International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

An Overview on Treatment of Cystic Benign Bone Tumors

Hossam mohamed khiry, Ahmed Mohamed Elattar, Ahmed Mohamed Mariey, Mohammed Hassan Abdellatief

Orthopedic Surgery Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Ahmed Mohamed Mariey

Email: ahmedmariey96@gmail.com,

Abstract:

Cystic benign bone tumors are among the most common osseous lesions encountered in children and young adults. They frequently occur in the metaphyseal–diaphyseal regions of long bones and may present with pain, swelling, or pathological fractures. Curettage remains the standard treatment, but the resulting defect requires filling. Bone grafts and synthetic bone substitutes are widely used to enhance healing and structural support.

Keywords: Benign bone tumor; Bone graft; Bone substitutes; Cystic bone lesion; Curettage; Musculoskeletal tumor.

Introduction:

Benign cystic bone tumors are among the most frequent osseous lesions in children and young adults, usually located in the metaphyseal–diaphyseal regions of long bones. They often present incidentally but can sometimes cause pain, swelling, or pathological fractures, requiring careful clinical and radiological assessment for proper diagnosis and management **(1).**

The most common types of cystic benign bone tumors include unicameral bone cysts, aneurysmal bone cysts, osteoblastoma, fibrous dysplasia, and giant cell tumor. These lesions have different clinical behaviors and radiographic features, making accurate differentiation crucial for treatment planning and prognosis **(2).**

Curettage is the standard surgical treatment for most cavitary benign bone tumors, with reported cure rates up to 90–95%. However, filling the residual defect after curettage is essential to prevent fractures and ensure bone healing. Bone grafts and synthetic bone substitutes are the two main options, each with distinct advantages and limitations **(3).**

Bone Graft:

Auto graft:

An autologous bone graft is commonly referred to as an autobone graft-is a surgical procedure in which bone tissue is harvested from one part of a patient's body and transplanted to another site within the same individual to aid in bone regeneration andhealing. Bone autograft used in Orthopedic Surgery for fracture non-union or bone defects, Autologous bone grafting is widely regarded as the "gold standard" in bone grafting procedures due to its excellent biological properties, including:

- Osteoconduction: provides a scaffold for new bone growth
- Osteoinduction: stimulates the differentiation of progenitor cells into osteoblasts
- Osteogenesis: contains live bone-forming cells (osteoblasts) **(4).**

Because the graft comes from the patient, there is no risk of immune rejection or disease transmission, unlike allografts (from donors) or xenografts (from animals).

Bone autograft used in Orthopedic Surgery for fracture non-union or bone defects, the most frequently used donor site is the iliac crest (pelvic bone), which provides a rich supply of both cortical and cancellous bone. Other donor sites include the tibia graft from proximal tibia and supply with Cancellous bone, fibular graft which supply with cortical bone and may be vascularized and distal radius which supply Cancellous bone and used in hand surgery, depending on the surgical need and location **(5).**

This refers to the form/consistency of the graft material:

1. **Cortical bone graft:**
   - Dense and strong
   - Provides structural support
   - Slower incorporation
   - Often harvested as ablock
2. **Cancellous bone graft:**
   - Spongy, porous bone
   - Rich in bone marrow and osteogenic cells
   - Rapid vascularization and incorporation
   - Commonly used for faster healing
3. **Corticocancellous graft**:
   - Combination of both cortical and Cancellous bone
   - Balances structural support and osteogenic potential

Advantages of autobone graft:

•High biological compatibility (no immune reaction).

• Contain live osteogenic cells.

• Superior healing potential compared to synthetic or donor grafts.

Limitations:

• Donor site morbidity: pain, infection, bleeding, or fracture.

• Limited quantity available, especially in small-framed or elderly patients.

• Longer operative time due to graft harvesting.

Bone Substitutes:

The most ideal bone substitute should include the ability of providing a scaffold for osteoconductivity and growth factors for osteoinductivity and should be structurally similar to real bone. The scaffold for ideal osteoconductivity should exhibit osseointegration and a 3D structure suitable for growing cells and blood vessels. In addition, it should have good biocompatibility, biodegradation, and biomechanics similar to surrounding bone tissues. Numerous bone substitutes that satisfy these conditions are commercially available in orthopedics. **(6)**

Ceramic and ceramic composites:

Ceramic bone substitutes are typical calcium-based synthetic bone substitutes that are already approved in terms of stability and effect. Given the problems with autogenous bone and allogeneic bone, osteoconductive ceramic with biodegradation draws considerable attention these days. For synthesized graft to exert its biological effects, several conditions are required: compatibility with surrounding tissues, chemical stability in body fluid,

biomechanical and physical compatibility, durability in sterilization process, reasonable price, and consistency of reliable quality. Today, various types of ceramic products are composed of calcium phosphate, including hydroxyapatite (HA) and tricalciumphosphate (TCP), or (calcium sulfate), or their compounds. **(7-10)**

Ceramic features no limitations of quantity, no risk of morbidity and infection of the donor site, and easy sterilization and storage. However, primary application of ceramics is mainly focused on bone defects, such as fracture with joint depression, because ceramics are fragile and have poor mechanical strength. Since the amount of resorption of ceramic varies depending on material, if resorption does not occur properly, it could possibly impede bone remodeling. As a result, the speed of bony union and the process of remodeling to obtain a proper strength are delayed. In addition, due to its fragility, it is difficult to mold ceramic into a desired shape during operation. The remodeling process relies mainly on ceramic biodegradability. At this time, material that is not absorbed biologically impedes the remodeling process and becomes a region of mechanical stress concentration. Too slow absorption impedes bone remodeling, and too fast absorption reduces mechanical stability and causes fibrous tissue formation instead of osteogenesis. **(11)**

Hydroxyapatite (HA):

HA is bioactive ceramic and a main mineral of bone. Given its density, HA with a porous structure is easily bio-absorbable and exhibits good osteoconductivity. Therefore, when it is introduced in vivo, surrounding bone tissues grows and gradually progresses through the bone substitution. Regarding the material features of HA, it can be inserted in line with a shape of a defective region. In addition, it is easily absorbed, does not generate metabolite impeding osteogenesis, and causes almost no foreign body reaction due to its excellent biocompatibility. HA has very high compression and tensile strength compared with TCP. Since HA is slowly degraded and retained in vivo for a long period of time, it impedes bone remodeling extends the mechanical vulnerability of new bone, and remains as permanent stressor. **(12)**

Tri-calcium phosphate (TCP):

Tri-calcium phosphate is osteoconductive calcium phosphate and has the most similar chemical composition to human bone. It has better absorption than hydroxyapatite (HA). It is more porous than HA and features weak mechanical strength and fast absorption. More porous TCP undergoes biodegradation within 6 weeks after its introduction into the bone defect. Since its compression and tensile strength is very similar to that of cancellous bone, it is used in regions with no mechanical load. Moreover, TCP has better osteoconductivity and biocompatibility than conventional bone cement with PMMA, and it is possible to inject TCP with a syringe into a bone defect or the screw insertion site in case of fracture fixation. As another main component, polyphosphate is highly concentrated in osteoblasts and is involved in mineralization of bone metabolism. In contrast of HA, ceramic TCP is biodegraded fast in vivo. It is biodegraded within 4–8 weeks after graft, and it is difficult to obtain proper bone formation during the early period. In consideration of these properties, biphasic ceramic with a mixture of HA and TCP is manufactured. Depending on the mixture ratio of these two components, it is possible to adjust the speed and degree of absorption and mechanical strength. **(13)**

Calcium phosphate cement (CPC):

The discovery of the first CPC occurred coincidentally via the observation of calcium phosphate solubility in 1986. CPC consists of calcium phosphate. Calcium phosphate cements (CPCs) are frequently used to repair bone defects. Currently, CPC are defined as a combination of one or more calcium phosphate powders which, upon mixing with a liquid phase, form a paste able to self-set and harden in situ in the bone defect site to form a scaffold. A body-temperature dissolution-precipitation reaction is one of the most important characteristics of CPC, which facilitates is ability to mold and fill the bone defect. Injectability, one of the advantages of CPC, allows application of CPC in minimally invasive surgery. Therefore, it is clinically used to fill metaphyseal or subchondral cortical defects caused by articular fracture. Since CPC has the material property of ceramic, bioabsorbable-enhancing additives, such as chitosan or Vicryl meshes, can be used to improve mechanical strength. CPC has osteoconductivity; it is gradually absorbed in the bone remodeling process and is replaced by a new bone. Currently, the paradigm has moved toward enhancement of biological interactions of CPC, such as

bone tissue engineering, in addition to improvement in the mechanical strength of CPC and the addition of cells and growth factors in cement. In addition, 3D printing for fabricating CPC scaffolds is rapidly developing with a high degree of accuracy. Here, 3D printed CPC offers specific benefits for clinical applications, including easy adaptation and fixation, reduced surgical time, and good esthetic results. Furthermore, with recent advances in tissue engineering, "tissue regeneration by natural tissues" instead of "tissue replacement by biomaterials" has been proposed and emphasized. This new emphasis on tissue engineering is enhanced by CPC's excellent biological interaction such as osteoconductivity, osteoinductivity, biodegradability and bioactivity. **(14)**

Calcium sulfate:

Calcium sulfate is clinically used to fill defects, such as bone cavities, and segmental bone defect, and moreover expansion use for spinal fusion and even for filling of harvest site of autogenous bone. Through recrystallization, it becomes a solid material and gives mechanical stability to its inserted region. Calcium sulfate normally undergoes biodegradation within 6–8 weeks after its insertion into the bone defect. Given its lack of porosity, calcium sulfate has limited osteoconductivity. Given its mechanical disadvantage and rapid resorption. Compared with calcium phosphate, calcium sulfate is not often used. **(15)**

Bone morphogenetic protein (BMP):

Urist et al. reported that the growth factors extracted from bone organic component were able to induce osteogenesis and named them bone morphogenetic proteins (BMPs). Many types of local growth factors are related to bone healing. Depending on similarities in composition, these growth factors are classified into approximately 20 multiprotein growth factor families or superfamilies. These growth factors include epidermal growth factor (EGF), insulin-like growth factor (IGF), fibroblast growth factor (FGF), platelet-derived growth factor (FDGF), and transforming growth factor (FGF). Among them, only BMPs that belong to the transforming growth factor superfamily are known to run all processes of new osteogenesis. After penetration of mesenchymal cells, BMPs are involved in a series of processes, including differentiation to chondrocytes, removal of cartilage, and osteogenesis. Depending on their levels, BMPs have a steep dose-response curve. If a large amount of BMPs are injected, osteoinduction occurs early, and a considerable amount of bone is generated. As the injection amount increases, direct osteogenesis is increased by intramembranous ossification rather than endochondral ossification. BMP-2, BMP-7 (OP-1), and BMP-6 have similar roles and activities in the process of osteogenesis. To obtain the same degree of osteoinduction, a little more BMP-5 is required. BMP-3 (Ostenogenin), which is the most distributed in bone, functions as negative modulator in osteogenesis. **(16)**

There are a few studies with a small number of randomized controlled trials only. The US Food and Drug Administration approved the use of BMP-2 for open tibial shaft fracture as a selective clinical indication and the use of BMP-7 for iliac nonunion and traumatic bone defect. BMP is used as an adjuvant for the spinal lumbar. When BMP-2 was used together with an allograft, its fusion rate was similar to that of autogenous bone graft. These BMPs account for only 0.1% of total bone proteins and are mainly found in cortical bone. Since BMPs exist in the extracellular matrix, it is impossible to obtain BMPs until the bone matrix is demineralized. Accordingly, to obtain several grams (g) of BMPs, several kilograms (kg) of bones are needed. In addition, regardless of high-quality purity, they can include impurities, potentially causing unexpected reactions and results. **(17)**

With the development of molecular cloning technology, these problems were solved by the creation of a large amount of recombinant human BMPs (rhBMP), which do not trigger immune reactions. In the rhBMP- or bovine BMP-based animal test, these substances exhibited considerably good results. According to the research in which partially purified bovine BMPs were used for canine thoracic vertebrae fusion, the use of BMPs and autogenous bone together had the highest success rate (71%). In the thoracic vertebrae fusion of canine posterolateral transverse processes with the use of rhBMP-2, it was possible to achieve faster fusion. Using an excess amount of BMPs physiologically can trigger osteolysis. Depending on patients and body regions, the requirement of BMPs varies. Regarding the side effect of BMPs in the cervical vertebrae, contraindications are reported. Therefore, tissue engineering approaches for long-term control and local transmission of these growth factors are a promising research area. Tissue engineering related to bone grafts have been conducted to provide

all the fundamental properties of an ideal bone graft; however, it has proven difficult to achieve vascularization in grafts which are large enough for use in clinical applications. **(18)**

Bone grafts versus synthetic bone substitutes in the treatment of benign bone tumors

Benign bone tumors represent an important chapter in the pathology of the musculoskeletal system, most commonly affecting young people under the age of 30 The most important clinical criteria essential for the diagnosis are age, sex, and location. **(19)**

The most common benign bone tumors diagnosed in orthopedic surgery are: osteochondroma, osteoid osteoma, osteoblastoma, giant cell tumor, bone aneurysmal cyst, fibrous dysplasia. An important feature is the lack of secondary determinations. Depending on the type and the location of benign bone tumors, the treatment can be non-surgical or surgical. In some cases, the treatment consists of "watchful waiting", but if the patients present persistent pain, surgical treatment is decided. **(20)**

The main objective of the surgical treatment is to restore the local anatomy, reduce pain and restore limb. Bone grafts have an important role in the treatment of bone defects caused by tumors, infections, trauma, and prosthetic revision surgery. **(21)**

In current practice, in orthopedics, the filling of bone defects is done with the help of autografts or synthetic bone substitute. Autografts are considered the "gold standard" in terms of grafting materials, due to the properties of osteogenesis, osteoinduction and osteoconduction, but also has some disadvantages: increased risk of infection, performing a new surgical incision. The synthetic bone substitute is an alternative to autografts, but it needs to have three important characteristics: biocompatibility, osteoconduction and osseointegration. Synthetic materials that have these characteristics are made of calcium, silicone, or aluminum. **(22)**

Mihai-Aurel et al. conducted a study on patients which were divided into two categories as follows: in the first group, there were 12 patients in whom the filling technique was performed with synthetic bone substitute, and the second group included 6 patients in whom the filling technique was performed by autograft.Patients evaluated, both pre- and post-operatively by clinical and imaging examination, with antero-posterior and profile radiographs and CT scans. **(23)**

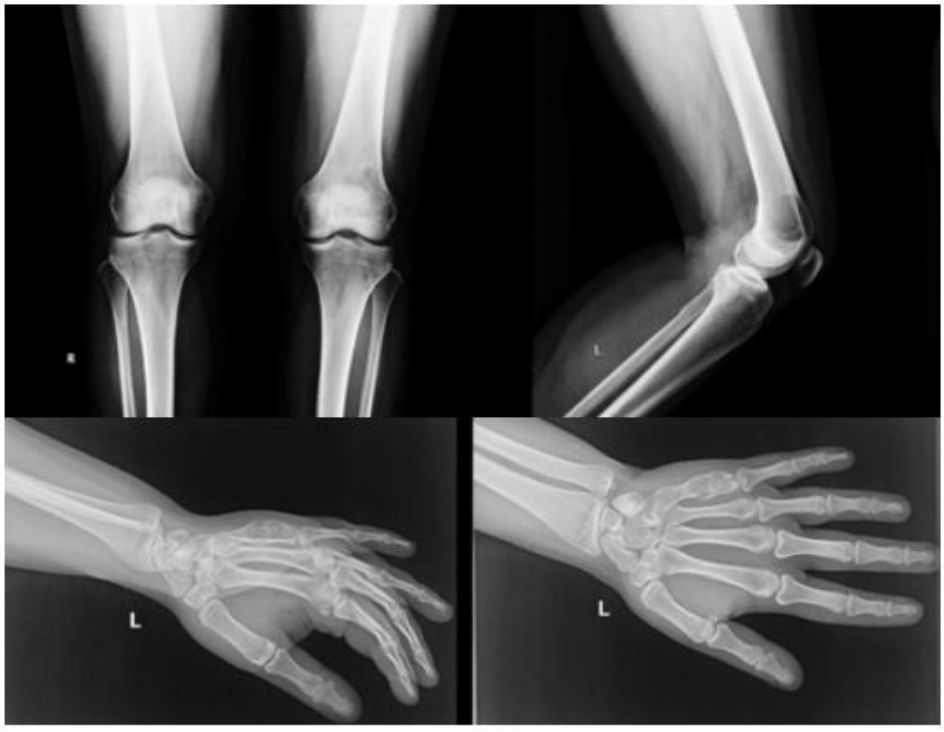

Figure 1: Preoperative radiographs. **(23)**

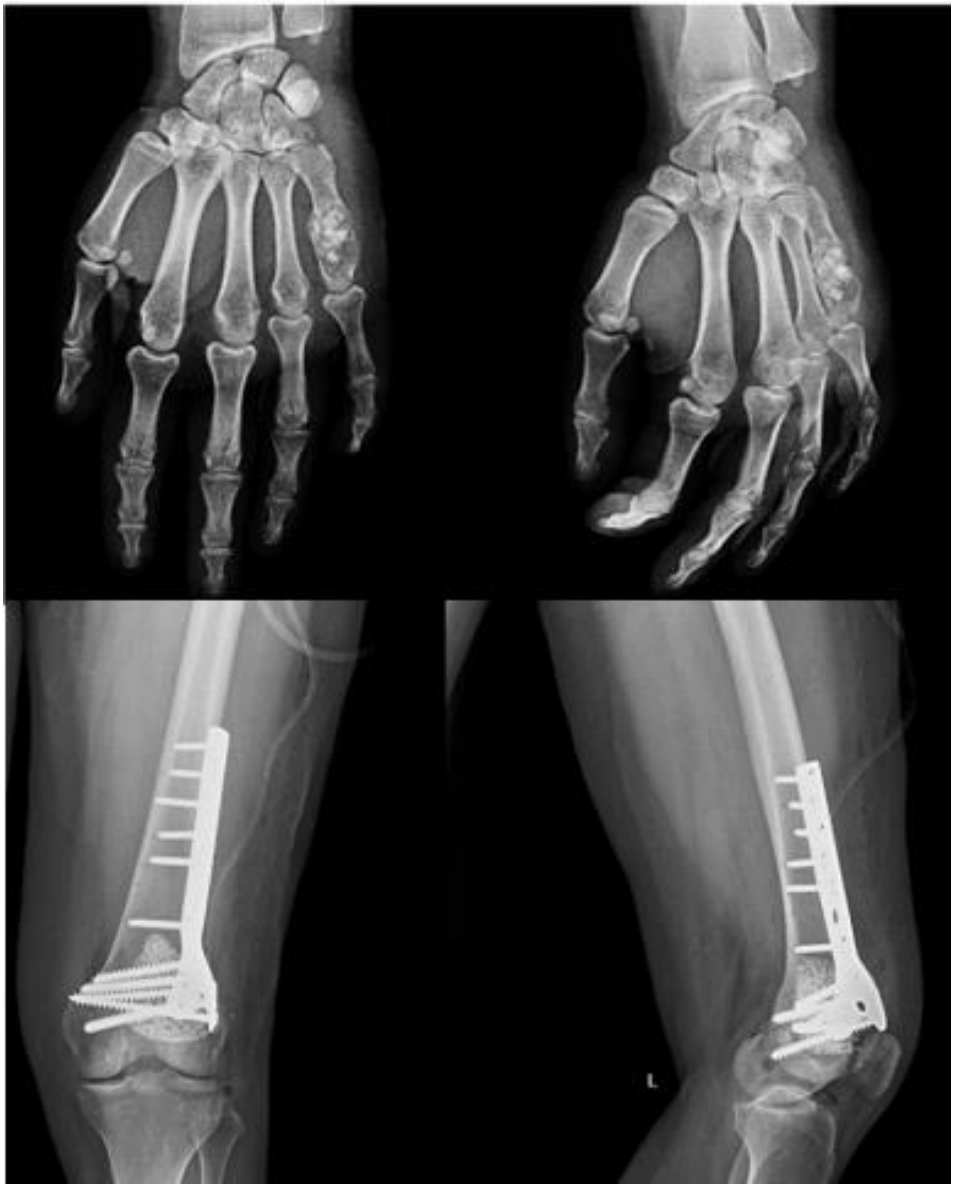

Figure 2: Autograft filling (left) and filling with synthetic bone substitute and reinforcement (right). **(23)**

References:

1. Eyesan SU, Idowu OK, Obalum DC, Nnodu OE, Abdulkareem FB. Surgical consideration for benign bone tumors. Niger J Clin Pract. 2011;14:186–92.
2. Jawad MU, Scully SP. In brief: classifications in brief: enneking classification: benign and malignant tumors of the musculoskeletal system. Clin Orthop Relat Res. 2010;468:2000–2.
3. Delawi D, Dhert WJ, Castelein RM, Verbout AJ, Oner FC. The incidence of donor site pain after bone graft harvesting from the posterior iliac crest may be overestimated: a study on spine fracture patients. Spine (Phila Pa 1976). 2007;32:1865–9.
4. Manyalich M, Navarro A, Koller J, Loty B, de Guerra A, Cornu O, et al. 2009. European quality system for tissue banking. Transplant Proc.;41:2035–2043.
5. Sohn HS, Oh JK. 2019 . Review of bone graft and bone substitutes with an emphasis on fracture surgeries. Biomater Res. Mar 14; 23:9.
6. An HS, Simpson JM, Glover JM, Stephany J. 1995. Comparison between allograft plus demineralized bone matrix versus autograft in anterior cervical fusion. A prospective multicenter study. Spine.; 20:2211–2216.

7. Ullmark G, Obrant KJ. 2002. Histology of impacted bone-graft incorporation. J Arthroplast.; 17:150–157.
8. Urist M, Mikulski A, Boyd S. A chemosterilized antigenextracted autodigested alloimplant for bone banks. Arch Surg. 1975;110(4):416–428.
9. Wildemann B, Kadow-Romacker A, Pruss A, Haas NP, Schmidmaier G. 2007. Quantification of growth factors in allogenic bone grafts extracted with three different methods. Cell Tissue Bank.;8:107–114.
10. Flattley T, Lynch K, Benson M. 1983.Tissue response to implants of calcium phosphate ceramic in the rabbit spine. Clin Orthop.;179:246–252.
11. Parikh SN. 2002. Bone graft substitutes in modern orthopedics. Orthopedics.;25:1301–1309. doi: 10.3928/0147-7447-20021101-27.
12. Finkemeier CG. 2002. Bone-grafting and bone-graft substitutes. J Bone Joint Surg Am.;84:454–464.
13. Lindner T, Kanakaris NK, Marx B, Cockbain A, Kontakis G, Giannoudis PV. 2009. Fractures of the hip and osteoporosis: the role of bone substitutes. J Bone Joint Surg Br.;91:294–303.
14. Xu HH, Wang P, Wang L, Bao C, Chen Q, Weir MD, et al. 2017. Calcium phosphate cements for bone engineering and their biological properties. Bone Res.;20(5):17056.
15. Zwingenberger S, Nich C, Valladares RD, Yao Z, Stiehler M, Goodman SB. 2012. Recommendations and considerations for the use of biologics in orthopedic surgery. BioDrugs.; 26:245–256.
16. Daluiski A, Engstrand T, Bahamonde ME, Gamer LW, Agius E, Stevenson SL, et al. 2001. Bone morphogenetic protein-3 is a negative regulator of bone density. Nat Genet.;27:84–88.
17. Slosar PJ, Josey R, Reynolds J. 2007. Accelerating lumbar fusions by combining rhBMP-2 with allograft bone: a prospective analysis of interbody fusion rates and clinical outcomes. Spine J.;7:301–307.
18. Baas J, Elmengaard B, Jensen TB, Jakobsen T, Andersen NT, Soballe K. 2008. The effect of pretreating morselized allograft bone with rhBMP-2 and/or pamidronate on the fixation of porous Ti and HA-coated implants. Biomaterials.;29:2915–2922.
19. Hakim DN, Pelly T, Kulendran M, Caris JA. 2015. Benign tumors of the bone: A review, Journal of Bone Oncology.; 4(2):37-41.
20. Offner D, Grade GF, Meisels I et al. 2019. Bone Grafts, Bone Substitutes and Regenerative Medicine Acceptance for the Management of Bone Defects Among French Population: Issues about Ethics, Religion or Fear? Cell Medicine. January.
21. Fernandez de Grado G, Keller L, Idoux-Gillet Y et al. 2018. Good substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. Journal of Tissue Engineering. January.
22. Nandi SK, Roy S, Mukherjee P, Kundu B, De DK, Basu D. 2010. Orthopedic applications of bone graft & graft substitutes: a review. Indian J Med Res. Jul; 132:15-30.
23. Mihai-Aurel C., Sergiu Andrei I., Bogdan s. , et al. 2021. Bone grafts versus synthetic bone substitutes in the treatment of benign bone tumors Romanian Journal of Orthopaedic Surgery and Traumatology, Volume 4, Issue 2, July-December. pp:67-70.