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Assessment of Overall Treatment Time in Curative Radiotherapy

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Abstract

In radiotherapy, spread is a radiobiological parameter that corresponds to the total duration of treatment expressed in days. The objective of the study is to evaluate adherence to the theoretical spread among patients receiving curative irradiation. This was a prospective study conducted within the radiotherapy department at the National Oncology Institute of Rabat, including 285 patients receiving curative irradiation, regardless of tumor localization, from December 1, 2021, to February 28, 2022. Reasons for missed sessions were collected during end-of-treatment consultations. The median age of our patients was 47 years (range: 36-78 years), with 62% being female and 38% male. Among them, 47.3% were employed. Transportation methods varied; public transportation accounted for 59.2%, taxis for 9.1%, and only 8.7% used personal transportation. Travel time from home to the oncology institute was less than 20 minutes for 12.6% of patients, between 20 and 60 minutes for 75.7%, and over 60 minutes for 11.7%. The most common tumor sites were the breast in 32.2% of cases and the prostate in 23.5% of patients. The theoretical spread was adhered to in 29.8% of cases. In 56.4% of cases, the extension was between 1 and 5 days, and in 13.3% of cases, it was between 6 and 12 days. Causes of spread extension were diverse, with equipment breakdowns and maintenance accounting for 52.1% of cases, intercurrent illness for 10%, holidays for 16%, and treatment refusal for 0.6%.

Evaluation of spread in radiotherapy is crucial as it represents a significant factor in local recurrence and indirectly affects distant progression, especially with prolonged treatment durations.

Keywords: Radiotherapy, Overall Treatment, Time factors

1. Introduction

In radiotherapy, the overall treatment time is the radiobiological parameter that corresponds to the total duration of treatment, expressed in days, while fractionation is determined by the total number of sessions and the time interval between each fraction. The conventional treatment involves delivering five sessions of 1.8 to 2 Gy per week, to achieve a total dose typically between 18 and 80 Gy, depending on the radiosensitivity of the tumors. The choice of fractionation and spread is guided by the therapeutic ratio concept, based on the linear-quadratic model (1).

Fractionation allows for the repair of sublethal lesions, repopulation, reoxygenation of the tumor tissue, and redistribution of cells in the cell cycle. (2) It is a crucial parameter in the genesis of late complications. The overall treatment time is a major parameter of therapeutic efficacy and acute

radiation toxicity and also a critical element in the genesis of late complications and an important factor in local recurrence and distant progression, especially with prolonged treatment duration. (3)The causes of spread extension can be numerous, with the most frequently encountered being acute side effects, accelerator breakdowns, and holiday breaks.

However, not all tissues react the same way to radiotherapy; at equal doses, rapidly renewing tissues are preserved by an increase in spread, as are most tumors, especially those with a short doubling time. This raises the dilemma for the radiation oncologist: on one hand, effectively treating the tumor while avoiding tumor repopulation, and on the other hand, protecting healthy tissues included in the irradiated area (4).

Previous clinical trials have confirmed that prolonging the spread has an unfavorable effect on local disease control and survival (5,6). The objective of this study was to evaluate if the theoretical spread was adhered to in a cohort of patients treated with curative intent radiotherapy, to identify potential reasons for its extension.

2. Materials and methods

Our study is a prospective descriptive study conducted within the radiotherapy department at the National Oncology Institute of Rabat, which has 4 linear accelerators. It included 285 patients receiving curative irradiation, regardless of tumor localization, from December 1, 2021, to February 28, 2022.

Inclusion criteria were: age over 18 years, histologically proven cancer, and indication for curative radiotherapy. Patients receiving palliative radiotherapy were excluded from the study.

The primary objective was to compare the theoretical spread to the actual spread of radiotherapy. The theoretical spread was defined as the total treatment duration in days, determined from the first day of treatment, the total number of fractions, and the number of fractions per week. The actual spread corresponded to the number of actual days between the first and last treatment sessions.

The secondary objectives were to specify the reasons for the extension of the spread. The reasons for missed sessions were collected prospectively by physicians using a dedicated questionnaire, which included the following items: equipment breakdown, maintenance, holidays, treatment toxicity, other illness, treatment refusal, refusal to wait, personal convenience, transportation difficulty, appointment error, other cause (to be specified). Additionally, clinical and logistical parameters were collected from the patient's computerized medical record system, ENOVA. These parameters included age, sex, transportation mode and time, tumor type, planned radiotherapy dose, number of fractions, need for unplanned hospitalization, concurrent chemotherapy or targeted therapy administration, and treatment position.

Statistical analysis was performed using the R statistical software. Qualitative values were analyzed using Chi-square tests. Quantitative values were analyzed using Wilcoxon, Mann-Whitney, and Kruskal-Wallis tests. The significance threshold was set at 5%.

3. Results

Two hundred and ninety consecutive patients were included in the study, and the records of 285 patients were evaluable. Five patients were excluded from the analysis. Three patients did not complete their treatment due to ongoing tumor progression during radiotherapy, and two patients had their fractionation modified due to hospitalization for a surgical emergency, during which radiotherapy had to be interrupted for more than 15 days.

The characteristics of the patients are described in Table 1. The majority were women (62%), with a median age of 47 years (range: 36-78 years), and 47.3% of cases were employed. Transportation methods varied; public transportation, personal vehicle, and taxi accounted for 77% of the means used, with a travel time of less than 40 minutes in 58.2% of cases. The most common tumor sites were the breast in 32.2% of cases and the prostate in 23.5% of cases.

Concurrent chemotherapy was administered to 96 patients (33.6%). Few patients (4.2%) required hospitalization within the radiotherapy department due to complications or side effects during their treatment.

The theoretical spread was adhered to in 29.8% of cases. In 56.4% of cases, the extension ranged from 1 to 5 days, and in 13.3% of cases, the extension was between 6 and 12 days (Figure 1).

Table 1: Characteristics of the studied population receiving a radiotherapy with curative intent

	Number	Percentage
Gender		
Male	108	38
Female	177	62
Age		
35-45 years	63	22.1
46–56 years	76	26.6
57–67 years	88	30.8
68-78 years	58	20.5
Professional activity		
Yes	135	47.3
No	150	52.7
Type of transport		
On foot	55	19.2
Bicycle	0	0
Scooter	0	0
Car	25	8.7
Public transport	169	59.2
Taxi	26	9.1
Multiple	10	3.8
Transport duration		
< 20 min	36	12.6
20–40 min	130	45.6
40–60 min	86	30.1
> 60 min	33	11.7
Hospitalization		
Yes	12	4.2
No	273	95.8
Tumor location		
Breast	92	32.2
Cervical	45	15.7

Endometrial	12	4.2
Prostate	67	23.5
Head and neck	43	15.08
Lung	16	5.6
Rectum	8	2.8
Other	2	0.92
Chemotherapy		
Yes	96	33.6
No	189	66.4
Treatment station		
1	73	25.6
2	92	32.2
3	50	17.5
4	70	24.7

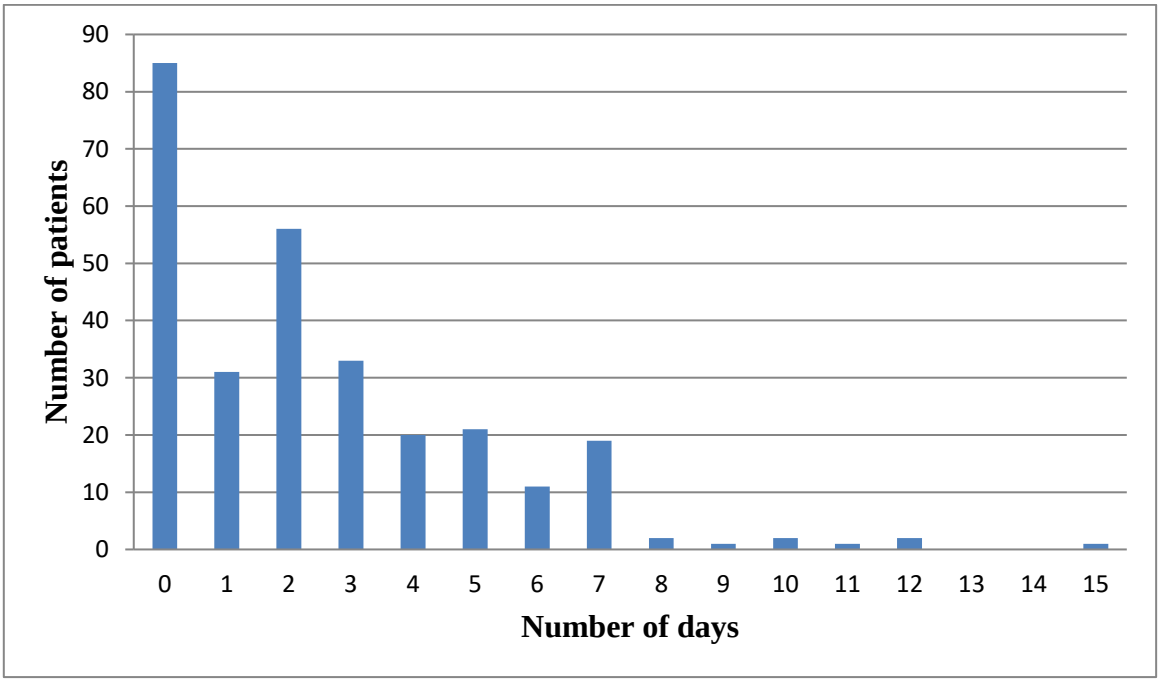

Figure 1: Number of day's difference between real and theoretical overall treatment time

The reasons for missed sessions are summarized in Table 2; equipment breakdown and maintenance accounted for the majority of reasons, 27.6% and 24.5% respectively. Medical reasons, including treatment toxicity and intercurrent illnesses, accounted for only 17.5% of interruptions.

Only two analysis parameters had a significant impact on theoretical spread in univariate analysis (Table 3): transportation time less than or equal to 40 minutes ($p = 0.031$) and treatment position ($p = 0.004$). Breakdowns were significantly more common in the first treatment position.

Table 2: Reasons for delayed fractions of radiotherapy

Reasons	Percentage (%)
Breakdown	27.6
Maintenance	24.5
Transportation issue	5.8
Treatment toxicity	7.5
Treatment refusal	0.6
Personal convenience	1.4
Communication or understanding issue	0.6
Intercurrent illness	10
Inadequate scheduling	6
Public holidays	16

Table 3: Radiotherapy delivered with curative intent: univariate analysis

	Number	Spread difference (average) [min-max]	Median spread difference	p
Sexe				0.091
Male	108	4.2 [0-35]	2	
Female	177	6.1 [0-31]	3	
Age				0.53
35-45 years	63	3.1 [0-29]	3	
46–56 years	76	3.5 [0-31]	2	
57–67 years	88	4.2 [0-29]	4	
68-78 years	58	5.1 [0-29]	3	
Professional activity				0.87
Yes	135	3.4 [0-36]	3	
No	150	4.1 [0-34]	2	
Type of transport				0.61
On foot	55	4.2 [0-21]	8	
Bicycle	0	0	2	
Scooter	0	0	4	
Car	25	2.6 [0-18]	3	
Public transport	169	4.3 [0-31]	2	
Taxi	26	3.2 [0-15]	2	
Multiple	10	4.1 [0-14]	3.5	
Duration of transport				0.031
< 40 min	166	4.1 [0-19]	2	
> 40 min	119	2.8 [0-26]	3	
Hospitalization				0.54

Yes	12	2.4 [0-22]	5	
No	273	3.1 [0-34]	3	
Tumor location				0.063
Breast	92	4.1 [0-19]	2	
Cervical	45	2.3 [0-9]	3	
Endometrial	12	5.3 [0-15]	5	
Prostate	67	3.1 [0-16]	6	
Head and neck	43	2.4 [0-29]	3.5	
Lung	16	4.5 [0-17]	4	
Rectum	8	6.1 [0-12]	3	
other	2	5.4 [0-19]	2	
Chemotherapy				0.23
Yes	96	4.6 [0-32]	3	
No	189	5.4 [0-32]	4	
Treatment station				0.004
1	73	4.1 [0-34]	3	
2	92	4.2 [0-32]	2	
3	50	3.4 [0-34]	5	
4	70	5.7 [0-32]	3	

4. Discussion

In our study, theoretical spread was adhered to in 71.2% of cases, with an average extension of 5.5 days and a median of 4 days, corresponding to a moderate increase in spread. Radiation-induced toxicity, leading to a temporary treatment interruption, affected 7.5% of patients, three of whom were concurrently receiving chemotherapy. The reasons for these interruptions were varied, including grade 3 epitheliitis, gastrointestinal side effects, and pain. Medical reasons, namely toxicity and intercurrent illnesses, accounted for less than 18% of all interruptions for the entire cohort, as well as for the subgroup of patients whose treatment was suspended for more than 10 days. It is crucial to minimize treatment interruptions during radiotherapy, emphasizing the importance of weekly consultations during radiotherapy to ensure regular patient follow-up and to adjust symptomatic treatments and supportive care in case of toxicity. (7).

Patient non-adherence, particularly treatment refusal, was found to be a rare cause of missed sessions, representing less than 0.6% of cases. Transportation modalities were diverse and numerous for our patients, given that the treatment center was located in the heart of the city of Rabat. An average travel time exceeding 40 minutes appeared to be a detrimental factor for adhering to the spread. To address this situation, a major corrective action would involve systematically evaluating, from the patient's referral, the relevance between their place of residence and the treatment facility, in order to potentially offer a closer center without resorting to a specific technique.

This study also underscores the importance of rigor in treatment planning and daily schedule management (8). Planning errors were observed towards the end of treatment. Therefore, it appears essential to raise awareness among paramedical staff involved in planning about the importance of adhering to the necessary spread.

In our study, the main cause of spread extension is attributed to technical constraints such as unplanned maintenance and breakdowns. One of the accelerators (the third one) experienced multiple breakdowns over a short period following scheduled maintenance. Consequently, the treatment position is a significant factor in the spread extension during univariate analysis.

Analysis of data collected by the National Radiotherapy Observatory reveals that in 2012, the average monthly number of hours per machine for treatment was 202 hours, and for maintenance and quality control, it was 28 hours (9,10). The average ratio of "non-treatment occupancy time to total occupancy time" was 12.4%. In case of machine downtime, 71% of centers rescheduled priority sessions to backup machines, 57% of centers had the option to increase the number of half-day openings, and 65% of centers modified the dose and fractionation of treatment. The report from the Royal College of Radiologists, which formulated recommendations for managing unplanned treatment interruptions, also suggests opening technical platforms in the UK on weekends and holidays (11).

It recommends that each center establish a procedure aimed at preventing or minimizing the extension of spread. A categorization of patients into three groups is proposed based on the evolutionary potential of the treated tumors and the curative or palliative intent. The first group concerns tumors with rapid evolution, the second group tumors with low evolutionary potential, and the third group patients treated with palliative intent. For each group, a maximum spread extension objective is defined: two, five, and seven days, respectively. Several compensatory measures are proposed, such as transferring patients from the first two groups to another machine, accelerating treatment (weekend or split-course), or increasing the dose per fraction or total dose. Additionally, the importance of opening technical platforms on most holidays is emphasized.

Hendry et al., as well as Dale et al., have described several methods to adhere to the spread, whether by modifying or not the dose per fraction, and/or by using a temporarily split-course regimen (12,13). Among these methods, one favored by the authors is weekend treatment while maintaining a constant dose per fraction, which helps limit late toxicity to healthy tissues.

The importance of adhering to the spread has been widely demonstrated, especially for cervical cancers and head and neck cancers (6,14-16). In our study, among the 45 patients treated for cervical cancer, the spread was less than 55 days in 71% of cases. For the remaining patients with a longer spread, it averaged 60 days (56; 67 days), with a median of 59 days. Among the 43 patients treated for upper aerodigestive tract tumors, the spread was only adhered to in 19% of cases and was on average extended by 9 days (0; 29 days; median 5 days). Toxicity was the main cause of spread extension. Other reasons included breakdowns, maintenance, and holidays.

For other tumor locations, data are less abundant, but some interesting publications have been found in the literature. For example, for locally advanced non-small cell lung cancers, Machtay et al. demonstrated that spread extension was correlated with a decrease in overall survival and progression-free survival rates, with an additional 2% risk of death per treatment day (17). Regarding prostate cancer, Perez et al. observed that a spread exceeding nine weeks increased the rates of pelvic and biochemical recurrence, while decreasing the specific survival rate for T2 tumors. However, this effect was attenuated when doses greater than 72 Gy were administered (18).

Regarding postoperative irradiation of breast cancer, Bese et al. demonstrated that any spread extension exceeding one week had a significant impact on 5- and 10-year local control rates, as well as overall survival rates. This difference was particularly pronounced for patients undergoing breast-conserving treatment (19).

Another approach used in some countries to alleviate logistical constraints is the development of hypofractionated radiotherapy. A literature review on the treatment of prostate and breast cancers, along with an analysis of potential benefits and risks, was recently published by Ray et al. (20). The results are promising for breast cancer, but the therapeutic benefit seems less clear for prostate cancer. The knowledge in radiobiology, along with all these studies, emphasizes the importance of remaining vigilant regarding adherence to spread in radiotherapy. The development of new techniques, the complexity of their implementation, and the necessary quality assurance should never lose sight of the importance of adhering to this fundamental parameter.

5. Conclusion

The evaluation of spread in radiotherapy is of crucial importance, as it is a determining factor in local recurrence and, indirectly, in distant progression, especially with prolonged treatment. In our study, spread was well adhered to, except for breakdowns and maintenance periods. Vigilance in adhering to the spread should be a priority to ensure quality treatment and optimize the chances of locoregional control.

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