

May 18th, 2013

Dear editor,

Please find enclosed the entitled manuscript in Word format (file name : 1268-review.doc)

Title: New insights for pelvic radiation disease treatment: Multipotential Stromal Cell is a promise mainstay treatment for the restoration of abdominopelvic severe chronic damages induced by radiotherapy.

Author: Alain CHAPEL, Sabine FRANCOIS, Luc DOUAY, Marc BENDERITTER, Jan VOSWINKEL

Name of journal: *World Journal of Stem Cells*

ESPS manuscript n°: 1268

The manuscript has been improved according to the suggestion of reviewers

1 Format has been updated

2 Revision has been made according to the suggestion of the reviewers

(1) The manuscript is a very short proposal of concept that suggests that MSC therapy should be useful for the treatment of Pelvic radiation disease. While I agree with all of the comment the author provides here, that are still other points that were not discussed and completely ignored. A balanced review of a topic would present both sides

- Other therapies of late severe effect of pelvic radiation disease are mentioned in sentences; (page and line reference??)

(2) Thank you a paragraph was added entitled: Treatments to manage post-radiotherapy pelvic damages

(3) The back side of this therapy should at least be mentioned as a caution to the reader and possible practitioners of the MSC therapy. It may be that the short-term effects far outweigh the possible long-term effects, but if this is the case, the authors should include the discussion of these ideas. As it is currently written, the manuscript is simply pro MSC, without any discussion of any possible untoward effects of this therapy.

-Untoward effects are mentioned in the paragraph: Untoward effects

(4) There are minor typographical errors that should be corrected.

-Minor errors were corrected.

- (5) I would suggest to stratify this more clearly - where should MSC been used. In which organs? Bowel, ureters? And also it should be mentioned that radiotherapy is changing - protons make less damage.

-The manuscript has been modify as requested

- (a) What are the most common post radiation damages?

-Most common radiation damages are mentioned in following sentences; The targeted organs of side effects of irradiation that are mostly studied are brain; salivary glands; mandible; skin; liver; heart; rectum/bladder; bone marrow.

- (b) Where can MSC be used - or are already in use.

- The following sentences were added:

Multipotential (mesenchymal) stromal (stem) cells (MSC) therapy are currently among the most advanced cell therapy tools, with the availability of three FDA-approved products, Prochymal, Provacel and Chondrogen. Stem cell-based approaches using MSCs are promising for the development of future therapy in therapeutics (9) to correct radiodermatitis (10), to improve haematopoiesis (11, 12) and to prevent Graft Versus Host Disease post-haematopoietic stem cell transplantation (13). Clinical studies have reported effects of MSC on gastrointestinal healing such as the reversion of colon peritonitis in patients with GVHD or the treatment of rectovaginal and perianal fistulas in patients with Crohn's disease (14).

- (c) Adding a table would be helpful,

- figure 1 which mentioned clinical trials to treat consequences of radiotherapy was added (is it a figure or a table?)

- (d) Please add that radiotherapy is doing better - protons have less damage.

- This is mentioned in sentence:

Proton therapy is an attractive method to attenuate toxicities of radiotherapy because of the decrease of integral radiation dose to normal tissues, which should lead to fewer late side effects. Unlike other types of radiation therapy that use x-rays to destroy cancer cells, proton therapy uses a beam of special particles called protons inducing less damage to the surrounding healthy tissue. There will be a lower risk of normal tissue toxicity associated with proton therapy because of a lower delivered dose outside of the target tissue (3).

3 References and typesetting were corrected.

Thank you again for considering our manuscript for publication in the *World Journal of Stem Cells*.

Sincerely yours,

A handwritten signature in blue ink, consisting of a stylized 'A' followed by a horizontal line that tapers off to the right.

Alain CHAPEL, PhD

Laboratory of Radio pathology and Innovative Therapies

Institute of Radioprotection and Nuclear Safety

Fontenay aux roses France

Email: alain.chapel@irsn.fr