PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	COMPARATIVE EVALUATION OF MINIMALLY INVASIVE 'TIBIAL TUBEROPLASTY' SURGICAL TECHNIQUE VERSUS CONVENTIONAL OPEN SURGERY FOR SCHATZKER II-III TIBIAL PLATEAU FRACTURES: DESIGN OF A MULTICENTRE, RANDOMISED, CONTROLLED AND BLINDED TRIAL (TUBERIMPACT STUDY)
AUTHORS	VENDEUVRE, Tanguy; MONLEZUN, Olivier; BRANDET, Claire; INGRAND, Pierre; Durand-Zaleski, Isabelle; GAYET, Louis-Etienne; GERMANEAU, Arnaud; KHIAMI, Frederic; ROULAUD, Manuel; HERPE, Guillaume; RIGOARD, Philippe

VERSION 1 – REVIEW

REVIEWER	Ahmed M. Thabet Texas Tech Uni Health Science center at El Paso
REVIEW RETURNED	16-Dec-2018

GENERAL COMMENTS	I like to thank the authors for their great work. I do not see any tables or graphs summarizing the results. It will very useful to report a summary of results. It is also useful to add another table summarizing the literature about the new technique.

REVIEWER	Oğuz Durakbaşa ACIBADEM KOZYATAĞI HASTANESİ
REVIEW RETURNED	25-Jan-2019

GENERAL COMMENTS	I have concerns about the study endpoints depicted in lines 5-7. The cut-off value for joint surface step-off is stated as 5mm. This value should be revised as 2mm (<=2mm). Step-off>2mm can not be accepted on the joint surface.

REVIEWER	Kiran Boyle Greater Glasgow and Clyde NHS, Scotland.
REVIEW RETURNED	05-Feb-2019

GENERAL COMMENTS	As Above

REVIEWER	Stig Brorson, Professor, MD, PhD, DMSc Department of Orthopaedic Surgery, Zealand University Hospital and University of Copenhagen
REVIEW RETURNED	27-Jun-2019

GENERAL COMMENTS	This is a protocol article for a randomized trial comparing standard osteosynthesis and a minimally invasive technique (tibial tuberoplasty) in operative treatment of tibial plateau fractures.

	The intervention is clinically relevant and the study is well planned and described. Please find below my specific comments. 1. Study population (p.5): Two distinct populations are defined. a. Is a bimodal distribution of the fracture population expected? Does it have implications for the planned statistical analysis? b. The authors state that 'The distinction between these populations will be included in the statistical analysis as a modifying factor'. Please define 'a modifying factor' and explain how it will be included in the statistical analysis. 2. Interventions (p.6): Please briefly define 'Conventional surgery'. 3. Study Endpoints (p.7): a. The primary endpoint is radiological step-off reduction with a cut-off value of 5 mm. Please reflect upon the measurement error of CT and provide some references. Can 4 mm. be distinguished from 6 mm.? b. A variety of secondary endpoints is listed including ROM, PROMs, and QoL measures. The authors should provide a rationale behind their choice of endpoints, the nature of the data obtained and some reflections on whether the study is adequately powered to detect clinically relevant differences for these endpoints. 4. Randomization method (p.8): The author will block-randomize stratified by center. How will they ensure an equal distribution of young and old patients (the bimodal distribution as mentioned above) in the two treatment arms? 5. Blindness (p.8): '…a blinded CT-scan evaluation will be performed by an independent imaging core lab.' Please explain how the CT-assessor can be blinded to the treatment allocation (cement vs plate). 6. Data analysis (p.9): Please specify exactly at what point the treatment allocation will be revealed. 7. Descriptive analysis (p.9): '…lost to follow-up will be described.' How will they be handled in the data analysis? 8. Timing of analysis (p.10): Please define '…mainly based on objective data.' 9. Safety: Please add a section discussing possible complications following tuberoplasty. Any plans for safety monitoring? Interim analyses? Steering group? Stopping rules? How can the investigators detect an unexpected failure of tuberoplasty?

VERSION 1 – AUTHOR RESPONSE

Answer to Ahmed M. Thabet (Rewiever 1) :
The aim of this article is to only present the clinical trial protocol. Moreover, we are in the patient recruitment phase, so we don't have any results yet.
We have added a table summarizing the literature about Tuberoplasty/Tibioplasty, according to your advice.

Answer to Oğuz Durakbaşa (Rewiever 2) :
Unfortunately, 5 mm of step-off on the CT-scan has been chosen for the main criterion to be consistent with the literature and with the sample size calculation according to our previous pilot study. So we can't change this cut-off value.
However, we totally agree with the fact that the reduction must be as close as possible to the anatomy: 0 mm. Indeed the better the reduction is, the better the result is. So we have a secondary objective integrating the notion of step-off measurements in continuous value which will undoubtedly allow us to conclude on this value at 2 mm or even at 1 mm.

Answer to Kiran Boyle (Rewiever 3) :
It was only mentioned ' As Above' in your comment. So, we hope it referred to comments of reviewers 1 and 2.

Answer to Stig Brorson (Rewiever 4) :
1a & 1b :
Clinical experience on tibial plateau fractures and observational studies based on discharge data show that the distribution of age is bimodal. To our knowledge no data are presently available to consider whether the expected outcome after fracture treatment and the expected effect size may differ or not between the two age groups (that age should be an effect modifying factor). But such an assumption seems reasonable so a potential effect modification should be anticipated.
Please see 'statistical analysis' sub-section for details in article.

2. 'Conventional surgery' section has been updated.

3a.
Clarifications about measurement error and potential bias in CT-scan evaluation have been added in article.

3b.
Secondary endpoints listed in the article are linked to study objectives described in the corresponding section. Unfortunatly, as we don't have necessary data in literature, it was hard to evaluate if the study is adequately powered for each secondary endpoint.

4.
Due to logistical constraints due to the delivery of medical devices, adding a supplementary stratification level for age stratum in the randomization process was not retained. In fact, dealing with a suspected effect modifier requires to stratify the analysis, not necessarily to stratify the randomization plan. Although some differences in age distribution may occur as a result of the randomization process, a strictly equal distribution of age groups is not necessary to assume the validity of the stratified analysis.

5.
Osteosynthesis and filling are totally at surgeon discretion, whatever the randomization group. Cement and plate can be used in each group. A statement has been added to clarify this point.

6.
For study participants : after J2 visit
For blinded investigator staff : after the blind review
For blind review committee members : after the blind review
A statement has been added to clarify this point.

7.
On an intent-to-treat basis, the full-analysis set will include every randomized patient with the exception of patients who retracted their consent before surgery. Due to the precocious timing of the primary endpoint (48h) no loss to follow-up is expected at this time.
In case of secondary endpoints, patients lost to follow-up will be described but not included in the analysis.

8.
‘Timing of analysis’ section has been updated in order to limit misunderstanding.

9.
According to French Health authority, this clinical trial has been classified as a clinical trial 'with minimal risks and constraints' (category 2 - Jardé law). So, a specific monitoring of safety is not necessary. We also collect Adverse Events and Serious Adverse Event (as describe in 'Study Objectives' and 'Study Endpoints'). In case of medical device failure, a declaration will be made by investigator to his/her materiovigilance officer, as in standard care.

Answer to Editorial Office :
A section has been added in Methods section, as per your request.

VERSION 2 – REVIEW

REVIEWER	Stig Brorson Zealand University Hospital and University of Copenhagen
REVIEW RETURNED	09-Aug-2019

GENERAL COMMENTS	I have no further comments. I wish the authors good luck with the study.