

Peer Review File

Article information: <http://dx.doi.org/10.21037/aoj-20-70>.

REVIEWER COMMENTS:

- **Reviewer Comment (RC) – First, native English language revision grammar editing is needed.**
 - ✓ Authors' Response (AR) – Thank you for this suggestion. The manuscript has been re-revised with attention to native English (US) grammatical and spelling standards.

- **RC – Second, although the rarity of the disease, 31 patients from two centers are few to demonstrate your hypothesis and it should be added in description of study limitations.**
 - ✓ AR – This has been added (lines 240-241).

- **RC – Moreover, the radiographic methodology and comparison with other imaging techniques now available should be more accurately discussed: surely, Xrays are more accessible, less expensive and represent the first diagnostic investigation after clinical exams for bone tumors, but many other imaging techniques like CT, MRI (even 3T) are essential for a correct diagnosis and their value should be better remarked. Also the description of typical radiographic features of Osteosarcoma should be added in the introduction.**
 - ✓ AR – We agree with the Reviewer that these matters are important. With respect to this manuscript, where we are using radiological imaging not as a diagnostic tool but in order to assess chemotherapy response, we have attempted to provide a thorough review of these advanced imaging modalities as they pertain to assessment of chemotherapy response (lines 232-239). With respect to the use of these modalities in the diagnosis and staging of osteosarcoma, we have added additional commentary on the use of these modalities for the work-up of osteosarcoma in the introduction.

- **RC – Line 50: please, describe the correlation between Huvos grading and % rate for evaluating poor or good response to chemotherapy.**
 - ✓ AR – This has been added.

- **RC – Line 58: what do you mean for human interpretation of tumor mineralization? Please, report previous Literature about subjective outcomes about this concern.**
 - ✓ AR – The intent here was to indicate that investigators visually scrutinized radiographs of patients with osteosarcomas, without the aid of computerized assessment. This text has been augmented and a citation added.

- **RC – Line 65: what do you mean for state-of the art image analysis technique? Please, better explain here.**
 - ✓ AR – Thank you, this text has been revised.

- **RC – Lines 73-76: chemotherapy protocol should be better described and cited as reference. Histologic evaluation of necrosis methods should be more accurately described.**
 - ✓ AR – The descriptions of the chemotherapy and necrosis evaluation have been augmented and cited.

- **RC – Line 80: why (6)?**
 - ✓ AR – We apologize, this citation was in error and has been removed.

- **RC – Line 90: ROIs abbreviation should be extended here and not in line 92. (ERH) is not essential.**
 - ✓ AR – Thank you for identifying this issue. This has been addressed.

- **RC – Line 141 and 144: references are not in right order.**
 - ✓ AR – We have updated the citations and this appears to be corrected.

- **RC – General: there are many not essential abbreviations in Discussion as they are not repeated a second time through following lines. Please remove them.**
 - ✓ AR – We agree with this assessment and have removed most of the abbreviations.