# Autografts, Allografts and Bone Substitutes in Lytic benign Bone Tumors and Tumour Like Lesions: A Comparative Study of Filling Defects and Healing in 90 Patients

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**Abstract:** *Background:* Extended curettage is treatment of choice for most benign lesions. To fill the defect after curettage remains a major problem particularly in children and in large cavities. We compared the results of allografts, autografts and bone substitutes in patients with benign bone tumors and tumour like conditions after curettage in view of healing of the lesion and their complications.

*Material and Methods:* Total 90 patients (54 males and36 females) of benign lytic bone tumors in extremities and amenable to curettage were included in this prospective study. Extended curettage was done using the sharp curettes and high-speed burr. The age of patient ranged from 6 years to 62 years. Giant cell tumor 33.3% (n=30) and aneurysmal bone cyst 30% (n=27) were the most common type of tumors in our series. There were twelve patients (13.3%) of enchondroma and ten patients each (11% each) of simple bone cyst and chondroblastoma. One patient had chondromyxoid fibroma. Mean tumor volume was 29.88 $cm^3$ (range 2.7 to 168.48). The defects were filled by either autograft, allograft or bone substitutes making the comparative groups. The mean follow up period was 46months (range 24–70).

*Results:* Autografts were used in 32 patients (35.6%) allografts in 28 (31.1%) and in remaining 30 cases (33.3%) bone substitutes were used. Autografts had shortest healing time with mean value of 6.77 ± 3.2 weeks (4–16 weeks) followed by bone substitutes 10.0± 2.4weeks (8-14 weeks). Allograft demonstrated maximum healing time with mean 11.25 ± 2.6weeks (range 8-16 weeks). Additional scar 100% (n=32), cosmetic deformity 6.25% (n=2), recurrence 6.25%(n=2) and infection 3.13%(n=1) were chief complications in autograft group. Serous discharge was observed in 64.3% (n=18) patients of allograft and in 23.3% (n=7) of bone substitute groups and one patient each in these two groups had infection respectively. There was one recurrence each in allograft and bone substitute groups respectively. Cost was big limiting factor for usage of bone substitutes in large cavities. Functional assessment was done by Musculoskeletal Tumor Society Rating Scale (MSTS) score while radiographic assessment of graft uptake by Irwin grading. The overall average Musculoskeletal Tumor Society (MSTS) score was 26.75 (range 24-30).

*Conclusion:* Autograft is the best material to fill the defect after extended curettage of benign lytic lesions of bone. Bone substitutes and allografts are the options if autograft not available like in children. We observed that in small cavities bone substitutes can be an effective alternative and in large cavities it is better to use either allograft alone or a combination of autograft.

**Keywords:** Autografts, allografts, bone substitutes, benign lytic lesions, bone, healing.

## 1. INTRODUCTION

Primary neoplasms of the skeleton are rare, amounting to only 0.2% of the overall human tumor burden [1]. Benign lytic lesions of bone occur most commonly during the first three decades of life and few of them like non-ossifying fibroma, simple bone cyst, enchondroma, bone infarcts etc may be asymptomatic and may be found incidentally on imaging for separate complaints, but they also can present with mild pain and localized swelling of short duration [2]. Further there are certain locally aggressive lesions like giant cell tumor, chondroblastoma, chondromyxoid fibroma, aneurysmal bone cysts and osteoblastomas [3]. Once an accurate diagnosis has been made on basis of radiographs and biopsy one can plan an appropriate line of treatment. Many benign bone tumors are treated adequately by curettage. Compared with resection, curettage is associated with a higher rate of local recurrence; however, curettage often allows for a better functional result. “Extended” curettage includes the use of adjuvants, such as liquid nitrogen, phenol, high speed burr, polymethyl methacrylate, or thermal cautery to extend destruction of tumor cells particularly in cases of giant cell tumor, chondroblastoma and chondromyxoid fibroma. The defect after curettage can be filled with autologous bone graft, allografts and bone substitutes [4,5].

This prospective study was designed to compare the healing and functional outcome using autologous bone grafts, allografts or bone substitutes for defects after curettage in benign lytic bone lesions.

## 2. MATERIAL AND METHODS

This prospective study was conducted in Department of Orthopaedics, at our institute between

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2010 and 2015. Total 90 patients (54 males and36 females) with mean age ranging from 6- 62 years (mean 22.5±12.6) with benign lytic bone lesions were randomly selected by chit method for the particular filler after curettage. Clinico-radiologically and histopathologically diagnosed benign tumors in extremities which were confined within the bone with 2/3rd intact circumferential cortex and amenable to curettage were included in the study. The malignant tumor and those benign lesions with extensive soft tissue infiltration on MRI and not amenable to curettage requiring excision were excluded from the study.

All patients underwent routine investigations including plain X-ray in two views i.e. anteroposterior and lateral views. Computerized Tomography (CT) Scan, and/or Magnetic Resonance Imaging (MRI) were done for the local extent of the lesions. A preoperative biopsy confirmed the diagnosis in all the cases. The volume calculation for cystic lesions was done as follows, where A = width, B = depth, and C = height. The most appropriate formula was used in each case depending on the radiological shape of the defect [6,7]. For cylinder defect = ABC × 0.785, i.e., (π × A/2 × B/2 × C) and for spherical defect = ABC × 0.52, i.e., (4/3× π × A/2 × B/2 × C/2).

Patients were operated after anaesthetic fitness and taking consent for the usage of type of graft. The patients where allografts were used they were explained all the pros and cons of these materials; various complications like serous discharge and infection including the chances of viral transmission and consent were taken.

### 2.1. Extended Curettage

Extended curettage was performed by the standard technique as discussed. A large cortical window was made in the cavity to have a good exposure and to prevent leaving the tumor cells around the corner, and under the overhanging shelves [8]. Extended curettage was done using the sharp curettes and high-speed burr. At the end of curettage, a pulsatile jet lavage system was used to wash any residual tumor cell. The defect after bone curettage was filled by autografts (Figure **1**), allografts (Figure **2**) or bone substitutes (Figure **3**) as per randomization done by chit method.

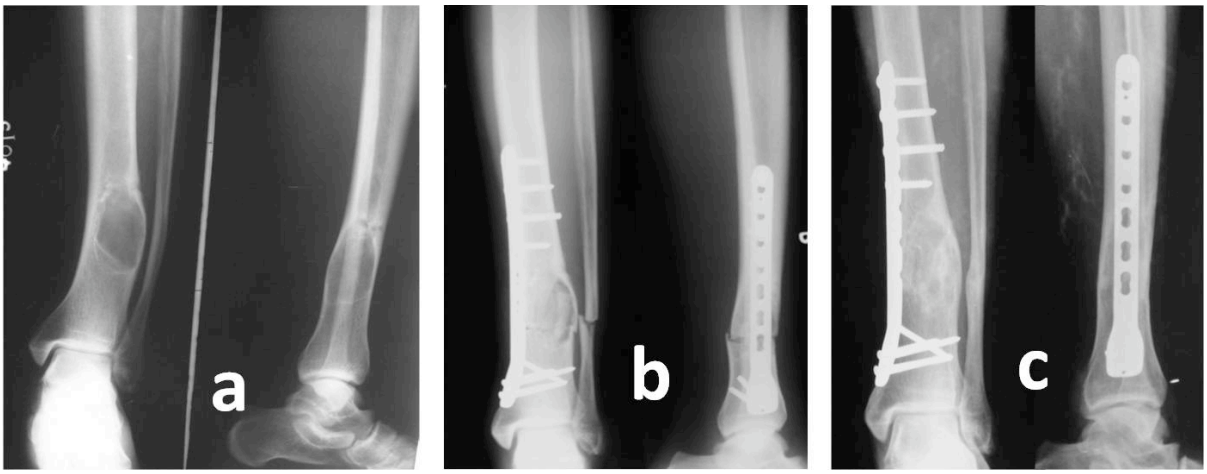


**Figure 1:** Showing bone cyst of distal tibia with varus deformity; (**a**) treated with curettage, aulologous bone grafting and deformity correction with osteotomy through the lesion and fibula; (**b**) and internal fixation with plating of tibia; (**c**) The lesion well healed with full correction of deformity.

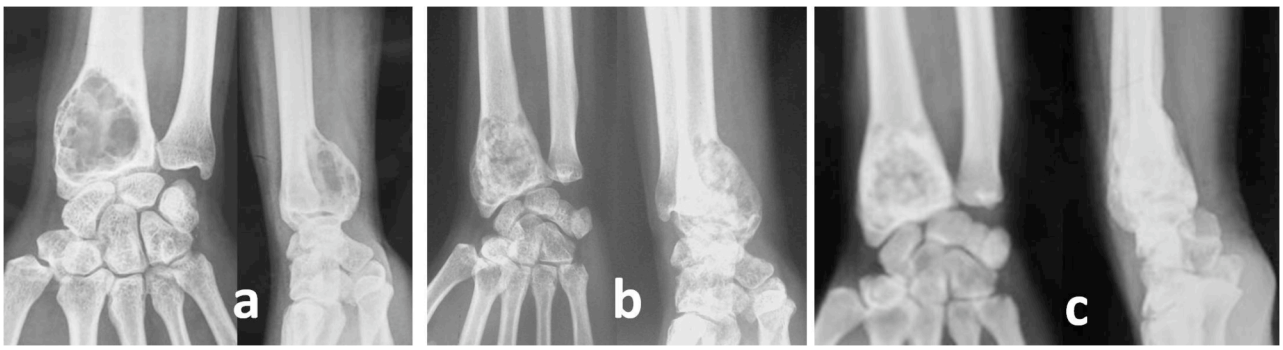


**Figure 2:** Showing giant cell tumour of distal radius; (**a**) treated with extended curettage and filling with decalcified allografts; (**b**) and it has well healed (**c**).

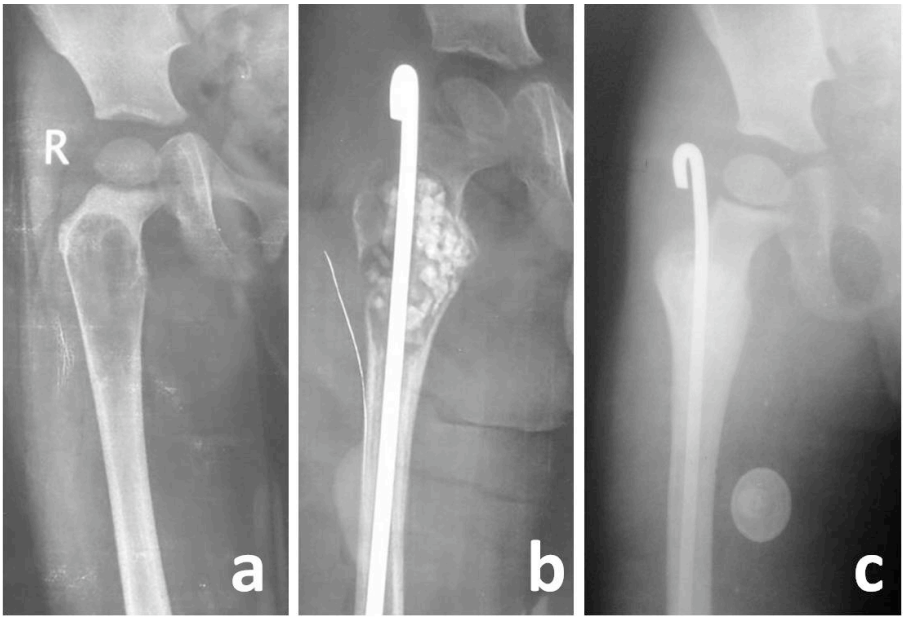


**Figure 3:** Showing the X-ray of a child of bone cyst in proximal femur; (**a**) treated with curettage, filling with β-tricalcium phosphate bone substitutes and prophylactic internal fixation with rush rod; (**b**) and the lesion healed well; (**c**) and the rod was removed after complete healing.

### 2.2. Autografts

The autografts were taken from the iliac crest in the older patients after taking separate trolley of instruments and changing the gloves of the whole team to avoid contamination of the graft harvest site. For young children falling in the autograft group we harvested autologous fibular strut instead of iliac crest having growth plate and lot of cartilage. The procured grafts were immediately and directly packed in to the curetted cavities with the aim that some of the osteoprogenitor cells may survive at the recipient site for osteoinduction along with the osetoconduction in the scaffold.

### 2.3. Allografts

We used femoral head allografts in all cases. The bone was removed during arthroplasties excluding the cases of tumors and infection. All the patients whose heads were taken for using as allografts were tested for HIV test, Australian antigen (hepatitis B surface antigen), hepatitis-C and venereal disease research laboratory test and the positive ones were excluded. We used hydrochloric acid treated decalcified bone as allografts. After removal of soft tissues, periosteum, and cartilage the bone was thoroughly washed with distilled water or normal saline and immersed in 0.6N hydrochloric acid (HCl). The grafts were stored in refrigerator for 3 to 5 days. The solution was changed every 24 hour. The partially decalcified bone was thoroughly washed to remove the acid and kept in 50–70% ethanol at 4°C temperature in simple domestic refrigerator. The stored bones were used within six months. At the time of use the allograft was cut into small granular pieces/chips, thoroughly cleaned and rinsed with sterile warm saline. The cavity was tightly packed with grafts.

### 2.4. The Bone Substitutes

β-Tricalcium phosphate (β-TCP) was used as bone substitute in all cases. The graft substitutes were mixed with patient's blood on the table and the cavity was snuggly packed with grafts.

Patients were evaluated clinically and radiologically at 6 weeks, 3 months, 6 months and 12 months interval thereafter. Functional assessment was done as per Musculoskeletal Tumor Society Rating Scale (MSTS) score [9] while radiographic assessment of graft uptake was done as per Irwin grading (Table **1**) [10]. The average time of bone healing in upper limb was judged by allowing routine activities (driving car and bike, combing hairs, lifting books and food plates etc) where as in lower limb, by allowing full weight bearing.

**Table 1: Irwin Grading for Radiological Assessment of Graft Uptake [10]**

| | |
|---|---|
| Stage I | Obvious margin |
| Stage II | Hazy margin |
| Stage III | Obvious incorporation |

**Table 2: Histopathological Diagnosis and Type of Graft Used**

| Histopathological diagnosis | Autograft (n=32) | Allograft (n=28) | Bone substitutes (n=30) | Total (n=90) |
|---|---|---|---|---|
| Giant cell tumor | 12 | 8 | 10 | 30 |
| Aneurysmal bone cyst | 8 | 10 | 9 | 27 |
| Enchondroma | 4 | 4 | 4 | 12 |
| Simple bone cyst | 3 | 3 | 4 | 10 |
| Chondroblastoma | 4 | 3 | 3 | 10 |
| Chondromyxoid fibroma | 1 | 0 | 0 | 1 |

## 3. RESULTS

The mean age of the patients was 22.5±12.6 years ranging from 6- 62 years. Peak incidence was observed in second and third decade (n=63, 70%). There was preponderance of male patients over the female patients with ratio of 3:2. Out of 90 patients, 54 were males while the rest 36 females. The most common lesion was giant cell tumor (n=30, 33.3%) followed by aneurysmal bone cyst (n=27, 30%). There were twelve patients (13.3%) of enchondroma and ten patients each (11% each) of simple bone cyst and chondroblastoma. One patient had chondromyxoid fibroma (Table **2**).

Femur was the most commonly involved bone (n=22, 19.8%) followed by radius (n=15, 16.7%). Humerus, fibula and tibia were involved in fourteen cases (15.5%) each while metacarpals were involved in six patients (6.7%). There was one case (1.1%) each located in ulna, phalanges, talus, calcaneum and metatarsal. 6 patients (6.7%) presented with preoperative pathological fracture and hence treated accordingly with relevant internal fixation. Mean tumor volume was highest in femur 71.17 $cm^3$ (range 28.26 to 168.48 $cm^3$). In tibia mean volume was 31.07 $cm^3$ (range 9.4-43.27 $cm^3$) and for lesions involving humerus was 29.98 $cm^3$ (range 15.6-46.4 $cm^3$). There were pathological fractures in six patients with destruction of circumferential bone all around with mean volume 87.4 $cm^3$. The range and mean tumour volumes in different groups are described in table **3**. The mean tumour volumes in autograft, allograft and bone substitute groups were 29.50, 32.83 and 27.31 $cm^3$ respectively.

**Table 3: Mean Tumor Volume in Different Groups**

| Study Groups | Mean Volume ($cm^3$) | Range ($cm^3$) |
|---|---|---|
| Autograft (n=32) | 29.50 | 7.6- 105.26 |
| Allograft (n=28) | 32.83 | 9.4 – 168.48 |
| Bone substitutes (n=30) | 27.31 | 2.7- 97.32 |
| Total (n=90) | 29.88 | 2.7 – 168.48 |

Autografts were used in 32 patients (35.6%), allografts were used in 28 cases (31.1%) and in remaining 30 cases (33.3%) bone substitutes were used (Table **3**). Among 32 patients of autograft group, 30 patients (93.8%) achieved Irwin grade III characterized by obvious incorporation of graft into host bone. Rest two patients (6.25%) were able to achieve grade II visualized as hazy margins on radiograph. All patients with allograft (n=28, 100%) achieved Irwin grade III (obvious incorporation) radiologically over the follow up period. Among bone substitute group 27 patients (88.9%) achieved Irwin grade III (Figure **4**) while 3 patients (10%) radiological grade II was


**Figure 4:** Showing the X-ray of a patient of giant cell tumour of distal tibia; (**a**) treated with curettage, filling with β-tricalcium phosphate bone substitutes; (**b**) and the lesion well healed and good incorporation of bone substitutes (**c**).

**Table 4: Graft Uptake as Per Irwin Grading**

| Irwin Grade | Autograft (n=32) | Allograft (n=28) | Bone Substitute (n=30) | Total (n=90) |
|---|---|---|---|---|
| Grade III | 28 (87.5%) | 23 (82.1%) | 24 (80%) | 75 (83.3%) |
| Grade II | 4 (12.5%) | 5 (17.9%) | 6 (20%) | 15 (16.7%) |
| Grade I | 0 (0) | 0 (0) | 0 (0) | 0 |

**Table 5: Comparison of Healing Time among Three Groups**

| Graft (No. of Cases) | Mean Healing Time | Range |
|---|---|---|
| Autograft (32) | 6.77 ± 3.2 weeks | 4 – 16 weeks |
| Allograft (28) | 11.25 ± 2.6weeks | 8 – 16 weeks |
| Bone Substitute (30) | 10.0 ± 2.4weeks | 8 – 14 weeks |
| Total (90) | 8.93 ± 3.4 weeks | 4 – 16 weeks |

**Table 6: Post-Operative Complications in Different Groups**

| Complications | Autograft (n=32) | Allograft (n=28) | Bone Substitute (n=30) | Total (n=90) |
|---|---|---|---|---|
| Serous Discharge | 0 | 18 (64.3%) | 7 (23.3%) | 25 (27.8%) |
| Infection | 1 (3.1%) | 1 (3.6%) | 1 (3.3%) | 3 (3.3%) |
| Recurrence | 2 (6.2%) | 1 (3.6%) | 1 (3.6%) | 4 (3.3%) |
| Additional surgical scar | 32 (100) | 0 (0) | 0 (0) | 32 (35.6%) |

achieved (Table **4**). Specific graft based analysis revealed that the autograft had shortest healing time with mean value of 6.77 ± 3.2 weeks (4–16 weeks) followed by bone substitutes 10.0± 2.4weeks (8–14 weeks). Allografts demonstrated maximum healing time with mean 11.25 ± 2.6weeks (range 8–16 weeks) (Table **5**). The bone substitutes were costlier for the patients however the allografts were available free in the institute.

Serous discharge was seen in allograft (n=18) 64.3% and bone substitute (n=7) 23.3%. However it resolved spontaneously in 14-21 days. Three patients (3.3%) developed infection; one patient with autograft resolved with change of antibiotics while in other patient infection could be controlled with removal of infected bone substitute. In one patient with allograft, infection resolved with removal of implant and insertion of antibiotic (vancomycin) beads. Recurrence was noted in four cases of giant cell tumors (3.3%), 2 with autograft and one each with allograft and bone substitutes respectively. These were treated with further surgeries i.e. one with resection and reconstruction with arthrodesis and three with further extended curettage and polymethylmethaacrylate cementation. No neurovascular deficit or fracture was seen in any of the patients. These complications are described in Table **6**. The overall average Musculoskeletal Tumor Society (MSTS) score was 26.75 (range 24–30). The mean follow up period was 46months (range 24–70).

## 4. DISCUSSION

Extended curettage followed by filling the cavity with autograft or allograft or bone substitute is recommended for most benign lytic lesions. Fresh autogenous cancellous possess all the essential properties, osteogenesis, osteoinduction and osteo-conduction and have no associated risk of viral transmission. Iliac crest is the most frequently chosen donor site as it provides easy access to good quality and quantity cancellous autograft. Harvesting autologous bone from the iliac crest has several downsides as it lengthens the overall surgical procedure and is usually complicated by residual pain and cosmetic disadvantages. In small children, the usual donor sites do not provide cortical grafts large enough to bridge defects or the available cancellous bone may not be enough to fill a large cavity or cyst;

with additional possibility of injuring the physis. Allografts or bone substitutes are preferred in this situation. Allografts are also indicated in the elderly patients who are poor operative risks and patients from whom not enough acceptable autogenous bone is available. The advantages of bone allograft harvested from cadaver sources include its ready availability in various shapes and sizes, avoidance of the need to sacrifice host structures and no donor-site morbidity. However they are associated with the transmission of infectious agents, particularly transmission of HIV and Hepatitis C, a concern virtually eliminated through tissue-processing and sterilization [4].

The ideal bone-graft substitute should be biocompatible, bioresorbable, osteoconductive, osteoinductive, structurally similar to bone, easy to use and cost-effective. Within these parameters a growing number of bone alternatives are commercially available for orthopaedic applications. They may serve as a matrix for bone regeneration and can be apposed to the surface of the bone or fill a defect or bone gap. One of the major advantages of bone graft substitute is their unlimited availability, the reduction in operating time and blood loss, and the exclusion of donor site morbidity. Calcium-sulphate (gypsum) has been the most popular substance. Other more recently introduced graft materials include β-tricalcium phosphate (β-TCP), and hydroxyapatite. Various studies have compared the efficacy of one group with the other [4,10].

It was also observed that increased tumor volume is a risk factor for pathological fracture and we had pathological fractures in six patients with destruction of circumferential bone all around with mean volume 87.4 $cm.^3$ Although no size limit has been internationally accepted but lesions with mean volume greater than 60 $cm^3$ have been proposed as at risk for fracture and further complications [6,7,11,12,13].

Although no criterion has been defined to accurately measure mean healing time but we observed that the healing time of autograft was significantly less as opposed to allograft and bone substitute (p=0.005 and p=0.038 respectively). Yang *et al*. compared allograft and bone substitutes and noted a significantly higher mean healing time in allograft compared to bone substitute group (p=0.000) and increased discharge post operatively in both groups. There were more complications in allograft group like infection (2%) and non union (4%) when used for larger cavities [14]. Glancy *et al*. [13] and Yercan *et al*. [15] compared autograft and allograft for benign lytic bone lesions in children and hand enchondromas respectively. Additional scar, cosmetic deformity and increased duration of surgery are problems specifically related to autografts. Increased serous discharge and risk of infection are potential hazards to allograft application. Recurrence rate is dependent more on type, size and extent of lesion and efficacy of extended curettage rather than type of graft used [13,15]. The bone substitutes and allografts have similar risk of increased discharge and infection. However the functional outcome is not much dependent on types of grafts used [13,15,16,17,18].

As compared to adults, the lesions in children, young adults and their metaphyseal location showed much better healing with all kind of fillers. This is because of good healing and osteogenic potential in the young individuals and presence of cancellous bone in metaphyseal area. But all 90 patients were satisfied with the procedure and with their functional outcome. Nonetheless cost is big limiting factor for usage of bone substitutes in large cavities in our subset of patients but it avoided donor site morbidity. The autografts should be directly packed in to the curetted cavities after their retrieval from the iliac crest so that some of the osteoprogenitor cells may survive at the recipient site for osteoinduction, osteoconduction, early healing and take up of graft. These should not be kept on instrument trolley even for few minutes. Further the recurrence dependents on the aggressiveness of the lesion, the quality (thoroughness) of the curettage, and the effectiveness of the adjuvant used for extended curettage as observed by Gupta *et al*. also [19].

The strength of this study is that there was good number of cases for comparison which were treated at a single institute by the same team of surgeons with a good length of follow up. Also there were comparable lesions in view of their numbers in each group treated with extended curettage. The weakness of this study includes that in each group there were different kinds of lesions with relatively different biological behavior with varying sizes at different locations.

After comparing our results of autografts, allografts and bone substitutes as an adjuvant with that of available literature, we observed that autograft is best material to fill the defect after extended curettage of benign lytic lesions of bone. Bone substitutes, if affordable, and allografts can act as other options if autografts not available in adequate amount. We want to convey that in small cavities bone substitutes can be

an effective alternative as the requirement will be more in larger cavities increasing the cost; however in large cavities it is better to use either allograft alone or a combination of autograft and allograft without increasing much morbidity.

## CONCLUSION

We conclude that use of allograft and bone substitute may not be as effective in view of their take-up as the autografts but their judicious use in scarcity of the latter for the big cavities in benign bone tumors is very much required and acceptable. There results have been almost comparable with autografts in terms of efficacy and related complications. Any filler is well taken up in children because of good healing and osteogenic potential in them. The required quantity of autografts for big cavities, the cost of bone substitutes; and the availability and apprehension of disease transmission in allografts become the limiting factors respectively.

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