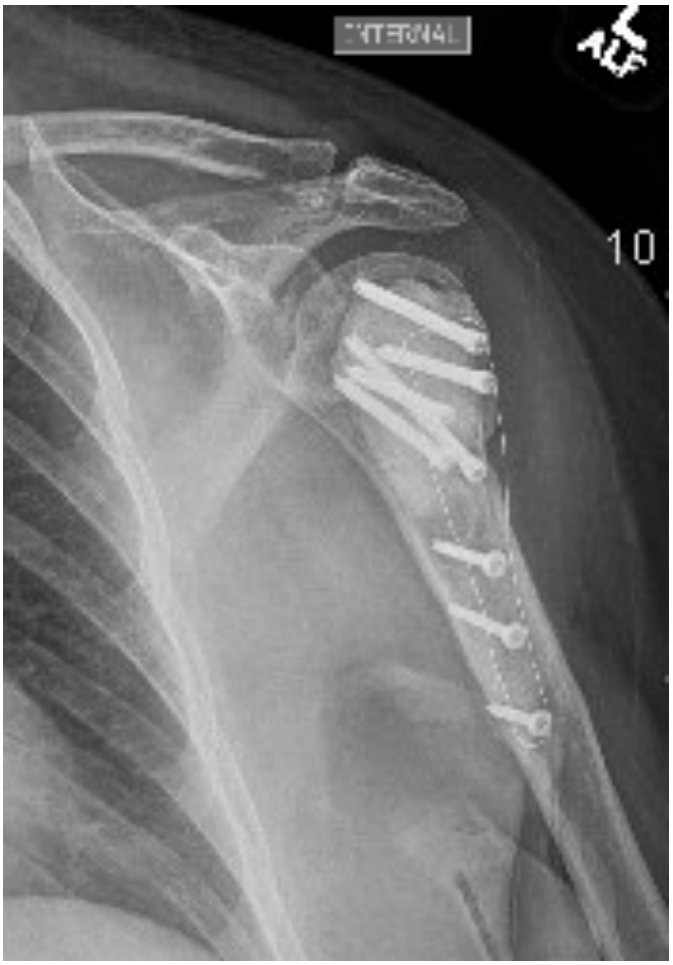
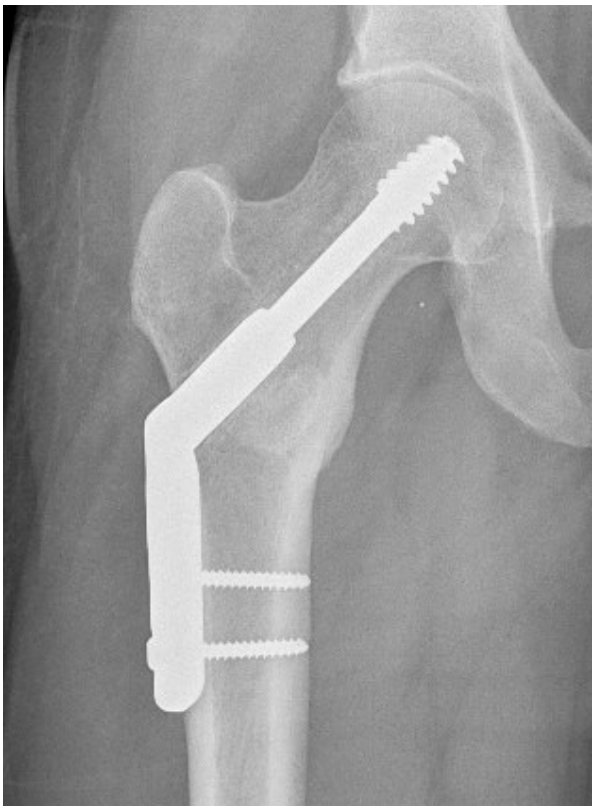


Figure 1c: NBS in calcar at 6 months post-op



CONCLUSIONS

NanoBone provides bone filling options in its use in the treatment of benign bone tumors even in a “hostile environment” such as bone treated with liquid nitrogen. It shows high biocompatibility and improves bone healing properties even in cavitied where bony apposition is not available. It is easily discernable on plain radiographs such that remodeling of bone as well as control of local recurrence of disease may be easily monitored. It acts as a scaffold for the host bone replacement to occur in an expected healing period of time. Because it is replaced by host bone, and allows for remodeling of that bone, it obviates the need for bone cement which as an inorganic inert substance, can adversely impact on future surgical procedures.

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