

The impact of national holidays on postoperative radiotherapy

A study from Canada

- Head and neck cancer is often treated by surgery followed by postoperative radiotherapy (PORT).
- Time factors, such as public holidays, impact the effectiveness of PORT.
- Dr Derek Wilke and colleagues from Dalhousie University in Canada have used a statistical model to explore the impact of different factors on cancer outcome.
- The study showed that missing four consecutive days of PORT increases risk of cancer recurrence.
- Wilke emphasises the need for considering planned interruptions when scheduling PORT treatments.

Head and neck cancer is one of the top 10 most common cancers worldwide, accounting for over 660,000 new cases and 325,000 deaths each year. There are more than 30 areas within the head and neck where cancer can develop, including the mouth and lips, throat, voice box, and salivary glands. Mouth cancer tends to be the most frequently diagnosed form of head and neck cancer.

Treatment is complex and depends on factors such as the type and location of cancer, the age of the patient, and patient performance status (the ability to perform certain activities of daily living such as self-care, housework, and physical activity). Many patients undergo surgery to remove the area affected by cancer, followed by postoperative radiotherapy (PORT), sometimes alongside chemotherapy. PORT is often used in patients when there is a high risk of the cancer returning.

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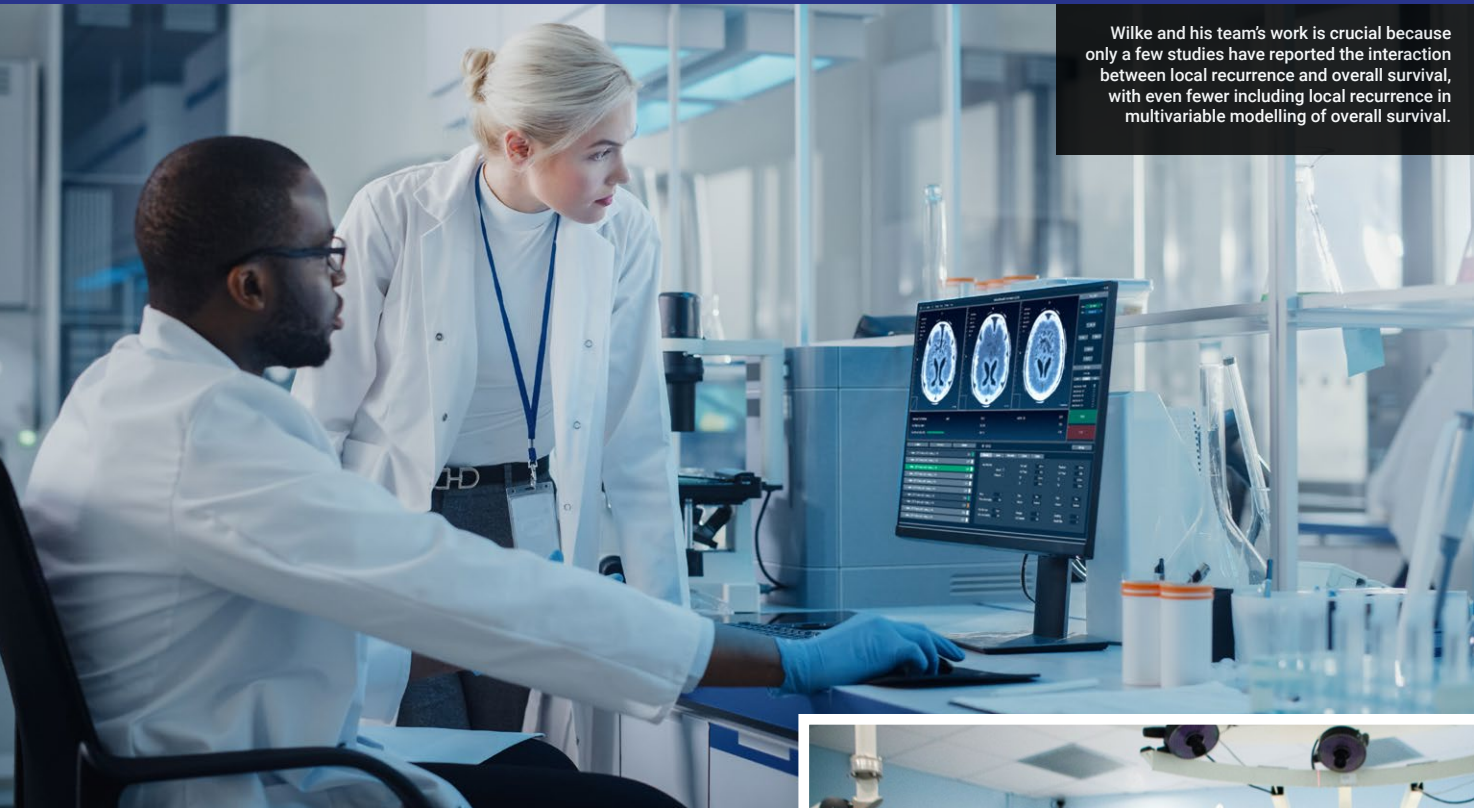
Globally, the five-year survival rate for head and neck cancer is around 50%. Dr Derek Wilke, radiation oncologist at the Nova Scotia Cancer Centre, and an assistant professor at Dalhousie University in Canada, highlights that prognosis can be improved by starting PORT within 6–7 weeks after surgery.

Previous studies have also shown that interruptions in PORT have a negative impact on the effectiveness of the treatment. While these are often unpredictable, there are some known factors that can impact radiation schedule, including public holidays.

Dr Wilke explains that public holidays in Canada can occur in pairs over consecutive days, or over weekends, spanning Friday–Monday. Radiation oncologists can account for these expected interruptions by accelerating radiotherapy, for example, by scheduling 2 sessions of radiotherapy in the same day. In addition to time factors, other aspects can influence the effectiveness of PORT, including how advanced the cancer is, tumour factors, and patient factors (such as age).

Predicting treatment outcomes

Multivariable statistical analysis can help explore and define the factors that have the most influence over a patient's predicted outcome. This allows healthcare professionals and patients to discuss the most appropriate treatment routes and issues, such as the timing of PORT, if appropriate. Some of the factors that will be reviewed include the risk of local recurrence, or the chance that cancer will come back in the area that underwent surgery. There is also



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a chance that the cancer could spread and grow back in a different area, known as distant metastases.

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Study findings

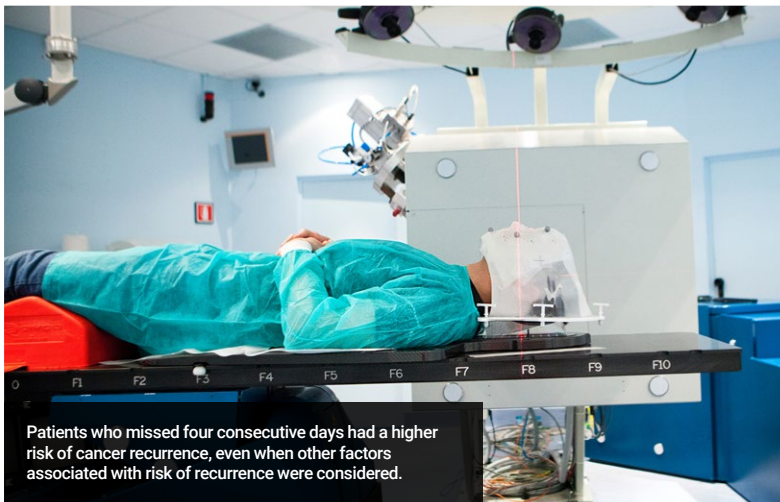
Wilke and colleagues used the provincial cancer registry in Canada to locate data for patients treated for squamous cell carcinomas of the head and neck region (HNSCCs) between 2007 and 2019. They identified 1,433 patients treated for HNSCC, of whom 338 were treated curatively by surgery followed by PORT. The results of the study showed that 69% of patients had a course of PORT interrupted due to national holidays (excluding other causes for interruptions).

The team found that missing one or two consecutive days of treatment did not seem to have a detectable impact, and could be accommodated by scheduling double sessions on a different day instead. However, patients who missed four consecutive days had a higher risk of recurrence, even when other factors associated with risk of recurrence were considered.

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The researchers also found that patients whose tumours regrow after surgical removal (early recurrence) had a poor prognosis, with a high risk of local and distant metastases. In contrast, patients who did not have any evidence of recurrence following surgery and radiation therapy had improved overall survival rates.

The multivariable modelling approach showed a significant impact of local recurrence and early recurrence on overall survival. Wilke suggests



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that from a methodological point of view, it is important that studies explicitly state whether local or early recurrence was included in the model. As the chance of local recurrence may change over time, it should be treated as a time-dependent variable and incorporated into any models as such.

Highlighting areas for improvement

There is an ongoing need to improve treatment approaches for patients with head and neck cancer. The team's work highlights potential areas where improvements could be made. Knowing that risk of recurrence increases after missing four consecutive days of PORT due to public holidays can change clinical practice. Wilke reports that the cancer centre he works with has already changed the way they plan and administer PORT to take this into account.

A lack of local recurrence was associated with a better prognosis, meaning that treatment options should be focused on improving and maintaining cancer management in a localised area. PORT should also be started as soon as possible after surgery to improve patient outcomes, in line with the findings of previous studies.

The research findings on the impact of planned interruptions, such as public holidays, on patient prognosis can be translated to other countries around the world who may experience similar issues. Radiotherapy centres can improve patient outcome after surgery and PORT by reviewing and amending their radiotherapy schedules and delivery.

Personal response

Apart from timing, what other factors should be considered when planning PORT?

I like to parse these factors into groups based on patient factors, tumour factors, and treatment factors. When considering whether to treat someone with radiation, increasing age is an adverse factor for recurrence, so we should be more aggressive in treating older patients and make them a priority. In terms of tumour factors, priority to receive radiotherapy in a timely manner is especially important for patients with tumour at the edge of what the surgeon surgically removed (positive surgical margins), and patients whose resected lymph nodes show growth of cancer cells outside the lymph node capsule (extracapsular extension). These patients also seem to benefit the most from the addition of chemotherapy given at the same time as radiation. Patients who have many lymph nodes affected by cancer are also at greater risk of early recurrence, so consideration should be given to do either a CT scan or MRI four weeks after surgery to look for this, as these patients have a very poor prognosis, even with subsequent radiation.

Treatment factors that are important include selecting the appropriate dose of radiotherapy as well as technique. Patients with positive margins should be treated with 33 treatments of radiotherapy and encouraged not to miss treatments. The morbidity of radiotherapy is much less in intensity with modulated radiotherapy (IMRT), or volumetric arc radiotherapy (VMAT), compared to 2-dimensional or 3-dimensional radiotherapy, due to the superior ability to spare normal tissues, leading to lesser side effects. If patients have unavoidable delays after surgery, and start radiation more than seven weeks after surgery, then there is sufficient evidence that treatment results can be improved, or maintained, by treating patients with six treatments per week as opposed to five treatments. This is termed accelerated radiotherapy.

Are other types of cancer treatment also equally affected by public holidays?

I recently ran a PubMed search using the terms 'public holidays and radiotherapy OR national holidays and radiotherapy'. Surprisingly, there appears to be no specific data on the effect of public holidays on outcome for cancers, other than head and neck cancer, that I could find. There is good data that prolonged radiotherapy

treatments for cancer of the cervix and anal canal lead to inferior outcomes, but adverse outcomes from missed treatments due to public holidays are not specifically addressed. Perhaps, they should be! Given the similar biology, I cannot imagine the results would be any different.

How did your research career lead you to focus on head and neck cancer?

I was fortunate to have worked with several expert radiation oncologists at the Princess Margaret Hospital in Toronto during my fellowship training who focused on treating head and neck cancer, like Dr Brian O'Sullivan, Dr Padraig Warde, and Dr Fei-Fei Liu, and consider them my mentors. Apart from developing innovative radiotherapy approaches, they were keen observers of the patients they treated, and prioritised publishing outcomes of their patients to further the understanding of head and neck cancer. This is an approach that I also enjoy. From a statistical analytic point of view, there appears to be an interesting relationship between local control and overall survival in head and neck cancer, which is a unique relationship to only a handful of scenarios in oncology.

Having a supportive team to work with is very important. The surgeons, medical oncologists, pathologists, radiologists, and my colleagues in radiation oncology are brilliant to work with and are very research-orientated and supportive of research ideas. Early on in my career, I had noticed that patients with early recurrence after surgery seemed to have an aggressive behaviour, and I was not sure if it was a function of time from surgery to radiotherapy, or some other intrinsic behaviour of the cancer. I had written a proposal for the current study in 2005, but it was not until 2019 that I had the opportunity to assemble a team to look at this, helped primarily by the steadfast work of Dr Michael Kim, who was a resident in our training programme at the time.



Details



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Bio

Dr Derek Wilke is a radiation oncologist at the Nova Scotia Cancer Centre, and an assistant professor at Dalhousie University. He received a Master of Science in Clinical Epidemiology at the Faculty of Health Policy, Management and Evaluation at the University of Toronto in 2005. Since his introduction to biostatistics at the graduate course level at University of Toronto, he has continued to develop his knowledge of statistics and SAS programming for the last 23 years, including time-to-event modelling and multivariable survival analyses. His current areas of clinical involvement include treatment of head and neck cancer, genito-urinary cancers, hematologic cancers, and stereotactic radiotherapy of spinal and bone metastases.

Collaborators

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Further reading

Kim, MS, Sheridan, M, Rajaraman, M, et al, (2023) [The impact of national holidays on postoperative radiotherapy of squamous cell carcinoma of the head and neck. Clinical and Translational Radiation Oncology](#), 42, 100668.

Hosni, A, Huang, SH, Chiu, K, et al, (2019) [Predictors of early recurrence prior to planned postoperative radiation therapy for oral cavity squamous cell carcinoma and outcomes following salvage intensified radiation therapy. International Journal of Radiation Oncology, Biology, Physics](#), 103(2), 363–373.

Harris, JP, Chen, MM, Orosco, RK, et al, (2018) [Association of survival with shorter time to radiation therapy after surgery for US patients with head and neck cancer. JAMA Otolaryngology – Head & Neck Surgery](#), 144(4), 349–359.

