Author’s response to reviews

Title: Robotic Stereotactic Ablative Radiotherapy for Renal Cell Carcinoma in Patients with Impaired Renal Function. A Single Center Study

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Author’s response to reviews:

Dear Prof. Dr. El-Hajj,

we thank you for finding our manuscript potentially acceptable for publication in “BMC Urology”. Please find enclosed our revised manuscript entitled “Robotic Stereotactic Ablative Radiotherapy for Renal Cell Carcinoma in Patients with Impaired Renal Function. A Single Center Study” which we like to submit to ‘BMC Urology’ for publication.

The constructive suggestions from the reviewer led us to improve our manuscript. We believe these revisions affirm and extend the significance of our conclusions.

We would appreciate if the revised manuscript will be considered suitable for publication by the Editorial Board of ‘BMC Urology’.
Sincerely Yours,

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Point to point reply:

We thank the reviewers for the close and thoughtful reading of our manuscript, for the interest in our work, and for valuable suggestions for improvement. We revised our manuscript based on the constructive suggestions from the reviewers. We believe these revisions extend the significance of our conclusions.

Reviewer(s)' Comments to Author:

Bassem Youssef, Reviewer #1:

This is an interesting retrospective study of Robotic SABR for Renal Cell Carcinoma. The paper is well written, and it is one of the first published studies that show the safety of Robotic SABR in patients with impaired renal function. It is limited by the small number of patients, and relatively short median follow-up. Below are few comments, for the author's consideration:

Line 83 - replace "online" by "continuous"

Online was replaced by continuous (Background section, line 83, page 3)

Line 84 - replace "movable" by "moving"

Movable was replaced by moving (Background section, line 84, page 3)

Line 117 - RCC was shown to have a lower ratio, (2.6-6.9) Ning et al Cancer 1997. It results in different EQD2 and BED estimates

According to the suggested a/ß 2.6-6.9 Gy for RCC we recalculated the biologically equivalent dose (BED) and the equivalent dose in 2 Gy fractions (EQD2). The calculated BED6.9 and EQD26.9 encompassing the PTV for single fraction were 107.5 Gy and 83.3 Gy, and 98.6 Gy and 76.4 Gy for the 3-fraction treatment. (Methods section, line 117-120, page 4)

In order to address the reviewer’s comment we added the suggested reference.

8. Ning S, Trisler K, Wessels BW, Knox SJ. Radiobiologic studies of radioimmunotherapy and external
(References, line 375-377, page 12)

Line 188 - Regimen not regime
Regimen was replaced by regimen (Results section, line 188, page 6)

Line 223 - Was there an observed rotation motion in the kidney? And if yes, was it accounted for and how?
Since only one marker was implanted, rotations could neither be directly detected nor corrected. However, geometric calculations have shown that a 3 mm margin appears to be sufficient also if small rotations (<5 °) occur.
This paragraph was added to the discussion as suggested by the reviewer (Discussion section, line 277-2794, page 9)

Line 244 - replace "and ablation by "ablative"
And ablation was replaced by ablative (Discussion section, line 244, page 8)

Line 245 - replace "is the possible alternative" by "are possible alternatives"
Is the possible alternative was replaced by are possible alternatives (Discussion section, line 245, page 8)

Line 257 - replace "wherever oncological" by "whenever oncologically"
Wherever oncological was replaced by whenever oncologically (Discussion section, line 257, page 9)

Clement Khoury, M.D., Reviewer #2:

This is a well written single-institution retrospective review of cases about the use of robotic SABR for RCC in patients with impaired renal function. It confirms the available data in the literature about the use, efficacy and safety of SABR in RCC, and adds on the application to patients with impaired renal function. Furthermore, the manuscript introduces new safety margins when it comes to motion management using CyberKnife MTS. As stated clearly in the manuscript, this a retrospective analysis with a limited number of patients and a short median follow up relative to renal toxicity.

We agree with the reviewer that larger clinical trials with long term follow up especially of renal function will help to define the clinical benefit of robotic SABR for the treatment of early stage RCC disease. The aim of our study was to evaluate our first experience using this technique to patients with preexisting kidney to further optimize its utility for patients who are at increased risk for progression to
end-stage renal disease due to partial nephrectomy or other ablative techniques. It is also correct that our study provided an important information regarding the margins to be used. A moderate expansion of the tumor (i.e. 3.0 mm) is sufficient for the CyberKnife MTS.