

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Minimally invasive surgery versus open surgery in the treatment of lumbar spondylolisthesis: study protocol of a multicenter randomised controlled trial (MISOS trial)
<b>AUTHORS</b>	Arts, Mark; Wolfs, Jasper; Kuijlen, Jos; de Ruiter, Godard

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Alex Alfieri, MD, PhD and Mohsen Yaish, MD Alex Alfieri, MD, PhD, IFAANS Chairman and Professor Neurological and Spinal Surgery Ruppiner Kliniken Brandenburg Medical School Campus Neuruppin Germany
<b>REVIEW RETURNED</b>	19-Jun-2017

<b>GENERAL COMMENTS</b>	<p>The Authors presented a promising a study protocol to compare the minimal invasive surgery of the spine with the conventional opens surgery. As this issue was not fully previously studied and due to the lack of level 1 randomized control studies, this study can be considered as a milestone, and should be encouraged for further development in the field of minimal invasive spinal surgery.</p> <p>Despite some of limitations, the study protocol is concisely written, well organized and justified. The introduction of the study seems to present an original concept. The design, as well the methodology of the study consists with its aims.</p> <p>Minor points of concern are the lack of references and that that the instruments to be used in every hospital are not well identified. It is not clear for me if they are going to use the same screw system of the same company or different systems.</p> <p>Moreover, the presence of neurological signs preoperatively und their Evolution postoperatively is not allocated in the study, which can actually be a good outcome measurement.</p> <p>Another good point of implemetation of the study should be the outcome measurement of the degree of reposition postoperatively in the patients whjth grad II spondylolisthesis .</p> <p>The fusion and its assessment using a conventional x-ray are categorized as one of the secondary outcomes. It is not clear according to which reference was the fusion defined radiologically as less than 2 ° in rotation and less than 1.25 mm in the sagittal plane.</p>
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<b>REVIEWER</b>	Josh Schroeder Hadassah Medical Center Jerusalem Israel none
<b>REVIEW RETURNED</b>	27-Jun-2017

<b>GENERAL COMMENTS</b>	please add what will go for fusion and decompression only
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<b>REVIEWER</b>	Tatsuya Ohtonari Department of Spinal Surgery, Brain Attack Center, Ota Memorial Hospital, Japan
<b>REVIEW RETURNED</b>	28-Jul-2017

<b>GENERAL COMMENTS</b>	This multicenter randomized control trial (MISOS trial) is well-organized study, compared between minimally invasive lumbar interbody fusion (LIF) and conventional open LIF in lumbar spondylolisthesis. The only problem in Methods section is the fact that patients who underwent each surgery noticed postoperatively which type of surgery was performed on them because of the position of skin incision and length, etc. However, this problem seems to be unavoidable, and authors also described this limitation truthfully in Randomization section in Methods and analysis. Except for this unavoidable bias described above, this report reaches enough to the level of publication and to the value of data-analysis.
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### VERSION 1 – AUTHOR RESPONSE

#### Reviewer 1.

- a. Regarding the used implants in the study, based on the surgeons preferences, we will use Zimmer-Biomet pedicle screws in one center, and Medtronic pedicle screws in the other center. Accordingly, the PLIF cages will depend on the surgeons preferences.
- b. Regarding neurological outcome, indeed we will document post operative neurological outcome but this is not the primary outcome measure. This is added in the text.
- c. The same for correction of spondylolisthesis, indeed we will measure degree of spondylolisthesis with postoperative correction in both groups. It is added as outcome measure in the text.
- d. The fusion will be determined by dynamic X-ray and the definition of fusion (< 1.25 mm and < 2 degree rotation) is based on our previous paper on cervical cages (Arts et. Al, Eur Spine J 2017; 2 years results of the CASCADE trial on silicon nitride versus PEEK cages). This reference is added to the reference list.

**Reviewer 2.** No comments

**Reviewer 3.** We agree with the reviewer that the study would be superior whenever blinding would be possible, which is not the case,