Individualized and optimized cancer radiotherapy

In the SA2001 course edition in Autumn 2022, the students in the master's programme in applied mathematics studied the following MSc theses from RaySearch Labs and Elekta Instrument on optimization on cancer radiotherapy, which relates to several SDGs, in particular SDG 3:

Battinelli, Cecilia, *Proton Arc Therapy Optimization*, 2019, (94 pages)

Olsson, Henrik, *Utilizing the Degrees of Freedom in Radiation Therapy Optimization*, 2017, (50 pages)

Norell, Emil, *Gamma Knife treatment planning with new degrees of freedom*, 2019, (73 pages)

Öström, Linn, *Post-processing of Monte Carlo calculated dose distributions*, 2019, (108 pages)

However, none of the reports above include the *gender dimension in the cancer radiotherapy optimization*. Your tasks will thus be to reflect first individually and then in groups (at the upcoming seminar) beyond the gender dimension and include the intersecting social factors. First, we take a quick look at the recent research on the gender dimension of cancer radiotherapy.

Wagner et al. [1] report from a workshop by European Society for Medical Oncology in 2018 to address the general lack of gender dimension in cancer treatment. Their conclusions are:

"Sex differences in cancer biology and treatment deserve more attention and systematic investigation. Interventional clinical trials evaluating sex-specific dosing regimens are necessary to improve the balance between efficacy and toxicity for drugs with significant pharmacokinetic differences. Especially in diseases or disease subgroups with significant differences in epidemiology or outcomes, men and women with non-sex-related cancers should be considered as biologically distinct groups of patients, for whom specific treatment approaches merit consideration."

The group of oncologists issued a consensus statement following the workshop (Table 2 in [1]). In that statement, one of the major open questions and challenges is:

"Sex differences may not only be limited to drug treatment: differences in anatomy and/ or tumour biology may also affect outcomes of surgery, radiotherapy, or combined modality treatments and need further investigation."

More recently, in 2020, researchers at the University of South Australia [2] report that:

"While disparities in radio sensitivity between genders have been well documented, most radiotherapy guidelines recommendations are based exclusively on population averages rather than demographic subgroups such as age, race and sex."

"While gendered medicine is not a particularly new concept, it has only come under the focus of the medical community in recent years, and as such the pool of available evidence is small. Our search strategy revealed only 8 papers which were relevant to the posed hypothesis, and over half of them were published in the last 3 years. Additionally, gender is rarely the focus of the article, and is instead a variable added as an afterthought. Small sample sizes and concurrent therapy (chemotherapy, surgery etc.) distort the results, leaving more an indication of an answer than a definitive statement."

"As healthcare marches progressively towards a system more tailored to the individual, gender is a factor that may not only have a profound effect, but can be implemented with relative ease."

More accessible presentations of paper [2] are found in [3] and [4], from which the following quotes are taken:

"Women are more likely to be cured of their cancer when undergoing radiotherapy than men are, but their side effects are likelier to be more severe."

"…women are generally more sensitive to radiation than men, but this is not considered in international guidelines for radiation dosages."

"Current guidelines suggest take into consideration weight, height and radiobiological responses of a general population, but have yet to consider gender."

"It is also important to collect data retrospectively so we can compare the radiotherapy outcomes for men and women who were prescribed radiotherapy for the same cancer."

"It is a double-edged coin for men, too. Because they are more radio-resistant than women, their healthy tissues are better protected when receiving radiotherapy with fewer side effects, but their long-term survival rates are shorter."

See also the 4-minute youtube video of the research on gender dimension on cancer radiotherapy: Radiotherapy: will it work for you?

In a recent article from February 2023, "*Sex differences in the diagnosis, treatment and prognosis of cancer: the rationale for an individualised approach*" the authors find:

"*Genetic and environmental factors (social or economic inequalities, power imbalances, and discrimination) that contribute to these differences adversely affect cancer patient health outcomes. Increased health professional awareness of sex differences is essential to the success of translational research and clinical oncological care.*"

and conclude:

"*This is a necessary and fundamental step towards* ***optimizing precision medicine that will benefit all individuals equally and equitably***."

The bold-faced part of the last sentence will be the starting point for your individual reflection question and upcoming seminar.

Question for the individual assignment

References [1–5] all indicate that the gender dimension applies to many aspects of cancer radiotherapy research, diagnosis, treatment, and prognosis, e.g., choice of research problem, method, data collection, analysis, impact, etc.

Following on your intersectional design discussions during the first two seminars and the rural electrification discussion on optimization towards SDGs, you should *study* one of the four MSc theses from previous students in Applied Mathematics and Computational Mathematics (Battinelli, Olsson, Norell or Öström) and reflect on the following question:

How can the intersecting social factors be included in a mathematical framework for more individualized and optimized cancer radiotherapy?

In the group work on the upcoming seminar, the context will be that you are a design team at RaySearch Labs or Elekta. You shall then use the Intersectional Design Cards (design levels 1–4) to improve and optimize individualized precision cancer radiotherapy. More detailed information will follow in the instructions for that group assignment.

[Summarize your main reflections in this text box and indicate which of the four MSc theses you have selected. Aim for ½ page of text.]

I select the article Öström, Linn, Post-processing of Monte Carlo calculated dose distributions. However, I am not quite certain of the task here. But I will do my best.

In order to include intersecting social factors in a Mathematical framework for more individualised and optimised Cancer radiotherapy, one could start by using them in the research as focus groups. By applying the project or research to the divided groups one could compare the specific results with the more general and draw conclusions from there. By, for instance, using the Monte Carlo calculated dose distributions on each focus group the result would be more individualised and optimised, since it can then be concluded what the differences between the groups are. Although, the computational time, which is one of the concerns in the article when using a high accuracy, will most likely be even longer. Regardless, considering different social factors such as age and sex and perhaps using parallel computing for efficiency; using the results for comparing differences and comparing to the general calculations one can consider the distinctions as well as similarities of the result in the future. Afterwards, one can use this "Denoising Autoencoder" to get a more specific result for each group and compare the efficiency of the use of it for each group, evaluating the use of it thereafter. Furthermore, as Öström points out, the article assumes every human head has an equal geometric distribution, although that is obviously not the case and also between different sexes the head shape might have a different distribution between different sexes as well, which is even further reasons for considering different social groups. Considering this partitioning, the calculations in this medicinal field will be more optimised, individualised as well as benefit individuals more equally and equitably.

References

[1] Wagner, A. D., et al., *Gender medicine and oncology: report and consensus of an ESMO workshop*, Annals of Oncology 30: 1914–1924, 2019, https://doi.org/10.1093/annonc/mdz414

[2] De Courcy, L., Bezak, E. & Larcu L. G., et al. *Gender-dependent radiotherapy: The next step in personalised medicine?* Critical Reviews in Oncology/Hematology, Volume 147, March 2020, https://doi.org/10.1016/j.critrevonc.2020.102881

[3] Fowler, M., *Radiotherapy outcomes potentially differ according to gender*, April 12, 2020, https://www.cancernetwork.com/view/radiotherapy-outcomes-potentially-differ-according-gender

[4] University of South Australia, *The pros and cons of radiotherapy: will it work for you?*, March 30, 2020, https://www.newswise.com/articles/the-pros-and-cons-of-radiotherapy-will-it-work-for-you?sc=dwhr&xy=10019792

[5] Vera, R., et al., "*Sex differences in the diagnosis, treatment and prognosis of cancer: the rationale for an individualised approach*", Clinical and Translational Oncology 25, 2069–2076, 2023, https://doi.org/10.1007/s12094-023-03112-w