Author’s response to reviews

Title: Irreversible Electroporation of Unresectable Soft Tissue Tumors with Vascular Invasion: Effective Palliation

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Author’s response to reviews: see over
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Maria Lourdes O. Catarroja
On behalf of Annie Bravo
Journal Editorial Office
Editor, BMC Cancer

RE: New Re-Submission Manuscript “Irreversible Electroporation of Unresectable Soft Tissue Tumors with Vascular Invasion: Effective Palliation”

Dear Editor:

Thank you for the additional review of our manuscript. We appreciate the time and effort that it takes to review these types of studies. We have revised our manuscript per the Editorial request. Please find a point by point description of those changes.

In Response to Reviewer 1:
1. In results it states that 107 patients underwent IRE for tumors with vascular invasion. Was this for liver tumors as well? How was vascular invasion defined? This has been better described in the abstract as well as the results section. This has been highlighted to ease of re-review.

2. Were all the open procedures done for pancreatic cancer? - No this has been added to the results section to better describe the technique.

3. Vascular resection was performed in 14 cases. Was the IRE done to improve the margins then? If so, should those patients be analyzed separately? Also, what was your criteria to decide if they underwent IRE for margins? The decision to perform IRE with resection has been significantly expanded within the results section

4. Were the patients who had vascular thrombotic events on anticoagulation prior to therapy? Yes, 2 were and this has been added to the results section

5. What were the causes of the peri-operative deaths? Were they attributed or related to the IRE? One was possibly related the other was not and this has been added to the results section

6. Can you show survival curves for the separate diseases (pancreatic vs liver)? Respectfully we would prefer not to present the data in this fashion. Given the significant heterogeneity of the liver patients and the heterogeneity of the care in the pancreatic patients we are concerned that this figure would be over-stating the results. The main goal of this manuscript is to demonstrate safety with locally advanced cancer. Thus we would like not to present the data in this fashion.
In response to Reviewer 2:
1. The conclusion in the abstract that local disease control and long local RFS demonstrate the superiority to other therapeutic options is not supported by the data. These are patients with different cancers in different anatomic locations with different therapeutic histories. It is difficult to conclude anything beyond the complication and actual local recurrence rates. – Thank you, we completely agree that this was an over reaching statement. This conclusion has been changed to convey a better message.

2. All of the complications should have an organ specific denominator. For example, for pancreas leaks, the denominator should be the number of patients with IRE performed in the pancreas. It's not clear what the denominator is currently. Yes we agree, all denominators have been inserted into the results section.

3. In the results section, the local recurrence free survival with all cancers combined is difficult to interpret. This goes back to comment #1 ? with a heterogeneous population of cancers it is difficult to make conclusions. The factors associated with recurrence are all different for different cancers. The discussion should be condensed and restructured removing most commentary about disease specific survival and local recurrence unless it is broken down by different diseases. We agree and have added that to the results section.

minor essential revisions

4. In the methods section vascular invasion is defined as a tumor less than 5mm from a major vascular structure. What is a major vascular structure? Perivascular may be a more accurate term, as vascular invasion does not represent what actually is occurring in many of these situations. We agree and we have changed this within the methods

5. Technical success is described in the methods. Later in the methods ablation success is described. What is the difference between these two? Thank you for this comment, technical success is defined as the ability to deliver at least 90 pulses while ablation success is the lack of viable tumor at 3 months.

6. The tables were not visible to me. Will upload them again.
7. What were the causes of perioperative death? We have added this description

Thank you for allowing us to resubmit our manuscript

Sincerely,

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