The Turning Point Modelling in Radiation Therapy for Breast Cancer Patients

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The VADA Program
Visual and Automated Disease Analytics
Graduate Training Program

Background

Facts about breast cancer in Canada:

- It is the 2^{nd} most common cancer in Canada.
- 1 in 8 Canadian women will be diagnosed with breast cancer in their lifetime.
- About 27, 400 women in Canada is diagnosed with breast cancer in 2020.

Radiation therapy (RT) helps almost in every stage of breast cancer:

- It is an effective way to reduce the risk of breast cancer recurring after surgery.
- It could be used to ease the symptoms caused by cancer that has spread to other parts of the body.

Thus, considering the complexity of RT patient scheduling, a simple first-come, first-served policy will generally perform poorly. A more efficient, more personalized algorithm for radiation therapy treatment fraction arrangement is in urgent need.

Objectives

The goal of this paper is to develop a data-driven scheduling algorithm for patients' treatment duration for RT of breast cancer using the data from CancerCare Manitoba, Canada.

- To explore the trajectory of the actual patients' RT treatment durations and, meanwhile, to detect whether a turning point exists.
- To examine the individual differences in the trajectories of the treatment duration and turning points.
- To examine how the trajectories and the turning point are associated with patient characteristics, including the Treatment Type, the Beam Energy, and the On-board Imaging usage.

Methods

The methods used to answer the research question will be: (1) using the data to find the best-fit model, (2) using the best-fit model to find the change point from the pre-assumed fractions, and (3) using the best-fit model with change point to find the related patient-specific characteristics.

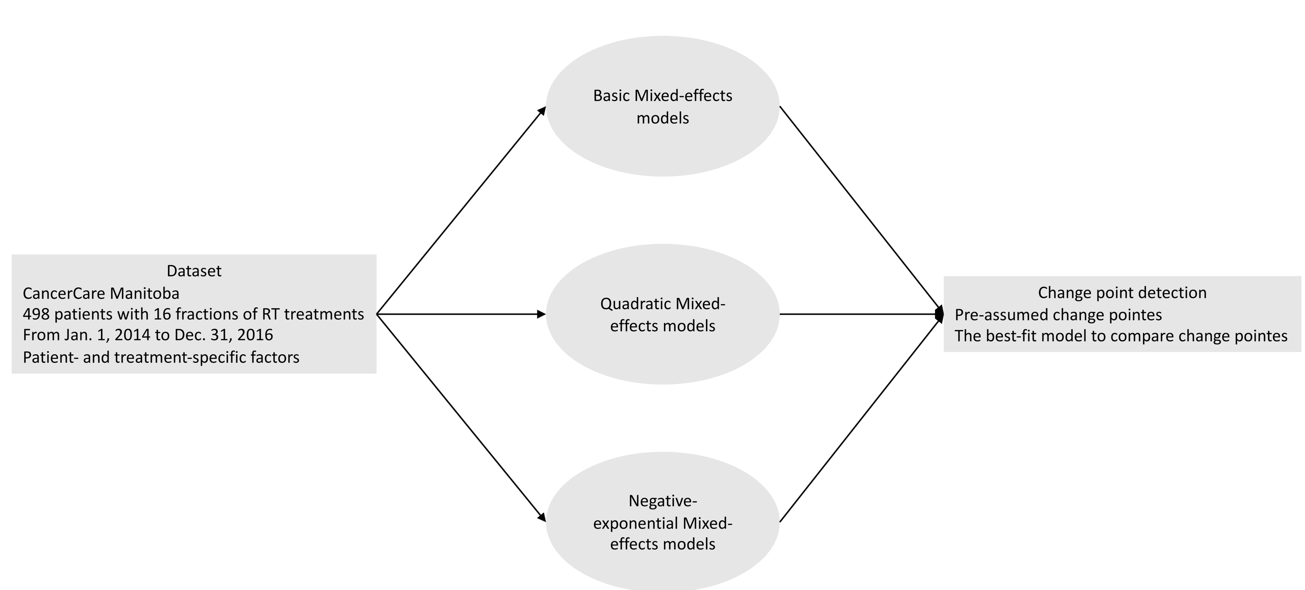

Fig. 1: Diagram of the methods.

Results

Quadratic and negative exponential mixed effects models were compared and BIC statistic was used to find better model.

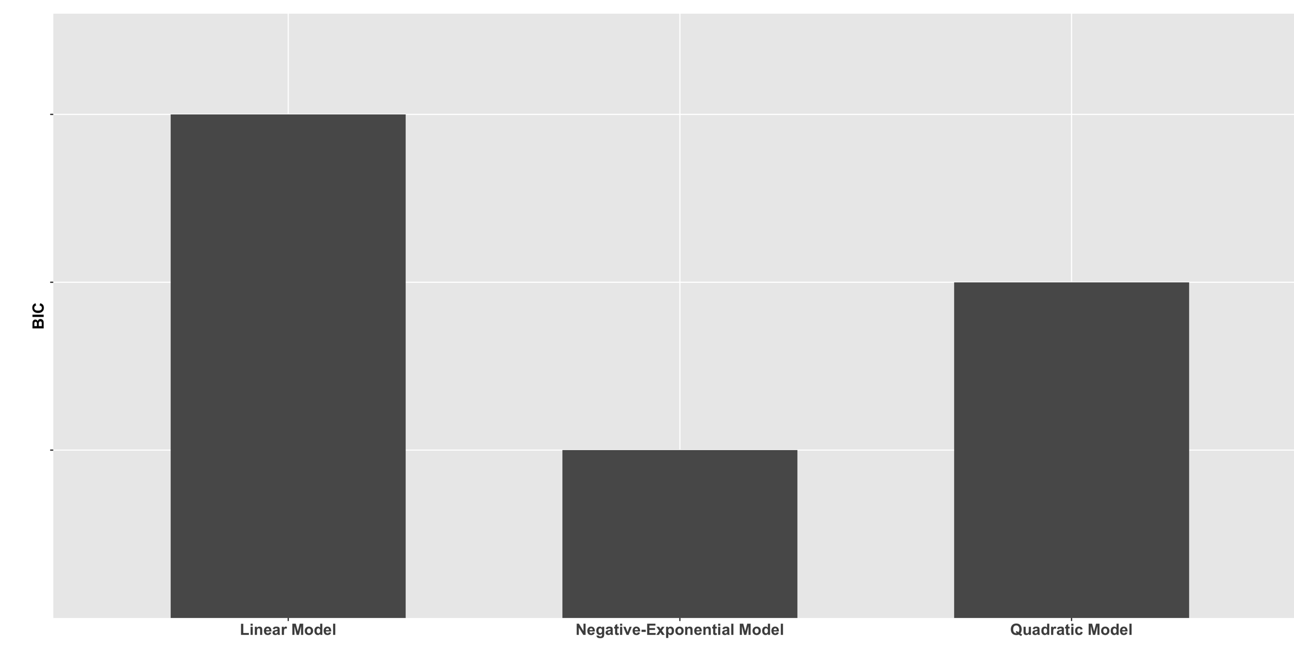

Fig. 2: Model Comparison.

The negative-exponential model shown below best described the population trajectory of RT treatment duration for breast cancer patiens. The initial starting value of treatment duration is estimated to be 12.34 mins and the change point was at the 10th fraction of treatment. We assumed that there is no difference between rate of change before and after the change point. However, there would be a 'jump' at the 10th fraction of treatment, which was estimated to be 0.31 min. It means that the patient averagely had a 0.31 min reduce in treatment time at the 10th fraction compared with their former treatment.

$$
\begin{aligned}
&y_{ij} = \alpha_{0i} + \alpha_{1i} \cdot e^{(-Time_{ij})} + I_j \cdot \alpha_{2i} + \varepsilon_{ij} \\
&I_j = \begin{cases} 0, & j < k \\ 1, & j \neq k \end{cases} \\
&\alpha_{0i} = \lambda_{00} + \xi_{0i} \\
&\alpha_{2i} = \lambda_{02} + \xi_{2i} \\
&\varepsilon_{ij} \sim N(0, \sigma_\varepsilon^2) \; and \; \begin{bmatrix} \xi_{0i} \\ \xi_{3i} \end{bmatrix} \sim N\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_0^2 & \sigma_{02}^2 \\ \sigma_{20} & \sigma_2^2 \end{bmatrix} \right)
\end{aligned}
\tag{1}
$$

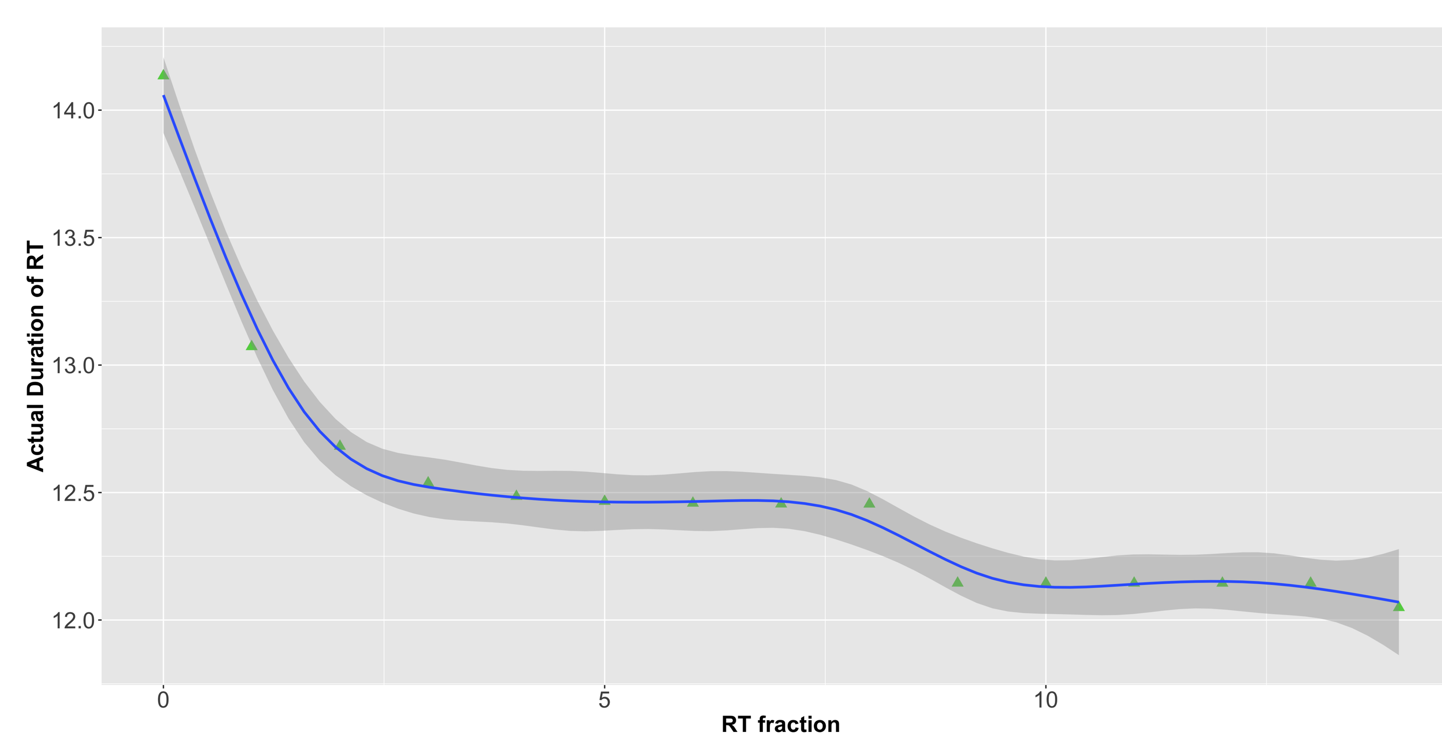

Fig. 3: The outcome of negative exponential model with the change point.

Conclusion

To examine how the actual RT treatment durations were changing during the treatment period, a series of piece-wise nonlinear mixed effect models were compared to determine the best prediction model for actual RT treatment durations. We employed the exhaustive attack methods to determine the turning point of the treatment.

	Phase I	Change Point	Phase II
Location	1st - 9th Fraction	10th Fraction	11th - 16th Fraction
Average Duration/Jump	10 - 18 mins	0.3 mins	9.7 - 17.6 mins

The scheduling of RT durations should also depend on treatment type, treatment beam energy, and on-boarding imaging use. A scheduling tool that can account for the different needs of individual patients would be very beneficial in meeting patient care and resource utilization goals by potentially increasing the treatment capacity.

At the same time, our study has several limitations and further analysis would be on these areas:

- According to the theory mentioned by Ning&Luo[2] that the misspecified turning point would lead us to the biased model fit indices, the model comparing with using the exhaustive attack methods were not the best solution in that when comparing with the results of the turning point models, the misspecified turning point was include, and the biased statistics were inevitable.
- An MI-based procedure was mentioned to solve such probllinear mixed-effects moem in latent growth curve models[1].
- Considering the timeline and the model complexity, we did not add the random part to the slope of time in the model resulting in the rate of change for each patient had to remain the same.
- Random change point models were an emerging area that parametrized the change point and let the individual-specific turning time happened by adding the random part to the change point parametrization. Determining the turning point becomes the problem of parameter estimation.

Acknowledgements

I wish to acknowledge the help provided by the technical and support staff in the department of applied mathematics at Nanjing Forestry University. I would also like to show my deep appreciation to my supervisor who helped me finalize my project. Besides, sincere gratitude will go to the VADA program, which provides the financial support of this research.

References

[1] Oi-Man Kwok, Wen Luo, and Stephen G West. "Using modification indexes to detect turning points in longitudinal data: A Monte Carlo study". In: *Structural Equation Modeling* 17.2 (2010), pp. 216–240.

[2] Ling Ning and Wen Luo. "Specifying turning point in piecewise growth curve models: challenges and solutions". In: *Frontiers in Applied Mathematics and Statistics* 3 (2017), p. 19.