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LEADING ARTICLE

A Scientific Rationale to Improve Resistance Training Prescription in Exercise Oncology

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Abstract To date, the prevailing evidence in the field of exercise oncology supports the safety and efficacy of resistance training to attenuate many oncology treatment-related adverse effects, such as risk for cardiovascular disease, increased fatigue, and diminished physical functioning and quality of life. Moreover, findings in the extant literature supporting the benefits of exercise for survivors of and patients with cancer have resulted in the release of exercise guidelines from several international agencies. However, despite research progression and international recognition, current exercise oncology-based exercise prescriptions remain relatively basic and underdeveloped, particularly in regards to resistance training. Recent publications have called for a more precise manipulation of training variables such as volume, intensity, and frequency (i.e., periodization), given the large heterogeneity of a cancer population, to truly optimize clinically relevant patient-reported outcomes. Indeed, increased attention to integrating fundamental principles of exercise physiology into the exercise prescription process could optimize the safety and efficacy of resistance training during cancer care. The purpose of this article is to give an overview of the current state of resistance training prescription and discuss novel methods that can contribute to improving approaches to exercise prescription. We hope this article may facilitate further evaluation of best practice regarding resistance training prescription, monitoring, and modification to ultimately optimize the efficacy of integrating resistance training as a supportive care intervention for survivors or and patients with cancer.

Key Points

- Current resistance training guidelines in exercise oncology remain largely underdeveloped. Increasing focal attention to integrating fundamental resistance training principles that underlie the adaptations to the exercise stimulus could improve resistance training prescription and its implementation in the treatment of survivors of and patients with cancer.
- Cancer survivors exhibit considerable heterogeneity in a myriad of physiological, functional, and psychological factors that influence daily readiness to train, resulting in the need to personalize the resistance training prescription to facilitate progress and adherence.
- Autoregulation (within a periodized model) may represent a feasible way of monitoring, adjusting, and personalizing resistance training stimuli more appropriately for individuals across the cancer control continuum.

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1 Introduction

Over the past 30 years, exercise oncology research has expanded remarkably. Resistance training is currently utilized in an array of oncology settings (i.e., various cancer sites, stages of cancer, and treatment types as well as pre-, during, and post-treatment settings) [1–9]. Indeed, resistance training has been demonstrated as safe and beneficial for attenuating many treatment-related adverse effects such as increased fatigue and diminished physical functioning and health-related quality of life (HRQoL) [1–9]. This has led to several international agencies recommending that exercise be implemented in supportive care approaches across the cancer control care continuum [3–5].

Nevertheless, despite considerable progress in research and growing recognition of the benefits of exercise in cancer care, current exercise oncology-based exercise prescription remains relatively basic and underdeveloped, particularly in regards to resistance training. Indeed, calls have recently been made for a more precise manipulation of training variables such as volume, intensity, and frequency (i.e., periodization), given the large heterogeneity of a cancer population, to truly optimize clinically relevant patient-reported outcomes [1]. The concept of autoregulation is particularly important in this context. Autoregulation refers to the ability to alter training volume, intensity, and ultimately the magnitude of the stimulus, based upon an individual's daily readiness [6, 7]. We posit that the inclusion of autoregulation within a periodization model can improve the exercise prescription, allowing for individualization and application of an appropriate training stressor and increasing the likelihood of maximizing the benefits of resistance training interventions upon clinically relevant outcomes of interest.

Moreover, recent literature has outlined four principles (individualization, specificity, progressive overload, and rest/recovery) that, if appropriately addressed, may optimize exercise prescription and adaptation implemented within cancer populations [1]. However, to our knowledge, no data exist that examine a periodized and autoregulated resistance training program within exercise oncology. Therefore, the purpose of this article is to propose how implementation of periodized and autoregulated resistance training programs in exercise oncology can address the four exercise oncology principles to enhance the feasibility and efficacy of integrating resistance training as a key supportive care intervention in the treatment of survivors of and patients with cancer [1].

2 Current Resistance Training Guidelines

The development of position statements from national and international governing bodies of exercise science in the late 2000s is testament to the growth of interest, awareness, and research in exercise oncology. These position statements support the safety and efficacy of resistance training in a cancer population and provide recommendations for prescription [5, 8]. The guidelines for resistance training in an exercise oncology setting (outlined in Table 1) focus on 1–3 days per week of large muscle group strength training at an intensity of 50–80% of one-repetition maximum (1RM), for 1–3 sets of 8–12 repetitions [5, 8].

Existing evidence clearly demonstrates that this prescription results in meaningful improvements in relevant functional, patient-reported, and fitness outcomes in survivors of and patients with cancer [9–15]. Nevertheless, given the multitude of resistance training variables that can be manipulated to obtain specific training adaptations, it is conceivable that broadly applying a generic prescription to such a diverse population as survivors of and patients with cancer may limit the full therapeutic potential of resistance training in the cancer rehabilitation setting. Indeed, the Australian Association for Exercise and Sport Science (now known as Exercise and Sports Science Australia [ESSA]) and the American College of Sports Medicine (ACSM) have both highlighted the critical need for future research to push the boundaries of exercise prescription to better understand what constitutes optimal dose and frequency duration of exercise and how individual characteristics can influence these [5, 8]. Moreover, recent publications have called for a more precise manipulation of training variables such as volume, intensity, and frequency (i.e., periodization), given the large heterogeneity of a cancer population, to truly optimize clinically relevant patient-reported outcomes [1, 16].

3 Periodization and Autoregulation

Periodization of training has evolved over decades of sport and exercise science research. Historically, periodization has been conceptualized as incorporating two main concepts:

1. The division of an annual training plan into smaller training phases, making it easier to plan, monitor, and adjust a training plan in an effort to optimize key outcomes.
2. Periodization structures training phases to focus on specific physiological characteristics to develop the highest possible levels of strength, hypertrophy, and endurance, among others [17]. Varying the focus of training also serves to reduce training monotony and strain, which is important as these are associated with illness, reduced performance, and injury [18–20].

Essentially, the manipulation of training variables such as volume, intensity, and frequency (i.e., periodization) is

Table 1 Recommendations of governing bodies for resistance exercise prescription in the cancer population

Governing body	Recommendation		
	Frequency	Intensity	Time
Exercise and Sports Science Australia Resistance Training [5]	1–3 times per week, with minimum 1 rest day between sessions	50–80% 1RM or 6–12RM	1–4 sets, 6–10 exercises
American College of Sports Medicine Resistance Training [8]	2–3 days per week	60–70% 1RM	1–3 sets of 8–12 repetitions

RM repetition maximum

an attempt to systematically structure training through phases to optimize physiological and psychological training adaptations.

Periodization has shown superior results for muscle performance (i.e., strength, hypertrophy, and endurance) in both general and athletic populations compared with non-periodized training (i.e., no manipulation of exercise variables) [21–23]. Periodization also encompasses various forms, including linear (LP), and non-linear (NLP) models. LP typically incorporates a gradual decline in volume and increase across each mesocycle (i.e., variables are changed every 4–6 weeks) [24, 25]. Conversely, NLP is characterized by more frequent alterations in intensity and volume (i.e., variables are changed daily or weekly) [46].

Unfortunately, despite the clear benefit of periodization, data examining this concept in clinical populations are scarce. However, Sasso et al. [1] recently described the possible benefits of implementing NLP for aerobic exercise rather than LP to optimize physiological and psychosocial adaptations in a cancer population. We believe this represents an important advance in the exercise prescription process targeting cancer populations. It also provides a foundation to propose that this approach may also be appropriate for resistance training in survivors of and patients with cancer. Indeed, resistance training periodization may serve to not only optimize strength and function but also prevent the onset of overtraining in a population where day-to-day fatigue is of heightened concern [26–28]. Despite the potential benefits of NLP in a cancer population, limitations remain because specific training days are pre-planned and thus may not appropriately account for fluctuations in daily physical and psychological readiness.

4 A Rationale for Autoregulation

Considerable heterogeneity exists in the cancer population (i.e., various demographics, medical history, cancer type, and treatment type, dose, duration), all of which may affect daily capacity, readiness, and motivation to train [1, 3, 29].

Cancer treatment is associated with a myriad of physiological and psychological side effects, many of which exhibit a ‘roller coaster’ effect, fluctuating in magnitude and severity throughout the course of treatment and survivorship phases [26–28]. Disruption of sleep quality/activity patterns is a common occurrence during chemotherapy, with the greatest disturbances seen in the first week after each infusion [30, 31]. Findings from additional studies suggest similar patterns are observed for fatigue and depression, with symptoms being the highest in the days following infusion and subsequently subsiding prior to the next infusion [26–28, 31–33]. Moreover, there is also evidence documenting variability in the incidence and magnitude of nausea in response to chemotherapy [34–36]. This, coupled with unfavorable musculoskeletal and cardiorespiratory changes, such as loss of muscle mass during androgen-deprivation therapy in prostate cancer [37], chemotherapy-induced peripheral neuropathy in breast cancer [38, 39], or reduced pulmonary function and exercise capacity in lung cancer [40, 41], emphasizes the highly individual response to cancer treatment. These fluctuations in physiological and psychosocial symptoms throughout the cancer continuum can greatly influence an individual’s readiness to train on a given day. Collectively, these findings underscore the critical need for individual exercise prescription that can be modified in response to these fluctuations and provide an appropriate training stimulus.

In light of the emerging evidence supporting the utility of autoregulation [42], it is reasonable to propose that an autoregulated approach within an NLP program may warrant consideration in exercise oncology. Such an approach can allow for flexibility in the daily selection of set and repetition schemes and training load based upon fluctuations in patients’ daily readiness to train, while coping with both the disease and treatment-related side effects [6, 7].

In a recent review, Sasso et al. [1] outlined four core principles of exercise prescription that should be considered when designing programs:

1. Individualization
2. Specificity

3. Progressive overload
4. Rest/recovery.

Furthermore, Sasso et al. [1] proposed the use of periodized aerobic programs for exercise oncology to enhance physical adaptations while coinciding with the outlined principles. Again, we propose this represents an important advance in contemporary exercise prescription approaches (Table 1), which could have meaningful implications for the implementation of resistance training as a supportive care intervention in cancer treatment.

Additionally, Table 1 provides ESSA/ACSM guidelines for resistance training in the cancer population that, similar to the aerobic exercise recommendations, likely do not adequately meet the principle of individualization, which consequently could diminish compliance with the other three principles. Specifically, since resistance training guidelines are currently confined to a small intensity range (50–80% of 1RM), repetition range (8–12), and number of sets (1–3), there is little flexibility to alter volume and intensity over time, which undermines the ability to apply progressive overload and individualization [8]. The use of generic guidelines may severely limit individualization and the opportunity for the exercise professional and patient to alter an exercise session based upon rest and recovery. Conversely, implementing periodized training in conjunction with an autoregulated daily loading strategy would allow resistance training in an exercise oncology setting to address the four key training principles outlined by Sasso et al. [1].

To coincide with the four principles of exercise oncology exercise prescription, we propose the utilization of an NLP model for resistance training in patients with cancer. More specifically, NLP has two subtypes: weekly undulating periodization (WUP) and daily undulating periodization (DUP). A WUP design specifies altering the number of repetitions and training focus each week, whereas a DUP configuration signifies changing the number of repetitions and intensity (percentage of 1RM) each day or training session (Table 2). The existing body of evidence demonstrates not only that NLP is superior to LP for skeletal muscle performance [43, 44] but also that DUP induces robust strength changes [45, 46], greater than those with LP in trained individuals [47–50] and similar adaptations for various periodization models in untrained individuals [51]. Furthermore, a recent meta-analysis compared LP with NLP across a range of untrained and trained populations and reported similar benefits for both periodization models for bench press and squat 1RM ($p = 0.37$ and $p = 0.72$, respectively). However, a trend towards NLP being more beneficial for leg press 1RM ($p = 0.07$), which is arguably an exercise more commonly used in clinical settings, was also noted [25]. Therefore, based upon the totality of results and ability to satisfy the exercise oncology training principles, we recommend that patients with cancer adopt a DUP design for resistance training.

When examining the four described exercise oncology training principles, DUP is particularly strong at addressing the concepts of specificity and progressive overload compared with other periodized configurations. An LP model lacks specificity due to spending an entire mesocycle without manipulating training variables (i.e., 12 repetitions at 60% 1RM for 4 weeks), which may lead to diminished neuromuscular efficiency with heavier loads [56]. However, a DUP model may prescribe 60, 70, and 80% 1RM sessions within the same week, precluding a long discontinuation of any specific repetition range and thus coinciding with the principle of specificity while staying adherent to a periodized program structure. Additionally, more robust strength adaptations in DUP than in LP will lead to a greater ability to increase volume over time to comply with the principles of progressive overload. Despite an undulating model of periodization fulfilling two of the established exercise oncology principles, a further two remain unaddressed if training days are pre-planned and load progression is fixed. Thus, implementing autoregulation within the periodized model is warranted to satisfy the individualization and rest/recovery principles.

5 Practical Application

Autoregulation is not a stand-alone model of periodization or training theory; rather it may be applied within a periodized model [45, 46] in three ways: to adjust intra-training load [45], to progress load from week to week [42, 46, 52],

Table 2 Examples of daily undulating periodization and linear periodization mesocycles[a]

Linear periodization	Weeks 1–3 3 × 10 (75% 1RM)	Weeks 4–6 3 × 8 (80% 1RM)	Weeks 7–9 4 × 6 (85% 1RM)
Daily undulating periodization	Monday 3 × 10 (75% 1RM)	Wednesday 3 × 8 (80% 1RM)	Friday 4 × 6 (85% 1RM)

RM repetition maximum

[a] In the absence of fractional plates, the percentage change is rounded to the nearest 2.5-kg or 5-lb increment

or to select a daily set and repetition scheme prior to the commencement of exercise [53]. Implementation of one or more of these autoregulation strategies will allow compliance with the principles of individualization and rest/recovery.

Moreover, it is well-established that the response of a patient with cancer to training must be monitored to ensure appropriate prescription [1, 3]. Therefore, monitoring progress will allow for daily load variations based upon individual differences in response to training such as accelerated or attenuated progress. Specifically, the resistance training-specific ratings of perceived exertion (RPE) scale has been demonstrated to be an effective strategy to gauge effort during a session and adjust training load [52]. The recently published RPE scale measures repetitions in reserve (RIR) in that during or upon completion of a set the patient records an RPE, which corresponds to an RIR as follows: 10RPE = 0RIR, 9RPE = 1RIR, 8RPE = 2RIR, and so forth. In other words, utilization of the RPE scale would allow a patient to estimate the amount of additional repetitions remaining at a given load until failure. It should be noted that, although this scale has been validated in both experienced and novice trainees [52], its application in a clinical setting has not yet been evaluated. Nevertheless, the RIR-based RPE scale has potential as a practical method to regulate daily training load that warrants consideration for implementation in resistance training programs targeting survivors of and patients with cancer.

For example, in a DUP training model, a specific training day may program 5 sets of 5 repetitions at a specific load; however, if the patient records a 10RPE/RIR on the first set, then the load can be lowered to ensure completion of the programmed training volume. Furthermore, an RPE range can be set for each session to target a specific physiological stress per set; for example, a training session may have a goal of the patient recording a 5–6RPE upon completion of each set. Additionally, objective load adjustments can be made using the RPE scale based upon the RPE goal. For example, using the goal of a 5–6RPE, if a 7RPE is recorded, a 3–5% load decrease will occur, with a 6–8% decrease occurring for a recorded RPE of 9 (Table 3). With this strategy, each patient can ensure the appropriate physiological stress is applied by complying with the individualization principle. It should be noted that, in the absence of fractional plates, practitioners and patients can round the percentage change to the nearest 2.5-kg or 5-lb increment when adjusting load based upon RPE. Moreover, since it is unlikely that a true 1RM will be performed in an exercise oncology setting, this RIR-based RPE scale allows patients to regulate intensity without performing a 1RM. However, it is suggested that patients be familiarized with the RPE scale because novice users do have a learning curve before accurate RPEs can be ensured [52].

Table 3 Theoretical framework for autoregulation using target rating of perceived exertion for sessions

Repetitions	
Warm-up	
Set 1 at established working weight	
Set 2 adjusted for RPE	
RPE response to established working weight	**Percentage adjustment**
9–10	−6 to 8%
7–8	−3 to 5%
5–6	No adjustment
3–5	+3 to 5%
1–2	+6 to 8%

RPE rating of perceived exertion

Furthermore, since considerable variability exists in the rate of response and adaptation to a training stimulus in a healthy population [54], it is plausible to suggest that the heterogeneity in training adaptation may be even larger among survivors of and patients with cancer at various stages of disease and treatment progression. In this case, pre-planned progression from week to week could lead to the incidence of failed repetitions, which in turn would alter the desired training volume. To avoid inappropriate progression, weekly load advancement could be implemented by monitoring RPE and adjusting the subsequent load accordingly (i.e., a low RPE for a set/session may warrant a larger increase in load for a subsequent session). Additionally, autoregulatory progressive resistance exercise (APRE) has been shown to yield superior strength adaptations than planned arbitrary progression [42]. To utilize APRE, a patient would perform one of the previous week's sets (typically the last set of the last day) to failure, and the performance (number of repetitions) would dictate progression; the more repetitions performed, the greater the load increase (Table 4).

Furthermore, it is well-established that sleep disruption, fatigue, and depressive symptoms are at their highest in the days following chemotherapy infusion, with daily fluctuations, and gradually subsiding prior to the subsequent infusion [26–28]. Accordingly, daily readiness to exercise, from both a physical capacity and a motivation perspective, can be significantly affected. These are important considerations since, in the absence of autoregulation, there is rigidity in pre-planned set, repetition, and intensity schemes for a particular day. For example, if a patient has the following weekly DUP setup (Monday 15 repetitions at a 1–4RPE, Wednesday 10 repetitions at 5–7RPE, and

Table 4 Perceived recovery status scale with target rating of perceived exertion. Adapted from Laurent et al. [61] with permission

Score	Recovery status	Expected effects on performance	RPE goal from recovery
10	Very well recovered/highly energetic	Expect improved performance	7–9
9			
8	Well recovered/somewhat energetic		
7		Expect similar performance	5–7
6	Moderately recovered		
5	Adequately recovered		
4	Somewhat recovered		
3		Expect reduced performance	1–4
2	Not well recovered/somewhat tired		
1			
0	Very poorly recovered		

RPE rating of perceived exertion

Table 5 Potential strategies for implementation of autoregulation within a periodized program

Intra session	Weekly adjustment	Daily load selection
The use of RPE/RIR from a set of repetitions to modify the load for subsequent sets	The use of RPE from a given session to modify the load in subsequent sessions	Use of perceived recovery status to determine an RPE goal for a given session
Target RPE/RIR 5–6. An RPE of 7 would result in decreasing load for subsequent set 3–5%	Target session 10 reps at 5–7RPE. A recording of 4–5RPE for session would result in a 3–5% increase in load for a subsequent session	Target session RPE 5–7. A perceived recovery score of 2 would result in an adjustment of target session RPE to 1–4

RIR repetitions in reserve, *RPE* rating of perceived exertion

Friday 5 repetitions at 7–9RPE), there is high probability that fatigue will mean a patient may not be ready for a lower-repetition higher-intensity session, which would violate the rest/recovery principle of exercise oncology training. Indeed, a recent investigation has shown the order of training session intensity within a week is important to manage fatigue and, when the principle of rest/recovery is violated within a DUP setup, performance outcomes are diminished [46]. Table 5 summarizes potential means for autoregulation to be implemented within a periodized design. Furthermore, it is imperative to state that the three methods of autoregulation are not mutually exclusive. For example, flexible NLP can be used to select a daily repetition and intensity zone and subsequently RPE can be used to alter load during the session.

It must also be noted that the proposed strategies can be implemented safely as supervised resistance training has been shown to reduce the risk of injury [55], and increased variation of loading schemes (i.e., periodization) can aid in avoiding staleness and plateaus in training [56]. Additionally, autoregulation strategies (i.e., flexible DUP) have increased training compliance compared with an inflexible weekly training order [57]. Moreover, it seems likely that even greater individualization of training programs, including autoregulated load assignment and specific exercise selection, will only be of further benefit to prevent injury and increase adherence in a clinical population. The benefits of resistance training in a cancer population extend beyond improved physical function and quality of life. Recent research has demonstrated that physical activity and, indeed, resistance training is associated with a reduction in cancer recurrence and in cancer-related and all-cause mortality [2, 58–60], highlighting the importance of maintaining an active lifestyle throughout survivorship. Thus, autoregulation strategies that facilitate participation in and adherence to physical activity may confer long-term benefits of overall and disease-free survival.

However, the following limitations do exist, and thus precautions must be taken when implementing the proposed strategies. First, the ability to accurately use RPE to assign intra-session training load improves with training and RPE scale-specific experience [53], thus patients should spend time recording RIR-based RPE before implementation. Second, if using the proposed APRE strategy, patients are cautioned to carefully evaluate daily fatigue levels as the previous week's performance may not be indicative of daily readiness. Third, since many of the proposed strategies are likely new to clinicians and patients, it is advisable to implement one strategy at a time to allow for adequate time and experience to promote adaptation and mastery of the approach. For example, periodization may be applied first for one mesocycle followed by RPE to assign training load for another mesocycle, and subsequently incorporating a flexible NLP strategy as well. Finally, we recommend that exercise oncology patients be supervised when beginning a resistance training program to aid in implementing the training techniques and principles appropriately, thereby facilitating the likelihood of safety, feasibility, and efficacy of the intervention.

6 Conclusions

The overarching purpose of the present article was to propose how implementation of periodized and autoregulated resistance training programs in exercise oncology can address the four exercise oncology principles that may enhance the utility of implementing resistance training as a supportive care intervention in the treatment of survivors of and patients with cancer. While the current guidelines provide some progress in HRQoL for patients with cancer, we suggest they can be further developed, with specific attention to the quality of exercise prescription and modification.

A substantial body of literature has demonstrated periodization and autoregulated resistance training models to be effective in healthy populations. We believe applying these strategies shows considerable promise for enhancing the potential benefits of resistance training for survivors of and patients with cancer beyond the current standard recommendations. This is due in part to the ability of an integrated periodization and autoregulation strategy to personalize the prescription and promote successful integration, adoption, and adherence with the four exercise oncology prescription principles of individualization, specificity, progressive overload, and rest/recovery. Consequently, we make the following recommendations for future research to ensure continued progress and improvement of resistance training prescription in exercise oncology:

- The RIR-based RPE scale should be investigated for validity in determining and monitoring resistance exercise intensity in a cancer population.
- Examinations of autoregulation within a periodization model compared with 'traditional' prescription approaches are warranted. It is critical that future inquiries systematically examine the safety, feasibility, and efficacy of implementing resistance training interventions incorporating these periodization and autoregulation principles within individuals across the cancer control continuum.
- Various exercise prescription strategies should be investigated in an attempt to discern the most appropriate form of monitoring, adjusting, and progressing resistance training in this population.
- It is also important to systematically compare the effects of an intervention using autoregulation within a periodized program with those of programs implementing fixed progression on key training adaptations and physiological and psychological outcomes.

We hope this article may facilitate further evaluation of the best practices regarding resistance training prescription, monitoring, and modification to ultimately optimize the efficacy of resistance training as a supportive care intervention for survivors of and patients with cancer.

Compliance with Ethical Standards

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