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Original Research

Outcomes of Hindfoot Arthrodesis Supplemented With Bioactive Glass and Bone Marrow Aspirate: A Retrospective Radiographic Study

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ABSTRACT

Foot and ankle surgeons continue to explore bone graft alternatives that will be comparable to the reference standard of autologous bone. The purpose of the present study was to consider the outcomes of hindfoot arthrodesis supplemented with bioactive glass in patients at risk of delayed union and nonunion. We performed a retrospective radiographic review of 29 consecutive patients (48 joints) who had undergone arthrodesis of ≥1 joint of the hindfoot (ankle, subtalar, talonavicular, calcaneocuboid). All patients included in the present study had a minimum of 1 documented risk factor for osseous nonunion (history of previous nonunion, trauma, smoking, diabetes, Charcot arthropathy, obesity, age >65 years at surgery). The patients were followed up for a minimum of 24 weeks or until radiographic healing had been achieved. We found 12 (25.0%) nonunions across all 48 joints supplemented with bioactive glass. We found 4 (16.7%) nonunions in the subtalar joint, 1 (11.1%) in the calcaneocuboid joint, and 1 (11.1%) in the talonavicular joint. We found that hindfoot arthrodesis procedures supplemented with bioactive glass resulted in an incidence of union comparable to that with autograft and other bone graft substitutes.

Nonunion is 1 of the most common and challenging complications encountered after hindfoot arthrodesis procedures. Nonunion can cause substantial morbidity and disability and often requires revision arthrodesis, with subsequent rates of success lower than those with the initial procedure (1–3). Despite modern joint preparation techniques, the incidence of nonunion in routine hindfoot arthrodesis has remained from 7% to 15% (3,4). The incidence of nonunion is likely even greater in patients with risk factors for bone healing, especially smoking and diabetes. A recent systematic review of 1262 ankle fusions reported an incidence of nonunion of 10% (5); however, it can be as great as 41%, as found in a cohort of posttraumatic arthritis cases (6).

Although they might not be indicated for the healthy patient undergoing a routine arthrodesis procedure, bone grafts and bone substitutes play an important role in the treatment of delayed unions, nonunions, and malunions and in patients with risk factors for bone healing. The autograft remains the reference standard and provides the essential components needed for bone healing (i.e., osteoinduction, osteoconduction, and osteogenesis). However, issues with donor site morbidity and the need for a second surgical site have led to an ongoing attempt to develop bone graft substitutes. Many of these substitutes have a biologic component that stimulates the host's natural healing mechanisms. These include bone morphogenic protein, platelet-derived growth factors (PDGFs), bone marrow aspirates (BMAs), and mesenchymal stem cells (7,8). In their level 2, prospective, multicenter study, DiGiovanni et al (9) studied 573 cases of hindfoot arthrodesis and compared recombinant human PDGF BB/β-tricalcium phosphate (rhPDGF-BB/β-TCP) with autografting and found a comparable incidence of nonunion—31% in the graft substitute group and 27% in the autograft group.

Bioactive glass is an inorganic, hard, solid, nonporous material consisting of calcium, phosphorus, and silicon dioxide. It contains both osteoconductive and osteointegrative properties by forming a mechanically strong chemical bond with hydroxyapatite, a natural bone inorganic salt providing a scaffold for new bone formation (10–15). This porous scaffold is resorbed by osteoclasts during bony deposition. The ionic constituents of the bioactive glass—silicon, sodium, and calcium—produces a deposition of calcium phosphate at its surface, attracting osteoblasts to create a matrix that promotes an osteostimulatory effect due to the electronegative forces. This leads to electrical bone growth stimulation by bonding of new bone to the scaffold (16–22).

Bioactive glass has been used in extensively as a bone graft supplement in orthopedic tumor defects, lumbar fusions, and spinal graft

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extensions (23) and as a bone graft expander in orbital floor reconstruction (24,25). However, no studies have documented its ability to supplement bone healing in foot and ankle arthrodesis procedures (26,27).

We were interested in studying the outcomes of osseous union in patients at risk of nonunion when using bioactive glass as a supplement to rearfoot arthrodesis. We hypothesized that bioactive glass could serve as a viable alternative with an incidence of union comparable to that of autograft and other bone graft substitutes. Our primary aim was to measure the incidence of radiographic union. Our secondary aim was to determine the risk factors for nonunion. We performed a retrospective radiographic cohort study to measure the incidence of union in a group of patients who had undergone rearfoot arthrodesis with ≥1 risk factor for nonunion.

Patients and Methods

After the Kaiser Permanente Northern California institutional review board approved the study, a retrospective medical record review was performed of consecutive patients treated by a single surgeon (G.W.) from January 2010 to December 2014 (5 years) who had undergone hindfoot arthrodesis supplemented with bioactive glass. The inclusion criteria were as follows: (1) patients who had undergone arthrodesis of ≥1 joint involving the hindfoot (defined as any of the following joints: ankle, subtalar, talonavicular, and calcaneocuboid joint); (2) ≥1 documented risk factor for osseous nonunion (history of previous nonunion, trauma, smoking, diabetes, Charcot arthropathy, obesity, age >65 years at surgery); and (3) supplementation of the fusion site with bioactive glass as documented in the operative report. Patients were identified by searching the electronic medical records using the Current Procedural Terminology codes 28715, 212085, 81.13, and 81.17 (American Medical Association, Chicago, IL). A total of 29 consecutive patients (48 joints) met the inclusion criteria. Of the patients included in the cohort, 4 had undergone surgery twice. Data were collected from the electronic health records, including age at surgery, gender, type of procedure, and the joint or joints operated on. Patients underwent arthrodesis in the supine position under general anesthesia with thigh tourniquet in place. The joints were prepared using standard joint preparation techniques, not limited to but including, curettage, drilling, and shingling with osteotome. All cases were fixated with rigid internal fixation, and bone graft supplementation with a mixture of bioactive glass/β-TCP (Vitoss Bone Graft Substitute; Stryker®, Kalamazoo, MI) and BMA (Fig.). A femoral head allograft was used in certain cases to fill larger defects. All patients remained non-weightbearing until radiographic union had been achieved. Postoperative radiographs were taken at 4- to 6-week intervals, until documentation of radiographic and clinical healing, as determined by the primary surgeon. The radiographs were then retrospectively and independently assessed by 1 of us (R.C.) to determine the presence of osseous union. Fusion was defined by the presence of osseous trabecular bridging involving ≥50% of the joint, with intact cortical borders and without a visible fracture line on radiographs obtained before 24 weeks postoperatively. Nonunion was defined by the lack of evidence of fusion on radiographs obtained after 24 weeks. Statistical tests, including the χ^2 test, t test, and univariate and multivariate logistic regression analysis, were performed by 1 of us (C.L.) and were used to analyze the patient demographic data and clinical outcomes. Statistical significance was defined at the 5% ($p \leq .05$) level. Logistic regression analysis was used to assess the predictor variables associated with nonunion. The primary aim of the present study was to measure the incidence of union at 24 weeks. The secondary aims were to measure the risk factors for nonunion. We hypothesized that hindfoot fusions supplemented with bioactive glass would achieve an incidence of union comparable to that of the autograft.

Results

Our study found 12 (25.0%) nonunions across all 48 joints supplemented with bioactive glass, with a mean interval to union of 13.2 ± 2.0 weeks (Table 1). Of the 12 nonunions, 6 (66.7%) were in the ankle joint, the greatest incidence of all joints observed. On bivariate analysis, a significant association was found between the joint type and the occurrence of nonunion ($p \leq .05$). When stratified by procedure type, 9 (27.3%) nonunions occurred in 33 procedures, and bivariate analysis showed no significant association among procedure types. When assessing patient risk factors that could contribute to nonunion, multivariate risk analysis demonstrated that the probability for nonunion was >6 times greater if the patient had a history of previous revision ($p = .085$; Table 2). Bivariate analysis of the patient risk factors for nonunion revealed a significant association between nonunion and a history of previous revision ($p \leq .05$) and patient age >65 years ($p \leq .05$; Table 3).

Discussion

Hindfoot arthrodesis in patients with risk factors for nonunion continues to challenge foot and ankle surgeons. Nonunion rates of ≤20% for triple arthrodesis have been reported, and isolated subtalar, talonavicular, and calcaneocuboid joint fusion has been reported in ≤16%, ≤35%, and ≤20%, respectively (28). The iliac crest autograft is generally considered the "historical" reference standard; however, a push continues for a new "standard" in the world of orthobiologic agents to avoid the need for donor site harvest and its associated morbidities.

Despite an abundance of data documenting the effects of bioactive glass in molecular and animal models (29–35), very few reported studies have considered the outcomes of bioactive glass in the clinical setting, most of which have been limited to spinal fusion. A

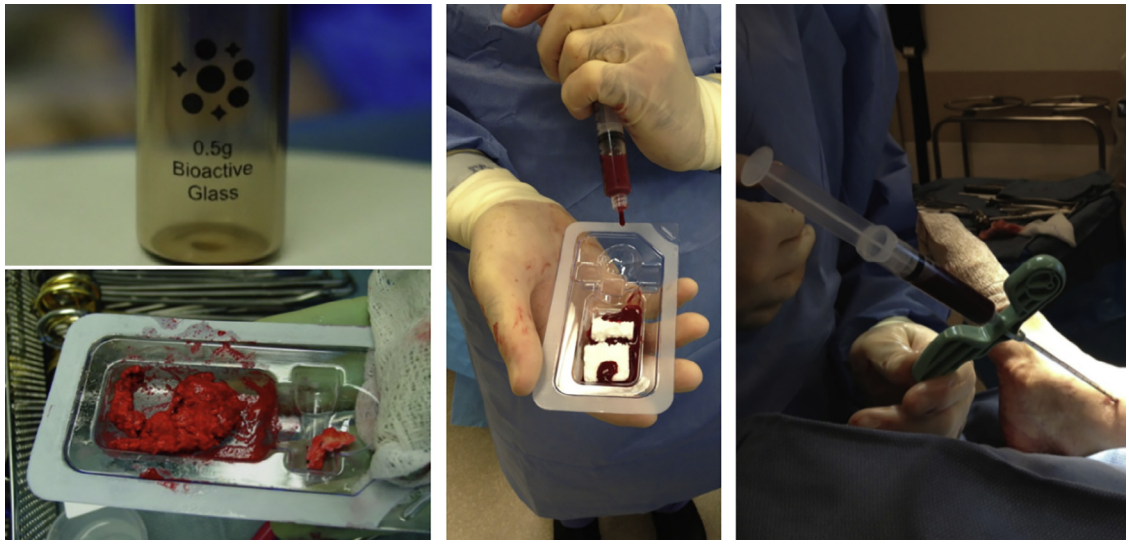

Fig. Preparation of bioactive glass with autogenous bone marrow aspirate.

Table 1
Outcomes of union stratified by joint location and procedure type (N = 48 joints in 29 consecutive patients)

Variable	Nonunion	Union	Total	Interval to Union (wk)
Joint type*				
Ankle (n = 9)	6 (66.7)	3 (33.3)	9 (18.8)	14.0 ± 2.6
Subtalar (n = 24)	4 (16.7)	20 (83.3)	24 (50.0)	13.0 ± 2.2
Calcaneocuboid (n = 6)	1 (16.7)	5 (83.3)	6 (12.5)	13.8 ± 1.5
Talonavicular (n = 9)	1 (11.1)	8 (88.9)	9 (18.8)	13 ± 2
Total (n = 48)	12 (25.0)	36 (75.0)	48 (100)	13.2 ± 2.0
Procedure type				
Isolated joint arthrodesis (n = 22)	6 (27.3)	16 (72.7)	22 (66.7)	13.2 ± 2.2
Double (subtalar and talonavicular) arthrodesis (n = 4)	0 (0)	4 (100)	4 (12.1)	12.3 ± 2.2
Triple arthrodesis (n = 4)	1 (25.0)	3 (75.0)	4 (12.1)	13.0 ± 1.0
Tibiotalocalcaneal (TTC) arthrodesis (n = 3)	2 (66.7)	1 (33.3)	3 (9.1)	NA
Total (n = 33)	9 (27.3)	24 (72.7)	33 (100)	13.2 ± 2.0

Data presented as n (%) or mean ± standard deviation.
* p Value ≤ .05.

prospective study by Rantakokko et al (23) considered the results of β-TCP with bioactive glass in the treatment of lumbar spine fractures with a 10-year follow-up period. In their study of 16 patients undergoing treatment with a combination of bioactive glass and autogenous bone, they found a 71% total fusion rate (23). However, bioactive glass used as a standalone bone substitute resulted in solid fusion in only 5 of 10 patients. Acharya et al (36) also studied cases of lumbar fusion and reported adverse reactions associated with bioactive glass compared with autogenous bone. They found a resorption rate of 95% in the cases showing poor consolidation but improved clinical outcome scores in 16 of 22 patients (36). A study by Ilharreborde et al (37) of the use of bioactive glass in lumbar fusion for the treatment of scoliosis found fewer changes in surgical correction of the thoracic curve in the bioactive glass group than in the autogenous bone group and decreased blood loss and lower complication rates. Kankare and Lindfors (38) used an antibacterial variant of bioactive glass in the treatment of vertebral defects in 3 cases of vertebral osteomyelitis with spondylodesis. After a 4-year follow-up period, fusion was observed in all patients, with complete neurologic recovery and no complications. Similarly, in a randomized prospective study, Lindfors et al (39) used bioactive glass to fill cavities of benign bone tumors and noted improved cortical thickness compared with autogenous bone at the 3-year follow-up point.

Table 2
Multivariate risk analysis for nonunion (N = 29 consecutive patients)

Predictor Variable	Odds Ratio	p Value*
History of previous revision (reference: no previous revision)	6.3	.085
History of prior trauma (reference: no previous trauma)	5.8	.160
Diabetes (reference: none)	2.9	.377
Smoker (reference: no)	0.7	.781
Charcot arthropathy (reference: no)	0.6	.777
Male gender (reference female gender)	0.7	.809

* Variables chosen for multivariable analysis based on multivariate $p < .1$.

Table 3
Prevalence of risk factors stratified by fusion procedure outcomes

Characteristic	Union (n = 73)	Nonunion (n = 33)	Total (n)	p Value*
History of previous revision	5 (13.9)	9 (75.0)	14	< .05
History of previous trauma	4 (11.1)	3 (25.0)	7	.238
Diabetes	15 (41.7)	4 (33.3)	19	.609
Smoker	14 (38.9)	6 (50.0)	20	.499
Charcot arthropathy	8 (22.2)	2 (16.7)	10	.682
Age >65 y	10 (27.8)	0 (0.0)	10	< .05
Obesity	17 (47.2)	9 (75.0)	26	.094

Data presented as n (%).
* p Values calculated using χ^2 and Fisher's exact tests.

To the best of our knowledge, the present study is the first that considered the use of bioactive glass and BMA in arthrodesis cases of the foot. We found 12 (25.0%) nonunions across all 48 joints supplemented with bioactive glass and BMA. This incidence of nonunion is comparable to that reported by DiGiovanni et al (9), who found an incidence of nonunion of 27% in rearfoot fusions treated with autograft and 31% for fusions treated with rhPDGF-BB/β-TCP. Our findings argue that a bone graft substitute consisting of bioactive glass and BMA can be considered a viable alternative to autograft to achieve an acceptable incidence of union in hindfoot arthrodesis procedures. We found 4 (16.7%) nonunions in the subtalar joint and 1 (16.7%) in the calcaneocuboid joint; however, we only found 1 (11.1%) nonunion in the talonavicular joint, the lowest incidence of all isolated joint categories. We found 6 (66.7%) nonunions in our ankle arthrodesis group, greater than the 10% to 40% previously reported (40). However, 4 of our 6 ankle nonunions were revision cases to treat a previous nonunion of the same joint. This was consistent with our multivariate risk factor analysis, which found that a patient would be 6 times more likely to develop nonunion if they had a history of previous nonunion, and also with that reported by previous studies (40).

The limitations of the present study included its retrospective nature and the variability in surgeon technique for joint preparation and fixation techniques and hardware choice. Another limitation was that the determination of radiographic healing was dependent on a single reviewer using plain film radiographs. We also did not have a control group to compare the incidence of nonunion when no bioactive glass was included. Our comparison for standard nonunion rates was limited to historical controls cited in previous data. Using historical controls could introduce differences in patient population and surgeon technique that could introduce bias to the discussion.

In conclusion, the present study has demonstrated that hindfoot arthrodesis procedures supplemented with bioactive glass result in an incidence of union comparable to that with autograft and other bone graft substitutes. Our findings continue to expand our knowledge in the search for an effective bone graft substitute.

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References

1. Cheng YM, Chen SK, Chen JC, Wu WL, Huang PJ, Chiang HC, Lin CY. Revision of ankle arthrodesis. Foot Ankle Int 24:321–325, 2003.

2. Kitaoka HB, Anderson PJ, Morrey BF. Revision of ankle arthrodesis with external fixation for non-union. J Bone Joint Surg Am 74:1191–1200, 1992.
3. Easley ME, Trnka HJ, Schon LC, Myerson MS. Isolated subtalar arthrodesis. J Bone Joint Surg Am 82:613–624, 2000.
4. Mulhern JL, Protzman NM, Levene MJ, Martin SM, Fleming JJ, Clements JR, Brigido SA. Is subtalar joint cartilage resection necessary for tibiotalocalcaneal arthrodesis via intramedullary nail? A multicenter evaluation. J Foot Ankle Surg 55:572–577, 2016.
5. Haddad SL, Coetzee JC, Estok R, Fahrbach K, Banel D, Nalysnyk L. Intermediate and long-term outcomes of total ankle arthroplasty and ankle arthrodesis: a systematic review of the literature. J Bone Joint Surg Am 89:1899–1905, 2007.
6. Frey C, Halikus NM, Vu-Rose T, Ebramzadeh E. A review of ankle arthrodesis: predisposing factors to nonunion. Foot Ankle Int 15:581–584, 1994.
7. Novicoff WM, Manaswi A, Hogan MV, Brubaker SM, Mihalko WM, Saleh KJ. Critical analysis of the evidence for current technologies in bone-healing and repair. J Bone Joint Surg Am 90(suppl 1):85–91, 2008.
8. DeLong WG Jr, Einhorn TA, Koval K, McKee M, Smith W, Sanders R, Watson T. Bone grafts and bone graft substitutes in orthopaedic trauma surgery: a critical analysis. J Bone Joint Surg Am 89:649–658, 2007.
9. DiGiovanni CW, Lin SS, Daniels TR, Glazebrook M, Evangelista P, Donahue R, Beasley W, Baumhauer JF. The importance of sufficient graft material in achieving foot or ankle fusion. J Bone Joint Surg Am 98:1260–1267, 2016.
10. Berbecaru C, Alexandru HV, Ianculescu A, Popescu A, Socol G, Sima F, Mihailescu I. Bioglass thin films for biomimetic implants. Appl Surf Sci 255:5476–5479, 2009.
11. Hafezi F, Hosseinnejad F, Fooladi AAI, Mafi SM, Amiri A, Nourani MR. Transplantation of nano-bioglass/gelatin scaffold in a non-autogenous setting for bone regeneration in a rabbit ulna. J Mater Sci Mater Med 23:2783–27926, 2012.
12. Meng DC, Rath SN, Mordan N, Salih V, Kneser U, Boccaccini AR. In vitro evaluation of 45S5 Bioglass®-derived glass-ceramic scaffolds coated with carbon nanotubes. J Biomed Mater Res A 99A:435–4447, 2011.
13. Xynos ID, Edgar AJ, Buttery LDK. Ionic products of bioactive glass dissolution increase proliferation of human osteoblasts and induce insulin-like growth factor II mRNA expression and protein synthesis. Biochem Biophys Res Commun 276:461–4658, 2000.
14. Mozafari M, Moztarzadeh F, Tahriri M. Investigation of the physico-chemical reactivity of a mesoporous bioactive SiO2–CaO–P2O5 glass in simulated body fluid. J Non Cryst Solids 356:1470–1489, 2010.
15. Mozafari M, Rabiee M, Azami M. Biomimetic formation of apatite on the surface of porous gelatin/bioactive glass nanocomposite scaffolds. Appl Surf Sci 257:1740–1749, 2010.
16. Hench LL, Splinter RJ, Allen WC. Bonding mechanisms at the interface of ceramic prosthetic materials. J Biomed Mater Res 2:117–141, 1971.
17. Hench LL, Paschall HA. Direct chemical bond of bioactive glass-ceramic materials to bone and muscle. J Biomed Mater Res 4:25–42, 1973.
18. Gross U. The interface of various glasses and glass ceramics with a bony implantation bed. J Biomed Mater Res 19:251–257, 1985.
19. Vrouwenvelder WCA. Histological and biochemical evaluation of osteoblasts cultured on bioactive glass, hydroxyapatite, titanium alloy, and stainless steel. J Biomed Mater Res 27:465–475, 1993.
20. Hench LL. The story of bioglass. J Mater Sci Mater Med 17:967–978, 2006.
21. Oonishi H, Kushitani S, Yasukawa E, Iwaki H, Hench LL, Wilson J, Tsuji E, Sugihara T. Particulate bioglass compared with hydroxyapatite as a bone graft substitute. Clin Orthop Relat Res 334:316–325, 1997.
22. Xynos ID, Edgar AJ, Buttery LDK, Hench LL, Polak JM. Ionic products of bioactive glass dissolution increase proliferation of human osteoblasts and induce insulin-like growth factor II mRNA expression and protein synthesis. Biochem Biophys Res Commun 276:461–465, 2000.
23. Rantakokko J, Frantzen JP, Heinanen J, Kajander S, Kotilainen E, Gullichsen E, Lindfors NC. Posterolateral spondylodesis using bioactive glass S53P4 and autogenous bone in instrumented unstable lumbar spine burst fractures; a prospective 10-year follow-up study. Scand J Surg 101:66–71, 2012.
24. Peltola M, Suonpaa J, Aitasalo K, Maattanen H, Anderson O, Yli-Urpo A, Laippala P. Experimental follow-up model for clinical frontal sinus obliteration with bioactive glass. Acta Otolaryngol Suppl 543:167–169, 2000.
25. Kinnunen I, Aitasalo K, Pollonen M, Varpula M. Reconstruction of orbital floor fractures using bioactive glass. J Craniomaxillofac Surg 28:229–234, 2000.
26. Daniels T, DiGiovanni C, Lau JT, Wing K, Younger A. Prospective clinical pilot trial in a single cohort group of rhPDGF in foot arthrodeses. Foot Ankle Int 31:473–479, 2010.
27. DiGiovanni CW, Baumhauer J, Lin SS, Berberian WS, Flemister AS, Enna MJ, Evangelista P, Newman J. Prospective, randomized, multi-center feasibility trial of rhPDGF-BB versus autologous bone graft in a foot and ankle fusion model. Foot Ankle Int 32:344–354, 2011.
28. Hreha J, Krell ES, Bibbo C. Role of recombinant human bone morphogenetic protein-2 on hindfoot arthrodesis. Foot Ankle Clin 21:793–802, 2016.
29. Detsch R, Rubner M, Strissel PL, Mohn D, Strasser E, Stark WJ, Strick R, Boccaccini AR. Nanoscale bioactive glass activates osteoclastic differentiation of RAW 264.7 cells. Nanomedicine (Lond) 11:1093–1105, 2016.
30. Andersson Ö, Karlsson KH. On the bioactivity of bioactive glass-ceramic materials to bone and muscle. J Non Cryst Solids 129:145–151, 1991.
31. Virolainen P, Heikkilä J, Yli-Urpo A, Vuorio E, Aro HT. Histomorphometric and molecular biologic comparison of bioactive glass granules and autogenous bone grafts in augmentation of bone healing. J Biomed Mater Res 35:9–17, 1997.
32. Välimäki VV, Moritz N, Yrjans JJ, Dalstra M, Aro HT. Peripheral quantitative computed tomography in evaluation of bioactive glass incorporation with bone. Biomaterials 26:6693–6703, 2005.
33. Lindfors NC, Hyvönen P, Nyyssönen M. Bioactive glass 1643 S53P4 as bone graft substitute in treatment of osteomyelitis. Bone 47:212–218, 2010.
34. Lindfors NC, Tallroth K, Aho AJ. Bioactive glass as bone-graft substitute for posterior spinal fusion in rabbit. J Biomed Mater Res 63:237–244, 2002.
35. Brink M, Turunen T, Happonen RP, Yli-Urpo A. Compositional dependence of bioactivity of glasses in the system Na2O-K2O-MgO-CaO-B2O3-P2O5-SiO2. J Biomed Mater Res 37:114–121, 1997.
36. Acharya NK, Kumar RJ, Varma HK, Menon VK. Hydroxyapatite-bioactive glass ceramic composite as stand-alone graft substitute for posterolateral fusion of lumbar spine: a prospective, matched, and controlled study. J Spinal Disord Tech 21:106–111, 2008.
37. Ilharreborde B, Morel E, Fitoussi F. Bioactive glass as a bone substitute for spinal fusion in adolescent idiopathic scoliosis: a comparative study with iliac crest autograft. J Pediatr Orthop 28:347–351, 2008.
38. Kankare J, Lindfors NC. Reconstruction of vertebral bone defects using an expandable replacement device and bioactive glass S53P4 in the treatment of vertebral osteomyelitis: three patients and three pathogens. Scand J Surg 2016 Feb 29. pii: 1457496915626834. [Epub ahead of print].
39. Lindfors NC, Heikkila JT, Koski I, Mattila K, Aho AJ. Bioactive glass and autogenous bone as bone graft substitutes in benign bone tumors. J Biomed Mater Res B Appl Biomater 90:131–136, 2009.
40. Hagen RJ. Ankle arthrodesis. Problems and pitfalls. Clin Orthop Relat Res 202:152–162, 1986.