



# Is a Bioceramic Glass Bone Graft Superior to Spongious Allografts in Femoral and Tibial Benign Bone Lesions?

# Femoral ve Tibial Benign Kemik Lezvonlarında Biyoseramik Cam Greftler Spongioz Allogreftlerden Üstün müdür?

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#### Abstract

Objective: this study aimed to examine the results of spongious and bioceramic bone graft applications in benign lesions of the lower extremity long bones.

Methods: Forty-seven patients, who applied to our hospital between the years 2007 and 2013; who received curettage-grafting for benign bone lesions in the long bones carrying lower extremity weight were examined retrospectively.

Results: In the bioceramic glass bone graft group, an increased average consolidation ratio, which is statistically significant compared to the spongious allograft group (p=0.002), was observed. When the fibrous dysplasia patients were considered a subgroup, the consolidation ratio in the bioceramic glass bone graft group was found to be significantly high compared to the spongious allograft group (p=0.029).

Conclusion: Bioceramic glass bone grafts are bone filler materials that hold radiologically superior and clinically similar results compared to spongious allografts. Having a statistically significant radiological consolidation success in fibrous dysplasia, which is a benign aggressive tumor, bioceramic glass bone grafts may be thought to be capable of being an advantage option for benign aggressive tumors.

Keywords: Bioceramic glass bone graft, spongious allograft, femur, tibia, benign bone lesion

# Öz

Amaç: Bu çalışmanın amacı, alt ekstremite uzun kemiklerindeki benign lezyonlarda uygulanmış spongioz ve biyoseramik cam greftin sonuçlarının incelenmesidir.

Yöntem: 2007 ile 2013 yılları arasında hastanemize başvuru yapmış, alt ekstremite yük taşıyan uzun kemiklerindeki iyi huylu kemik lezyonlarına yönelik küretaj-greftleme operasyonu yapılan kırk-yedi hasta retrospektif olarak incelendi.

Bulgular: Biyoseramik cam greft grubunda, insan kaynaklı spongioz allogreft grubuna kıyasla, istatistiksel olarak anlamlı, artmış ortalama konsolidasyon oranı görülmüştür (p=0,002). Fibröz displazi hastaları sub-grup olarak değerlendirildiğinde; biyoseramik cam greft grubundaki konsolidasyon oranı, insan kaynaklı spongioz allogreft grubuna kıyasla anlamlı olarak yüksek bulunmuştur (p=0,029).



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#### Öz

**Sonuç:** Biyoseramik cam greftler, insan kaynaklı spongioz allogreftlerle karşılaştırıldığında radyolojik olarak üstün, klinik olarak benzer sonuçlara sahip kemik dolgu materyalleridir. Biyoseramik cam greftlerin; benign agresif tümör olan fibröz displazideki radyolojik konsolidasyon başarısının istatistiksel olarak anlamlı olmasından dolayı, benign agresif tümörlerde avantajlı bir seçenek olarak düşünülebilir.

Anahtar Kelimeler: Biyoseramik cam greft, spongioz allogreft, femur, tibia, benign kemik lezyonları

# Introduction

The gold standard is autogenous bone graft applications while there are several graft material usages for treating bone defects resulting from congenital anomalies, diseases, tumoral lesions, atrophy, or surgical excisions. An autogenous graft holds some difficulties such as generating a second surgery region, risk of having a tumor, increase in patient morbidity, and the possibility of being incapable of obtaining the desired amount of bone graft. These situations led researchers to seek an ideal bone graft material that can substitute autogenous bone grafts. MacEwen first implemented allograft in humans with the purpose of child humerus reconstruction in 1881<sup>(1)</sup>. Until quite recently, orthopedic surgeons possessed only autologous bones and allografts as bone resources. Today, several different options have been improved using tissue engineering applications. Bioactive glass grafts are the products of this technology. The recent research has served for increasing the osteoconductive, osteo-inductive, and osteogenic features of bone grafts obtained via synthetic ways.

The aim of treatment in benign bone lesions is to provide an osteo-conductive effect rather than a biological effect. Therefore, autograft or bioceramic grafts can be used for these lesions. The current study seeks a solution to partial healing on spongious allografts and to shed light on the literature. There is no previous study on this issue in our knowledge.

# **Materials and Methods**

In this study, patients, who applied to our hospital between the years 2007 and 2013 and who were given curettagegrafting for benign bone lesions in their long bones carrying lower extremity weight were examined retrospectively after the approval of the İzmir Tepecik Education and Research Hospital Research Ethics Committee (date: 24.11.2015, decision no: 22).

Inclusion criteria were that the tumor was located in the femur or tibia and was treated with curettage and grafting using a bioceramic glass bone graft or spongious allograft. The criteria of exclusion from the study have been determined as lesions located were not femur and tibia; malign bone tumor, non-ossifying fibroma (NOF), fibrous cortical defect (FCD), and osteoid osteoma cases, severe systematic diseases, nonattendance for follow-up.

During this period, 123 patients underwent curettage and grafting operations. Seventy-six (62%) patients were excluded because the tumor was outside the femur or tibia (n=63), two patients had malignant bone tumors, eight patients had NOF-FCD or osteoid osteoma, one patient had advanced systemic disease, and two patients had nonattendance for follow-up.

Forty-seven (38%) patients who did not meet the exclusion criteria were included in the study. There were 29 patients (62%) treated with spongious allograft in group 1, and 18 patients (38%) treated with bioceramic glass bone grafts in group 2.

Physical examination findings, surgery records, and radiological findings were evaluated.

X-rays of affected bones were taken preoperatively; and the second week, the first month, the third month, the sixth month, the first year, and following years postoperatively for a checkup, and their visual analogue scale (VAS)<sup>(2)</sup> and lower extremity functional scale (LEFS)<sup>(3)</sup> scores were calculated and evaluated.

Preoperative lesion volume and the amount of graft used in the operation were calculated in cm<sup>3</sup>. The lesion volume was calculated in a computer environment on magnetic resonance images. Additionally, patients with fibrous dysplasia were evaluated as a subgroup.

The groups were evaluated among each other following the staging of the tumors<sup>(4)</sup>.

All patients in the study received the same surgical technique, opening a cap on the bone, curettage of the mass, the application of chemical cauterization with 1% formaldehyde and 70% alcohol, respectively, each for five minutes, a lot of irrigation with physiological saline solution and filling with bone graft materials. The operation was performed by a single surgeon.

Cefazolin was given to all patients on the day of the operation and the day after the operation in 3 equal doses of 50 mg/kg for 2 days with the purpose of prophylaxis.

The spongious bone graft used in this study has crushed and freeze-dried primer form (Tranzgraft by Aziyo Biologics) while bioceramic glass bone graft has granule and bioglass primer form. A bioceramic glass bone graft is composed of silicon dioxide (45%), calcium oxide (24.5%), disodium oxide (24.5%) and pyrophosphate (6%) (GlassBoneR by Noraker).

#### **Statistical Analysis**

Statistical Package for Social Sciences version 17 was used for statistical analysis. The normality of continuous data was evaluated with the Shapiro-Wilk test. If the distribution of data was evaluated as normal, a t-test was used for statistical comparison. In the case of non-normally distribution, the Mann-Whitney U test was used. Categorical data were compared with the Fisher exact test. A p-value <0.05 was set as statistically significant.

#### Results

The study included 47 patients, 19 (40%) of whom were males. The average age was found to be 23.08 (7-57) (Table 1). Twenty-three of the patients had lesions located on femurs and twenty-four located on tibias. No statistically significant differences were found between the graft materials used when considered in terms of age, gender, and location (p>0.05).

Radiological consolidation success is achieved by proportioning the volume of the consolidated region on average 16.36 months (6-48) after curettage and grafting was evaluated.

The average pain score (out of 10, according to VAS) at the end of the follow-up period in the spongious graft group was  $1.07\pm0.96$  (0-3) while it was  $1.0\pm0.84$  (0-3) in the bioceramic glass bone graft group (p=0.898).

The average lower extremity function score percentage (out of 100, according to LEFS) at the end of the follow-up period in the spongious graft group was  $93.75\pm3.67\%$  (86.25-100) whereas it was  $94.51\pm3\%$  (88.75-100) in the bioceramic glass bone graft group (p=0.581).

The preoperative volume of tumors of the 47 patients was 43.15 (7-150) cm<sup>3</sup> on average and the average amount of graft applied to all the patients was 58.21 (8-180) cm<sup>3</sup> (Table 2). The average tumor volume was 45.79 cm<sup>3</sup> and the average amount of graft used was 67.93 cm<sup>3</sup> in the spongious allograft group, whereas the average tumor volume was 38.89 cm<sup>3</sup> and the average amount of graft used was 42.55 cm<sup>3</sup> in the bioceramic glass bone graft group (Figure 1). The rate of average tumor volume and the average amount of grafts used were calculated as  $62.14\pm17.38\%$  (33-92) in the spongious allograft group while they were calculated as  $89.11\pm7.07\%$  (70-100) in the bioceramic glass bone graft group (p<0.001).

When we examine the consolidation ratio according to the graft material used, 15 (52%) of the patients who received spongious bone graft were greater than 90%; 7 (24%) were between 80 and 90; 7 (24%) were below 80% [2 (7%) were 50%>], and 15 (83%) of the patients who received bioceramic glass bone graft were above 90%, and 3 (17%) were between 80 and 90% (Figure 2). The average consolidation ratio at the end of the follow-up period was  $82.58 \pm 15.55\%$  (35-98) in the spongious graft group while it was  $93.78 \pm 3.67\%$  (87-99) in the bioceramic glass bone group (p=0.002).

The average consolidation ratio in fibrous dysplasia, which is a tumoral lesion with a benign aggressive course, was identified as  $71.5\pm7.76\%$  (62-81) in the spongious allograft group (n=4) whereas it was found to be  $96.75\pm1.50\%$  (95-98) in the bioceramic glass bone graft group (n=4) (p=0.029).

Ten of the tumors were interpreted as stage 1; 29 were stage 2, and eight were stage 3 according to Enneking benign tumor staging (Figure 3). In the spongious allograft group, the statistical results between stage 1 and stage 2 were non-significant (p=0.097); the statistical result was significant between stages 1 and 3 (p=0.032); the statistical result was non-significant between stages 2 and 3 (p=0.129). In the bioceramic glass bone graft group, the statistical result was significant between stages 1 and 2 (p=0.01); the statistical result was non-significant between stages 1 and 2 (p=0.01); the statistical result was non-significant between stages 2 and 3 (p=0.167), the statistical result was significant between stages 2 and 3 (p=0.009) (Table 3).

Examples from several cases in the study are shown in Figures 4, 5.

The graphics of the patients with the lowest consolidation ratio identified in both groups are demonstrated in Figures 6, 7.

Table 1. Demografic characteristics and scoring							
Case	Age	Sex	Pathology	Stage	Follow-up (month)	LEFS %	VAS
1	8	М	FD	2	24	95.0	0
2	7	F	FD	3	12	92.5	1
3	20	М	SBC	1	6	93.75	1
4	28	F	GSBT	2	6	88.75	3
5	51	F	PS	3	6	91.25	2
6	56	F	SBC	1	7	92.5	1
7	15	F	FD	1	11	95.0	1
8	20	F	КВ	2	36	95.0	0
9	14	F	ABC	3	36	91.25	2
10	47	F	FD	2	6	95.0	1
11	9	М	ABC	1	36	98.75	0
12	28	F	SBC	2	6	93.75	1
13	18	F	SBC	1	12	97.5	0
14	26	М	SBC	1	11	93.75	1
15	16	F	ABC	2	12	97.5	0
16	9	F	FD	2	12	100.0	0
17	27	F	FD	2	16	88.75	3
18	17	F	SBC	1	6	95.0	1
19	24	F	ABC+GSBT	2	36	93.75	1
20	11	М	ABC	3	24	86.25	3
21	31	F	ABC	2	6	93.75	1
22	8	F	ABC	2	6	90.00	2
23	57	М	GSBT	2	6	91.25	2
24	11	F	SBC	2	24	96.25	1
25	16	М	ABC	2	12	97.5	0
26	11	М	ABC	2	12	96.25	1
27	45	М	Н	2	12	93.75	1
28	14	М	FD	2	18	97.5	0
29	15	F	L	1	7	98.75	0
30	16	F	ABC	1	18	93.75	1
31	10	F	ABC	2	36	92.5	1
32	18	М	ОВ	2	12	96.25	0
33	9	М	FD	2	24	95.0	1
34	20	М	ABC+GSBT	2	18	90.0	2
35	30	F	L	2	48	96.25	1
36	46	F	HS	2	12	93.75	1
37	19	F	ABC	2	18	100.0	0

Case	Age	Sex	Pathology	Stage	Follow-up (month)	LEFS %	VAS
38	16	М	SBC	3	48	88.75	2
39	15	М	EG	1	18	98.75	0
40	26	F	GSBT	3	6	86.25	3
41	52	М	EC	2	24	91.25	2
42	18	М	FD+ABC	3	6	91.25	1
43	26	F	EC	2	6	93.75	1
44	28	F	L	2	6	95.0	0
45	47	F	FA	2	9	91.25	2
46	13	М	ABC	2	24	98.75	0
47	17	М	OB	3	12	97.5	1



Figure 1. Volume of tumor and graft amount

# Discussion

Bioceramic bone glass and spongious allografts are bonefilling materials that can be used in bone tumor. In this study, it was observed that consolidation rates were statistically significantly higher in the bioceramic bone graft group especially in the fibrous dysplasia group.

The ratio of the mean tumor volume and the amount of graft applied was higher in the bioceramic glass bone graft group compared to the other groups. This situation is thought to be developing out of the structural features of bioceramic glass bone graft.

In a randomized prospective study; Lindfors et al.  $^{\scriptscriptstyle(5)}$  evaluated twenty-five patients in a total of two groups with benign

bone lesions, in one that they used bioceramic glass bone graft and autograft after curettage. No difference in cavity volume was identified between the two groups after thirtysix months. In the following period, an increase in cortical thickness was observed to be higher in the bioceramic glass bone graft group compared to the autograft group. In our study, spongious allograft was implemented instead of autograft, and the consolidation ratio was found to be higher in bioceramic glass bone graft compared to the spongious allograft.

In their study, Sponer et al.<sup>(6)</sup> used bioceramic glass bone graft in a population of one hundred six patients with benign bone lesions, tibial plateau fractures, total hip replacement, and bone infections. The average length of follow-up was 3.2 years.

Table 2.	Graft materials, volume and con	solidation ratio		
Case	Graft material: Sg: 1 Bg: 2	Volume of the tumor (cm <sup>3</sup> )	Graft amount (cm <sup>3</sup> )	Consolidation ratio (%)
L	1.0	150	180	81
2	2.0	83	90	98
3	1.0	96	120	92
1	1.0	60	65	95
5	2.0	82	85	99
6	2.0	98	106	96
7	2.0	15	16	98
3	1.0	14	30	82
9	1.0	50	90	35
LO	1.0	20	45	72
1	1.0	13	30	92
2	1.0	11	30	93
.3	2.0	30	32	98
4	1.0	10	30	94
.5	1.0	32	90	93
.6	2.0	8	10	95
.7	2.0	26	26	96
.8	2.0	40	42	94
9	1.0	29	45	88
20	1.0	22	30	72
21	1.0	18	30	92
22	1.0	24	45	66
23	2.0	70	74	87
<u>2</u> 4	2.0	7	10	92
<u>24</u> 25	2.0	22	26	88
25 26	1.0	54	90	82
20 27	2.0	27	32	91
28	1.0	38	60	71
28 29	2.0	32	37	93
30	2.0	27	32	95
31	1.0	10	30	97
32	1.0	12	30	96
33	1.0	42	60	62
34	1.0	54	75	83
35	1.0	26	30	74
36	2.0	28	32	92
37	1.0	25	30	98
8	1.0	43	60	44
89	1.0	16	30	97
0	1.0	143	180	92
1	1.0	115	150	91
12	1.0	67	90	88
13	1.0	72	105	82
14	2.0	39	42	92
15	2.0	52	58	88
16	1.0	62	90	91
7	2.0	14	16	96



- ■%90< (%)
- **8**%80-90 (%)
- %80> (%)



Figure 3. Enneking staging

Table 3. Comparison of consolidation rate					
	Consolidation rate				
Stage	Spongious allograft	Bioceramic glass bone graft			
1	93.75±2.36% (92-97)	95.67±2.06% (93-98)			
2	84.45±10.78% (62-98)	91.22±3.11% (87-96)			
3	66.2±25.69% (35-92)	97.67±1.53% (96-99)			



Figure 4. Spongious allograft samples



Figure 5. Bioceramic bone graft samples



Figure 6. Patient sample with lowest consolidation rate of spongious allograft



Figure 7. Patient sample with lowest

No a patient possessed radiological findings revealing a soft tissue reaction, periosteal reaction or irritation, or bone loss. Radiographs displayed that trabecula persisted on bioactive glass. In our study, as well, bioceramic glass bone graft was used only on benign bone lesions; and there was no radiological evidence of soft tissue reaction, periosteal reaction or irritation, or bone loss, which shows consistency with this study.

Sponer et al.<sup>(7)</sup> followed seventeen patients with long bone diaphyseal defects for 7 years and ascertained that bioceramic glass bone grafts are impractical in diaphyseal defects but they can be convenient bone filler materials in metaphyseal defects. In our study, 8 of the patients who were given bioceramic glass bone graft had mass located in the diaphyseal region and ten had the mass in the metaphyseal region. No significant difference was identified when the average consolidation ratios were statistically compared as diaphyseal and metaphyseal regions (p=0.972).

In one of their research, Sponer and Urban<sup>(8)</sup> concluded that bioceramic glass bone grafts can be recommended for especially metaphyseal defects instead of autograft and allografts that are frequently used on patients with the juvenile bone cyst. In our study, as well, results were fruitful on the patient group of bioceramic glass bone graft used on the juvenile age group.

Schepers et al.<sup>(9)</sup>, in their study, evaluated the use of bioactive glass particles as fillers on bone lesions and compared them to two hydroxyapatite (HA) materials (calcitite and interpore

200). The osteoconductive effect was observed to be stronger in the cases of bioactive glass. When bioactive glasses are applied, they form a porous matrix that helps osteogenic cells develop by connecting to collagen, growth factors, and fibrin. They have absorbable and nonabsorbable types. They cannot be used with antibiotics or mixtures of bonebuilding increaser materials. They are more durable than HA implants<sup>(10,11)</sup>.

It was demonstrated in Day et al.<sup>(12)</sup> research that bioactive glass-ceramics raise the secretion of angiogenic growth factors *in vitro* and escalate the formation of new vessels.

Lin et al.<sup>(13)</sup> detected in their study that bioactive glass is gradually biodegraded and absorbed by the living bone. An optic microscope used in histological examination revealed that osteocytes grow into bioactive glass. Microscopic examination was not performed in our study, but it was found to be clinically and radiologically compatible with this study.

#### **Study Limitations**

This study has some limitations. The most important limitation is its retrospective design. The other important limitation is that the number of included patients was quite low.

# Conclusion

Bioceramic glass bone grafts are bone filler materials that possess radiologically superior and clinically similar findings compared to spongious allografts. The statistically significant radiological consolidation success of bioceramic glass bone grafts on FD, which is a benign aggressive tumor, causes the thought that they can be a good option toward the devastating effects of benign aggressive tumors. Bioceramic glass bone grafts are available to be used for adults and children. They can substitute spongious allografts and other modalities. Early results are promising. More comprehensive and long-term monitoring studies are required for more precise results.

#### Ethics

**Ethics Committee Approval:** The study were approved by the İzmir Tepecik Education and Research Hospital Research Ethics Committee (date: 24.11.2015, decision no: 22).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

#### **Authorship Contributions**

Concept: G.İ., A.K., M.İ., Design: G.İ., A.K., M.İ., Data Collection or Processing: G.İ., A.K., M.İ., Analysis or Interpretation: G.İ., A.K., M.İ., Literature Search: G.İ., A.K., M.İ., Writing: G.İ., A.K., M.İ.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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