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*Reviewed by 02353682*

I would suggest minor revisions: 1) Authors should quote other RFA technological development such as bipolar RF needles and use of multiple RF needles, promising approaches for large tumors. 2) In the LITT section a large Italian experience dealing with laser ablation of HCC is not mentioned (Pacella et al Journal of Oncology 2008).

**Author Response:**

- 1) We have described the types of RF needles in the revised manuscript as suggested.
- 2) The Italian study in the context of LITT has been included in the revised manuscript.

*Reviewed by 00241247*

Thank you for allowing me to review this manuscript. I congratulate the authors on a concise, well-written, and easy to read review. 1. It would be very useful for the readers if you can insert a table comparing the energy based therapies, specifically radiofrequency, irreversible electroporation, and microwave. Specific comparators to have for this would be collateral damage, ease of dose titration, cost, and duration of therapy. 2. What can you tell us about tissue specificity for each of these energy sources? Specifically, since microwave and radiofrequency are primarily thermal methods ablation whereas irreversible electroporation uses a different non-thermal mechanism, please outline for us the tissue specificity both pathology (tumor) versus normal anatomic structures, such as nerves, arteries, vessels, and hepatic architecture. 3. Please comment and provide some guideline as to when and where therapies may be used in combination because of complementary effects. 4. Please reference basic cellular or tissue studies to explain the mechanism of action of irreversible electroporation wherever possible. 5. Can you provide any information

on specificity between tumor types and the type of energy delivery? 6. Please comment on methods to access the site for energy delivery – intravascular, intravenous, transhepatic, intraperitoneal, or laparoscopic, and please discuss whether one energy source has a preferential route or vantage point for delivery. Your discussion on focused ultrasound was interesting. Please discuss invasive, as well as non-invasive routes for ultrasound delivery that may be available in the future.

#### Author Response

- 1) A tables including comparison of the RFA vs MWA vs IRE has been included
- 2) Tissue specificity of various techniques has been included in the technique
- 3) The use of combination therapies has been included
- 4) The mechanism of action of IRE has been referenced
- 5) Methods to access the site of energy delivery have been discussed in the revised version
- 6) Invasive as well as non-invasive routes for focussed ultrasound have been discussed