Author's response to reviews

**Title:** Sunitinib Combined with Proton Beam Radiation for the Treatment of Chondrosarcoma: a Case Report

**Authors:**

Jennifer Dallas (jennifer.dallas@medicine.ufl.edu)
Iman Imanirad (iman.imanirad@medicine.ufl.edu)
Rajiv Rajani (rajanr@ortho.ufl.edu)
Roi Dagan (rdagan@ufl.edu)
Sukanthini Subbiah (Sukanthini.Subbiah@medicine.ufl.edu)
Rebecca Gaa (gaar@shands.ufl.edu)
Wayne A. Dwarica (Dwariwa@shands.ufl.edu)
Alison M. Ivey (aivey@ufl.edu)
Robert A. Zlotecki (zlotera@ufl.edu)
Robert Malyapa (malyapa@ufl.edu)
Danny J. Indelicato (dindelicato@floridaproton.org)
Mark T. Scarborough (scarbmt@ortho.ufl.edu)
John D. Reith (reith@pathology.ufl.edu)
C. Parker Gibbs (cpgibbs@ortho.ufl.edu)
Long H. Dang (long.dang@medicine.ufl.edu)

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**Author's response to reviews:** see over
Dear Members of the Editorial Board,

We are re-submitting a revised version of our manuscript titled “Sunitinib combined with proton beam radiation for the treatment of chondrosarcoma: a case report?” for your re-consideration as a case report in Journal of Medical Case Reports.

We would like to take this opportunity to thank you for considering our manuscript, as well as the reviewers for their time and comments on the manuscript. Below, we have detailed the changes that have been incorporated into this revised manuscript.

Thank you very much for your time and consideration.

Sincerely yours,

Long H. Dang MD PhD

Reviewer’s comment:

Since you postulate the mechanism of sunitinib is blocking PDGFR, VEGFR in chondrosarcoma, it would be of interest if you can show some staining of phosphorylated receptors in the tumor sample that you have shown.

Authors’ response:

We have done immunohistochemistry on the patient’s tumor samples using anti-PDGFR antibody, and found that PDGFR is not expressed in tumor cells. We postulate several possible mechanisms for clinical efficacy with sunitinib. First, sunitinib may have a purely anti-angiogenic effect in chondrosarcoma, inhibiting VEGFR on endothelial cells and
PDGFR on pericytes. Second, PDGFR may be expressed at low level beyond the detection limits of our assay, and PDGF-alpha and PDGF-beta may be overexpressed in the tumor cells and have autocrine growth stimulating effects. Sunitinib treatment would inhibit his autocrine growth pathway. Third, the tumor cells may express at low level a PDGFR-alpha or PDGFR-beta with an activating mutation, and sunitinib would inhibit its signaling.