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# A Study of Giant cell Tumor of Bone following Denosumab Treatment

Authors
**Dr Rahmat Ali (Ms (ortho), MCh(ortho) )[1], Dr Rajendra Chaudhry (MD Medicine)[2*]**
[1]Professor and H.O.D (Ortho department), Maharishi Vashishtha Autonomous State Medical College, Basti, UP
[2]Professor and H.O.D (Medicine Department), Maharishi Vashishtha Autonomous State Medical College, Basti, UP., India
*Corresponding Author
**Dr Rajendra Chaudhry (MD Medicine)**
Professor and H.O.D (Medicine Department), Maharishi Vashishtha Autonomous State Medical College, Basti, UP., India

**Abstract**
*Giant cell tumor (GCT) is a nonmalignant neoplasm composed of multinucleated giant and mononuclear stromal cells. This study aimed to compare imaging findings of GCT pre- and post-denosumab treatment, including lesion size, percentage of signal intensity/density change, and time of initial objective tumor response. This will have a great impact on selection of most appropriate imaging technique to accurately measure therapy response and its related complications, which would influence the physicians to tailor the treatment regimen to suit each patient. Based on the ICDS criteria, most patients with giant cell tumor of bone show objective tumor response to denosumab.*
**Keywords:** *Giant cell tumor, Denosumab, Magnetic resonance imaging, RANKL. GCTB.*

## Background

Giant cell tumor (GCT) is a nonmalignant neoplasm composed of multinucleated giant and mononuclear stromal cells. The stromal cell population is a mesenchymal osteoblast precursor, which is the neoplastic component of GCT. GCT has an aggressive osteolytic nature related to activation of receptor activator of nuclear factor-kappa B ligand (RANKL) expressed by its giant cells. GCT accounts for approximately 6% of all primary bone tumors and 20% of benign bone neoplasms in adults. Nearly half of most GCT lesions occur in the knee with a fewer than 5% of lesions seen in other sites such as the distal radius, proximal humerus and vertebral bodies. After intralesional surgery combined with allograft or cement, the local recurrence rate of these lesions has been reduced to 12–14%. In nearly one tenth of patients, malignant transformation occurs at recurrence, and 1–4% has pulmonary metastasis despite its benign histopathology. Currently, denosumab is one of the treatment modality used in such challenging GCT cases. It is an FDA approved monoclonal antibody that acts as RANKL inhibitor, which prevents bone destruction and induces sclerosis and remineralization. RANKL plays a crucial role in GCT; it is expressed by the neoplastic stromal component and mediates recruitment of the monocytic precursors, which then develop

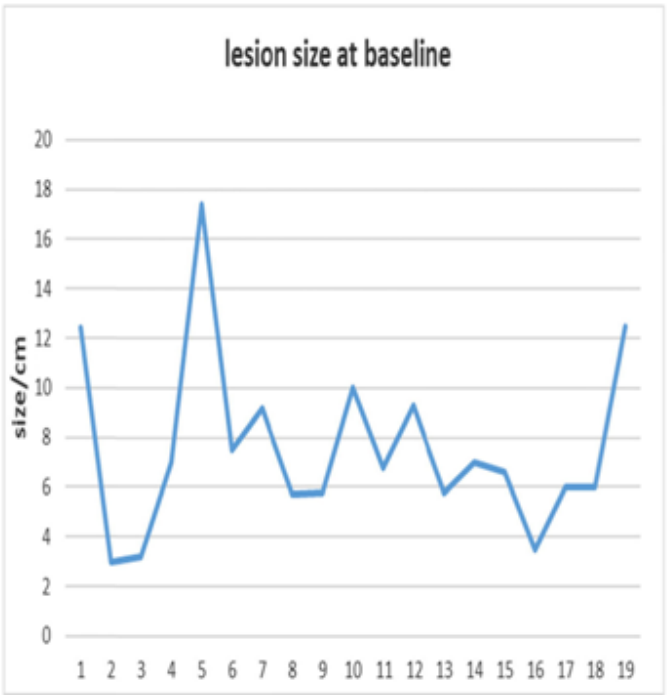
osteoclast-like cells and erode bone. This study aimed to compare imaging findings of GCT pre- and post-denosumab treatment, including lesion size, percentage of signal intensity/density change, and time of initial objective tumor response. This will have a great impact on selection of most appropriate imaging technique to accurately measure therapy response and its related complications, which would influence the physicians to tailor the treatment regimen to suit each patient.

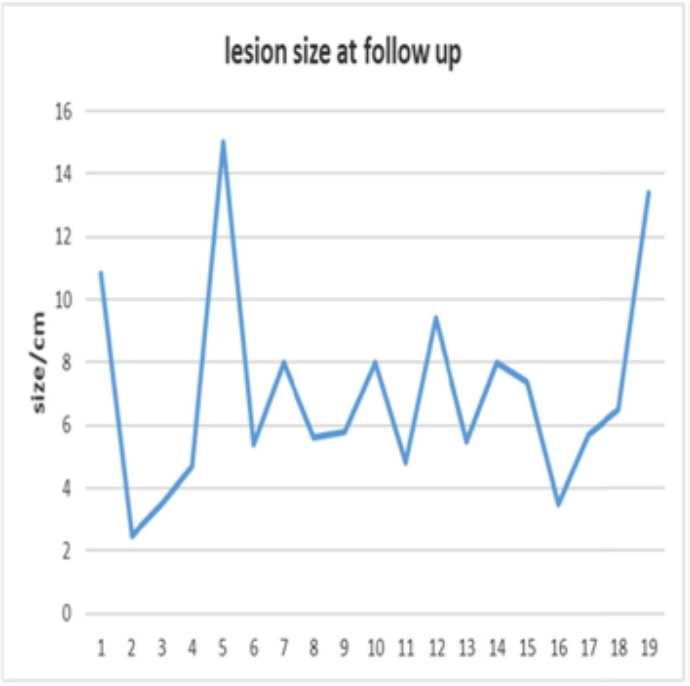
**Method** -

This study reviewed the data of 20 patients with radiologically and pathologically proven GCTB treated with denosumab at MVASMC- Basti, between April 2019 to January 2021. The exclusion criteria included absence of baseline or post-treatment imaging follow-up and the use of concurrent alternative treatment. Patients were administered 120 mg denosumab subcutaneously every 4 weeks based on a standard treatment regimen. The baseline clinical data, demographic profile, therapeutic regimen, and imaging findings on plain radiograph, CT scan, and MRI scan at baseline and 24-month follow-up were reviewed. The lesion size, textural/signal pattern, and time to first objective tumor response were evaluated using available modalities by two musculoskeletal radiologists blinded to the investigator assessment.

**Results**

This study included 10 patients with an average age of 30.7 ± 10.2 years of whom nearly two third patients had primary GCT, one third had recurrence. As per ICDS, 6 patients (84.2%) had an objective tumor response and 5 (78.9%) had an increase in density or decrease in signal intensity. The median time to first objective tumor response was approximately 23 weeks. Almost half of the patients underwent surgical resection following treatment with no documented cases of recurrence. None of the patients developed pathological fracture or malignant transformation during or after the course of treatment. However, one case of osteonecrosis of the maxilla developed in a patient 3 years after the start of treatment which needed cessation of denosumab administration.



## Discussion

We detected a positive tumor response in the majority of patient with GCT following denosumab treatment using ICDS assessment criteria. The effectiveness of denosumab in reducing the stage of disease and sharpening the tumor margin prior to surgical resection has been established. In this study, denosumab was used to decrease the stage of the local disease prior to surgical resection in 57%of patients and control the progression of recurrent locally aggressive or unresectable lesions in the remaining patients. However, it does not prevent recurrence in patients who have been treated surgically previously. Recurrence and metastasis to the lung and lymph nodes on baseline imaging were observed in two patients, and two patients achieved objective tumor response at the target lesions and metastatic lesions. In patients with GCT, skeletal-related complications, such as pathological fracture and malignant transformation, with an incidence of approximately 30% and 2–5%, respectively, can occur especially after radiotherapy.

## Conclusion

Based on the ICDS criteria, most patients with GCTB show objective tumor response to denosumab. MRI and plain radiographs detected tumor response in our cases, but many institutions prefer a combination of CT and plain radiograph which seems to be a better alternative for a more accurate assessment considering the availability of HU as an objective measure.

## Reference


1. Xu S, Adams B, Yu XC, Xu M (2013) Denosumab and giant cell tumour of bone-a review and future management considerations. Curr Oncol.
2. Luengo-Alonso G, Mellado-Romero M, Shemesh S, Ramos-Pascua L, Pretell-Mazzini J (2019) Denosumab Treatment for giant-cell tumor of bone: a systematic review of the literature. Arch Orthop Trauma Surg.
3. Qi WX, Tang LN, He AN, Yao Y, Shen Z (2014) Risk of osteonecrosis of the jaw in cancer patients receiving denosumab: a meta-analysis of seven randomized controlled trials. Int J Clin Oncol.
4. Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, Li SM (1982) Giant-cell tumor of bone: analysis of two hundred and eight cases in Chinese patients. J Bone Joint Surg Am 64(5):755–761.
5. ECR 2014 / C-1095 / Imaging of giant cell tumors of bone. European Congress of Radiology.
6. Chawla S, Henshaw R, Seeger L et al (2013) Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol.
7. Choi H, Charnsangavej C, Faria SC et al (2007) Correlation of computed tomography and positron emission tomography in patients with metastatic gastrointestinal stromal tumor treated at a single institution with imatinib mesylate: proposal of new computed tomography response criteria. J Clin Oncol. 25(13):1753–1759.
8. Rock MG, Sim FH, Unni KK et al (1986) Secondary malignant giant-cell tumor of bone. Clinicopathological Assessment Of Nineteen Patients. J Bone Joint Surg Am. 68(7):1073–1079.
9. Branstetter DG, Nelson SD, Manivel JC et al (2012) Denosumab induces tumor reduction and bone formation in patients with giant-cell tumor of bone. Clin Cancer Res.
10. Turcotte RE, Wunder JS, Isler MH et al (2002) Giant cell tumor of long bone: a Canadian Sarcoma Group study. Clin Orthop Relat Res.

11. Mcgrath PJ (1972) Giant-cell tumour of bone: an analysis of fifty-two cases. J Bone Joint Surg Br 54(2):216–229.
12. Campanacci M, Baldini N, Boriani S, Sudanese A (1987) Giant-cell tumor of bone. J Bone Joint Surg Am 69(1):106–114.
13. Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk GR Jr (2013) Giant cell tumor of bone: review, mimics, and new developments in treatment. Radiographics.
14. Bertoni F, Bacchini P, Staals EL (2003) Malignancy in giant cell tumor of bone. Cancer. 97(10):2520–2529.
15. Ueda T, Morioka H, Nishida Y et al (2015) Objective tumor response to denosumab in patients with giant cell tumor of bone: a multicenter phase II trial. Ann Oncol.