

## OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-19-00049

**Title:** Neuromodulation and ablation with focused ultrasound – toward the future of noninvasive brain therapy

**Reviewer's Name:** Attilio Marino

**Reviewer's country:** Italy

**Date sent for review:** 2019-01-28

**Date reviewed:** 2019-02-07

**Review time:** 10 days

### COMMENTS TO AUTHORS

In the manuscript "Neuromodulation and ablation with focused ultrasound - toward the future of noninvasive brain therapy", authors presented the state of the art, the main challenges and future directions of the focused ultrasound-mediated neuromodulation and ablation. The article is well written and scientifically interesting but few minor changes will be necessary before to publish the paper.

-Concerning ablation mediated by focused ultrasound, the possibility to ablate cancer tissue should be mentioned and the following papers should be cited (1-First noninvasive thermal ablation of a brain tumor with MR-guided focused ultrasound; doi: 10.1186/2050-5736-2-17. 2-Magnetic resonance-guided interstitial high-intensity focused ultrasound for brain tumor ablation. doi: 10.3171/2017.11.FOCUS17613)

-Concerning neuromodulation by ultrasound, please include an example showing as the ultrasound frequency affect the neural modulation; moreover, in the future perspective of the ultrasound-mediated neuromodulation, the possibility to amplify the ultrasound excitatory effects by coating neurons with biocompatible piezoelectric nanotransducers should be mentioned and the following papers should be cited (1-Piezoelectric nanotransducers: The future of neural stimulation; DOI: 10.1016/j.nantod.2016.12.005. 2-Piezoelectric Nanoparticle-Assisted Wireless Neuronal Stimulation; DOI: 10.1021/acsnano.5b03162).

## OPEN PEER REVIEW REPORT 2

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-19-00049

**Title:** Neuromodulation and ablation with focused ultrasound – toward the future of noninvasive brain therapy

**Reviewer's Name:** Carlos Paz

**Reviewer's country:** Mexico

**Date sent for review:** 2019-01-28

**Date reviewed:** 2019-02-09

**Review time:** 12 days

### COMMENTS TO AUTHORS

#### General comment

This review references two types of approach for minimally invasive surgical procedures. In the first place, ultrasound technology as a non-invasive option for the treatment of movement disorders. Using focused ultrasound guided by high intensity magnetic resonance (MRgFUS) that is as effective and durable comparable to conventional surgeries. Others that would function as emerging for MRgFUS injury include tumor ablation, obstructive hydrocephalus, and thrombolysis. Meanwhile, focused low-intensity ultrasound (LIFUS) is being explored for its ability to precisely modulate brain circuits without the need of an incision. However, this review does not provide us with sufficient information to determine the effects not only on the skull, but also on the entire trajectory of the ultrasound beam. In addition, the long-term effects are not known, nor what neurotransmitters are being affected, nor the inflammatory processes that are generated. I understand that this review focuses on ultrasound surgical procedures; it can probably be enriched with other surgical procedures that have minimal invasion such as the selective lesion of excitatory neurons with kainic acid, for the control of epileptic seizures. These lesions are circumscribed to a group of excitatory neurons and the unknown effects are avoided by the ultrasound beam.

#### Minor comments

This revision lacks a summary it is important to add it to give a main idea of work.