Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2017 April 01; 97(5): 1061–1065. doi:10.1016/j.ijrobp.2016.12.030.

Continuous Activity Monitoring during Concurrent Chemoradiotherapy

Nitin Ohri, M.D.,

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, 111 East 210th Street, Bronx, New York 10467, (718) 920-7750, ohri.nitin@gmail.com

Rafi Kabarriti, M.D.,

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

William R Bodner, M.D.,

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Keyur J Mehta, M.D.,

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Viswanathan Shankar, Dr.P.H.,

Department of Epidemiology & Population Health, Albert Einstein College of Medicine

Balazs Halmos, M.D.,

Department of Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Missak Haigentz Jr., M.D.,

Department of Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Bruce Rapkin, Ph.D.,

Department of Epidemiology & Population Health, Albert Einstein College of Medicine

Chandan Guha, M.B.B.S., Ph.D.,

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Shalom Kalnicki, M.D., and

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Madhur Garg, M.D.

Correspondence to: Nitin Ohri.

This work was presented in abstract form at the 2016 ASTRO Annual Meeting.

The authors have no conflicts of interest to disclose.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine

Abstract

Background—Wearable activity monitors are widely available and marketed as fitness trackers. We performed a prospective trial testing the feasibility and utility of acquiring activity data as a measure of health status during concurrent chemoradiotherapy.

Methods—Ambulatory patients who were planned for treatment with concurrent chemoradiotherapy with curative intent for cancers of the head and neck, lung, or gastrointestinal (GI) tract were provided with activity monitors prior to treatment initiation. Patients were asked to wear the devices continuously throughout the radiotherapy course. Step count data were downloaded at weekly during radiotherapy and two and four weeks after radiotherapy completion. The primary objective was to demonstrate feasibility, defined as collection of step counts for 80% of the days during study subjects' radiotherapy courses. Secondary objectives included establishing step count as a dynamic predictor of unplanned hospitalization risk.

Results—Thirty-eight enrolled patients were treated with concurrent chemoradiotherapy. Primary diagnoses included head and neck cancer (n=11), lung cancer (n=13), and a variety of GI cancers (n=14). Step data were collected for 1524 out of 1613 days (94%) during patients' radiotherapy courses. Fourteen patients were hospitalized during radiotherapy or within four weeks of radiotherapy completion. Cox regression modeling demonstrated a significant association between recent step counts (3-day average) and hospitalization risk, with a 38% reduction in the risk of hospitalization for every 1,000 steps taken each day (HR = 0.62, 95% CI: 0.46 to 0.83, p=0.002). Inferior quality of life scores and impaired performance status were not associated with increased hospitalization risk.

Conclusion—Continuous activity monitoring during concurrent chemoradiotherapy is feasible and well-tolerated. Step counts may serve as powerful, objective, and dynamic indicators of hospitalization risk.

INTRODUCTION

Preoperative, definitive, or postoperative radiotherapy plays a role in the curative treatment of a variety of solid tumors. Concurrent chemotherapy can both exacerbate acute radiotherapy toxicities and introduce new side effects^{1,2}. Acute treatment toxicities frequently lead to treatment interruptions and/or hospitalizations³, which detract from treatment efficacy^{4,5} and place burdens on the health care system^{6,7}. In this pilot study, we tested the feasibility of using commercially-available fitness trackers for assessing patients with head and neck, lung, or gastrointestinal cancers throughout the course of concurrent chemoradiotherapy. We also performed exploratory analyses testing associations between activity level and unplanned hospital admission.

METHODS

Patients

Adult patients with ECOG performance status 0-2 who were planned for a course of fractionated radiotherapy with concurrent chemotherapy with curative intent for cancers of the head and neck, lung, or gastrointestinal tract were eligible for this trial. Patients who used a cane or walker to ambulate were ineligible. All study subjects signed informed consent prior to enrollment on this observational, prospective, IRB-approved trial. This trial is registered on ClinicalTrials.gov (NCT02649569).

Assessments

At the time of study registration, a commercially available fitness tracker (Garmin, Lenexa, KS) was placed on the patient's non-dominant wrist and paired with a computer in our department. Patients were asked to wear the device continuously throughout the course of the study. Patients were evaluated by a physician prior to radiotherapy initiation, weekly during radiotherapy, and then two and four weeks after radiotherapy completion. Each evaluation included a history and physical examinations, toxicity assessment using CTCAE version 4.03, completion of the EORTC QLQ-C30 quality of life survey, and activity data download.

Statistical Methods

The primary study objective was to demonstrate the feasibility of continuous activity monitoring, defined as collection of step counts for 80% of the days during study subjects' radiotherapy courses. Secondary objectives included characterization of step count dynamics throughout patients' treatment courses and evaluation of associations between step counts and quality of life data, treatment interruptions, and hospitalizations. The intended sample size was 40 subjects.

For each patient, a baseline activity level was defined as the average daily step count observed prior to radiotherapy initiation. A linear mixed effects model with random slopes using a restricted maximum likelihood procedure was used to model daily step count (average value over the past 3 days⁸) during radiotherapy as a function of patient age, diagnosis, time since radiotherapy initiation, and day of the week (weekend v. weekday).

Cox regression models with time-dependent and time-fixed covariates were used to identify predictors of first hospitalization during the study period. Time-dependent covariates included recent step counts (averaged over the previous three days), most recent ECOG performance status, and most recent average quality of life score (scaled from 0 to 100⁹). Step data collected during hospitalizations were not used to fit the Cox models, as subjects in the hospital were no longer at risk for first hospitalization.

Statistical analyses were performed using STATA version 14 and R version 3.3.1.

RESULTS

Study Subjects and Step Data

A total of 43 subjects signed study consent between June 2015 and December 2015. Five subjects were excluded from this analysis due to device loss prior to treatment initiation (n=1), consent withdrawal (n=1), or change in treatment plan to definitive resection (n=1) or palliative radiotherapy (n=2). Characteristics of the remaining 38 patients are displayed in Table 1.

Continuous use of activity monitors was well-tolerated. Step data were collected for 1524 out of 1613 days (94%) during patients' radiotherapy courses. During the study period, subjects completed a median of 9 quality of life surveys and had performance status documented on a median of 15 occasions.

The median average daily step count prior to radiotherapy initiation was 5,103 steps/day (range: 1,882 to 15,078 steps/day). Multivariable linear mixed effects modeling demonstrated that daily step count was significantly associated with timing in the radiotherapy course (-43 steps per day after radiotherapy initiation, 95% CI: -66 to -21, $p<0.001$) and day of the week (1,386 fewer steps on weekends compared to weekdays, 95% CI: 1,164 to 1,607, $p<0.001$).

Toxicities and Hospitalizations

Non-hematologic toxicity scores during the observation period, which spanned from the initiation of radiotherapy until four weeks after radiotherapy completion, are summarized in Table 2. Fourteen out of 38 patients (37%) were hospitalized during the observation period. Hospitalizations occurred a median of 40 days (range: 2 to 69) after initiation of radiotherapy (Figure 2). Cox regression models (Table 3) demonstrated that low recent step counts were associated with increased risk of hospitalization. Impaired performance status and low quality of life scores were not associated with increased hospitalization risk.

DISCUSSION

We found that continuous activity monitoring during concurrent chemoradiotherapy using a fitness tracker was feasible and well-tolerated. Wireless access clients that sync data automatically every time a subject enters the clinic are now available, which will further simplify daily patient monitoring.

Exploratory analyses suggest that step counts may serve as dynamic predictors of short-term hospitalization risk during chemoradiotherapy. This may be an important finding, as unplanned hospitalization rates in large series range from 14-37%¹⁰⁻¹³. Activity monitoring may serve as a simple and effective tool for predicting treatment complications and provide a window to intervene before severe toxicities occur. A follow-up trial testing this concept is underway.

We did not find that impaired physician-scored performance status or low global quality of life score was associated with increased hospitalization risk. This may be related to our

limited sample size, or it could result from limitations in these assessment tools¹⁴⁻¹⁶. We believe that activity monitoring provides a new dimension of objective information that will complement physician assessments and patient-reported outcomes and serve as a valuable tool in the management of cancer patients across many settings.

Acknowledgments

This work was supported by a Paul Calabresi K12 Career Development Award for Clinical Oncology.

This work, including the cost of subjects' wearable devices, was supported by a Paul Calabresi K12 Career Development Award for Clinical Oncology. Subjects received no other remuneration for participation in this trial.

References

1. Aupérin A, Le Péchoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *Journal of Clinical Oncology*. 2010; 28:2181–2190. [PubMed: 20351327]
2. Furuse K, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer. *Journal of Clinical Oncology*. 1999; 17:2692–2692. [PubMed: 10561343]
3. Kachnic LA, Winter K, Myerson RJ, et al. RTOG 0529: a phase 2 evaluation of dose-painted intensity modulated radiation therapy in combination with 5-fluorouracil and mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal. *International Journal of Radiation Oncology* Biology* Physics*. 2013; 86:27–33.
4. Fowler JF, Lindstrom MJ. Loss of local control with prolongation in radiotherapy. *International Journal of Radiation Oncology* Biology* Physics*. 1992; 23:457–467.
5. Ohri N, Rapkin BD, Guha C, et al. Radiation Therapy Noncompliance and Clinical Outcomes in an Urban Academic Cancer Center. *International Journal of Radiation Oncology* Biology* Physics*. 2016
6. Lang K, Sussman M, Friedman M, et al. Incidence and costs of treatment-related complications among patients with advanced squamous cell carcinoma of the head and neck. *Archives of Otolaryngology–Head & Neck Surgery*. 2009; 135:582–588. [PubMed: 19528407]
7. Cipriano LE, Romanus D, Earle CC, et al. Lung cancer treatment costs, including patient responsibility, by disease stage and treatment modality, 1992 to 2003. *Value in Health*. 2011; 14:41–52. [PubMed: 21211485]
8. Tudor-Locke C, Burkett L, Reis J, et al. How many days of pedometer monitoring predict weekly physical activity in adults? *Preventive medicine*. 2005; 40:293–298. [PubMed: 15533542]
9. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the national cancer institute*. 1993; 85:365–376. [PubMed: 8433390]
10. Hanna N, Neubauer M, Yiannoutsos C, et al. Phase III study of cisplatin, etoposide, and concurrent chest radiation with or without consolidation docetaxel in patients with inoperable stage III non-small-cell lung cancer: The Hoosier Oncology Group and US Oncology. *Journal of clinical oncology*. 2008; 26:5755–5760. [PubMed: 19001323]
11. Vera-Llonch M, Oster G, Hagiwara M, et al. Oral mucositis in patients undergoing radiation treatment for head and neck carcinoma. *Cancer*. 2006; 106:329–336. [PubMed: 16342066]
12. Bamias A, Karina M, Papakostas P, et al. A randomized phase III study of adjuvant platinum/docetaxel chemotherapy with or without radiation therapy in patients with gastric cancer. *Cancer Chemother Pharmacol*. 2010; 65:1009–1021. [PubMed: 20130877]
13. Haj Mohammad N, Hulshof MC, Bergman JJ, et al. Acute toxicity of definitive chemoradiation in patients with inoperable or irresectable esophageal carcinoma. *BMC Cancer*. 2014; 14:56. [PubMed: 24485047]
14. Taylor AE, Olver IN, Sivanthan T, et al. Observer error in grading performance status in cancer patients. *Support Care Cancer*. 1999; 7:332–5. [PubMed: 10483818]

15. Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. *Br J Cancer*. 2001; 85:1634–9. [PubMed: 11742480]
16. Hutchinson TA, Boyd NF, Feinstein AR, et al. Scientific problems in clinical scales, as demonstrated in the Karnofsky index of performance status. *J Chronic Dis*. 1979; 32:661–6. [PubMed: 489706]

We performed a prospective trial demonstrating the feasibility of collecting activity data using a commercial fitness tracker during concurrent chemoradiotherapy for cancers of the head and neck, lung, or gastrointestinal tract. We also found that daily step count was a powerful predictor of short-term hospitalization risk. Activity monitoring should be explored as a tool to aid in the evaluation and management of patients receiving cancer therapy.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

Daily step count data. Each line represents one patient. Step counts are smoothed using a moving average function for clarity. Triangles denote patients' first hospital admissions.

Figure 2.

Patients' first hospitalizations during or after chemoradiotherapy. Tick mark indicates censoring due to loss to follow-up

Table 1

Patient Characteristics.

Age, median (range)	64 (33 to 82)
Gender, n (%)	
Male	23 (61%)
Female	15 (39%)
Diagnosis, n (%)	
Head and Neck Cancer	11 (29%)
Lung Cancer	13 (34%)
Gastrointestinal Cancer	14 (37%)
Esophageal Cancer	1 (3%)
Gastric Cancer	5 (13%)
Pancreatic Cancer	3 (8%)
Rectal Cancer	2 (5%)
Anal Cancer	3 (8%)
ECOG Performance Status, n (%)	
0	16 (42%)
1	19 (50%)
2	3 (8%)
Treatment Type, n (%)	
Preoperative	2 (5%)
Definitive	31 (82%)
Postoperative	5 (13%)
Radiotherapy Dose, median (range) *	54 Gy (45 to 70)

* excludes one patient whose treatment was discontinued after three fractions due to intracerebral hemorrhage causing hemiparalysis.

Table 2

Non-hematologic treatment-related toxicities.

	Number of Subjects (%)			
Toxicity	Grade 0	Grade 1	Grade 2	Grade 3
Cough	29 (76)	9 (23)	0 (0)	0 (0)
Dermatitis	12 (32)	14 (37)	12 (32)	0 (0)
Diarrhea	30 (79)	6 (16)	2 (5)	0 (0)
Dyspnea	29 (76)	6 (16)	3 (8)	0 (0)
Dysphagia/Esoophagitis	15 (39)	11 (29)	11 (29)	1 (3)
Fatigue	25 (66)	12 (32)	1 (3)	0 (0)
Oral Mucositis	19 (50)	12 (32)	7 (18)	0 (0)
Nausea	18 (47)	15 (39)	5 (13)	0 (0)
Pain	26 (68)	9 (23)	3 (8)	0 (0)
Vomiting	26 (68)	12 (32)	0 (0)	0 (0)
Xerostomia	28 (76)	9 (23)	1 (3)	0 (0)

Table 3

Cox regression models evaluating predictors of hospitalization.

	Univariate Models	
Covariate	HR (95% CI)	p-value
Daily Step Count (per 1000 [*])	0.62 (0.46, 0.83)	0.002
Age (per year)	1.03 (0.97, 1.09)	0.350
Male Gender (v. Female)	1.31 (0.45, 3.85)	0.625
Most Recent QoL Score	0.98 (0.96, 1.00)	0.104
Most recent ECOG PS		
0	[reference]	-
1	0.20 (0.06, 0.74)	0.016
2	0.98 (0.25, 3.83)	0.977
Diagnosis		
Head & Neck Cancer	[reference]	-
Lung Cancer	0.90 (0.27, 2.99)	0.870
GI Cancer	0.74 (0.20, 2.70)	0.647

^{*} Daily step count represents the average daily value over the past 3 days.