www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

Fatigue trajectories by wearable remote monitoring of breast cancer patients during radiotherapy

Angela Barillaro[1,5], Chiara Feoli[1,5], Adriano Tramontano[2], Marco Comerci[2], Mara Caroprese[1], Renato Cuocolo[3], Oscar Tamburis[2], Mario Petrazzuoli[1], Maria Anna D'Arienzo[1], Antonio Farella[4], Caterina Oliviero[4], Stefania Clemente[4], Laura Cella[2]✉, Mario Magliulo[2], Manuel Conson[1]✉ & Roberto Pacelli[1]

The aim of this pilot study was to assess the compliance of breast cancer (BC) patients with fitness tracker (FT) monitoring program during radiotherapy (RT) and to characterize radiation-induced fatigue (RIF) status through objective evaluation using FT-collected parameters. Thirty-six BC patients were invited to wear FT during their RT course for continuous monitoring of heart rate (HR) and step counts (STP). RIF assessment was performed weekly, according to CTCAE v5.0 and dichotomized into G0 vs. any-grade. A novel concept based on patient Repeated Activity Window (RAW) was introduced to evaluate HR and STP variations during RT. Several Machine Learning (ML) methods were trained to characterize RIF on the basis of HR and STP collected data. RIF of any grade was reported by 17 out of 36 patients (47%) included in the study. None of patient clinical variables were significantly correlated with RIF. All patients accepted the FT monitoring program, and for 32 patients FT collection efficiency was greater than 60%. For each patient, a distinct distribution of RAWs was identifiable over RT and across the entire patient cohort, with a total of 7950 RAWs processed. Six features related to RAWs, HR and STP were identified as associated with RIF. The best-performing classifier was the Bagged Trees model, showing a cross-validated ROC-AUC of 89% (95% CI 88–90%). This study confirms the feasibility of continuous biomedical monitoring of BC patients by FT. We successfully identify objective indicators of RIF through HR and STP variation measures within each patient's RAW, thus providing a novel and practical approach to assess and manage RIF. This can significantly aid medical staff in evaluating RIF trajectories, potentially leading to better individualized care strategies and improved patient outcomes.

Keywords Fitness tracker, Radiation-induced fatigue, Breast cancer, Quality-of-life

Cancer is a complex disease in which outcome, in addition to its biological behavior and stage, is also influenced by the global performance status (PS) of the patient that is an indicator of prognosis, eligibility for treatment, and patient's quality of life (QoL)[1–3]. When visiting a cancer patient, a performance score is assigned[4], which is based on possible comorbidities, their autonomy in daily life activities, and their treatment needs. This score takes into account factors such as the frequency of care required, the assistance needed for self-care, and any limitations in daily activity. However, the two available systems for defining PS often prove to be too subjective, which can lead to incorrect therapeutic choices[5]. Hence, it might be beneficial to integrate an objective assessment of activity to enhance the evaluation of PS.

Breast cancer (BC) patients represent a long-term survivor group, and the impact of the therapy on their QoL is significant[6]. Radiotherapy (RT) is generally well tolerated[7], however, radiation-induced fatigue (RIF) is a frequent side effect reported by patients that can reduce activity and affect QoL[8].

It is widely recognized that moderate physical activity improves the QoL of cancer patients through various interconnected mechanisms. These include improved insulin sensitivity with consequent reduction in blood sugar levels, a positive impact on sleep quality, decreased levels of fat tissue (resulting in reduced production of

[1]Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy. [2]Institute of Biostructures and Bioimaging, National Research Council, Naples, Italy. [3]Department of Medicine, Surgery, and Dentistry, University of Salerno, Fisciano, Italy. [4]Unit of Medical Physics and Radioprotection, University Hospital Federico II, Naples, Italy. [5]These authors contributed equally: Angela Barillaro and Chiara Feoli. ✉email: laura.cella@cnr.it; manuel.conson@unina.it

pro-inflammatory cytokines), increased muscle mass and strength (leading to deceased fatigue), and a positive impact on mood through the release of endorphins[9].

Several Bluetooth Low Energy Fitness Activity Trackers (FT)[10–12] are available on the market, which are capable of detecting parameters such as steps per minute, sleep level, blood pressure, heart rate, blood oxygen saturation[13–15]. While these devices were not originally designed for medical purposes, they have the potential to aid in remote monitoring, requiring minimal compliance, and providing objective health information[16]. However, to fully exploit the capabilities of such wireless body sensors, appropriate development frameworks, methodologies, techniques, and implementation tools are required for effectively support this growing technology in a clinical setting[17–20].

The objective of the current pilot study was to introduce a new methodology for BC patients monitoring using FT during their RT course. This aimed to: (i) determine the feasibility and patient compliance with the FT monitoring program during RT, (ii) analyze patient activity trajectories using biomedical data gathered from FT devices, and (iii) identify the most appropriate FT-collected data able to provide an objective assessment of RIF, thereby enhancing the accuracy of therapeutic decisions and improving patient care.

Materials and methods

Patients and data collection

A total of 36 BC patients undergoing RT at Federico II University Hospital in Naples, Italy, were invited to participate in a monitoring protocol by wearing an FT device during RT and instructed to wear them throughout the entire day. All participants signed informed consent and the patient data were analyzed anonymously. This study was approved by the local Ethics Committee (Comitato Etico per le Attività Biomediche, Università Federico II, Napoli, protocol code n. 222-10, 9th March 2017). All experimental protocols and procedures were performed in accordance with the guidelines of the Federico II University of Naples.

Patients received moderately hypofractionated or conventional RT fractionation schedule, depending on whether the target volume included the chest wall and/or elective nodes. All fractionation schedules consisted of one fraction a day, five fractions a week. The treatment duration was 3–5 weeks. Patient and treatment related characteristics were collected. Treatment-related toxicity assessment, including RIF, was performed weekly according to CTCAE version 5.0. For subsequent data analysis, RIF was dichotomized into G0 and any-grade (G1–G2).

Fitness activity trackers

The FT devices (Veepoo H03 smart watch) served as wearable sensors for gathering biomedical data such as step counts (STP), heart rate (HR), sleep level and oxygen saturation. The primary endpoint of the present study was the collection of STP and HR parameters with the aim of characterizing variations in patient habits during RT. In Supplementary Material Table S1, the sampling rates for the STP and HR set by the manufacturer were reported.

The battery life of FT devices lasted approximately 3 days. For this reason, patients were asked to replace their device every 2 days with a new one fully charged.

The used devices were capable of monitoring patient data independently, without the need for a smartphone or internet connection, as they utilized internal memory to store the collected data. In addition, these devices do not require any patient interaction. A gateway located in the RT department[21,22], collected the data stored in the memory of the FT as soon as the patient entered the waiting room.

No patient personal information was stored in the device according to General Data Protection Regulation (GDPR) recommendations. A dedicated in-house application hosted on the gateway and developed for the needed tasks[23] pre-processed the anonymized data and sent to the hospital server. Data were available to the medical staff throughout the therapy course thanks to a web application[21] specifically designed for the use case scenario. Briefly, the patient was invited by the medical staff to wear the FT continuously during domestic/outside activities and during rest. Upon arrival at the RT department, the data were downloaded from the FT memory to the gateway. Data aggregation by patients and activities were made available to the medical staff in the form of graphs. The doctor integrated this information with that from the clinical interview (clinical visit, administration of questionnaires). The patient left the hospital and the process repeated for all the radiation treatment course (Fig. 1a).

The acceptance rate of the FT monitoring protocol was defined as the ratio of participants to the total number of patients to whom FT was proposed.

A collection efficiency was introduced as the ratio of HR collected and HR collectible during RT time, considering the device's acquisition performance. Compliance rate was accordingly defined as the ratio of patients who wore FT from the beginning to the end of RT with a collection efficiency greater than 60% to the total patients wearing the FT.

Data extraction

FT data extraction process consisted of two distinct phases.

In a first phase, the data collected from FT were preprocessed to standardize the data sampling frequency. STP and HR were, by design, characterized by a different sampling rate, necessitating sampling synchronization for further processing. In the preprocessing step, data gaps (occasionally missing observations[24]) were also removed.

In a subsequent phase, it was necessary to define patient "activity windows". Each patient is indeed characterized by her own habits, which determine various activity windows throughout the 24-h day[25,26]. To recognize and characterize the repeated activity windows (RAWs) that recur throughout the RT duration, we designed a dedicated algorithm[27] developed in MATLAB® (MathWorks, Natick, MA) and described in detail in Appendix 1. In such defined RAWs, it was possible to effectively evaluate FT biomedical parameters (Fig. 1b,c).

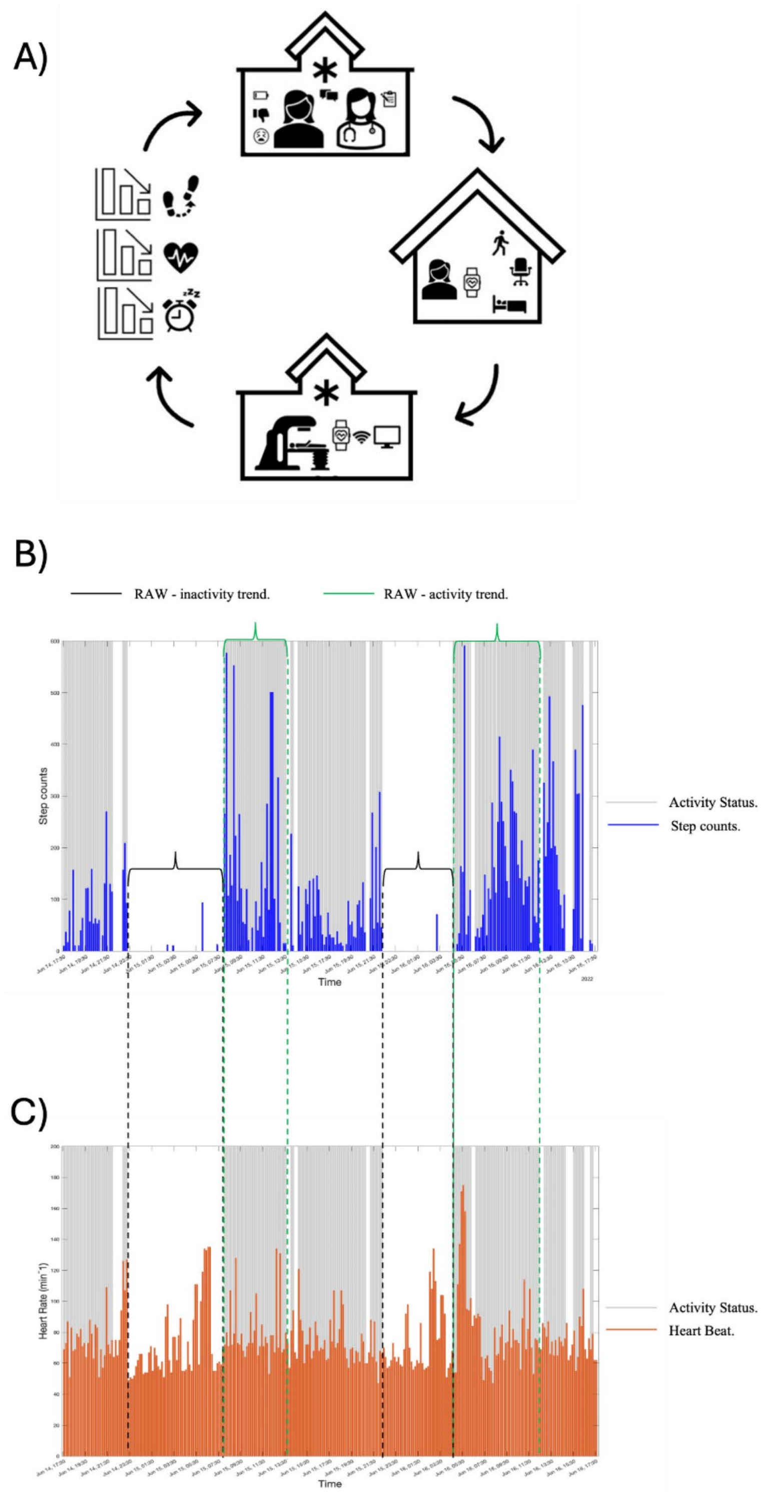

Fig. 1. (**A**) Workflow of data collection by fitness tracker (FT) throughout the radiation therapy course. (**B**) Step counts (STP) and activity status data extraction during two days. Two Repeated Activity Windows (RAWs) on two consecutive days are marked in green (active trend) and red (inactive trend). They may refer to possible patient habits. (**C**) Heart Rate data extraction in the same time span as showed in (**B**).

In particular, for each patient, it was possible to identify HR and STP variations within their RAWs and the following features were accordingly identified: start timestamp, end timestamp, duration, RAW start time, RT day, activity status (1 vs. 0), STP mean, HR mean, STP sum, HR sum, STP standard deviation, HR standard deviation, mean ΔSTP/ΔTimestamp. A detailed description of each feature is provided in Table 1.

	RAW features	Description
1	Start timestamp	The time at which the RAW starts (format: yyyy:mm:dd hh:mm:ss)
2	End timestamp	The time at which the RAW ends (format: yyyy:mm:dd hh:mm:ss)
3	Duration	The duration of RAW in seconds
	RAW start time	The time of day (00:24) at which the RAW starts
5	RT day	The number of days between the start of the RT and the start of RAW
6	HR sum	The sum of the HR in a RAW
7	STP sum	The sum of the STP counts in a RAW
8	HR standard deviation (SD)	The standard deviation of HR in a RAW
9	STP standard deviation (SD)	The standard deviation of STP in a RAW
10	HR mean	The mean of the HR sampled between two consecutive timestamps in a RAW
11	STP mean	The mean of the STP sampled between two consecutive timestamps in a RAW
12	Mean ΔSTP/ΔTimestamp	The mean patient speed registered in a RAW calculated as mean of [STP($i+1$) − STP(i) /timestamp($i+1$) timestamp(i)] with i timestamp index in a RAW
13	Activity status	Binary value associated to activity (1) and inactivity (0) windows

Table 1. Description of the extracted repeated activity window (RAW) related features. *HR* Heart rate, *STP* Step counts.

Statistical analysis

Patient, disease and treatment-related characteristics were examined according to the development of RIF. Categorical variables were expressed as percentages and tested by Pearson's χ^2-test or Fisher's exact test when appropriate; the median and the range were used to describe all continuous variables and Mann–Whitney U-test was employed for analyzing them.

Subsequently, to identify possible association between the RAW features described in Table 1 and RIF, data of participants who were fully compliant to FT monitoring program were randomly divided in two sets: a training dataset and a test dataset, maintaining a 5:1 ratio. Fine Tree Machine Learning (ML) algorithm[24] was used to identify candidate RIF associated features, including possible nuisance clinical variables significantly correlated with RIF. Feature selection was then performed using an ANOVA-based feature ranking algorithm[28], with a threshold set at a value of 3 for the importance score, taking into account the population size. Following variable selection, we tested four commonly used classification methods in ML: Fine Tree, Bagged Trees, Neural Network, K-Nearest Neighbors (KNN)[29,30]. By comparing the performance of these different algorithms, we aimed to identify the most effective model for characterizing RIF based on the selected features.

Each model's performance was assessed on the training data using fivefold cross-validation to ensure robustness and to mitigate overfitting. The methods were trained by Classification Learner available in MATLAB 2023b.

The Fine Tree algorithm was set with the fine tree preset, a maximum of 140 splits, and the maximum deviance reduction as split criterion. The Ensemble algorithm was set with a Bag preset, 279 learners and a maximum of 6122 splits. The Neural Network algorithm was set with 3 fully connected layers, each layer having a size of 10. The KNN algorithm was set with the coarse KNN preset with 100 neighbors, a Euclidean distance metric, and equal distance weighting. The test dataset was used to assess the predictive capability of the trained models. The classification performance of the models was evaluated by accuracies from both train and test dataset, and Receiver Operating Characteristics (ROC)–Area Under the Curve (AUC) (train and test dataset).

Results

Study population

All 36 patients had a good performance score. RIF was reported by 17 out of 36 patients (47%). Patient clinical and treatment characteristics were described in Table 2. At univariable analysis, none of the patient clinical variables was significantly correlated with RIF.

An overview of RIF experienced by patients during RT is provided in Supplementary Material, Table S2. Of note, all patients except one (97%) experienced dermatitis, mostly G1; 12 patients (33%) experienced G2 dermatitis.

FT compliance

All patients accepted to participate in the monitoring program (100% acceptance rate). One patient wore the device continuously but only for the first RT week, reporting discomfort after a certain period and she was accordingly excluded from further analysis.

Three patients wore the FT for the entire treatment duration, though not continuously and the data collection efficiency resulted to be less than 60%. For 32 patients the FT data collection efficiency was over the set threshold of 60%. Accordingly, the final compliance rate was 89%.

Clinical and treatment feature	All (n = 36)	Fatigue G0 (n = 19)	Fatigue Any-grade (n = 17)	p-value
Age	55.5 (31–72)	56 (31–72)	55 (39–68)	0.802
KPS (%)				
90	15 (42%)	6 (32%)	9 (53%)	0.285
100	21 (58%)	13 (68%)	8 (47%)	
BMI	26.6 (21.5–39.5)	26.6 (22.5–39.5)	26.5 (21.5–37.4)	1
Normal	15 (42%)	7 (37%)	8 (47%)	0.738
Overweight or obese	21 (58%)	12 (63%)	9 (53%)	
Smoke				
Current/former	7 (19%)	5 (26%)	2 (12%)	0.408
Heart comorbidity	15 (78%)	8 (16%)	7 (41%)	0.736
Surgery				
Conservative	28 (78%)	17 (89%)	11 (64%)	0.114
Radical	8 (22%)	2 (11%)	6 (35%)	
Histotype				
Ductal	13 (36%)	6 (32%)	7 (41%)	0.73
Lobular	4 (11%)	2 (11%)	2 (12%)	1
NST	16 (44%)	9 (47%)	7 (41%)	0.749
NR	3 (11%)			
Stage				
0–1	16 (44%)	8 (42%)	11 (64%)	0.202
2–3	20 (56%)	11 (58%)	16 (94%)	
Adjuvant CHT	5 (14%)	4 (21%)	1 (6%)	0.187
Neoadjuvant CHT	9 (25%)	4 (21%)	5 (29%)	0.706
Target therapy	6 (11%)	1 (5%)	5 (29%)	0.081
Endocrine therapy	33 (92%)	17 (89%)	16 (94%)	0.543
IHC				
Luminal	29 (81%)	16 (84%)	3 (18%)	0.402
HER2+	4 (11%)	0 (0%)	4 (24%)	0.050
Triple negative	2 (6%)	2 (6%)	0 (0%)	0.486
Target				
Breast	32 (89%)	18 (95%)	14 (82%)	0.326
Chestwall	4 (11%)	1 (5%)	3 (18%)	0.326
N	10 (28%)	3 (16%)	7 (41%)	0.139
Laterality				
Right	14 (39%)	8 (42%)	6 (35%)	0.742
Left	22 (61%)	11 (58%)	11 (64%)	1
Bilateral	1 (3%)	1 (5%)	0 (0%)	1
Dmax prescriprion dose BED_4 (Gy)	83 (66.8–90.6)	83 (66.8–90.6)	83 (75–90.6)	0.433

Table 2. Clinical and treatment characteristics of the whole, study population, and according to fatigue, with statistics. *KPS* Karnofsky Performance Score, *BMI* Body Mass Index, *IHC* Immunochemistry, *N* Nodes.

Repeated activity windows

For each patient, a distinct distribution of RAWs was identifiable over the course of RT treatment days. Across the entire patient cohort, a total of 7950 RAWs were collected. The mean values of RAWs related features for the whole cohort and according to RIF development were reported in Supplementary Material Table S3.

The dataset of RAWs was split into a training set (6315 RAWs, 25 patients) and a test set (1635 RAWs, 7 patients). Eleven features were selected by Fine Tree as candidate features while 6 were identified as associated with RIF, based on their ANOVA-derived importance score (Fig. 2). These features include start timestamp, RAW start time, HR mean, HR standard deviation, STP standard deviation, mean ΔSTP/ΔTimestamp.

All tested ML models demonstrated moderate to good predictive performance for RIF (Table 3 and Fig. 3), with accuracies ranging from 70 to 80% in the training set. Confusion matrices for all models are reported in Supplementary Material Fig. S1.

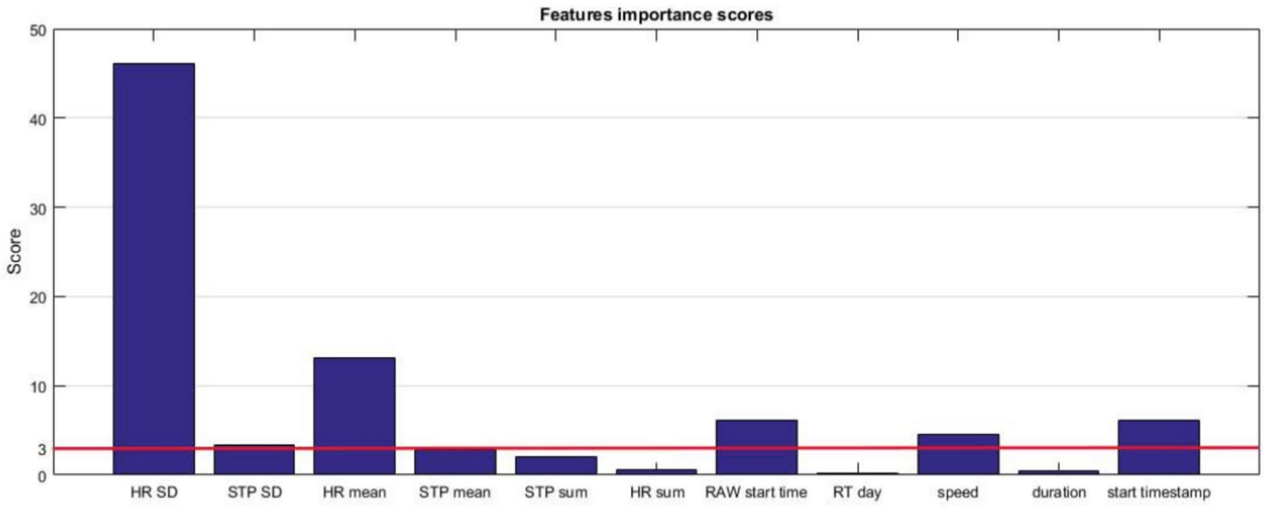

Fig. 2. Feature importance scores selected by Analysis of Variance (ANOVA) algorithm. The red dashed-line indicates an importance score of 3; 6 features have an importance score major or equal to 3.

Performance	Bagged tree	Fine tree	Neural network	KNN
Accuracy (training)	80%	77%	76%	70%
Total cost (training)	1286	1452	1531	1987
Accuracy (test)	85%	86%	73%	72%
Total cost (test)	268	175	449	496
Time (s)	255	25	15	2
AUC (training)	89%	86%	86%	76%
95% CI (training)	(89–90)%	(85–87)%	(85–86)%	(74–77)%
AUC (test)	86%	93%	86%	55%

Table 3. Performance measures for each machine learning model.

Discussion

The pandemic era has introduced significant changes in healthcare, marked by the implementation of telemedicine and remote monitoring. The interest in the use of non-medical tracking devices for medical purposes is, therefore, growing[31]. While it is not yet well known how FT can play their role, various studies have analyzed adherence to remote tracking, sleep and activity levels among oncological patients. Monitored physical activity seems to correlate with clinician assessed performance status[11] and possibly with toxicity in cancer patients: step counts per day could serve as an adjunct to performance status assessment and a possible help to identify vulnerable populations[32]. Various studies have focused their attention on the role of physical activity during preoperative treatments. In pancreatic cancer patients, moderate exercise can reduce surgical complications and accelerate recovery from surgery[33]. During chemotherapy for breast cancer, patients typically experience a decrease in physical activity. Adherence to interventions aimed at reversing this trend appears to be higher among younger patients and receiving adjuvant chemotherapy[34]. If several studies have explored biomedical monitoring before, during or after chemotherapy or surgery[19] there is a paucity of research[35–38] regarding the monitoring of cancer patients during their RT course (Supplementary Material Table S4). The preliminary results of a pilot study by Sher et al.[38] about wearable activity monitoring during RT for a large sample of head and neck malignancies, have been recently published. Although not meeting the compliance goal, most patients did use the wearable device; their signal could not identify patients requiring hospitalization or significantly more pain medication, but the finding of reduced STP before a significant reduction in quality of life was suggestive. Association between biomedical parameters and QoL had already described by Lowe et al.[35], showing that, in a sample of patients bearing brain metastases undergoing palliative whole brain RT, sedentary behavior was associated with better physical functioning but with worse psychosocial functioning. The study was limited by malfunctioning of accelerometers. Moreover, those patients are characterized by a low level of physical activity since baseline which can hardly be increased. Ohri et al.[36] have more concretely demonstrated the possibility to identify vulnerable patients during RT; performing continuous activity monitoring during concurrent chemoradiotherapy on 38 patients with different primaries, a significant association was found between recent step counts and hospitalization risk.

Notably, BC is a more common malignancy, and BC patients represent a better-prognosis group with long-term survivors. One of the main side effects related to RT is fatigue, although it is not completely clear how it

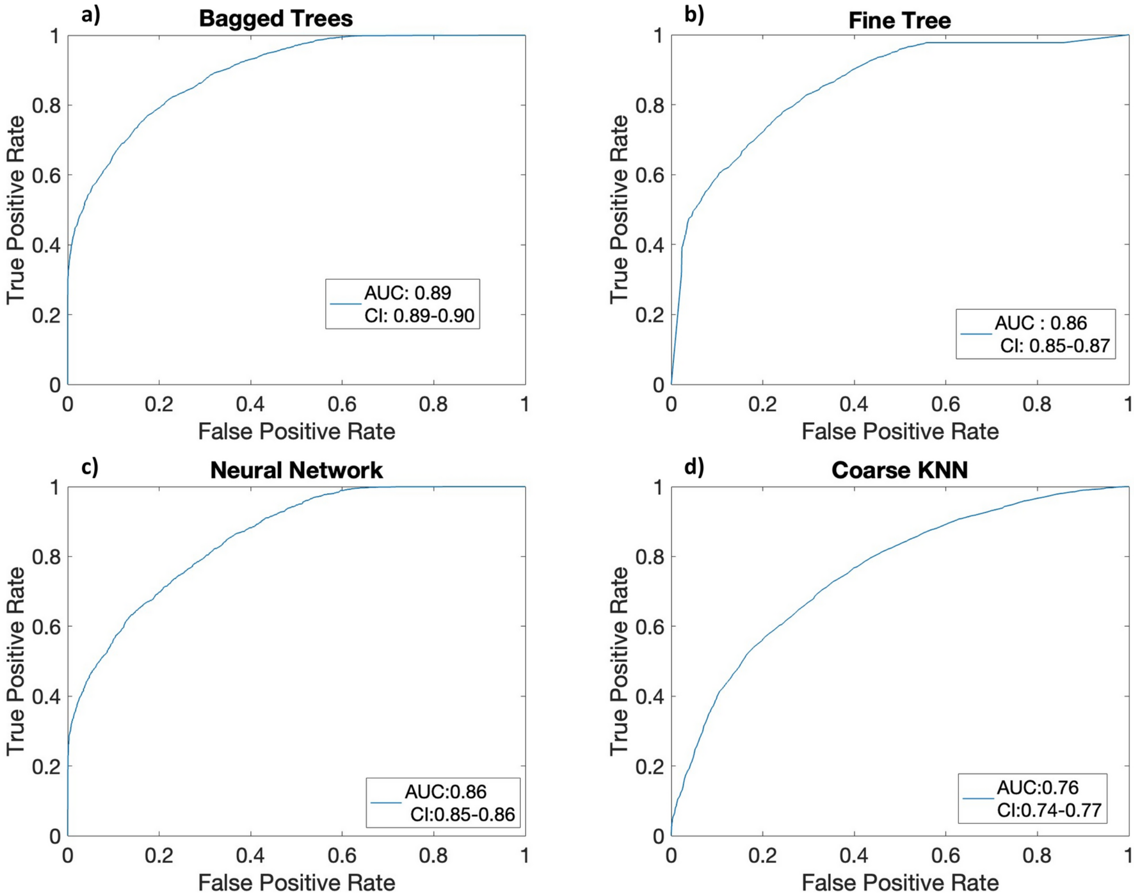

Fig. 3. Model ROC curves on the training dataset: bagged trees model (**a**), fine tree model (**b**), neural network model (**c**), K-nearest neighbors model (**d**).

impacts on physical activity. Champ et al.[37] selecting ten patients, found transient changes in activity levels during RT. Despite its limitation -above all, the small sample size- they identified the path of RT as an opportune time to start implementing changes prior to survivorship for BC patients.

The present study represents a pilot, primarily aimed at assessing the compliance of BC patients in continuously wearing FT during 3–5 weeks of RT. Our primary goal was to characterize RIF trajectories using objective data collected by these wearable devices. To achieve this, we identified time windows for observing patients' daily habits by introducing RAWs and the related features, including HR and STP variations. Champ et al.[37] in their study indeed highlighted significant variability in activity levels among women undergoing RT. This inter-patient variability, potentially due to differing daily habits, prompted us to adopt a novel approach based on the innovative concept of RAWs, allowing us to effectively evaluate HR and STP variations during RT. This approach enabled us to define a kind of fingerprint of each patient activity level.

As expected, BC patients undergoing adjuvant RT proved to be highly compliant. While all patients agreed to wear the FT, continuous monitoring was inadequate for 11% of patients due to interruptions or discontinuities in data collection caused by patient tolerance levels in wearing the device. In addition to patient tolerance, we also considered data collection efficiency to ensure the quality of the collected data, which was directly related to the device's acquisition performance. The FT's acquisition performance was potentially affected by two key factors: (a) limited battery life, leading to interruptions and data gaps in each patient's dataset, and (b) improper or inconsistent use of the device by the patient, causing a loss of information about daily activities. Despite these challenges, only 9% of patients had data collection efficiency below the set threshold.

Various ML algorithms were then tested to capture patterns in the collected FT data that translate these features into an objective description of RIF. The ML algorithms that have been utilized in this study are Fine Tree, Bagged Trees, Neural Network, and KNN which have helped us achieve the results presented in the paper. These algorithms were chosen for their diverse approaches to classification and their proven effectiveness in different contexts. Fine Tree and Bagged Trees represent decision tree-based models, with Fine Tree offering a simple and interpretable model, while Bagged Trees enhance robustness by reducing overfitting through ensemble learning. Neural Networks are powerful in capturing complex, non-linear relationships in data, although they may require significant computational resources and risk overfitting with small datasets. K-Nearest Neighbors (KNN) is an instance-based method known for its simplicity and effectiveness in low-dimensional spaces, but it can struggle with high-dimensional data and large datasets due to increased computational complexity. By comparing these methods, we aimed to balance model complexity, interpretability, and predictive accuracy.

Notably, the Bagged Trees model exhibited the highest performance, achieving a training-AUC of 89% (95% CI 88–90%) and test-AUC of 86%, while the worst performance was observed with KNN model achieving a training-AUC of 76% (95% CI 74–77%) and a test-AUC of 55% (Fig. 3).

A subset of the extracted RAW features resulted to be important in the description of the RIF status. Specifically, the instants at which the RAWs start provide us with information about the general patterns of patients' activities, enabling intra-patient analysis. Differently, the time of the day at which the RAW starts provides us with information about the daily patient habits, allowing for inter-patient analysis. As regard to STP and HR within RAWS, the standard deviations of step counts and heart rates give a description of the variation in intra-RAW fatigue. The mean HR and mean speed are instead indicative of the variation in patient activity assessable between RAWs.

The supervised learning method suggested that the objective data collected by FT could be useful to define RIF status in patients undergoing RT. Thanks to its sensitivity and specificity, the bagged trees showed to be a powerful tool to characterize RIF over RT time, basing on data collected.

Among the limitations of our study, technical issues related to the chosen FT devices stand out, including the above-mentioned low battery life. Out of the box, the FT's battery lasted about a week, but after several charge/discharge cycles, it only lasted three days. This may be due to the manufacturer using lower-grade components for the batteries. The short battery life hindered baseline and post-discharge data acquisition, limiting data collection efficiency. This was due to the decision not to require patients to recharge their FTs independently, aiming to maintain the study's non-invasiveness. Another contributing factor to the short battery life was the non-configurable sampling frequency. While lowering the heart rate (HR) sampling rate could have extended battery life, it might have resulted in information loss. Additionally, the most significant technical limitation affecting the proposed methodology was the limited memory capacity of the FTs. These devices could only store data from the current day and the previous two days, meaning patients returning to the RT department on a Monday, after weekend treatment break, would have their Friday data lost. To address these challenges, one of the biggest design hurdles involved developing a fully reliable gateway application to collect data from the FTs. The application must efficiently manage multiple FTs in cases where several monitored patients were in the RT waiting room simultaneously, as well as handle retries for unsuccessful downloads due to patients moving in and out of the gateway's range. This process was made more complex by the slow transmission rate of Bluetooth Low Energy, which extended the time needed to download data from FT memory.

Additionally, the small number of enrolled patients may have impacted method performance, as evidenced by the fine tree model performance reported in Table 3. However, to our knowledge, this study represents the first experience in monitored biomedical data analysis among cancer patients using the methodological approach based on RAWs.

The promising preliminary results encourage us to continue enrolling more patients to extend and validate our findings. Our study indeed prospectively opens up several potential clinical applications. Specifically, we have demonstrated that a highly subjective symptom like fatigue can be predicted with reasonable accuracy using wearable devices. This finding offers a model that supports the broader implementation of remote monitoring for cancer patients. The reduction in hospital visits not only addresses the immediate needs brought on by the pandemic but also reflects a growing demand for more accessible healthcare. This shift holds potential benefits across various aspects, including improved patient quality of life, mobility, sustainability, hospital efficiency, and cost-effectiveness.

Conclusions

While remote monitoring in cancer patients is not a novel concept, our experience stands out as one of the few instances observed among BC patients undergoing RT. Our findings highlight BC patients as a particularly compliant group for continuous biomedical monitoring. By FT monitoring of HR and STP within patient's activity windows, healthcare providers may be helped in performing an evaluation of RIF trajectories based on objective data. Investigating the long-term impact of remote monitoring on patient outcomes—such as quality of life, treatment adherence, and survival rates—could provide valuable insights into the clinical utility of these technologies. By validating these approaches in larger trials, remote monitoring could become a standard component of cancer care, enhancing patient autonomy while reducing the burden on healthcare systems.

Data availability

The datasets used and/or analyzed during the current study available from the corresponding authors on reasonable request.

Received: 26 April 2024; Accepted: 4 November 2024
Published online: 08 November 2024

References

1. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. *Psychol. Med.* **28**, 551–558 (1998).
2. Maratia, S., Cedillo, S. & Rejas, J. Assessing health-related quality of life in patients with breast cancer: a systematic and standardized comparison of available instruments using the EMPRO tool. *Qual. Life Res.* **25**, 2467–2480 (2016).
3. Groenvold, M. Health-related quality of life in early breast cancer. *Dan Med. Bull.* **57**, B4184 (2010).
4. Broderick, J. E. et al. Patient reported outcomes can improve performance status assessment: a pilot study. *J. Patient Rep. Outcomes* **3**, 41 (2019).

5. Malterud, K. Subjective symptoms without objective findings—a challenge for theory and practice of general medicine. *Ugeskr Laeger* **163**, 6729–6734 (2001).
6. Mokhtari-Hessari, P. & Montazeri, A. Health-related quality of life in breast cancer patients: Review of reviews from 2008 to 2018. *Health Qual. Life Outcomes* **18**, 338 (2020).
7. Pacelli, R. et al. Technological evolution of radiation treatment: Implications for clinical applications. *Semin. Oncol.* **46**, 193–201 (2019).
8. Kowalczyk, L. et al. Radiotherapy-induced fatigue in breast cancer patients. *Breast Care (Basel)* **16**, 236–242 (2021).
9. Milne, H. M., Wallman, K. E., Gordon, S. & Courneya, K. S. Effects of a combined aerobic and resistance exercise program in breast cancer survivors: a randomized controlled trial. *Breast Cancer Res. Treat.* **108**, 279–288 (2008).
10. Beg, S. et al. Wearable smart devices in cancer diagnosis and remote clinical trial monitoring: Transforming the healthcare applications. *Drug Discov. Today* **27**, 103314 (2022).
11. Gupta, A. et al. Feasibility of wearable physical activity monitors in patients with cancer. *JCO Clin. Cancer Inform.* **2**, 1–10 (2018).
12. Liu, J. et al. Multi-wavelength photoplethysmography enabling continuous blood pressure measurement with compact wearable electronics. *IEEE Trans. Biomed. Eng.* **66**, 1514–1525 (2019).
13. Riaz, F. *et al.* Pervasive blood pressure monitoring using Photoplethysmogram (PPG) sensor. *Future Gener. Comput. Syst.* **98**, (2019).
14. Nabeel, P. M., Karthik, S., Joseph, J. & Sivaprakasam, M. Arterial blood pressure estimation from local pulse wave velocity using dual-element photoplethysmograph probe. *IEEE Trans. Instrum. Meas.* **67**, 1399–1408 (2018).
15. Henriksen, A. et al. Using fitness trackers and smartwatches to measure physical activity in research: analysis of consumer wrist-worn wearables. *J. Med. Internet Res.* **20**, e110 (2018).
16. Tramontano, A., Scala, M. & Magliulo, M. Wearable devices for health-related quality of life evaluation. *Soft Comput.* **23**, 9315–9326 (2019).
17. Gravina, R. & Fortino, G. Computational aspects in body sensor networks (BSNs): From operating systems to data fusion. In *Encyclopedia of Sensors and Biosensors (First Edition)* (ed. Narayan, R.) 173–185. https://doi.org/10.1016/B978-0-12-822548-6.00136-9 (Elsevier, 2023).
18. Pirbhulal, S., Zhang, H., Wu, W., Mukhopadhyay, S. C. & Zhang, Y.-T. Heartbeats based biometric random binary sequences generation to secure wireless body sensor networks. *IEEE Trans. Biomed. Eng.* **65**, 2751–2759 (2018).
19. Chow, R. et al. The use of wearable devices in oncology patients: A systematic review. *Oncologist* **29**, e419–e430 (2024).
20. El-Adawi, E., Essa, E., Handosa, M. & Elmougy, S. Wireless body area sensor networks based human activity recognition using deep learning. *Sci. Rep.* **14**, 2702 (2024).
21. Tramontano, A., Scippacercola, F. & Magliulo, M. Estimating quality of life variation using BLE wearable devices on android based architecture. *Int. J. Radiat. Oncol. Biol. Phys.* **102**, e286 (2018).
22. Feoli, C. et al. PO-1250 Biomedical parameters identification for radiotherapy-induced fatigue evaluation:proof of principle. *Radiother. Oncol.* **182**, S1000–S1001 (2023).
23. Magliulo, M. & Tramontano, A. Cardiac monitoring of frail oncological outpatient using wearable devices. In *2017 E-Health and Bioengineering Conference (EHB)* 697–700. https://doi.org/10.1109/EHB.2017.7995519 (2017).
24. Kolgotin, A., Müller, D., Chemyakin, E. & Romanov, A. Improved identification of the solution space of aerosol microphysical properties derived from the inversion of profiles of lidar optical data, part 2: simulations with synthetic optical data. *Appl. Opt.* **55**, 9850–9865 (2016).
25. Morlock, M. et al. Duration and frequency of every day activities in total hip patients. *J. Biomech.* **34**, 873–881 (2001).
26. Chaurasia, P., McClean, S., Scotney, B. & Nugent, C. Duration discretisation for activity recognition. *Technol. Health Care* **20**, 277–295 (2012).
27. Tramontano, A. *et al.* Deploying unsupervised learning for daily activity windows analysis in cancer patients. https://doi.org/10.1109/MetroXRAINE58569.2023.10405824 (2023).
28. Deo, R. C. Machine learning in medicine. *Circulation* **132**, 1920–1930 (2015).
29. Montazeri, M., Montazeri, M., Montazeri, M. & Beigzadeh, A. Machine learning models in breast cancer survival prediction. *Technol. Health Care* **24**, 31–42 (2016).
30. Beam, A. L. & Kohane, I. S. Big data and machine learning in health care. *JAMA* **319**, 1317–1318 (2018).
31. Colbert, G. B., Venegas-Vera, A. V. & Lerma, E. V. Utility of telemedicine in the COVID-19 era. *Rev. Cardiovasc. Med.* **21**, 583–587 (2020).
32. Ward, W. H. et al. Feasibility of fitness tracker usage to assess activity level and toxicities in patients with colorectal cancer. *JCO Clin. Cancer Inform.* **5**, 125–133 (2021).
33. Parker, N. H. et al. Physical activity and exercise during preoperative pancreatic cancer treatment. *Support Care Cancer* **27**, 2275–2284 (2019).
34. Dreher, N. et al. Fitbit usage in patients with breast cancer undergoing chemotherapy. *Clin. Breast Cancer* **19**, 443-449.e1 (2019).
35. Lowe, S. S. et al. Associations between objectively measured physical activity and quality of life in cancer patients with brain metastases. *J. Pain Symptom Manag.* **48**, 322–332 (2014).
36. Ohri, N. et al. Continuous activity monitoring during concurrent chemoradiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* **97**, 1061–1065 (2017).
37. Champ, C. E. et al. Assessing changes in the activity levels of breast cancer patients during radiation therapy. *Clin. Breast Cancer* **18**, e1–e6 (2018).
38. Sher, D. J. et al. Pilot study of a wearable activity monitor during head and neck radiotherapy to predict clinical outcomes. *JCO Clin. Cancer Inform.* **6**, e2100179 (2022).

Acknowledgements

Dr. O. Tamburis and A. Tramontano acknowledge the support of the European Union's Horizon Europe Research and Innovation Program (HORIZON-CL6-2022-GOVERNANCE-01) under grant agreement No. 101086521—OneAquaHealth (Protecting urban aquatic ecosystems to promote One Health). Dr. M. Magliulo acknowledges the support of "NUTRAGE -NUTRIZIONE, ALIMENTAZIONE & INVECCHIAMENTO ATTIVO"—DM MUR n. 844.

Author contributions

A.B. and C.F. wrote the main manuscript text and analyzed data. C.F., M.C, A.T. and O.T. implemented the software. M.C., A.F. M.P., C.O., S.C., M.A.A. followed the patients and data curation. R.P., M.C., A.T., M.C. and L.C. conceptualization, review and editing. All authors reviewed the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-78805-5.

Correspondence and requests for materials should be addressed to L.C. or M.C.

Appendix 1

The algorithm introduced in the text, and detailed below, leverages a combination of Boolean logic, predefined thresholds, and sliding time windows to classify periods of activity and inactivity for patients.

Based on the functionality of the Fitness Tracker (FT) deployed in our study (Veepoo H03 smart watch), 144 Time Points (TP) are identified each day with:

$$\Delta TP = TP_{i+1} - TP_i = 10mins$$

Each TP_i contains values for the parameters Step Counts (STP) and Heart Rate (HR). A dichotomous variable (DV) to classify patient activity (1) or inactivity (0) is associated with each TP_i depending on the trend of the STP values. Specifically, a DV value of 1 is associated with STP values > 20, and 0 otherwise. The threshold value of STP = 20 was identified because, upon analyzing the historical series of STP values collected during monitoring, it emerged that all outliers had an STP value ≤ 20.

Activity Windows are defined as time intervals of no less than 30 minutes during which the patient is likely active. This duration was mainly determined, beyond literature analysis [25, 26],on a preliminary analysis of the specific habits reported by patients enrolled in the study.

The algorithm subsequently evaluates time intervals of 4 TPs: if at least 3 values of DV are the same within that interval, it provides a consistent indication of whether or not there was activity. In other words, if DV = 0 in 3 out of 4 TPs, it can be concluded with some certainty that there was no activity in that interval. Conversely, if DV = 1 in 3 out of 4 TPs, it is plausible to assume that there was activity.

The steps of the algorithm are as follows:

1. In the first step, the first 4 TPs (from TP1 to TP4) of treatment day 1 are evaluated, i.e., the TPs for the time interval from 12:05 am to 12:35 am. The possible scenarios are:
    - There are 3 STP values above the threshold; all 4 TPs are assigned a DV value of 1;
    - There are 3 STP values below the threshold; all 4 TPs are assigned a DV value of 0;
    - There are two values above the threshold and two values below the threshold; the two TPs above the threshold are assigned a DV value of 1 while the other two TPs are assigned a DV value of 0;
2. The observation window of the 4 TPs shifts by one TP. The new evaluation interval is from TP2 to TP5, i.e., from 12:15 am to 12:45 am. The possible scenarios are:
    - There are 3 STP values above the threshold; all 4 TPs are assigned a DV value of 1;
    - There are 3 STP values below the threshold; all 4 TPs are assigned a DV value of 0;
    - There are two values above the threshold and two values below the threshold; all 4 TPs are assigned a DV value equal to that of the TP immediately preceding the first TP of the window under examination (in this case TP1) since, with 5 STP values, a 3:2 ratio between values above and below the threshold is created;

This means that, in the algorithm's iteration, the DV values associated with the TPs in the window can be overwritten based on the specific STP sequences of the windows under examination.

3. Step 2 is repeated throughout the day up to the observation window [TP141-TP144], corresponding to the interval 11:25 pm - 11:55 pm, assigning DV values to each TP, occasionally overwriting previously calculated DV values as indicated in step 2.

4. At the end of the day, the last associated DV value is checked for each TP_i to identify Activity Windows, i.e., sequences of TP_i where the DV value is 1. Sequences of TP_i where the DV value is 0 identify non-activity windows.

5. The algorithm evaluates all treatment days to highlight activity windows for each day.

It was thus possible to identify Activity Windows that recur during treatment days. Two Activity Windows (even on non-consecutive days) are comparable if the distances between the initial TPs and those between the final TPs do not exceed 2 TPs, i.e., 20 minutes. Formally, given two activity windows AW1 and AW2:

$$\left|TP_{in|AW1} - TP_{in|AW2}\right| \leq 2TP$$

$$\left|TP_{fin|AW1} - TP_{fin|AW2}\right| \leq 2TP$$

If a window repeats for more than 40% of the RT, it is considered a Repeated Activity Window, and the biomedical parameters collected within it during monitoring are analyzed.

An example of the first 7 iterations of the algorithm (on sample data) is shown in Figure A.1.

Figure A.1

		TP1	TP2	TP3	TP4	TP5	TP6	TP7	TP8	TP9	TP10
STP		*87*	*4*	*90*	*18*	*89*	*84*	*15*	*0*	*8*	*15*
DV	*It. #1*	1	0	1	0						
	It. #2		~~0~~ 1	1	~~0~~ 1	1					
	It. #3			1	~~0~~ 1	1	1				
	It. #4				~~0~~ 1	1	1	~~1~~ 1			
	It. #5					1	1	~~1~~ 0	~~0~~ 1		
	It. #6						~~1~~ 0	0	0	0	
	It. #7							0	0	0	0
	Final	***1***	***1***	***1***	***1***	***1***	***0***	***0***	***0***	***0***	***0***
		ACTIVITY					NO ACTIVITY				

Supplementary Materials

To

Fatigue trajectories by wearable remote monitoring of breast cancer patients during radiotherapy

Table S1. Data acquisition range and sampling rate for step counts (STP) and heart rate (HR)

Parameter	Data acquisition range	Sampling rates
STP	00.00-24:00	15 min
HR	00.00-24:00	08.00 - 24.00: 10 min 00.00 - 08.00: 1 min

Table S2. Radiation-induced fatigue (RIF) and its grading during the weeks of radiation therapy (RT), along with a summary of the maximum fatigue reported by patients.

RIF grading	**Timing**						Summary
	Baseline (n=36)	week #1 (n=36)	week #2 (n=36)	week #3 (n=36)	week #4 (n=33)	week #5 (n=11)	
G0	33 (92%)	30 (83%)	26 (72%)	24 (66%)	21 (64%)	5 (46%)	19 (53%)
G1	3 (8%)	4 (11%)	4 (11%)	6 (17%)	5 (15%)	3 (27%)	9 (25%)
G2	0 (0%)	2 (6%)	6 (17%)	6 (17%)	7 (21%)	3 (27%)	8 (22%)
Any	3 (8%)	6 (17%)	10 (28%)	12 (34%)	13 (36%)	6 (54%)	17 (47%)

Table S3. Mean values of Repeated Activity Windows **(**RAWs) related features for the whole cohort and according to radiation-induce fatigue (RIF).

RAWs feature	**Overall (N=7950)**	**RIF**	
		G0 (N=3722)	**any-grade (N=4228)**
Duration (sec)	7556.2	7575.0	7539.6
RAW start times (00-24)	13.9	14.1	13.6
STP mean	56.6	56.8	56.2
HR mean (min^{-1})	75.8	76.4	75.4
STP Sum	797	825.1	772.3
HR sum (min^{-1})	888.9	906.3	873.7
HR Standard Deviation	9.6	10.2	9.0
STP Standard Deviation	49.6	50.9	49.1
RT day	13	14	13
ΔSTP/ΔTimestamp (min^{-1})	-1.9	-2.1	-1.7

Abbreviations: HR: Heart Rate, STP: Step counts

Table S4. Previous studies exploring biomedical parameters during radiotherapy.

Author, year	**population**	**parameters**	**Results**
Lowe, 2014 [35]	31 BM	triaxal movement	association between sedentary behavior and better physical functioning but worse psychosocial one
Ohri, 2017 [36]	11 HN 13 lung 14 GI	step counts	association between physical activity and hospitalization risk
Champ, 2017 [37]	10 BC	step counts calories burned sleep metrics	statistically significant but not clinically relevant changes in step counts, distance, and calories. No significant change in sleep
Sher, 2022 [38]	51 HN	step counts	no association with hospitalization or more pain medication request, but association with oncoming reduction in QoL

Abbreviations: BM Brain Metastases; HN Head and Neck; GI Gastrointestinal

Figure S1. Bagged Trees confusion matrices related to the training set (a) and test set (b).