Received: 15.1.2008 **Accepted: 6.4.2008**

Original Article

Local recurrence in giant cell tumor of bone: Comparative study of two methods of surgical approach

Khodamorad Jamshidi, Sam Sami*,*
*Hamid Reza Modares-Nejad**, Ali Jahansoz****

Abstract

BACKGROUND: Most experts accept the use of curettage, phenol, and cement as the best treatment to prevent recurrence of giant-cell tumors. The purpose of this investigation was to analyze the effect of cement as a filling material and compare it with bone graft and the effect of high-speed burr in local recurrence of giant cell tumor after curettage.

METHODS: We retrospectively reviewed 168 consecutive patients diagnosed with giant cell tumor at the three most common sites (distal femur, proximal tibia, and distal radius) to determine the pattern of local tumor recurrence. Only patients who had intralesional excision of primary tumor by curettage without a surgical adjuvant were included.

RESULTS: A total of 168 patients with primary giant cell tumor were treated with curettage. The female to male ratio was 1.4: 1 and the mean age was 34 years (range: 17-68 years). The minimum follow-up was 24 months and the median follow up was 75 months. The knee region was involved in 135 (80.4%) patients. There were 10 (5.9%), 130 (77.4%) and 28 (16.7%) patients in Campanacci grade I, II and III, respectively. Tumor surgery was supplemented with high speed burring in 88 (52.4%), bone cement in 82 (48.8%) and bone grafting, either autograft or allograft in 86 (51.2%) patients. The recurrence rates were 18.2% and 37.5% for curettage with or without high speed burring, respectively. For 46 (27%) recurrent lesions treated by curettage, the recurrence rate was 35%. The nature of the filling material used did not show any significant impact on the outcome of recurrence rate.

CONCLUSIONS: Despite the high rates of recurrence after treatment of giant-cell tumor with curettage, the results of the present study suggested that the high-speed burr is effective in reducing the rate of recurrence. The risk of local recurrence after curettage with a high-speed burr and reconstruction with bone graft is similar to that observed after using cement. It is likely that the adequacy of the removal of the tumor rather than the use of adjuvant modalities is what determines the risk of recurrence.

KEYWORDS: Giant cell tumor, recurrence, bone graft, cement.

JRMS 2008; 13(5): 223-229

Giant cell tumor of bones is an unusual neoplasm that accounts for 4% of all primary tumors of bone.[1] Usually, the age of patients ranges from 20 to 55 years, and the peak age incidence is in the third decade of life, with slight female predominance (1.2:1). It is a locally aggressive tumor, which involves the ends of long bones in skeletally mature individuals in more than 80% of cases, and 75% of them occur around the knee joint.[1] The tumor on occasion invades the articular space, also involving the ligaments and the synovial membrane. Extension to an adjacent bone through the joint occurs in 5 per cent of the

*Assistant Professor of Orthopedic Surgery, Iran University of Medical Sciences, Tehran, Iran.
**Orthopedic Surgeon, Iran University of Medical Sciences, Tehran, Iran.
***Orthopedic Resident, Iran University of Medical Sciences, Tehran, Iran.
Correspondence to: Dr Hamid Reza Modares-nejad, Orthopedic Surgeon, Iran University of Medical Sciences, Tehran, Iran.
e-mail: Dr_modares@yahoo.com

tumors. Less frequently, giant cell tumors occur in the vertebrae (2-5%) and in the sacrum (10%).[1] Giant cell tumor is characterized by its typical location in the epiphysis of long bone. Rarely, when it occurs in teenagers with an open physis, the metaphyseal area may be involved first.[2,3] This tumor is well known for its potential to recur after treatment such as curettage or incomplete resection, which leaves microscopic residuals.[4,5] Recurrence can develop in the bone or soft tissues and although both reflect relapse of disease, the sequelae of recurrence can vary as a function of the site and extent. Historically, the rate of local recurrence after curettage and bone grafting has been reported to range between 25% and 50%.[6-10] This has led surgeons to enhance their surgical procedure with adjuvants such as liquid nitrogen,[11,12] acrylic cement,[13,14] phenol,[6,15,16] hydrogen peroxide,[17] locally delivered chemotherapy,[18] or radiation therapy. The latter has been associated with malignant transformation in the past,[6,19,20] but the risk of this complication recently has been challenged and may be different with modern radiotherapy modalities.[21,22] Wide resection is associated with much better local control, but it often impairs limb function because it implies the sacrifice of a significant segment of bone.[8,23,24] Adjuvant liquid nitrogen has been reported to provide the best local control but its use has not gained popularity because handling the product is difficult and pathologic fractures have been frequent.[11,12] Although acrylic cement initially seemed to enhance local control,[21,25] this has been challenged.[6,23] Comparably low local recurrence rates have been reported using modern surgical techniques without the addition of adjuvant.[26] Compared with other filler material such as autograft or allograft bone, cement is easy and inexpensive to use, provides immediate stability allowing early weight-bearing may avoid the necessity of internal fixation, and allows for early detection of recurrence as a lytic defect at the bone-cement interface.[27,28] Cement also can be used when a fracture is present.[29] The risk of joint degeneration after cementation seems to be minimal,[30-32] although some authors prefer to interpose bone chips between cartilage or subchondral area and cement in an attempt to prevent joint degeneration.[4] The purpose of this investigation was to analyze the effect of cement and high speed burring in recurrence rate of giant cell tumor after curettage. The primary hypothesis was that the use of any one or a combination of them would not provide better local control.

Methods

We retrospectively identified the records of 205 patients from the database maintained by the Orthopedic Oncology Service of our hospital between 1975 and 2004. We included all patients diagnosed with primary giant cell tumor arising in the distal femur, proximal tibia, and distal radius with a minimum follow-up of 2 years after treatment. Patients with multifocal lesions involving one or more of these sites were not included. Only patients who had intralesional excision of tumor by curettage were included and any patient who originally had been treated elsewhere was excluded from this study. Base on these criteria, 168 cases of 205 patients were entered in the study. Seventy-five tumors were in the distal femur, 53 were in the proximal tibia, and 40 were in the distal radius. Medical records and radiographs were reviewed for all patients for whom a local recurrence developed. Anatomic site of the tumor, first surgical procedure, and timing of the local recurrence were determined. The pathology of the primary and locally recurrent tumor was confirmed in all cases. Radiographs were assessed for adequacy and thoroughness of initial treatment and site of recurrence (bone or soft tissue), and location within the bone (subchondral or metaphyseal bone). Local recurrences were analyzed in eight groups: patients who were treated by simple curettage and bone graft (group A), simple curettage and cementing (group B), curettage with high-speed burring and bone graft (group C), curettage with high-speed burring and cementing (group D), cementing with or without burring (group E), bone graft with or without burring (group F). Burring with cement or bone graft

(group G), simple curettage with cement or bone graft (group H). There was not significant statistical difference among these groups for sex, age, location and grading of tumor. Analysis of the data was focused on the effect of cement and high-speed burr in local recurrence of tumors. The data analyzed with Epi-info software (version 3.4.1).

Results

The average age of the 168 patients was 34 years (range of 17-68 years). There were 99 females and 69 males (female to male ratio was 1.43:1). Age and sex distribution among cases with GCT are shown in figure 1. Campanacci grading was as follows: grade 1, ten patients, grade 2, 130 patients and grade 3, 28 patients (Figure 2). Seventy-five tumors were in the distal femur, 53 were in the proximal tibia, and 40 were in the distal radius. The distal femur and the proximal tibia accounted for 76% of all locations. The follow up ranged from 24 to 192 months (median, 74 months). The average follow-up did not differ between patients who had a recurrence and patients who did not have a recurrence (P = 0.08). After curettage, a high-speed burr was used in 88 patients (group E). The cavity was filled with bone graft in 86 patients (Figure 3) (autograft only in 18 patients and allograft in 68 patients) and cement in 82 patients (group F) (Figure 4). Forty-six patients of the 168 had developed a local recurrence (27.4%). Forty-two patients had the first recurrence in bone and four patients developed a soft tissue recurrence as their first recurrence. Twenty tumors recurred in the distal femur, sixteen recurred in the proximal tibia, and ten recurred in the distal radius. Recurrence in proximal tibia (30.2%) was more than that in distal parts of femur (26.7%) and radius (25%), but there was not a statistical difference between the primary sites of the tumor and the recurrence sites. The average recurrence occurred at 30 months (range, 6–54 months) and there was no statistical difference between the times of recurrence in different locations (p value = 0.125). The local recurrence rate in the groups was shown in the table 1. The group that received curettage was analyzed to determine whether patients who received cement had recurrences less often than patients who received grafts but no statistical difference in the recurrence rate was found (p value = 0.117). Statistical difference in the recurrence rate was found between patients who received high-speed burring curettage and who had simple curettage (p value = 0.0487). Patients presenting with a local recurrence had a significantly higher risk of having another recurrence with a rate of 35% ($p < 0.05$) if they got curettage again; 32 of 46 patients with local recurrence were operated with curettage again and recurrence rate of them was 35%. Others were operated with resection and allograft or oncologic prosthesis and recurrence rate of them was only 7%. No significant statistical effect on local recurrence rate was identified for gender, tumor location and Campanacci grading for the groups.

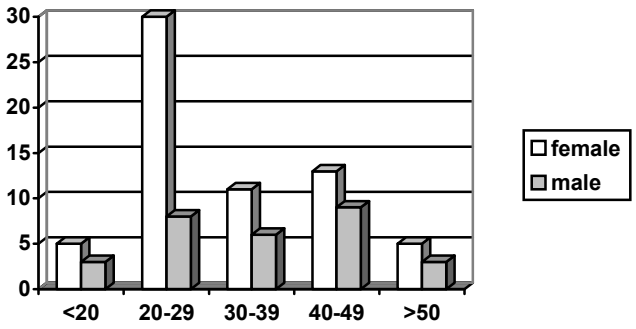

Figure 1. Age and sex distribution among cases with GCT.

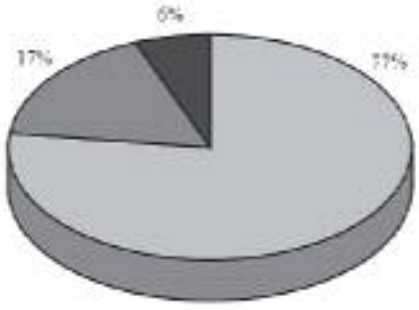

Figure 2. Distribution of cases according to Campanacci grading. I II III

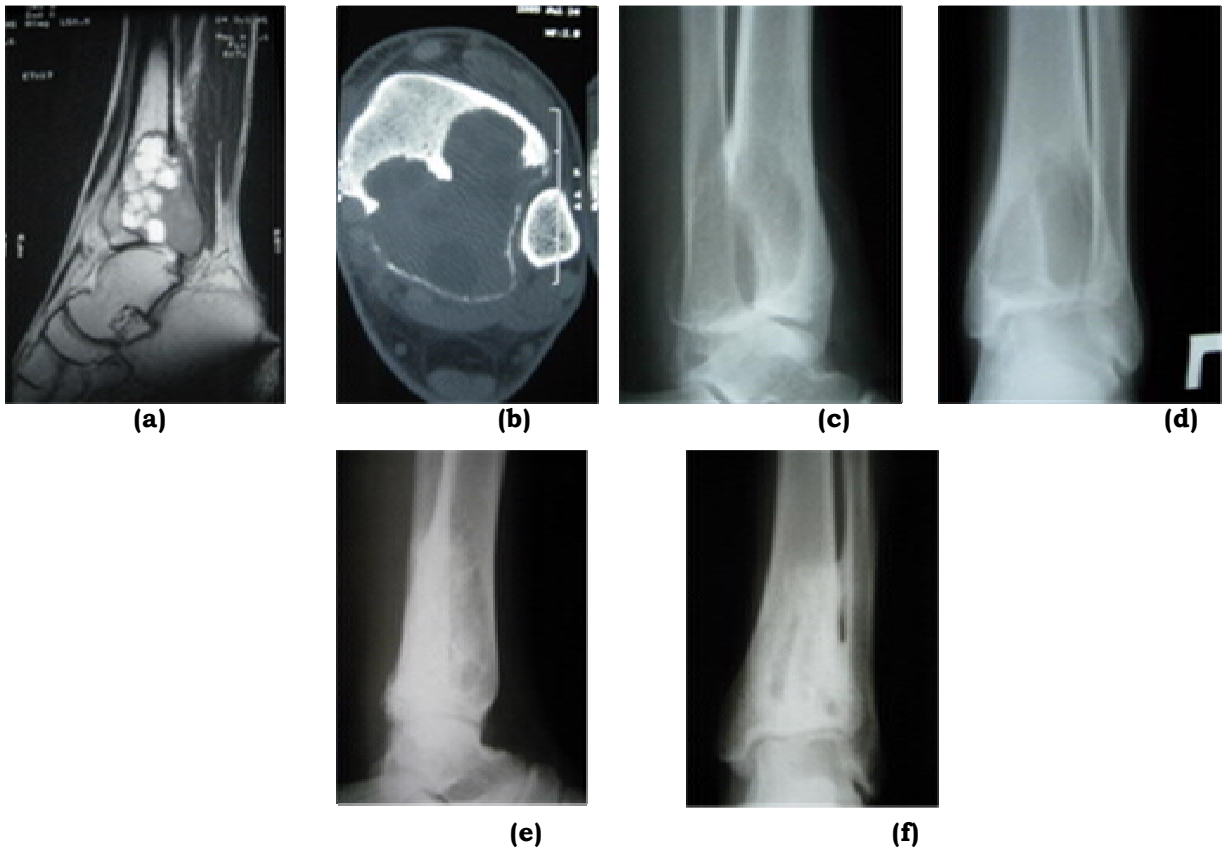

Figure 3. A 17 year old male with left distal tibia giant cell tumor; AP x-ray (a), Lateral x-ray (b) CT-scan (c), MRI (d), AP and lateral x-ray 2 years after curettage with high speed burr and bone graft without recurrence (e, f).

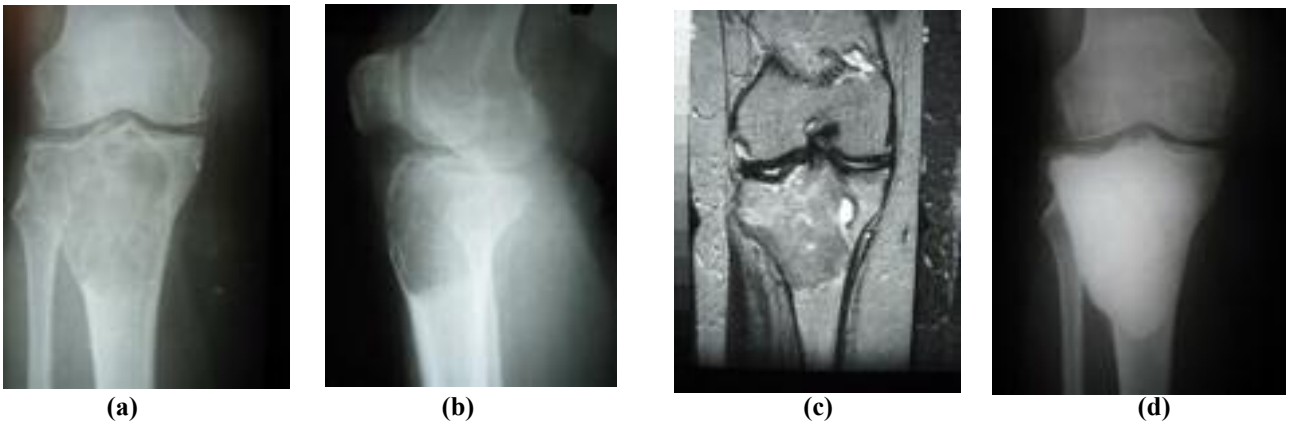

Figure 4. A 51 year old female with right proximal tibia giant cell tumor; AP x-ray (a), Lateral x-ray (b), MRI (c), AP x-ray 2 years after curettage with high speed burr and cementing without re-currence (d).

Table 1. Local recurrences were analyzed in eight groups.

Group	Number of Patients	Recurrence	Percent
A	40	17	42.5
B	40	12	30
C	46	10	21.7
D	42	7	16.7
E	82	19	23.1
F	86	27	31.4
G	88	17	19.3
H	80	29	36.2

We included only the patients whom had curettage with bone graft or cement and we excluded patients whose initial surgery were other kinds like wide excision and allograft or oncologic prosthesis. Then we did not analyze the first surgical procedure type versus recurrence except those that were explained. We explained that no significant statistical effect on local recurrence rate could be identified for gender, tumor location and Campanacci grading for the groups. The histology types were not considered in this study because the new classification don't accept any histologic grading for giant cell tumor as the last one that divided it into high and low grades. In the most pathologic reports of our patients, the histology grading was not reported.

Discussion

The adequacy of the tumor removal is critical to the successful management of GCT. Treatment-related factors including intraoperative techniques to minimize the risk of local tumor recurrence in the bone and soft tissue are critical determinants of local tumor control. Technical aspects such as sufficient exposure, isolation of the tumor, careful manipulation of the tumor to avoid contamination of the soft tissues, thoroughness of the curettage, intracavitary burring, addition of surgical adjuvants, and sufficient osseous reconstruction are contributory factors that affect local tumor recurrence and metastasis. Acrylic cement initially was reported to have an adjuvant role in the treatment of giant cell tumor of bone.[6,13] Proposed mechanisms involved either the toxicity of the acrylic monomer or thermal necrosis induced by cement polymerization.[33] O'Donnel et al[25] challenged this idea when they reported a series of patients with giant cell tumors treated with cement compared with other filling materials and found no difference in local recurrence. With respect to curettage and bone cement, the reported rate of local recurrence by O'Donnell et al using curettage and bone cement was 33.3% that decreased to 16.6% when mechanical burr was used; so they recommended using the burr at the end of all procedures. In addition, when the lesion reached the subchondral bone in weight bearing areas they put a layer of bone cement first under the subchondral plate to support it and then fill the rest of the cavity either by bone cement or bone graft. In our study, the overall recurrence rate was 36.2% after curettage without high-speed burring. The recurrence rate when high speed burring has been used was 19.3%. There was no significant difference between cement and bone graft in local recurrence but there was significant difference between curettage with high-speed burr and without it. The use of the mechanical burr easily can extend the curettage and allow for a more controlled debridement of the cavity walls to minimize damage to uninvolved tissues while it may reduce the residual disease observed. The current report suggests an improvement in the local control rate of these tumors with modern curettage techniques. In this study we compared the role of filling material and high-speed burr but O'Donnel's study focused only on the filling material. The recurrence rate when cementing and burring was done to gether was less than that in bone graft without burring but the difference was not significant. The recurrence rates in our study were a little more than that in O'Donnel's study. As reported previously, no correlation could be found between Campanacci radiographic classification and the risk of recurrence[13,34] that have been shown in our study. The successful treatment of local recurrence after intralesional excision by curettage is site-of-recurrence specific and treatment spe-

cific. The soft tissue recurrences were observed less frequently and were readily addressed with no adverse sequelae. In our series, soft tissue recurrences without bone recurrences were observed in only four cases.

Conclusions

Despite the high rates of recurrence after treatment of giant-cell tumor with curettage, the results of the present study suggested that the high-speed burr is effective in reducing the rate of recurrence. The risk of local recurrence after curettage with a high-speed burr and reconstruction with bone graft was similar to that observed after use of cement. It is likely that the adequacy of the removal of the tumor rather than the use of adjuvant modalities is what determines the risk of recurrence.

References

1. Wulling M, Engels C, Jesse N, Werner M, Delling G, Kaiser E. **The nature of giant cell tumor of bone.** *J Cancer Res Clin Oncol* 2001; 127**:** 467-474.
2. Hoeffel JC, Galloy MA, Grignon Y, Chastagner P, Floquet J, Mainard L et al. **Giant cell tumor of bone in children and adolescents.** *Rev Rhum Engl Ed* 1996; 63**:** 618-623.
3. Picci P, Manfrini M, Zucchi V, Gherlinzoni F, Rock M, Bertoni F et al. **Giant-cell tumor of bone in skeletally immature patients.** *J Bone Joint Surg Am* 1983; 65**:** 486-490.
4. Campanacci M, Capanna R, Fabbri N, Bettelli G. **Curettage of giant cell tumor of bone. Reconstruction with subchondral grafts and cement.** *Chir Organi Mov* 1990; 75**:** 212-213.
5. Capanna R, Fabbri N, Bettelli G. **Curettage of giant cell tumor of bone. The effect of surgical technique and adjuvants on local recurrence rate.** *Chir Organi Mov* 1990; 75**:** 206.
6. Campanacci M, Baldini N, Boriani S, Sudanese A. **Giant-cell tumor of bone.** *J Bone Joint Surg Am* 1987; 69**:** 106-114.
7. Dahlin DC. **Bone Tumours, General Aspects and Data on 6,221 Cases.** 3rd edition. Springfield: IL. Charles C Thomas; 1978.
8. Liu HS, Wang JW. **Treatment of giant cell tumor of bone: a comparison of local curettage and wide resection.** *Changgeng Yi Xue Za Zhi* 1998; 21**:** 37-43.
9. Trieb K, Bitzan P, Dominkus M, Kotz R. **Giant-cell tumors of long bones.** *J Bone Joint Surg Am* 2000; 82**:** 1360-1361.
10. Unni KK. **Dahlin's Bone Tumors: General Aspect and Data on 11087 Cases.** 5th edition. Philadelphia: PA. Lippincott- Raven; 1998.
11. Malawer MM, Bickels J, Meller I, Buch RG, Henshaw RM, Kollender Y. **Cryosurgery in the treatment of giant cell tumor. A long-term followup study.** *Clin Orthop Relat Res* 1999; 176-188.
12. Marcove RC, Weis LD, Vaghaiwalla MR, Pearson R, Huvos AG. **Cryosurgery in the treatment of giant cell tumors of bone. A report of 52 consecutive cases.** *Bull Hosp Joint Dis* 1978; 39**:** 12-34.
13. Bertoni F, Present D, Sudanese A, Baldini N, Bacchini P, Campanacci M. **Giant-cell tumor of bone with pulmonary metastases. Six case reports and a review of the literature.** *Clin Orthop Relat Res* 1988; 275-285.
14. Bini SA, Gill K, Johnston JO. **Giant cell tumor of bone. Curettage and cement reconstruction.** *Clin Orthop Relat Res* 1995; 245-250.
15. Durr HR, Maier M, Jansson V, Baur A, Refior HJ. **Phenol as an adjuvant for local control in the treatment of giant cell tumour of the bone.** *Eur J Surg Oncol* 1999; 25**:** 610-618.
16. Oda Y, Miura H, Tsuneyoshi M, Iwamoto Y. **Giant cell tumor of bone: oncological and functional results of long-term follow-up.** *Jpn J Clin Oncol* 1998; 28**:** 323-328.
17. Nicholson NC, Ramp WK, Kneisl JS, Kaysinger KK. **Hydrogen peroxide inhibits giant cell tumor and osteoblast metabolism in vitro.** *Clin Orthop Relat Res* 1998; 250-260.
18. Zhang Y, Hou C, Chen A. **[A preliminary clinical observation of giant cell tumor of bone treated by adriamycin-loaded chitosan drug delivery system].** *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 1998; 12**:** 280-282.
19. Boriani S, Sudanese A, Baldini N, Picci P. **Sarcomatous degeneration of giant cell tumours.** *Ital J Orthop Traumatol* 1986; 12**:** 191-199.
20. Rock MG, Sim FH, Unni KK, Witrak GA, Frassica FJ, Schray MF et al. **Secondary malignant giant-cell tumor of bone. Clinicopathological assessment of nineteen patients.** *J Bone Joint Surg Am* 1986; 68**:** 1073-1079.

21. Chakravarti A, Spiro IJ, Hug EB, Mankin HJ, Efird JT, Suit HD. **Megavoltage radiation therapy for axial and inoperable giant-cell tumor of bone.** *J Bone Joint Surg Am* 1999; 81**:** 1566-1573.
22. Nair MK, Jyothirmayi R. **Radiation therapy in the treatment of giant cell tumor of bone.** *Int J Radiat Oncol Biol Phys* 1999; 43**:** 1065-1069.
23. Persson BM, Ekelund L, Lovdahl R, Gunterberg B. **Favourable results of acrylic cementation for giant cell tumors.** *Acta Orthop Scand* 1984; 55**:** 209-214.
24. Yip KM, Leung PC, Kumta SM. **Giant cell tumor of bone.** *Clin Orthop Relat Res* 1996; 60-64.
25. O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, Mankin HJ. **Recurrence of giant-cell tumors of the long bones after curettage and packing with cement.** *J Bone Joint Surg Am* 1994; 76**:** 1827-1833.
26. Blackley HR, Wunder JS, Davis AM, White LM, Kandel R, Bell RS. **Treatment of giant-cell tumors of long bones with curettage and bone-grafting.** *J Bone Joint Surg Am* 1999; 81**:** 811-820.
27. von Steyern FV, Kristiansson I, Jonsson K, Mannfolk P, Heinegard D, Rydholm A. **Giant-cell tumour of the knee: the condition of the cartilage after treatment by curettage and cementing.** *J Bone Joint Surg Br* 2007; 89**:** 361-365.
28. Remedios D, Saifuddin A, Pringle J. **Radiological and clinical recurrence of giant-cell tumour of bone after the use of cement.** *J Bone Joint Surg Br* 1997; 79**:** 26-30.
29. Dreinhofer KE, Rydholm A, Bauer HC, Kreicbergs A. **Giant-cell tumours with fracture at diagnosis. Curettage and acrylic cementing in ten cases.** *J Bone Joint Surg Br* 1995; 77**:** 189-193.
30. Frassica FJ, Gorski JP, Pritchard DJ, Sim FH, Chao EY. **A comparative analysis of subchondral replacement with polymethylmethacrylate or autogenous bone grafts in dogs.** *Clin Orthop Relat Res* 1993; 378-390.
31. Frassica FJ, Sim FH, Pritchard DJ, Chao EY. **Subchondral replacement: a comparative analysis of reconstruction with methyl methacrylate or autogenous bone graft.** *Chir Organi Mov* 1990; 75**:** 189-190.
32. Lavoie S, Turcotte RE, Berthiaume MJ, Doyon J. **The arthrogenic effect of cementation for the treatment of giant cell tumor of the knee**. *J Bone Joint Surg* 80[S1], 14. 1998.
33. Mjoberg B, Pettersson H, Rosenqvist R, Rydholm A. **Bone cement, thermal injury and the radiolucent zone.** *Acta Orthop Scand* 1984; 55**:** 597-600.
34. Vult von SF, Bauer HC, Trovik C, Kivioja A, Bergh P, Holmberg JP et al. **Treatment of local recurrences of giant cell tumour in long bones after curettage and cementing. A Scandinavian Sarcoma Group study.** *J Bone Joint Surg Br* 2006; 88**:** 531-535.