**Case report** 

# A Case Study of Exercise Adherence during Stereotactic Ablative Radiotherapy Treatment in a Previously Active Male with Metastatic Renal Cell Carcinoma

# Michael C. Hartland <sup>1</sup>, Kade Davison <sup>1</sup>, Maximillian J. Nelson <sup>1</sup>, Jonathan D. Buckley <sup>1</sup>, Gaynor Parfitt <sup>1</sup> and Joel T. Fuller<sup>2</sup>

<sup>1</sup> Alliance for Research in Exercise, Nutrition and Activity (ARENA), School of Health Sciences, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia; <sup>2</sup> Faculty of Medicine and Health Sciences, Macquarie University, New South Wales, Australia

#### Abstract

Stereotactic Ablative Radiotherapy (SABR) is increasingly replacing thoracotomy for resection of lung cancers and oligometastatic lung lesions but it is not known whether exercise can be maintained during SABR, the major side-effect of which is fatigue. This case study describes a 57-year-old male who exercised regularly (above American College of Sports Medicine minimum weekly exercise guidelines) and continued to exercise during SABR for a renal cell metastasis in his left lung. His exercise program included 5x60-minute moderate intensity aerobic exercise sessions and 3x45-minute resistance exercise sessions per week for 12 weeks post-treatment. Cardiorespiratory fitness and strength, as well as self-reported fatigue, depression, anxiety, physical wellbeing and sleep quality were assessed at baseline and fortnightly. Exercise adherence was 98% and no adverse events occurred. Fatigue was elevated from Weeks 2-8, which adversely impacted exercise intensity perception. Minimal changes were observed in cardiorespiratory fitness, depression, anxiety and sleep quality, but strength decreased, and physical wellbeing was improved above baseline levels. This is the first reported clinical case of exercise during SABR for a lung carcinoma. The data suggest that exercise may be feasible for patients undergoing SABR and may improve physical wellbeing. Larger controlled studies are needed to confirm these findings.

**Key words:** Supportive cancer care; aerobic exercise; resistance exercise; maximal oxygen uptake; muscle strength; fatigue.

## Introduction

In the United States in 2015 it was estimated that there were 221,220 new lung cancer diagnosis and 158,040 lives lost, with a 5-year relative survival rate reported to be as low as 18.0% (Siegel et al., 2015). Stereotactic Ablative Radiotherapy (SABR) is increasingly being used as a primary treatment for early stage lung carcinoma as well as in the treatment of oligometatstic lesions in selected patients. SABR involves the delivery of a small number of large, highly focused doses of radiation over few fractions using multiple small fields or arcs. A major proposed advantage of SABR over conventional external beam radiotherapy is reduced radiation toxicity as a result of a sharp dose gradient fall off beyond the tumour, and it has recently been reported to be as effective as surgery for early lung cancer with regard to treatment tolerance and survival outcomes (Chang et al., 2015; Videtic et al., 2013; Zimmermann et al., 2005).

A growing body of research has demonstrated numerous health benefits from exercise participation during and after cancer treatment (Fuller et al., 2018; Speck et al., 2010). In 2010, the American College of Sports Medicine (ACSM) released a roundtable consensus on exercise guidelines for cancer survivors that included evidence for the introduction or maintenance of exercise during treatment (Schmitz et al., 2010). These guidelines suggest that, unless specifically contraindicated, the goal for cancer patients and survivors should be the same as for age-matched healthy adults. Exercise can improve outcomes for cancer survivors by preserving muscle mass (Winters-Stone et al., 2011; Galvao et al., 2009) and cardiovascular health (Courneya et al., 2007; Courneya et al., 2003), attenuating fatigue (Fuller et al., 2018) and enhancing quality of life (Schneider et al., 2007; Courneya et al., 2003). However, while the ACSM guidelines recommend that cancer survivors aim to complete at least 150 minutes per week of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise (Speck et al., 2010), they also point out that given the diversity of cancers and treatment regimens, some of which may impact on the capacity to engage in exercise, a "one size fits all" approach to exercise prescription is not appropriate. As SABR is a newer treatment approach there are no published data indicating whether exercise can be maintained whilst undergoing treatment, the major side effect of which is fatigue (Lagerwaard et al., 2012; Haasbeek et al., 2011). The aim of this case study was to determine whether the ACSM exercise guidelines could be adhered to during SABR to the lung, and secondly to report on any changes in physiological or psychological function or wellbeing.

# **Case report**

## Patient

A 57-year-old male (height: 1.87m; mass: 93kg) presented for an opinion regarding treatment for a metastatic renal cell carcinoma situated in the superior lobe of the left lung. The metastasis was detected on routine follow-up Computed Tomography imaging. It developed at the site of previous metastectomy for pathologically proven renal cell carcinoma. Aside from the renal metastasis, the patient presented in good health, had professional qualifications in exercise science and was completing 435 minutes of gymbased moderate-intensity exercise per week, which is above the minimum threshold of the ACSM guidelines for healthy populations and cancer survivors. Weekly exercise included 5 x 60 minutes of cycling on a stationary bike at a moderate intensity (rating of perceived exertion [RPE] = 13) and 3 x 45 minutes of resistance exercise.

The patient's previous oncology history included a parotidectomy to remove pleomorphic adenomas (January 2010), a thyroidectomy via full neck dissection for papillary thyroid cancer (October 2010), a simple left nephrectomy to treat stage 1 renal cell carcinoma (November 2010), radioactive iodine treatment to treat papillary thyroid cancer (December 2010), external beam radiotherapy (30 fractions over 6 weeks) to treat thyroid cancer N1bspread to lymph nodes at other cervical levels on the sides of the neck (February 2011), a robotic-assisted laparoscopic radical prostatectomy for stage 1 prostate cancer (June 2013), and a metastectomy for pathologically proven renal cell carcinoma to the superior lobe of the left lung (December 2013). The stage 2 renal carcinoma reoccurred in the superior lobe of the left lung at the time of this case study (June 2015).

The renal cell metastasis in the left lung was treated with a course of SABR that consisted of 48 Gy in four fractions on alternate days (i.e. over an 8-day period) dosed to the 74% isodose line using a 3D conformal SABR technique. Outcome measures were assessed prior to SABR treatment and then fortnightly for 12 weeks. All measurements were recorded at least 4 hours fasted and 24 hours after any exercise. The patient's treating medical team were made aware of all symptoms throughout the study. The patient provided written informed consent prior to participation. The University of South Australia Human Research Ethics Committee indicated that ethical approval was not required for this study because the patient is an author of the case study and consents to its publication. All procedures conformed to the Declaration of Helsinki.

#### **Exercise program**

The exercise program was advised and monitored by an Accredited Exercise Physiologist (AEP; Exercise and Sport Science Australia, QLD, Australia). The patient maintained his pre-diagnosis exercise regime throughout the observation period. Aerobic exercise was performed on a stationary bicycle at 60-70% maximum heart rate (HR max), which was equivalent to the patient's pre-treatment aerobic exercise intensity of RPE 13. HR based intensity was used instead of RPE because the patient's high fatigue made it difficult for him to perform any exercise at all without exceeding RPE 13.

Resistance training involved 6 exercises (chest press, upright seated row, triceps extension, biceps curl, chest fly, shoulder extension) performed using 3 sets of 8-10 repetitions for each exercise. Progression of resistance training focused on increasing resistance and then repetitions whereby once three sets of ten repetitions could be accomplished weight was increased to the next increment. Exercise progression took into consideration degenerative changes in the shoulder of the patient. Progression was delayed if increasing the exercise resistance caused large increases in shoulder pain.

#### Primary outcome measure

The primary outcome of interest was continued adherence to the patient's pre-treatment exercise program. Adherence was defined as a composite measure comprising scores of exercise session attendance, exercise intensity compliance and exercise contamination. Attendance referred to the number of minutes of exercise achieved per week as a percentage of the number of minutes prescribed. The patient recorded physical activity using the Godin leisure time index (Godin and Shephard, 1997). Contamination referred to any change in physical activity modes from baseline participation (i.e. commencing a new type of exercise program). Compliance referred to meeting the prescribed intensity of exercise and was reported as a percentage. Aerobic exercise compliance was based on the patient's ability to meet the prescribed intensity of 60-70% HR max. Mean aerobic exercise compliance was calculated across exercise sessions. Resistance exercise was prescribed in sets and repetitions and the percentage of the total prescribed load was used to measure compliance. For example, if 3 x 8 repetitions of a 20 kg biceps curl were prescribed the total prescribed load was 480 kg, and if 3 x 6 20 kg repetitions were completed, compliance was 360/480 = 75%. This process was repeated for each resistance exercise and session to determine the mean resistance exercise compliance. Overall compliance was defined as the mean of aerobic and resistance exercise compliance. Overall adherence was calculated as the mean of overall compliance and attendance plus or minus any contamination. Exercise test protocols performed for the purpose of this case study were not considered as contamination.

#### Secondary outcome measures

Maximal oxygen uptake (VO<sub>2Max</sub>) was measured using an indirect calorimeter (ParvoMedics TrueOne 2400, Parvo Medics, USA) during an incremental exercise test to exhaustion on an electronically braked cycle ergometer (Ergoselect 200, Ergoline, Germany). HR was recorded throughout using a personal HR monitor (RS800CX, Polar Electro OY, Finland) to facilitate prescription of relative aerobic exercise intensity. A ramp protocol was used where power output commenced at 80 watts and increased by 15 watts per minute until exhaustion. The criteria for a valid VO<sub>2Max</sub> test was identified as a plateau in VO<sub>2</sub> with increasing exercise intensity and an RER >1.1 based on the most commonly used criteria in previous studies (Midgley et al., 2007). An additional sub-maximal perceptually regulated exercise test (PRET) to predict VO2Max was performed on alternate weeks to the actual VO<sub>2Max</sub> testing and comprised 4 stages of 3-minute duration at RPE 9, 11, 13, and 15 based on the Borg 6-20 scale (Borg, 1998). This was conducted in accordance with the validated methodology published previously (Eston et al., 2008). The participant adjusted the power output of the bike to achieve the necessary RPE during the first 30 seconds of each 3-minute exercise stage. Power output, HR and VO<sub>2</sub> were recorded during each 3-minute exercise stage to assess effects of SABR on the relationship of RPE with power output, HR and  $\dot{VO}_2$ . A difference of 7.5% was considered the minimal detecta-

The patient's 8-repetition maximum (8RM) for the seated row and biceps curl was used to assess upper body muscle strength. Strength testing using 8RM is reliable (Taylor and Fletcher, 2012), valid (Taylor and Fletcher, 2013) and specific to the 3 sets of 8-10 repetitions that were used in the patient's exercise program. A difference of 10.0% was considered the minimal detectable change in 8RM based on previous test-retest (Romano et al., 2013) and population sample (Segal et al., 2009) data collected during upper body exercises. Upper body exercises involving pushing movements (such as chest or shoulder presses) could not be performed at the intensity required for 8RM testing without pain due to severe osteoarthritis. Similarly, lower body strength was not assessed, due to knee osteoarthritis. Grip strength in the dominant hand was measured using a hand-grip dynamometer (Jamar, Illinois, USA). A difference of 13.2% was considered the minimal detectable change in grip strength based on previous test-retest data collected in older adults (Wang and Chen, 2010).

Blood pressure and HR were measured in supine using digital oscilometry (A and D Medical Saltama, Japan) following fifteen minutes of rest. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were measured by spirometry (Model 6000 Alpha, Vitalograph, Ennis, Ireland) with the best of three measures recorded. The minimum detectable change in FVC and FEV1 was 330 and 160 ml, respectively (Tweeddale et al., 1987). Disability associated with breathlessness was assessed using the Medical Research Council (MRC) breathlessness scale (Stenton, 2008). The MRC breathlessness scale consists of five statements that describe a range of respiratory disability from none (Grade 1) to almost complete incapacity (Grade 5) (Bestall et al., 1999).

Physical wellbeing was assessed using the Functional Assessment of Cancer Therapy-Lung (FACT) physical wellbeing subscale (Yellen et al., 1997). A difference  $\geq 3$  was considered the minimally important difference in physical wellbeing (Steel et al., 2006). The Hospital Anxiety and Depression Scale (HADS), a 14-item selfreport screening tool, was used to assess anxiety and depression (Zigmond and Snaith, 1983). The HADS used cutoff scores based on the severity of anxiety and depression, dividing patients into four categories: normal (score  $\leq 7$ ), mild (score 8-10), moderate (score 11-14), and severe (score >14). Fatigue was measured using the 9-item Brief Fatigue Inventory (BFI). The patient scored each item on a 0-10 numeric scale, with 0 indicating "no fatigue" and 10 indicating "fatigue as bad as you can imagine" (Mendoza et al., 1999). A global fatigue score was determined by calculating the average score across the 9 items and used to categorise the patient as experiencing mild (score  $\leq 3$ ), moderate (score 4-6) or severe (score >6) fatigue. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI), a nine item self-rated questionnaire which assessed sleep quality and disturbances, with a score greater than five indicating that the person was a poor sleeper (Buysse et al., 1989).

## Statistical analysis

Changes in cardiorespiratory fitness and health, and muscle strength from baseline were compared against minimum detectable change values reported in the literature. Changes from baseline that were greater than the minimum detectable change were considered likely to be true changes. Minimum detectable changes in VO<sub>2Max</sub>, 8RM, and grip strength were calculated from test-retest reliability results reported in the literature using MDC = $1.96\sqrt{2(SEM)}$ , where MDC is the minimum detectable change and SEM is the standard error of measurement. When previous literature had reported the intra-class correlation coefficient (ICC) instead of the SEM, the SEM was calculated using  $SEM = SD\sqrt{1 - ICC}$ , where SD is the group standard deviation. Typical errors for each outcome measure were calculated based on the standard deviation of the repeated measurements that were taken on the patient from baseline to Week 12.

# Results

No adverse events arose during the study period although the patient did report 6/10 pain on a numeric pain rating scale for the ribs adjacent to the site of SABR, which was anticipated by the treating radiation oncologist. This discomfort did not stop the patient from exercising and the patient did not request pharmacological pain management from his treating medical team. The patient maintained his 435 minutes of weekly gym-based exercise throughout the treatment and recovery phase with an attendance rate of 100%. Compliance to aerobic training was 100% based on HR measures of exercise intensity. Compliance to resistance training was 96% with sets and reps being maintained from baseline, but at a reduced load by 10% per exercise from Week 2 due to fatigue. The Godin Leisure Time Index scores did not change during the study observation period indicating no exercise contamination. Thus, the overall adherence rate for the intervention was 98%.

Despite maintaining his pre-treatment exercise regime, the patient experienced several changes in physiological and psychological measurements over the observation period. Following treatment,  $\dot{V}O_{2Max}$  as measured by the incremental test to exhaustion, was slightly decreased (~7% reduction) at Weeks 2, 4, and 6 (Figure 1), but these reductions were less than the minimum detecatable change (7.5%). The patient was able to reach a valid  $\dot{V}O_{2Max}$  in all seven tests over the 12 week period, as evidenced by a plateau in  $\dot{V}O_2$  despite increasing power output, RER>1.10, and HR in excess of his age predicted maximum.

In contrast to the incremental test to exhaustion, the PRET prediction of  $\dot{VO}_{2Max}$  was decreased by over 50% six weeks after treatment and remained 9% below baseline values at the end of the 12-week observation period (Figure 1). These reductions in predicted  $\dot{VO}_{2Max}$  were all greater than the minimum detectable change (7.5%). Before treatment, the aerobic exercise intensity of RPE 13 corresponded to a HR of 120 bpm but after one radiation dose it corresponded to 90 bpm (which represented only a light intensity when expressed as %HR max) and a HR of 120 bpm corresponded to an RPE of 17 (which represented a very hard intensity based on perceived level of exertion).



Figure 1. Maximal oxygen uptake assessed by an incremental exercise test to exhaustion and a sub-maximal perceptually regulated exercise test (PRET) before and 12 weeks after stereotactic ablative body radiation therapy. A difference of 2.3 ml/kg/min was considered the minimal detectable change based on previous test-retest data. Typical errors for the patient were 1.0 ml/kg/min (incremental exercise test) and 5.5 ml/kg/min (PRET). \* Decreased from baseline by more than the minimum detectable change.

	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	<b>Typical Error</b>					
Muscle Strength													
Upright row 8RM (kg)	40.0	33.0*	33.0*	33.0*	33.0*	33.0*	33.0*	2.6					
Bicep curl 8RM (kg)	15.0	12.5*	12.5*	12.5*	12.5*	12.5*	12.5*	0.9					
Hand-grip dynamometer (kg)	37.0	35.0	34.0	33.0	33.0	36.0	36.0	1.6					
Cardiorespiratory Health													
Heart rate resting (bpm)	54	56	54	52	57	52	56	2					
Systolic blood pressure (mmHg)	128	128	129	133	126	129	117	5					
Diastolic blood pressure (mmHg)	73	70	77	72	70	71	61	5					
FVC (L)	5.44	5.08*	5.20	5.32	5.18	5.20	5.24	0.11					
FEV1 (L)	4.31	4.06*	4.12*	4.17	4.07*	4.15	4.16	0.08					
MRC breathlessness scale (Grade 1-5)	1	2	3	3	1	1	1	1					

 Table 1. Muscle strength and cardiorespiratory health at baseline and 12 weeks after stereotactic ablative body radiation therapy.

8RM, eight-repetition maximum; FEV1, forced expiratory volume in 1-second; FVC, forced vital capacity; MRC, Medical Research Council. \* Decreased from baseline by more than the minimum detectable change.

The patient's 8RM for the upright row and bicep curl decreased following treatment by 18% and 17%, respectively (Table 1). These values remained decreased at Week 12 (Table 1). Reductions in 8RM were greater than the minimum detectable change (10.0%). Grip strength was slightly reduced following treatment (<11% reduction) at Week 2, 4, 6, and 8 (Table 1). These reductions were less than the minimum detectable change (13.2%).

The patient's FVC reduced by more than the minimum detectable change (330 ml) at Week 2 following treatment (Table 1). The patient's FEV1 reduced by more than the minimum detectable change (160 ml) at Week 2, Week 4, and Week 8 following treatment (Table 1). The patient reported increased disability due to breathlessness for the first 6 weeks after treatment (Table 1). The patient reported shortness of breath when hurrying or walking up a slight hill (MRC Grade 2) for the first 6 weeks and walking slower than most people on level ground due to breathlessness (MRC Grade 3) from Week 2 to Week 6 following treatment (Table 1).

Self-reported fatigue increased from mild (BFI = 1) at baseline to moderate (BFI = 6) at Week 2 and severe (BFI = 7) at Weeks 4 and 6 (Table 2). The patient was still reporting moderate fatigue (BFI = 4) at Week 12.

The patient's physical wellbeing assessed with the FACT-F decreased from baseline by more than the

	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Typical Error				
FACT-F												
Physical wellbeing	15	16	12*	12*	16	18†	19†	3				
Hospital Anxiety & Depression Scale												
Depression [qualitative descriptor]	17 [severe]	18 [severe]	17 [severe]	17 [severe]	16 [severe]	16 [severe]	16 [severe]	1				
Anxiety [qualitative descriptor]	19 [severe]	20 [severe]	19 [severe]	19 [severe]	15 [severe]	15 [severe]	15 [severe]	2				
Brief Fatigue Inventory												
Fatigue [qualitative descriptor]	1 [mild]	6 [moderate]	7 [severe]	7 [severe]	5 [moderate]	4 [moderate]	4 [moderate]	2				
Pittsburgh Sleep Quality Index												
Sleep quality [qualitative descriptor]	15 [poor]	14 [poor]	15 [poor]	15 [poor]	12 [poor]	12 [poor]	13 [poor]	1				
Duration of sleep (hours)	5	5	5	5	6	6	5	<1				

Table 2. Patient reported outcomes at baseline and 12 weeks after stereotactic ablative body radiation therapy.

\* Physical wellbeing decreased from baseline by more than the minimally important difference. † Physical wellbeing increased from baseline by more than the minimally important difference.

minimally important difference at Week 4 and 6 (Table 2). However, physical wellbeing improved after Week 6 and was increased from baseline by more than the minimally important difference at Week 12 (Table 2).

The patient reported severe depression and anxiety scores on the HADS at baseline and throughout the 12week post-treatment observation period (Table 2). Similarly, the patient reported poor sleep quality on the PSQI at baseline and each post-treatment assessment (Table 2).

# Discussion

The principal findings from this case study were that ACSM guidelines for exercise could be maintained by an already active patient while undergoing a cancer treatment that is recognized for producing high levels of fatigue, and that physical and psychological function remained relatively unchanged. Notably, the patient's perception of their physical wellbeing was increased above baseline levels by the end of the intervention, which suggests there may be benefits to maintaining ACSM exercise guidelines during SABR that should be investigated in future controlled studies. The level of exercise participation achieved during and post SABR treatment may not have been possible under the alternate treatment option of thoracotomy, which is associated with long recuperation periods and permanently reduced lung function (Gottschalk et al., 2006; Reeve et al., 2010).

This was the first investigation into the feasibility of maintaining an exercise clinic-based aerobic and resistance exercise program in a cancer patient undergoing lung SABR. Case study research provides unique insights into the feasibility and efficacy of management strategies applied in real-world settings. This is particularly relevant for exercise-based management strategies in cancer patients because it is recognized that exercise prescriptions need to be individualized based on each patients' fitness, comorbidities, medical management, treatment side-effects, and disease trajectory (Schmitz et al., 2010). Although findings of this case study should be generalized with caution, the opportunity to report a detailed individualized response in a case study format has important value for clinicians looking to implement this approach in practice.

Traditionally most investigators report adherence as a percentage of the number of sessions attended out of a total possible number of prescribed sessions (Knols et al., 2005; Pinto et al., 2009). However, this approach provides limited insight into how well the prescribed exercise dose was achieved (Nilsen et al., 2018). In this investigation it was considered more accurate to report exercise adherence as a composite measure including measures of both session attendance and exercise intensity compliance with each having equal weighting in the final adherence score. With respect to attendance, exercise trials in lung cancer patients typically report it between 72 to 85% (Jones et al., 2007; 2008; 2009). The higher attendance in the current study may be due to the patients' previous exercise history which indicated that he was exceeding ACSM physical activity guidelines (Speck et al., 2010), combined with being an exercise professional with undergraduate qualifications in exercise science. Studies have previously reported a positive relationship between pre-treatment exercise behaviour and attendance in exercise interventions during cancer treatment (Courneya et al., 2002; 2004).

The increase in fatigue reported in the current study is not uncommon, with fatigue being one of the most reported unmanaged symptoms of cancer patients post radiotherapy (Mock et al., 2001; Curt et al., 2000). The precise mechanisms driving radiotherapy induced fatigue have yet to be determined but are expected to include physiological, haematological and psychological factors. The patient maintained his regular exercise regime despite the accumulation of very high fatigue. However, he did indicate that the use of HR guided intensity rather than RPE made it uncomfortable and difficult to maintain due to this resulting in a very high RPE during exercise. This presents an issue for clinicians in selecting suitable exercise intensities, particularly for sedentary cancer patients and survivors unaccustomed to exercise and experiencing fatigue. A recent report by Dennett favoured moderate intensity exercise regardless of prescription methods (Dennett et al., 2016). The difficulty lies in quantifying what constitutes moderate intensity exercise during cancer treatments as this case report suggests that there is dissociation between actual (i.e. HR) and perceived (i.e. RPE) intensity with radiation treatment. We speculate that the disassociation is likely caused by the increased fatigue and breathlessness that was reported by the patient. Alternatively, haematological changes (i.e. anaemia) are common in cancer patients (Stone and Minton, 2008) and could increase perceived exercise intensity. However, haematological side effects are expected to be less for SABR treatment compared to conventional

radiation therapy (Chang, 2015) so this explanation may be less likely. Nevertheless, it could be argued that immediately post-treatment RPE 13 may be the more appropriate moderate intensity prescription given that 60-70% of HR maximum proved difficult to maintain.

Aside from the baseline measurements, the PRET estimates of  $VO_{2Max}$  did not approximate the  $\dot{V}O_{2Max}$  values obtained from the incremental test to exhaustion. This finding contrasts with the expected high levels of agreement between PRET and incremental test to exhaustion measurements of VO<sub>2Max</sub> (Eston et al., 2008). Notably, fluctuations in the PRET estimates of VO<sub>2Max</sub> appeared to more closely match the fluctuations in BFI and the MRC than the incremental test to exhaustion, FVC and FEV1. The PRET, BFI and MRC are all perception-based measurements, which may explain why they tended to behave similarly. If correct, the changes witnessed in the PRET in the first week were more likely the result of fatigue from the SABR treatment as opposed to actual reductions in cardiorespiratory fitness because maximum aerobic capacity demonstrated only minimal fluctuations that were less than the minimum detectable change. This finding may have important implications for using PRET to establish and track exercise capacity during cancer treatment, but this requires further research in larger cohorts.

Anecdotally, the patient reported that maintaining exercise participation based on HR, which resulted in a high RPE, encouraged feelings of empowerment as he expected the exercise program would improve his chances of survival. These reflections were not supported in the depression and anxiety reporting from the HADS, which remained in the severe category throughout the intervention. This is inconsistent with the literature where exercise participation during treatment has been shown to enhance mood state (Fuller et al., 2018). These contrasting results may be partially attributed to the patient being unsure whether SABR treatment had been successful until after this observation was completed. As such, his uncertainty about the efficacy of choosing this newer treatment over the more widely used surgical approach may have exacerbated feelings of depression and anxiety, although this cannot be determined from the current data as it was not possible to include a control condition.

Notably, the patient reported physical wellbeing scores were improved above baseline scores by the end of the intervention period, indicating a potential benefit of exercise on post-SABR quality of life. This is consistent with previously reported benefits of exercise on quality of life in patients undergoing other forms of cancer treatment (Fuller et al., 2018). Objective measures of strength and cardiovascular fitness were not improved above baseline but this maintenance can be considered a positive outcome given the potential for deterioration due to cancer and side effects of treatment (Lakoski et al., 2012). It is unlikely that the patient's improved physical wellbeing can be attributed to strength and fitness benefits of exercise because those outcomes did not change. Instead, it is possible that the improvement related to dimensions of the FACT physical wellbeing subscale (i.e. "I have nausea", "I have pain", "I feel ill") that are somewhat independent of muscle strength and cardiovascular fitness. Moreover, the subjective nature of the physical wellbeing scores may have contributed to the apparent improvement. The baseline measures were taken in the context of a known metastatic lung carcinoma that was pending treatment whereas the post intervention measures were taken when the patient had seemingly successfully completed the treatment process. This contextual difference may have resulted in lower self-reported physical wellbeing scores at baseline.

Aside from the typical sample size issues associated with a case study, an important consideration in interpreting this study is that it reports on a highly motivated individual with a professional background in exercise science. The subject of this case study is also a doctoral research student and an author of this manuscript, which may have contributed in part to higher motivation and subsequently his adherence rate to the exercise. However, every effort was made to ensure rigour and objectivity in the data collected to avoid any bias. Some of the key observations of this study including the changes in mood and fatigue have occurred largely in spite of the motivations and unconscious bias of the subject rather than as a result of them. The high adherence needs to be interpreted in the context of very high motivation, but the other observations are valid and robust indicators of the physiological and psychological response to the treatment process. Additionally, the observation that the high motivation and adherence in this case study might be linked to the patient's exercise science knowledge highlights the importance of patient education within any exercise intervention.

# Conclusion

The ACSM and many other key organisations suggest that exercising during and after cancer treatment can aid in attenuating issues such as muscle degeneration, reduced cardiovascular health, fatigue, loss of function and reduced quality of life. Clinical trials are now showing that SABR may rival surgery as first line treatment for localized cancers, and the non-invasive protocol means an individual can continue exercising, thereby maintaining their strength, cardiovascular health and physical function, as well as potentially mitigating symptoms of fatigue and negative changes in health-related quality of life. This potential for improved exercise remains untested in large controlled studies and conclusive inferences cannot be made based on this case study. Nevertheless, the fact that the patient was able to maintain exercise behaviours during and after SABR is an important observation, as is the divergence of RPE and HR-based methods of exercise intensity prescription. Further research, using controlled study designs, is required to confirm these findings and determine what clinical benefits might accrue from prescribing exercise based on these different methods for defining intensity.

## Acknowledgements

No sources of funding were used to complete this research. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The case study described in this article complies with the current laws of the country in which they were performed. One of the authors was the subject of this case study. The authors declare no other conflicts of interest.

#### References

- Bestall, J.C., Paul, E.A., Garrod, R., Garnham, R., Jones, P., Wedzicha, J. (1999) Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 54, 581-586.
- Borg, G. (1998) Borg's perceived exertion and pain scales. Human kinetics, Champaign, IL.
- Buysse, D.J., Reynolds, C.F. 3rd, Monk, T.H., Berman, S.R., and Kupfer, D.J. (1989) The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28, 193-213.
- Chang, J.Y. (2015) Stereotactic ablative radiotherapy: aim for a cure of cancer. Annals of Translational Medicine 3, 12.
- Chang, J.Y., Senan, S., Paul, M.A., Mehran, R.J., Louie, A.V., Balter, P., Groen, H.J., McRae, S.E., Widder, J., Feng, L. and van den Borne, B.E. (2015) Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *The Lancet Oncology* 16, 630-637.
- Courneya, K.S., Friedenreich, C.M., Sela, R.A., Quinney, H.A. and Rhodes, R.E. (2002) Correlates of adherence and contamination in a randomized controlled trial of exercise in cancer survivors: an application of the theory of planned behavior and the five factor model of personality. *Annals of Behavioral Medicine* 24, 257-268.
- Courneya, K.S., Mackey, J.R., Bell, G.J., Jones, L.W., Field, C.J. and Fairey, A.S. (2003) Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. *Journal of Clinical Oncology* 21, 1660-1668.
- Courneya, K.S., Segal, R.J., Mackey, J.R., Gelmon, K., Reid, R.D., Friedenreich, C.M., Ladha, A.B., Proulx, C., Vallance, J.K., Lane, K. and Yasui, Y. (2007) Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *Journal of Clinical Oncology* 25, 4396-4404.
- Courneya, K.S., Segal, R.J., Reid, R.D., Jones, L.W., Malone, S.C., Venner, P.M., Parliament, M.B., Scott, C.G., Quinney, H.A. and Wells, G.A. (2004) Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. *Journal of Clinical Epidemiology* 57, 571-579.
- Curt, G.A., Breitbart, W., Cella, D., Groopman, J.E., Horning, S.J., Itri, L.M., Johnson, D.H., Miaskowski, C., Scherr, S.L., Portenoy, R.K. and Vogelzang, N.J. (2000) Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. *The Oncologist* 5, 353-360.
- Dennett, A.M., Peiris, C.L., Shields, N., Prendergast, L.A. and Taylor, N.F. (2016) Moderate-intensity exercise reduces fatigue and improves mobility in cancer survivors: a systematic review and meta-regression. *Journal of Physiotherapy* 62, 68-82.
- Eston, R., Lambrick, D., Sheppard, K. and Parfitt, G. (2008). Prediction of maximal oxygen uptake in sedentary males from a perceptually regulated, sub-maximal graded exercise test. *Journal of Sports Sciences* **26**, 131-139.
- Fuller, J.T., Hartland, M.C., Maloney, L.T. and Davison, K. (2018) Therapeutic effects of aerobic and resistance exercises for cancer survivors: a systematic review of meta-analyses of clinical trials. *British Journal of Sports Medicine* 52, 1311.
- Galvao, D.A., Taaffe, D.R., Spry, N., Joseph, D. and Newton, R.U. (2009) Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. *Journal of Clinical Oncology* 28, 340-347.
- Godin, G., and Shephard, R. (1997) Godin leisure-time exercise questionnaire. *Medicine and Science in Sports and Exercise* 29, 36-38.
- Gottschalk, A., Cohen, S.P., Yang, S. and Ochroch, E.A. (2006) Preventing and treating pain after thoracic surgery. *Anesthesiology* 104, 594-600.
- Haasbeek, C.J., Lagerwaard, F.J., Slotman, B.J. and Senan, S. (2011) Outcomes of stereotactic ablative radiotherapy for centrally

located early-stage lung cancer. *Journal of Thoracic Oncology* **6**, 2036-2043.

- Jones, L.W., Eves, N.D., Peddle, C.J., Courneya, K.S., Haykowsky, M., Kumar, V., Winton, T.W. and Reiman, T. (2009) Effects of presurgical exercise training on systemic inflammatory markers among patients with malignant lung lesions. *Applied Physiology*, *Nutrition, and Metabolism* 34, 197-202.
- Jones, L.W., Eves, N.D., Peterson, B.L., Garst, J., Crawford, J., West, M.J., Mabe, S., Harpole, D., Kraus, W.E. and Douglas, P.S. (2008). Safety and feasibility of aerobic training on cardiopulmonary function and quality of life in postsurgical nonsmall cell lung cancer patients: a pilot study. *Cancer* 113, 3430-3439.
- Jones, L.W., Peddle, C.J., Eves, N.D., Haykowsky, M.J., Courneya, K.S., Mackey, J.R., Joy, A.A., Kumar, V., Winton, T.W. and Reiman, T. (2007) Effects of presurgical exercise training on cardiorespiratory fitness among patients undergoing thoracic surgery for malignant lung lesions. *Cancer* 110, 590-598.
- Knols, R., Aaronson, N.K., Uebelhart, D., Fransen, J. and Aufdemkampe, G. (2005) Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. *Journal of Clinical Oncology* 23, 3830-3842.
- Kohrt, W.M., Malley, M.T., Coggan, A.R., Spina, R.J., Ogawa, T., Ehsani, A.A., Bourey, R.E., Martin, W.H. 3rd and Holloszy, J.O. (1991) Effects of gender, age, and fitness level on response of VO2max to training in 60-71 yr olds. *Journal of Applied Physiology* **71**, 2004-2011.
- Lagerwaard, F.J., Verstegen, N.E., Haasbeek, C.J., Slotman, B.J., Paul, M.A., Smit, E.F. and Senan, S. (2012) Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. *International Journal of Radiation* Oncology · Biology · Physics 83, 348-353.
- Lakoski, S.G., Eves, N.D., Douglas, P.S., Jones, L.W. (2012) Exercise rehabilitation in patients with cancer. *Nature Reviews Clinical Oncology* 9, 288-296.
- Mendoza, T.R., Wang, X.S., Cleeland, C.S., Morrissey, M., Johnson, B.A., Wendt, J.K. and Huber, S.L. (1999) The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer* 85, 1186-1196.
- Midgley, A.W., McNaughton, L.R., Polman, R. and Marchant, D. (2007) Criteria for determination of maximal oxygen uptake: a brief critique and recommendations for future research. *Sports Medicine* 37, 1019-1028.
- Mock, V., Pickett, M., Ropka, M.E., Lin, E.M., Stewart, K.J., Rhodes, V.A., McDaniel, R., Grimm, P.M., Krumm, S. and McCorkle, R. (2001) Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Practice* 9, 119-127.
- Nilsen, T.S., Scott, J.M., Michalski, M., Capaci, C., Thomas, S.M., Herndon, J.E. Sasso, J., Eves, N.N., Jones, L.W. (2018) Novel methods for reporting of exercise dose and adherence: An exploratory analysis. *Medicine and Science in Sports and Exercise* 50, 1134-1141.
- Pinto, B.M., Rabin, C. and Dunsiger, S. (2009) Home-based exercise among cancer survivors: adherence and its predictors. *Psycho-Oncology* 18, 369-376.
- Reeve, J., Stiller, K., Nicol, K., McPherson, K.M., Birch, P., Gordon, I.R. and Denehy, L. (2010) A postoperative shoulder exercise program improves function and decreases pain following open thoracotomy: a randomised trial. *Journal of Physiotherapy* 56, 245-252.
- Romano, N., Vilaça-Alves, J., Fernandes, H.M., Saavedra, F., Paz, G., Miranda, H., Simão, R., Novaes, J. and Reis, V. (2013) Effects of resistance exercise order on the number of repetitions performed to failure and perceived exertion in untrained young males. *Journal of Human Kinetics* 39, 177-183.
- Schmitz, K.H., Courneya, K.S., Matthews, C., Demark-Wahnefried, W., Galvão, D.A., Pinto, B.M., Irwin, M.L., Wolin, K.Y., Segal, R.J., Lucia, A. and Schneider, C.M. (2010) American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Medicine and Science in Sports and Exercise* 42, 1409-1426.
- Schneider, C.M., Hsieh, C.C., Sprod, L.K., Carter, S.D. and Hayward, R. (2007) Cancer treatment-induced alterations in muscular fitness and quality of life: the role of exercise training. *Annals of Oncology* 18, 1957-1962.
- Segal, R.J., Reid, R.D., Courneya, K.S., Sigal, R.J., Kenny, G.P.,

Prud'Homme, D.G., Malone, S.C., Wells, G.A., Scott, C.G. and Slovinec D'Angelo, M.E. (2009) Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. *Journal of Clinical Oncology* **27**, 344-351.

- Siegel, R.L., Miller, K.D. and Jemal, A. (2015) Cancer statistics, 2015. CA: a Cancer Journal for Clinicians 65, 5-29.
- Speck, R.M., Courneya, K.S., Mâsse, L.C., Duval, S. and Schmitz, K.H. (2010) An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Journal of Cancer Survivorship* 4, 87-100.
- Steel, J.L., Eton, D.T., Cella, D., Olek, M.C. and Carr, B.I. (2006) Clinically meaningful changes in health-related quality of life in patients diagnosed with hepatobiliary carcinoma. *Annals of Oncology* 17, 304-312.
- Stenton, C. (2008) The MRC breathlessness scale. Occupational Medicine 58, 226-227.
- Stone, P.C. and Minton, O. (2008) Cancer-related fatigue. European Journal of Cancer 44, 1097-1104
- Taylor, J.D. and Fletcher, J.P. (2012) Reliability of the 8-repetition maximum test in men and women. *Journal of Science and Medicine in Sport* 15, 69-73.
- Taylor, J.D. and Fletcher, J.P. (2013) Correlation between the 8-repetition maximum test and isokinetic dynamometry in the measurement of muscle strength of the knee extensors: A concurrent validity study. *Physiotherapy Theory and Practice* **29**, 335-341.
- Tweeddale, P.M., Alexander, F. and McHardy, G.J. (1987) Short term variability in FEV1 and bronchodilator responsiveness in patients with obstructive ventilatory defects. *Thorax* 42, 487-490.
- Videtic, G.M., Reddy, C.A. and Sorenson, L. (2013) A prospective study of quality of life including fatigue and pulmonary function after stereotactic body radiotherapy for medically inoperable earlystage lung cancer. *Supportive Care in Cancer* 21, 211-218.
- Wang, C.Y. and Chen, L.Y. (2010) Grip strength in older adults: testretest reliability and cutoff for subjective weakness of using the hands in heavy tasks. *Archives of Physical Medicine and Rehabilitation* 91, 1747-1751.
- Winters-Stone, K.M., Dobek, J., Nail, L., Bennett, J.A., Leo, M.C., Naik, A. and Schwartz, A. (2011) Strength training stops bone loss and builds muscle in postmenopausal breast cancer survivors: a randomized, controlled trial. *Breast Cancer Research and Treatment* 127, 447-456.
- Yellen, S.B., Cella, D.F., Webster, K., Blendowski, C. and Kaplan, E. (1997) Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. Journal of Pain and Symptom Management 13, 63-74.
- Zigmond, A.S. and Snaith, R.P. (1983) The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* **67**, 361-370.
- Zimmermann, F.B., Geinitz, H., Schill, S., Grosu, A., Schratzenstaller, U., Molls, M. and Jeremic, B. (2005) Stereotactic hypofractionated radiation therapy for stage I non-small cell lung cancer. *Lung Cancer* 48, 107-114.

# **Key points**

- This is the first reported clinical case of exercise during stereotactic ablative radiotherapy for a lung carcinoma.
- Fatigue during and after stereotactic ablative radiotherapy altered the relationship between the perception of exercise intensity and heart rate and compromised the rating or perceived exertion-based exercise prescription.
- The patient's ability to adhere to the exercise and the lack of adverse events suggests that continuing to exercise may be feasible for patients undergoing stereo-tactic ablative radiotherapy.
- Exercise improved physical wellbeing, but larger randomised controlled studies are needed to confirm this finding.

#### AUTHOR BIOGRAPHY



Michael C. HARTLAND Employment

Lecturer, Division of Health Sciences, University of South Australia, Adelaide, Australia. Degree

# B.Ex.Phys(Hons)

**Research Interests** 

Exercise based interventions for improving the health of cancer survivors.

E-mail: Michael.hartland@unisa.edu.au

#### Kade DAVISON Employment

Program Director for Clinical Exercise Physiology

Degree

PhD

#### **Research Interests**

Clinical Exercise Service Models, Exercise Oncology, Exercise Physiology. **E-mail:** kade.davison@unisa.edu.au

Maximillian J. NELSON

# Employment

Lecturer in Exercise and Sport Science, Division of Health Sciences, University of South Australia, Adelaide, Australia Degree

#### PhD Research Interests

Exercise induced fatigue, performance, physical training, autonomic dysfunction, recovery

**E-mail:** max.nelson@unisa.edu.au





# Jonathan D. BUCKLEY

#### Employment

Professor, Division of Health Sciences, University of South Australia, Adelaide, Australia. Degree

## PhD Research Interests

Physical activity and nutrition for improving health and human performance. **E-mail:** jon.buckey@unisa.edu.au.edu.au

Gaynor PARFITT

## Employment

Associate Professor, Division of Health Sciences, University of South Australia, Adelaide, Australia Degree

# PhD Research Interests

Exercise intensity regulation and physical activity intervention for physical and psychological health.

E-mail: gaynor.parfitt@unisa.edu.au

## Joel T. FULLER Employment

Physiotherapy Lecturer, Faculty of Medicine and Health Sciences, Macquarie University, New South Wales, Australia. Degree

#### PhD Research Interests

Exercise monitoring, injury prevention, and exercise-based interventions for improving health and physical performance. **E-mail:** joel.fuller@mq.edu.au

# 🖂 Joel T. Fuller

Faculty of Medicine and Health Sciences, Macquarie University, 75 Talavera Rd, Macquarie Park 2109 NSW, Australia