Reviewer’s report

Title: Autologous cell-derived tissue engineered cartilage for repairing articular cartilage lesions in the knee: study protocol for a randomized controlled trial

Version: 0 Date: 08 Jul 2017

Reviewer: Gianfranco Di Gennaro

Reviewer's report:

The protocol presented here is very interesting and its development can produce genuine value and hope for patients with cartilage lesions.

However, before its acceptance and conduction, clearness should be done concerning planning and analysis. The final aim is to get clear interpretations of results and clinical impacts.

I've got a question concerning inclusion criteria: why do you consider an age range of 14-50. Does it mean that intervention can't be considered for older people?

On exclusion criteria: statements as "Poor health", "Blood diseases" are very "large" and unspecific. I suggest to give more precise criteria to avoid biases related to recruitment.

In the paragraph: "interventions_ Therapeutic approach": when you say "....if the patient's condition meets the surgical requirement, we will extract cartilage from the fossa intercondylar non-weight-bearing area during the first surgery...". If no surgical requirement is met, are patients withdrawn from the study?

I don't understand what the Primary Endpoint exactly is. You use objective and subjective evaluations: do you analyze it separately? Do you use a global score?

Statistical Analysis: in general the paragraph is too poor to be accepted.

Which dataset will you analyze? Intention to treat? Per-Protocol? Specify: results in protocols like yours could be very different.

No sample-size calculation is reported: what's the expected power of the results you will obtain?

You only consider bivariate tests. chi-square, t-test, rank sum. I strongly suggest to use a multivariable approach and consider the introduction of surgeon effect as random component in the model.
For example, try read this paper http://www.sciencedirect.com/science/article/pii/S1053077013004023 on the impact of surgeons in cardiac outcomes. It can be extended to your surgery protocols too.

Gianfranco Di Gennaro

**Level of interest**

Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

**Quality of figures**

All images and figures within the manuscript should be genuine i.e. without evidence of manipulation. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. If you have concerns about the veracity of the figures you should choose the first option below.

**Statistical review**

Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.

**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

Gianfranco Di Gennaro

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal