

December 09, 2013



**Title:** Unilateral peripheral neuropathic pain: the role of neurodiagnostic skin biopsy

**Author:** Michelangelo Buonocore

**Name of Journal:** *World Journal of Clinical Cases*

**ESPS Manuscript NO:** 6136

Dear Editor,

thank you for publishing the manuscript in the World Journal of Clinical Cases.  
The manuscript has been improved according to the suggestions of referees.  
Please find enclosed the answers to the queries of the reviewers.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Michelangelo Buonocore'.

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REVIEWER 1 (00742049)

REF 1

Query 1

The article ... was too short

Answer 1

The article has been thought to be a short review. Anyway, following this and other suggestions I added new text and references to the previous manuscript.

Query 2

References ... only about 10 of them were direct reports on the use of NSB.

Answer 2

As suggested, I added several new references on the use of NSB.

Query 3

For this reason, a systematic review is considered ...

Answer 3

The article has been thought to be a short review and not a systemic review. That's why the topic was limited to the possible use of NSB for the diagnosis of unilateral neuropathic pain and not for all the possible forms of neuropathic pain.

REVIEWER 2 (00722438)

REF 2

Query 1

(The article) is not a thorough review of the published literature ... it does not meet the expectation of a research paper or a review article.

Answer 1

Again, the article has been thought to be a short review and not a systemic review, neither a research paper!

REVIEWER 3 (00875981)

REF 3 - Query 1

Figure 3 refers to Epidermal Nerve Fibre Density as EISR. Shouldn't it be ENFD?

REF 3 - Answer 1

The figure 3 is correct. It shows the values of EISR and not of ENFD. However, in the legend I wrongly repeated the meaning of EISR and not of ENFD. I amended it accordingly.

REF 3 - Query 2

Figure 1 would be more interesting if it also showed the results from an abnormal subject.

REF 3 - Answer 2

I followed the suggestion adding a second figure (Fig 2) that shows the abnormal finding of a unilateral, complete epidermal denervation, in a patient with post-herpetic neuralgia.

REF 3 - Query 3

A table or algorithm that guides the clinician through the sequence of testing for neuropathic pain would be useful. If possible, it would be useful to identify which test(s) is/are best based on suspected diagnostic entities.

REF 3 - Answer 3

Many thanks to the referee for this suggestion. According to the specific diagnostic properties of neurophysiological tests and NSB, I prepared a new figure (Fig 3) showing a diagnostic sequence that can be useful to confirm the

diagnosis of unilateral peripheral neuropathic pain.

REF 3 - Query 4

It would be very interesting to discuss the role of skin biopsy in small-fiber polyneuropathy and fibromyalgia.

REF 3 - Answer 4

I think that the suggestion is inappropriate because small-fiber polyneuropathies and fibromyalgia are diffuse and bilateral diseases. Aim of the article was indeed to describe only the possible use of NSB in unilateral peripheral neuropathic pain conditions.

REF 3 - Query 5

Some institutions suggest that the results of neurodiagnostic skin biopsy might take as long as a month to process. If so, isn't this a limitation of the procedure?

REF 3 - Answer 5

Yes it is. I thank the referee for the suggestion. The time needed is not so long (usually 2-3 weeks), but surely it is a time-consuming method. Accordingly, I added this limitation in the new version of the manuscript.