

ORIGINAL ARTICLE



Assessing the utilization of radiotherapy near end of life at a Finnish University Hospital: a retrospective cohort study

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ABSTRACT

Background: Palliative radiotherapy can improve quality of life for cancer patients during the last months of life. However, very short life expectancy may devastate the benefit of the treatment. This single center study assesses the utilization of radiotherapy during the last weeks of life.

Material and methods: All cancer patients ($N = 38,982$) treated with radiotherapy ($N = 11,395$) in Turku University Central Hospital during 2005–2013 were identified in the database consisting of electronic patient records. One fourth ($N = 2904$, 25.5%) of the radiotherapy treatments were given during the last year of life. The last radiotherapy treatments and the time from the last radiotherapy treatment to death were assessed in regards to patients' age, cancer diagnosis, domicile, place of death and the treatment year. Treatments given during the last two weeks of life were also assessed regarding the goal of treatment and the reason for possible discontinuation.

Results: The median time from the last fraction of radiotherapy to death was 84 d. During the last two weeks before death ($N = 340$), pain (29.4%) was the most common indication for radiotherapy. Treatment was discontinued in 40.6% of the patients during the last two weeks of life, and worsening of general condition was the most common reason for discontinuity (70.3%). The patients receiving radiotherapy during the last weeks of life were more likely to die in tertiary care unit. During the last year of life single-fraction treatment was used only in 7% of all therapy courses. There was a statistically significant ($p < .05$) decrease in the median number of fractions in the last radiotherapy treatment between 2005–2007 (8 fractions) and 2011–2013 (6 fractions).

Conclusions: Up to 70% of the treatments during the last two weeks of life were not delivered to alleviate pain and utilization of single fraction radiotherapy during the last year of life was infrequent. These observations suggest that practice of radiotherapy during the last weeks of life should be revisited.

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Introduction

Radiotherapy is an effective palliative treatment option for patients with advanced and metastatic cancer and approximately half of all radiotherapy courses are delivered with palliative intent [1,2]. Radiotherapy is used to relieve pain, neurologic symptoms, bleeding and obstruction, and thus to improve the patient's quality of life also during the last months of life. Indicators of quality of end-of-life (EOL) care consist of the use of chemotherapy, number of hospitalizations, emergency room visits and use of intensive care unit [3]. According to the international guidelines, single fraction radiotherapy is recommended to alleviate the symptoms of advanced cancer, although the optimal use during the end of patients' life is still undetermined [4,5].

The use of radiotherapy during the last weeks of life may, however, have limited benefit and may actually impair the quality of life for patients and their families. Inappropriate use of radiotherapy generates unnecessary hospital stays and

expenses and should be avoided. There is no clear agreement on the indicators of overuse of radiotherapy during the final weeks of life, however, it has been suggested that radiotherapy administered during the last 14 or 30 d of life might be a useful quality indicator [6]. The time from the treatment to symptom control varies from weeks to months [7] and limits the use of radiotherapy for patients with poor prognosis.

In Finland, the patterns of the use of radiotherapy during the last month of patients' life are unknown and better understanding of current clinical routine is needed in order to design better palliative interventions in the future. Finnish publicly funded healthcare system provides cancer therapy for all citizens, with minimal cost to patients. Turku University Central Hospital (TUCH) provides 100% of the radiation therapy in the region of South Western Finland. Electronic patient records provide real world data of all therapies received by patients visited in TUCH. In this study, we assessed the schedule and goal of radiotherapy received by

cancer patients during the last two weeks of life during the years 2005–2013. Additionally, we also describe radiotherapy treatments delivered during the last year of life. Our focus was on the cancer diagnoses and fractionation of radiotherapy, and during the last two weeks of life, also indication and potential discontinuity of the radiotherapy. The documentation was based on electronic patient data.

Material and methods

Study design

TUCH is one of five academic hospitals in Finland and has a population of approximately 480,000 people, in the south-west part of Finland, comprising an area of 10,900 square kilometers. TUCH is the single center providing cancer care in the region. The radiotherapy unit at TUCH provides care for approximately 1500 patients annually. A total of 11,395 patients received radiotherapy between 2005 and 2013, and one fourth ($N=2904$, 25.5%) of these treatments were given during the last year of life.

Data sources

In TUCH, patient records are electronic, including systematically documented information on patient hospitalization, outpatient clinic visits, ICD-10-codes, laboratory values, radiological exams performed, radiotherapies given and intravenously administered medications. All recordings by clinicians, therapists and nurses were included. This extensive amount of information concerning all patients treated in the hospital was collected from multiple operative IT-systems for secondary use and combined with patients ID to form the database.

Cohort selection

From the database, all patients with cancer diagnosis between the years 2005 and 2013 were identified by the Center of Clinical Informatics ($N=38,982$). During that time period, 11,395 patients received radiotherapy, of which 2904 (25.5%) during their last year of life. All deceased cancer patients receiving radiotherapy during the last year of life were included in the study.

Utilization of radiotherapy during the last year of life was recorded in relation to the patient's age, gender, cancer diagnosis, residency and time and place of death. For all cancer patients who died and had received radiotherapy during the last year of their life, the last implemented radiotherapy treatment was included in the analysis. To assess the use of radiotherapy during the last two weeks of life, patient records of all the patients who received radiotherapy during the last two weeks of their life ($N=340$) were identified and checked also for the indication of the treatment, curative or palliative intent and possible discontinuation of the treatment plan.

Study objectives

The main objective was to assess the use of radiotherapy during the last two weeks of life in terms of curative or

palliative intent, indication and possible discontinuity of the treatment.

The secondary objective was to assess the last given radiotherapy treatment and the time from the last treatment to death in regards to patient characteristics, including gender, age, cancer type, domicile, place of death and the treatment year. The number of fractions (1, 2–5, 6–10, 11–20 >20) and the total dose of radiation (Gy) was also included. To assess the use of radiotherapy by age, patients were divided into four groups by age at death: under 60 years ($N=629$, 21.7%), 60–69 years ($N=907$, 31.3%), 70–79 years ($N=891$, 30.7%) and over 80 years ($N=477$, 16.4%). To assess the use of radiotherapy by cancer type, the patients were divided into fourteen diagnostic groups: (1) head and neck, (2) esophageal and gastric, (3) colorectal, (4) pancreatic, (5) lung, (6) skin, (7) breast, (8) gynecological, (9) prostate, (10) other urologic, (11) primary central nervous system (CNS), (12) lymphoma, (13) hematological malignancies (including leukemia), and (14) 'other cancers' including, for example, sarcomas, neoplasm of the mediastinum and pleura and cancer of unspecified origin. To assess the use of radiotherapy by domicile, the patients were divided into four cohorts by the distance between the domicile of the patient and the hospital: under 20, 20–50, 50–100 and >100 km. The place of death was assessed as a University Hospital in comparison or other location. To assess the use of radiotherapy by treatment year, the patients were divided into three cohorts by the year of radiotherapy administration: 2005–2007 ($N=941$, 32.4%), 2008–2010 ($N=975$, 33.6%) and 2011–2013 ($N=988$, 34.0%).

The tertiary objective of the study was to assess the use of radiotherapy in different regions of body during the last year and last two weeks before death. The anatomical locations of the radiotherapy targets were divided into the following regions: brain, spine, abdomen, thorax, pelvis, extremities, head and neck, prostate, breast and other. These locations may include bone, soft tissue or visceral targets.

This registry-based study was done with the permission of the authorities of Turku University Central Hospital. According to the Finnish law, no Ethics Committee approval was needed.

Statistical analyses

The time from the last radiotherapy to death was investigated using Kaplan–Meier analysis. The differences in EOL radiotherapy treatment by year of administration, patient domicile, age, diagnostic group or radiotherapy target site were analyzed using the log-rank test. Statistical significance was set at $p < .05$. Medians and means together with their respective standard errors were used as statistical descriptors of the data. Wilcoxon rank sum test or Kruskal–Wallis test was used to compare the medians between the two or more comparison groups, respectively, for an overall characterization of the patients and their treatment. All statistical analyses were performed using R version 3.1.3 (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

Results

Of the 340 patients who were treated during the last two weeks before death, 97.1% ($N=330$) received radiotherapy with palliative intent. Nearly half of these treatments were discontinued ($N=138$, 40.6%) due to general worsening of patient's condition (70.3%, $N=97$), death of the patient (21.0%, $N=29$), and other reasons such as patients own wish (8.7%, $N=12$). The indications for palliative radiotherapy were pain (29.4%), followed by brain-symptoms caused by primary tumor or metastases (20.0%), local symptoms caused by the tumor, such as hematuria, dysphagia, edema (17.4%), paraparesis or other radicular or local symptom caused by the changes in spine (12.4%), dyspnea and other respiratory symptoms (9.7%), primary or secondary tumor growing through the skin or mucosa (5.3%), vena cava superior syndrome (2.1%) and other (0.9%).

The median time between the last fraction of radiotherapy and death was 84 d (range, 0–365 d). There was no significant difference in the time between the last radiotherapy treatment and death between the study periods ($p > .05$ for all, log-rank test).

The characteristics of patients receiving radiotherapy during the last year of life are presented in Table 1. For these patients, the median number of fractions was seven in their last administered radiotherapy course. Of the treatments given during the last year of life, 7% consisted of a single fraction and 77.3% of ≤ 10 fractions (Figure 1). The median number of fractions decreased over the years from 8 in 2005–2007 to 6 in 2011–2013 ($p = .032$, Wilcoxon test). The number of fractions differed in the last administered radiotherapy course between metastases and primary tumors. For example, the median number of fractions for patients receiving radiotherapy for brain metastases was five and for primary CNS tumors eight.

The use of radiotherapy varied, as expected, by diagnosis (Table 1 and Figure 2). From all the diagnostic groups lung cancer, lymphoma, skin cancer and the group 'other cancers' were treated closer to death than the other groups ($p < .0001$, log-rank test). The gender did not influence the time from the last treatment day to death ($p = .15$). There was a tendency toward more aggressive treatment in the age group 60–69 compared to groups 70–79 ($p = .062$) and >80 ($p = .061$). The distance between domicile and the radiotherapy unit affected the time from the last treatment to death. Patients living >100 km from the hospital were treated least frequently near death and had a median of 110 d to death from the last treatment. For other groups it was 80–83 d. The difference was statistically significant in each pairwise comparison ($p < .001$).

The most frequently treated anatomical locations during the last year of life were the brain, spine and thorax (Figure 3). Primary as well as secondary tumors were targeted. One-third (27.8%, $N=185$) of the patients receiving radiotherapy to the brain had a primary CNS-tumor (C70–C72), the rest (72.2%) had brain metastases. From the patients who received radiotherapy to the thorax region, 44.8% ($N=240$) were diagnosed with lung cancer (C34).

Table 1. Characteristics of patients receiving radiotherapy during the last year of life.

	Median	Range
Age		
Female	68 years	
Male	69 years	
Time from the last fraction of radiotherapy to death	84 days	0–365 days
Radiotherapy dose	20.0 Gy	1–70.5 Gy
	n = 2904	%
Gender		
Female	1251	43.1 %
Male	1653	56.9 %
Time from the last fraction of radiotherapy to death		
6 months to 1 year	696	24.0 %
3 months to 6 months	688	23.7 %
1 month to 3 months	854	29.4 %
2 weeks to 1 month	326	11.2 %
< 2 weeks	340	11.7 %
Age groups		
<60	629	21.7 %
60–69	907	31.3 %
70–79	891	30.7 %
>80	477	16.4 %
Largest diagnose groups		
Lung	596	20.5 %
Breast	335	11.5 %
Prostate	319	11.0 %
Primary CNS	234	8.1 %
Esophagus and gastric	189	6.5 %
Lymphoma	174	6.0 %
Colorectal	173	6.0 %
Head and neck	121	4.2 %
Skin	120	4.1 %
Other	643	11.2 %
Distance between domicile and hospital		
<20 km	1346	46.3 %
20–50 km	348	12.0 %
50–100 km	869	29.9 %
>100 km	341	11.7 %
Treatment year		
2005–2007	941	32.4 %
2008–2010	975	33.6 %
2011–2013	988	34.0 %

There was an association between the place of death and receiving radiotherapy near EOL. Of the patients who received radiotherapy during their last year of life, one fifth (20.2%, $N=588$) died in the University Hospital; the corresponding percentage for patients receiving radiotherapy two weeks prior to death was 46.4%. Thus, half of the patients who received radiotherapy during their last two weeks of life died in the hospital.

Discussion

In this assessment of EOL care at Turku University Central Hospital, we demonstrated that one fourth (25.5%) of all radiotherapy courses delivered in our radiotherapy unit were received by patients during their last year of life. Approximately half of the last treatment courses delivered during the last weeks of life were discontinued and only one third of these therapies were aimed to alleviate pain. Nearly

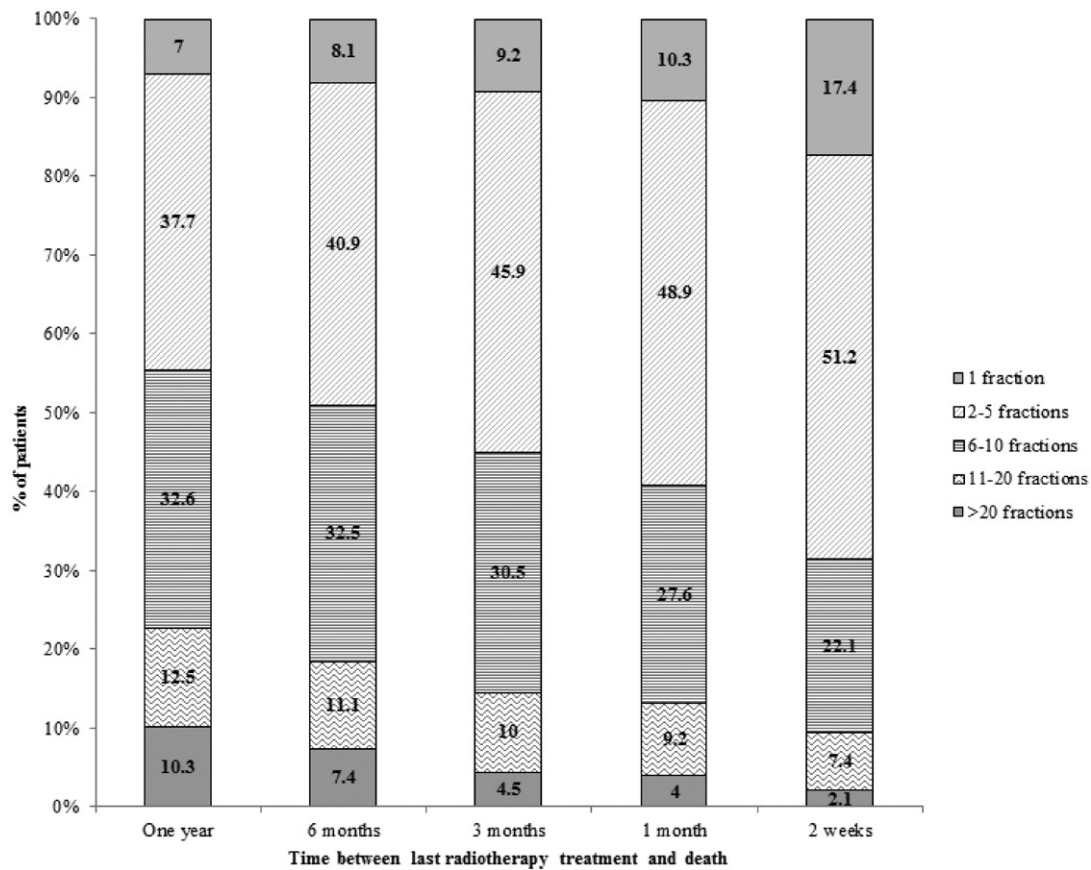


Figure 1. The distribution of radiotherapy fractions in the last treatment plan for cancer patients who were treated during the last year of life. The doses and fractions are the actually given doses. One year includes the other time periods also.

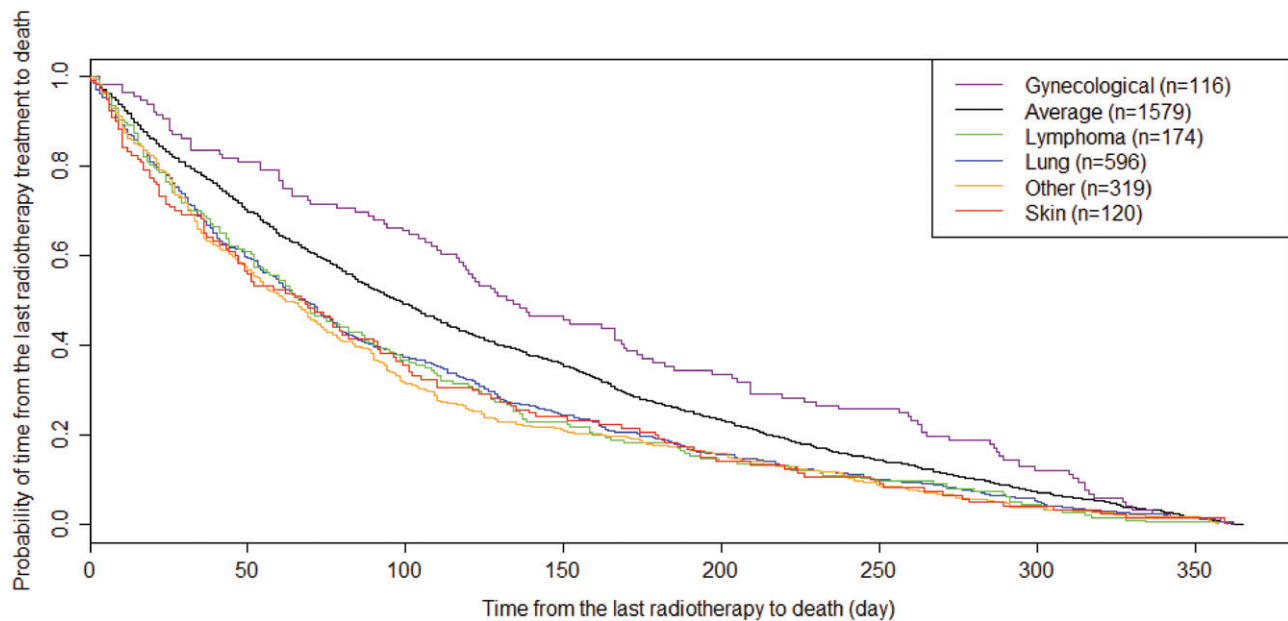


Figure 2. Probability of time from the last radiotherapy treatment to death for the diagnostic groups that differed significantly from the average. Lung cancer ($p < .001$), skin cancer ($p = .01$), lymphoma ($p = .007$) and group 'other cancers' ($p < .001$) were treated closer to death whereas gynecological malignancies were treated least frequently near death ($p = .02$).

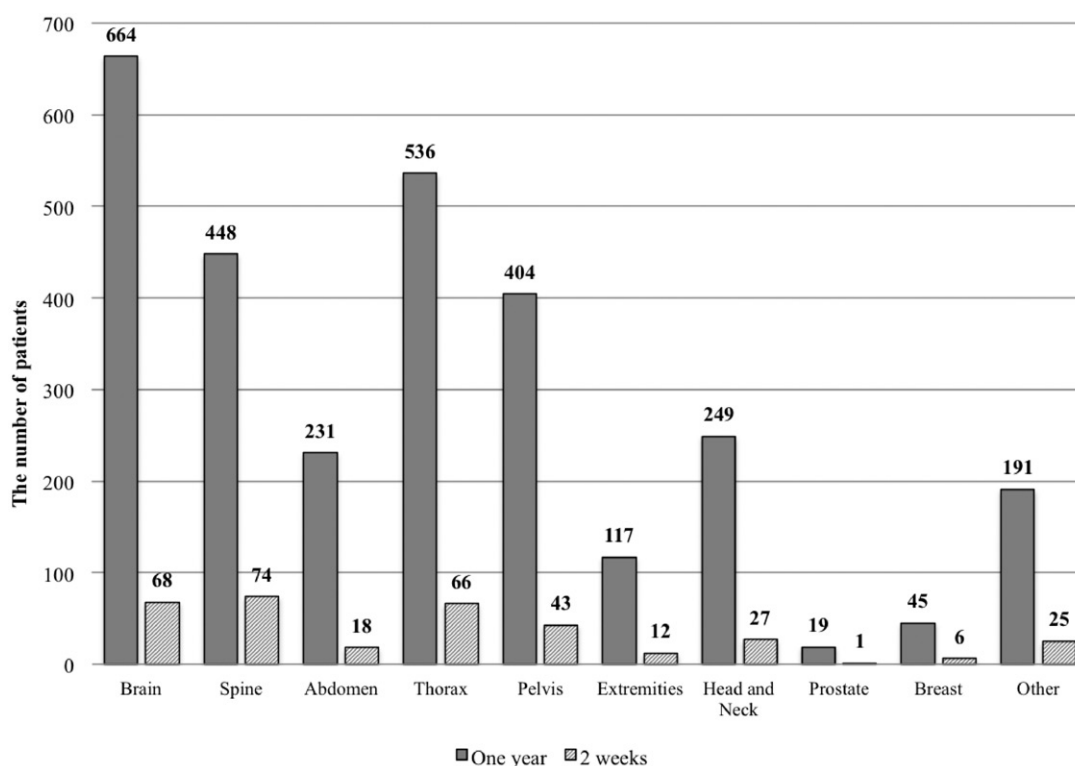


Figure 3. Anatomical treatment site in patients receiving radiotherapy during the last year ($N = 2904$) and last two weeks of life ($N = 340$).

half of the patients receiving radiotherapy during the last weeks of life died in the tertiary care hospital. Single fraction radiotherapy was used infrequently to alleviate the symptoms of patients with advanced cancer – only in 7% of patients at end of life. In our study, the median time between the last fraction of radiotherapy and death was 84 d.

The optimal use of radiotherapy near the end of patients' life is unknown. Evidence from a Dutch study [7] indicates that single fraction radiation should have a more pronounced role in the palliative treatment of cancer patients near end of life, and this is also supported by the guidelines of the American Society for Radiation Oncology (ASTRO) [5]. According to the ASTRO guidelines, 30 Gy in 10 fractions, 24 Gy in 6 fractions, 20 Gy in 5 fractions and 8 Gy in a single fraction can all provide excellent pain control and minimum side effects for the management of bone metastases. Even if longer treatments require less repeated treatment against recurring pain, single-fraction therapy is obviously more convenient for patients and their caregivers, especially, if the distance to the hospital is long [8]. Treatment with 8 Gy in a single fraction is non-inferior and less toxic than longer treatments according to the results of a controlled trial run worldwide in nine countries [4]. Still, our own patients received single-fraction radiotherapy relatively rarely, although all radiotherapies during the last months of life were not delivered only because of pain but also to alleviate other symptoms. However, the infrequent use of single fraction radiotherapy may reflect poor compliance with current guidelines or overly optimistic evaluation of patients' prognosis.

Comparing the overall use of radiotherapy during the last months of patients' life with earlier studies is challenging, as study designs and inclusion criteria have varied. One month

prior to death, 5.0–11.7% of the patients with advanced cancer have been reported to receive radiotherapy in contemporary studies [9–13]. In our hospital, 14.9% of all patients receiving radiotherapy during the last year of life received radiotherapy during the last month of life, representing rather aggressive culture of practice near end of patients' life. On the other hand, a shorter time between the last fraction of radiotherapy and death has also been reported (39 d) than in our series of patients (84 d) [14].

In a Canadian study, 22.3% of all patients received palliative radiotherapy in the last 9 months of life, while in a large North American study, 41% of patients received palliative radiotherapy at any time [15,16]. In the United States, approximately half of the patients who received radiation therapy were treated with palliative intent [1,2]. Along with the clinical factors, such as diagnosis, prognosis, comorbidity and age, also socioeconomic factors, such as gender, ethnic background, income, hospice care and residency have been associated with the use of radiotherapy near the end of patients' life [9–11,13–16]. In our own series of patients only the diagnosis and the distance between the domicile and the treatment unit had a significant impact on the usage of radiotherapy during the last months of patients' life.

In our study, the median number of fractions for patients receiving radiotherapy for brain metastases was five. Whole-brain radiotherapy given in five 4 Gy fractions over one week provides similar survival and symptom control as longer protocols [17,18]. In the future, fewer fractions may be preferred as more conformal radiation techniques are used, for example, stereotactic irradiation and hippocampus-sparing whole-brain radiotherapy, which is less deleterious on cognitive function.

The overall aggressiveness of cancer care near end of patients' life may be increasing – this concerns radiation as

well as non-radiation treatments. Two retrospective studies from the United States and Canada with more than 28,000 and 227,000 patients, respectively, reported a trend toward more intensive EOL cancer care. In these studies emergency room visits, chemotherapy use, hospitalizations and intensive care unit admissions were evaluated [19,20]. In contrast, however, among elderly patients, the trend in the use of radiotherapy in the last 30 d of life was decreasing [10]. In our study, no trend toward more aggressive usage of radiotherapy over time was detected. On the contrary, the number of fractions decreased during the last years of the study period, which indicates that there is a decreasing trend in the use of radiotherapy fractions and that adherence to guidelines may be improving.

The use of radiotherapy varied between the diagnostic groups, as expected. In accordance with our own study, previous studies have reported the tumor site to be a predictor of the use of palliative radiotherapy [9,11,13–16,21]. Patients with breast and prostate cancer require less radiotherapy at the end of life, as death approaches. The progression of advanced breast and prostate cancer may be slow, and the patient, family and physician have time to adapt to the circumstances and the progression of the metastatic disease. However, for patients with more aggressive cancer and course of the disease, like lung cancer and cerebral gliomas, the time from diagnosis to death is often shorter and hence, the treatment patterns may be more aggressive during the last months of life. In this study, 11.4% of the lung cancer patients received radiotherapy during the last two weeks of their life, which is in line with earlier findings, where 10% of patients with non-small cell lung cancer received palliative radiotherapy over a comparable time period [22].

Finland is sparsely populated and distances to health service units may be quite long. The Turku University Hospital district also includes a vast archipelago where there are no rapid highways and where some areas are reached by waterway only. These geographical and logistic hurdles may explain why patients living beyond a distance of 100 km to the hospital were treated significantly less aggressively, following the wish of the patients or caregivers to receive treatment closer to home. Some patients live also outside of the TUCH hospital district and may have received palliative radiotherapy in another hospital closer to home.

This study should be interpreted in the context of its limitations. The strength of the study is the population-based profile of the material. However, although comprehensive data are available in electronic patient records, there are also some limitations. For instance, the aim of the radiotherapy treatment plan curative versus palliative was not documented in the files, even if the number of fractions and the total dose may be used to estimate the intent of radiotherapy. The terminology palliative versus curative radiotherapy treatment plan is not based clearly on the intent of the treatment rather the intensity of the plan. For example, definitive radiotherapy of gliomas is seldom exactly curative although may prolong life expectancy of the patient with the disease. Although ICD-codes included the codes for metastatic disease, the actual date of the first appearance of metastasis of the neoplastic diseases was not documented reliably and the

stage of the disease or the performance status was not recorded in the structured files. Due to the complexity of the data, blood values were not included in the analysis. In the future, the electronic patient records and data recording in everyday patient contacts should be developed in regards to produce appropriate data documentation for the assessment of the quality of the care.

Conclusions

This 9-year cohort study on real world data identified from electronic patient records in southwest Finland revealed that only 30% of radiotherapy within the last two weeks of life was given to alleviate pain. Thus, the indication of up to 70% of the treatments may be questioned. Nearly half of the treatments delivered during the last two weeks of life were discontinued and patients receiving radiotherapy during the last weeks of life were more likely to die in a tertiary care unit. Therefore, more widespread adoption of prognostic tools to identify the EOL patients is warranted. One fourth of the radiotherapy resources were used to treat cancer during the last year of patients' life. Single-fraction radiotherapy was used infrequently near the end of patients' life. On the other hand, a trend toward shorter radiotherapy courses was observed, and only 20% received more than 10 fractions in the last realized radiotherapy plan. Overall, optimal use of radiotherapy near the end of patients' life remains a challenge. Culture of practice of EOL care should be revisited and adherence on international guidelines should be facilitated.

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Disclosure statement

The authors declare that they have no conflicts of interest.

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