

Internship offer

Using clustering methods to describe the radiotherapy dose to the heart after treatment for a childhood cancer

Context: Survival rates have raised significantly after childhood cancer, due to improvements on the therapeutic approaches, but so have chronic iatrogenic effects of cancer treatments (radiotherapy and chemotherapy), such as valvulopathy. Recent advancements in dose reconstruction allow for in depth understanding of the radiation dose distribution that could ensure useful predictive models and therefore effective and personalized medical follow-up of cancer survivors.

Objective: Take into account the heterogeneity of the heart-dose via clustering to model the occurrence of a valvulopathy after radiotherapy for a childhood cancer.

Material: The French Childhood Cancer Survivors Study (FCCSS) consists of 7670 5-year survivors that were diagnosed between 1946 and 2000 and we dispose individual matrices of voxelised dosimetric dose reconstruction for 3907 out of the 4081 survivors that were treated with radiotherapy for their first cancer.

Method: For the first part, the student will have to check for clustering tendency, define the optimal number of clusters per patient, evaluate clustering techniques to group voxels according to both dose intensity and spatial characteristics (comparison of different methods like hierarchical clustering and k-means is encouraged) and make a choice on the optimal technique to apply. For the second part, they will have to weigh the clusters and perform an association analysis to model the occurrence of a valvulopathy in the FCCSS in a time-to-event model that they will have to compare with a baseline model of the risk of a radio-induced valvulopathy (e.g. a classic Cox model adjusted on the mean dose to the heart).

Supervision: The intern will be co-supervised by two PhDs, one from the field of biostatistics and epidemiology and one from the field of applied mathematics (biomathematics and mathematical modeling of living systems), as well as one PhD student.

Aims:

- Exploration and short description of the data
- Application and comparison of clustering techniques
- Adjustment of a time-to-event model and comparison with a baseline model

Profile: We are looking for a creative and motivated Master 2 student with a background on applied mathematics, statistics, biostatistics, machine learning, data science, with strong programming skills in R or Python.

Practical aspects:

- Duration: 6 months
- Starting date: according to the curriculum of the Master
- Gratification: according to legal standards
- Location: Institut Gustave Roussy and/or partially remotely

Application process: Please send your CV (one page) and your motivation letter (250-300 words) via email to all of the supervisors (contact below)

Contact:

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References:

- [1] C. Veres *et al.*, "Retrospective Reconstructions of Active Bone Marrow Dose-Volume Histograms," *Int. J. Radiat. Oncol.*, vol. 90, no. 5, pp. 1216–1224, Dec. 2014, doi: 10.1016/j.ijrobp.2014.08.335.
- [2] W. Dörr and T. Herrmann, "Cancer induction by radiotherapy: dose dependence and spatial relationship to irradiated volume," *J. Radiol. Prot. Off. J. Soc. Radiol. Prot.*, vol. 22, no. 3A, pp. A117-121, Sep. 2002, doi: 10.1088/0952-4746/22/3a/321.
- [3] "A Comparative Study of Clustering Algorithms," *Science Alert*. <https://scialert.net/fulltext/?doi=itj.2006.551.559> (accessed Jan. 24, 2022).
- [4] L. Cella *et al.*, "Predicting radiation-induced valvular heart damage," *Acta Oncol.*, vol. 54, no. 10, pp. 1796–1804, Nov. 2015, doi: 10.3109/0284186X.2015.1016624.

Key-words: radiotherapy, dose reconstruction, clustering, spatial heterogeneity, valvulopathy, childhood cancer survivors, late effects