

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-18-00269

Title: Aligned fibers enhance nerve guide conduits when bridging peripheral nerve defects focused on early repair stage

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Reviewer's country: Italy

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COMMENTS TO AUTHORS

This is a novel study giving important new data about neural tissue engineering

Study design and Method are rigorous and results well sound.

However, some concerns must be issued as follows:

1. In the title it should be pointed out this is an experimental study on rats
2. In Introduction page 3 line 27 No mention of alternative methods such as nerve allografts, autologous and alloplastic nerve conduits, end-to-side nerve coaptation. Should be mentioned and some basic references should be introduced (1-6)
3. In Experimental Section page 3 line 55 The extended name of the compound should be used first and the abbreviation in parentheses. Polycaprolactone (PCL)
4. In Experimental Section page 7 line 41 Some data are missing. Please point out which parameters did you analyze (nerve diameter, fiber, area), as it is written in the session RESULTS and at which magnification each of these parameters was evaluated.
5. In Discussion page 10 A paragraph should be added pointing out that why did the Authors use the lower limb (sciatic nerve) instead of the upper limb (which could apply for better objective functional studies (7)
6. In Discussion page 10 line 43 It has largely been shown in literature (1, 2, 4) in particular if we think to clinical series, that conduits may be effective for short nerve gaps. This consideration is too hazardous and should be corrected taking into account this is an experimental study.

Suggested references to be added:

1) Bontioti EN, Kanje M, Dahlin LB (2003) Regeneration and functional recovery in the upper extremity

of rats after various types of nerve injuries. *J Peripher Nerv Syst* 8: 159-168.

2) Tos P, Battiston B, Nicolino S, Raimondo S, Fornaro M, Lee JM, Chirila L, Geuna S, Perroteau I.

Comparison of fresh and predegenerated muscle-vein-combined guides for the repair of rat median nerve.

Microsurgery. 2007;27(1):48-55

3) Geuna S, Tos P, Raimondo S, Lee JM, Gambarotta G, Nicolino S, Fornaro M, Papalia I, Perroteau I, Battiston B.

Functional, morphological and biomolecular assessment of posttraumatic neuro-muscular recovery in the rat forelimb model.

Acta Neurochir Suppl. 2007;100:173-7

4) Battiston B, Tos P, Conforti LG, Geuna S.

Alternative techniques for peripheral nerve repair: conduits and end-to-side neurorrhaphy.

Acta Neurochir Suppl. 2007;100:43-50

5) Papalia I, Magaudda L, Righi M, Ronchi G, Viano N, Geuna S, Colonna MR.

Epineurial Window Is More Efficient in Attracting Axons than Simple Coaptation in a Sutureless (Cyanoacrylate-Bound) Model of End-to-Side Nerve Repair in the Rat Upper Limb: Functional and Morphometric Evidences and Review of the Literature.

PLoS One. 2016 Feb 12;11(2):e0148443

6) Geuna S, Papalia I, Ronchi G, d'Alcontres FS, Natsis K, Papadopoulos NA, Colonna MR.

The reasons for end-to-side coaptation: how does lateral axon sprouting work?

Neural Regen Res. 2017 Apr;12(4):529-533

7) Papalia I, Tos P, Stagno d'Alcontres F, Battiston B, Geuna S (2003) On the use of the grasping test in the rat median nerve model: a re-appraisal of its efficacy for quantitative assessment of motor function

recovery. J Neurosci Methods 127: 43-47