Reviewer's report

Title: Quantification of Heterogeneity Observed in Medical Images

Version: 2 Date: 7 December 2012

Reviewer: Giampaolo Tomasi

Reviewer's report:

- The authors did a very good job in addressing my previous comments, especially in terms of the issue of shape. I recommend publication; this is a nice piece of work in an extremely interesting and difficult field.

- Minor Essential Revisions
In the first version of the paper the authors claimed that they used FBP for reconstruction. In the second version they mentioned OSEM. Which is correct?
- The CSI statistics introduced in eq.3 is sometimes referred to as CSISA (shape aware), sometimes as CSI. It is better to start using the SA subscript in eq.3 and use it throughout the manuscript. Also when they introduce CSISU (lines 182-195) the authors should use this symbol (CSISU) and use it throughout the manuscript. Note that lines 202 and 203 the authors used CSIA and CSIU, which should be corrected to CSISA and CSISU.
- line 242. Please report the p-value corresponding to that value of ro.

Discretionary Revisions

- I would suggest to erase the results presented in lines 225-233.
- The discussion on the application to 3D images is important and should be expanded. For instance the strategy of using the Euclidean line could in theory be used also for a 2D image. Also, the two different strategies (Bresenham algorithm vs. Euclidean line+interpolation) should be discussed a little bit better. The details of the type of interpolation necessary for the Euclidean line could be discussed.

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

Quality of written English: Acceptable

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'