## Author's response to reviews

**Title:** Cluster detection methods applied to the Upper Cape Cod cancer data

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**Author's response to reviews:** see over

**Summary of revisions:**

Our thanks to all of the reviewers for their attention to our manuscript. Your comments have helped improve our paper, and we appreciate the time and effort you have spent. On the basis of the reviews, we attempted to strengthen the explanation of the goals of our paper, and to clarify and focus the discussion to areas most relevant to our stated purpose. Additional information on the data and several maps were added.

**Reviewer: DG**

- We have made an effort to improve the statement of the purpose of the paper. In particular we tried to reemphasize the point that we are not interested in comparing and interpreting results, but instead focus on the methodology and what we may learn about these three methods of cluster detection by considering real data. Most of these changes are reflected in the revised Background section.

- We have also expanded the Data section somewhat, although we feel that because our focus is not on the analysis of this data set per se, it is better to direct readers to the articles that describe the data comprehensively. We have added the number of cases and controls for each of the latency assumptions considered.

- After some discussion, we felt that the description of each method, although not a thorough treatment, was still important to our goals for the paper. We agree that there may be more than is needed for an unsophisticated reader, but we would rather include more detail than needed instead of less. These sections can certainly be skimmed by those not interested in the statistical details of the methodology, and references to more detailed discussions are provided for readers who would like a more complete treatment. Additionally, we wish to counteract an increasing tendency to apply statistical methods as a "black box" approach, and be explicit about the details of the methodology in so far as they are relevant to our interpretation of the results.

- The third paragraph of the Background section now addresses our reasoning for the methods chosen. We hope that in future work, researchers with expertise in other cluster detection methods will contribute to the discussion that we have begun.

- We made a concerted effort to modify our language to remove the impression that we are unsympathetic to the spatial scan. To the contrary, we acknowledge the superiority of the scan statistic in published power comparisons and further discuss situations where the scan statistic may provide valuable information about the presence of clustering in real data.

- Maps of the most likely cluster, as identified by the spatial scan statistic, have been added.

**Reviewer: MK**

- In the last paragraph of the GAM subsection (Methods section), we have clarified the interpretation of the local p-values generated by the GAM method. We emphasize that the multiple testing issue is problematic if using these local p-values for the purposes of hypothesis testing, which we advise against. The p-value for the global deviance statistic, which is the p-value we report when comparing across the three methods, does not need adjustment for multiple comparisons.

- Additional references have been added at the suggestion of the reviewer.

- Rather than tabulate the relative risks for the scan statistic and GAM, we have included these values in figure captions (for the scan statistic) or the map legends (GAM).

- Discussion and results have been revised to address several of the points raised, including the strength of evidence of the resulting p-values and the complementary nature of test statistics.

**Reviewer: DW**

- Many of the issues raised by the reviewer have been addressed directly above (see response to reviewer DG). We have clarified the connection between the data and the analysis to emphasize that the data provide a platform for comparing methods that can not be provided by simulations alone. Interpretation of the results is made in the context of the strengths and limitations of each of the methods, and not with the goal of epidemiological findings for breast cancer on Cape Cod.

- The issue of including further data sets to perform additional comparisons across methods had been raised before. After careful consideration, we feel that maintaining a tighter focus on the three data sets analyzed here is preferable to a more wide-ranging analysis of many more data sets. The reviewer's other suggestion, eliminating the real data completely and focusing on the methodology, is reasonable if our goal were to solely consider methodological aspects. But we feel that the inclusion of real data is essential to our purposes in this paper, and have tried to find some middle ground between the two extremes of no data and a comprehensive examination of all available data.

- With no a priori intention to examine particular patterns in these data, we are more interested in learning about the complementary nature of the various test statistics and gaining information from the results of several methods. Thus the fact that the results of hypothesis testing differ across the three methods should be considered and explored, rather than treated as a case of false positives or false negatives.