Reviewer’s report

Title: Changes in bone marrow lesions in response to weight loss in obese knee osteoarthritis patients: A prospective cohort study

Version: 1 Date: 27 October 2012

Reviewer: Jeffrey Driban

Reviewer’s report:

Overall, the authors present a manuscript that explores interesting and well-defined questions. While the manuscript overall is well written there are several points that could be clarified to help further evaluate the methods and results (noted below).

• Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. Abstract/Methods: It may be helpful if it is clarified that BML scores were dichotomized based on decreases in BML scores (responders) and nonresponders.

2. Abstract/Results: The abstract could be clarified to help the reader determine that “weight loss” was evaluated as loss > 10% or <10%. Based on text it is not clear if weight loss was evaluated as a continuous variable or not.

3. Purpose Statement and Methods/Interventions: The study design seems to be a comparative effectiveness design that compares two programs (LED and VLED). There is no control group and therefore it may be important for the authors to reflect this in their purpose statement or note in the discussion how the lack of a control group may impede an accurate assessment of the study’s primary aim (“investigate the changes in BMLs after 16-week weight loss intervention…”). For example, this study design may be more appropriate to investigate the differences in BML changes between two different weight-loss interventions. Or, based on the analyses it appears the interventions were used to evaluate the association between weight loss and BML change.

4. Methods/Interventions: It may be helpful if the authors reiterate that participants were randomly allocated to either treatment group.

5. MRI analysis: Please clarify how the target knee was selected if both knees were equally symptomatic.

6. MRI analysis: Did the study team ensure that the participants were scanned with the same send/receive flex coil at baseline and follow-up (medium or large)? Please clarify in the text.

7. MRI analysis: Please clarify who performed the BLOKS scoring. On Page 4 it indicates that MB and HG performed the BLOKS grading but then in the last sentence of the section it appears that “HG performed all the BLOKS…”

8. MRI analysis: It may be helpful to the reader if the intra-reader agreement and
inter-reader agreement were reported separately? Are the reported values based on weighted kappas? It may be helpful to report the BML agreement separate from the other BLOKS scores since the BML scores were particularly important in these analyses. Were the kappas based on the sum of BML score, max BML score, or individual region scores? Ideally, the intra- and inter-reader kappas for sum and max BMLs would be provided.

9. Radiographic Measurements: What ICC models were used to evaluate the intra- and inter-reader mJSW? It would be helpful if those were included in the sentence.

10. Radiographic Measurements: What was the intra-reader agreement for KL grades?

11. Knee joint alignment: What was the reliability for this measurement?

12. Isometric maximal voluntary contraction: It may be helpful to the reader to see the order that the muscle groups were tested, the duration of isometric contraction, and the rest interval between trials.

13. Statistical Methods: Did the authors try to model weight loss as a continuous variable? It appears figure 1 might do this but the analysis is not described.

14. Statistical Methods: Please clarify if weight loss was evaluated based on percent baseline weight or percent baseline BMI (or both).

15. Statistical Methods: When describing the calculation for LSC it may be helpful to describe how SE was derived.

16. Statistical Methods/Results: How were participants with no baseline BMLs handled in the analyses since their BMLs could not improve?

17. Results: The text indicates that 81% of knees had KL grade 1-2 but Table 1 suggests that the median was KL3 with an IQ of 2-3. Is this a discrepancy?

18. Results: It may be helpful if the authors clarified how the affected compartment was defined and the distribution of affected compartments (e.g., percent with medial tibiofemoral, percent with lateral tibiofemoral).

19. Results: What was the distribution of weight loss in both groups? Based on the figure it appears that the <10% group had considerable weight-loss and included many people near the cut point.

20. Results: The authors note “there were no differences in BML responses in the underlying RCT…” does this suggest there were no group differences?

21. Results/Statistical Methods: Did the authors attempt to control for knee alignment which could influence loading on the affected compartment?

22. Results/Statistical Methods: What statistical tests were used to explore the association between BML change and clinical symptom change? Did the authors adjust for patient characteristics?

23. Limitations: Did the authors measure physical activity? If the inflammation and loading are important aspects to the associations between BMLs, obesity, and symptoms then perhaps physical activity is an important variable in these analyses.
• Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Throughout Document: It may be helpful for the reader if abbreviations are defined when they are first used (e.g., ACR, MRI, BMI).

2. Abstract/Methods: It may be beneficial to the reader if units of measure were added after the BMI of 30 and age of 50.

3. Results (2nd paragraph): It may be beneficial to the reader if units of measure were added after the BMI.

4. Figure: It may be helpful to the reader if the y-axis was labeled with whole units (e.g., 1,2,3). Is the x-axis based on weight loss or BMI loss?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests