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Effects of Radiochemotherapy on Muscle Oxygen Saturation in Locally Advanced Lung Cancer Patients

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ABSTRACT

Objective: This study aimed to investigate the effects of curative radiochemotherapy on muscle oxygen saturation dynamics using the Moxy oxygen monitor in individuals with locally advanced lung cancer.

Materials and Methods: A prospective study was conducted at Atatürk University Sports Sciences Application and Research Center. Male patients aged 30–70 years with a diagnosis of locally advanced lung cancer were recruited from the Radiation Oncology Clinic of Erzurum Regional Training and Research Hospital. Before and after curative radiochemotherapy, participants performed a low-intensity acute aerobic walking exercise protocol on a treadmill for 10 minutes. Muscle oxygen saturation (SmO_2) and total hemoglobin (tHb) levels in the rectus femoris muscle were monitored during and after the test using near-infrared spectroscopy with the Moxy monitor. Data were analyzed using SPSS 26.0 software.

Results: The results demonstrated a significant increase in total hemoglobin values in both the right and left legs following curative radiochemotherapy.

Conclusion: Curative radiochemotherapy positively influenced muscle oxygen saturation and total hemoglobin levels, suggesting a potential improvement in muscle oxygenation dynamics in patients with locally advanced lung cancer.

Keywords: Moxy Oxygen Monitor, SmO2, Locally Advanced Lung Cancer, Curative Radiochemotherapy

1. INTRODUCTION

The Moxy oxygen monitor is a muscle oxygen monitor that can measure local oxygen saturation (SmO2) and total hemoglobin (Thb) using near-infrared spectroscopy, thanks to the sensor embedded in the skin. Data storage and telemetric capability are safe for assessing localized O_2 [1]. Technically, these devices illuminate the skeletal muscle with infrared light. By sensing the light reflected from it as a result of the amount of light absorbed by the tissue, they recognize variables such as hemoglobin, deoxyhemoglobin, oxyhemoglobin, and total hemoglobin. They can measure muscle oxygen saturation as a percentage (%). [2]

Oxygen is essential for eukaryotic life. The increase in body size of humans and other vertebral creatures requires a physiological infrastructure to maintain oxygen homeostasis and provide adequate oxygen delivery to the tissues. Oxygen is an important element necessary for energy gain in maintaining homeostasis and for the organism's survival. Hypoxia, a decrease in oxygen level, results in many changes at the cellular level. While hypoxia occurs in natural physiological processes such as embryonic development, it also occurs in pathophysiological conditions such as inflammation and solid tumor formation. [3,4] Hypoxia is a major consequence of tumor growth in cancerous cells. Lung cancers have hypoxia and when the tumor increases in mass, the blood supply is impaired because it is far from the blood vessels. This, in turn, impairs the regulation of the hypoxic environmental repair mechanism, thereby accelerating cancer development. Hypoxia is a common pathological feature commonly observed in solid tumors due to decreased or insufficient oxygen supply. [4,5] In addition, the presence of oxygen is an important prognostic factor known to increase the response of tumor cells to radiotherapy. Due to the size of the tumoral mass in the lung and pressure on the airways, shortness of breath and consequently hypoxemia will inevitably increase. [4,5] Curative radiochemotherapy is a treatment whose main goal is to cure the tumor or reduce the local recurrence rate. Although the treatment plan in curative radiochemotherapy covers an average of 5-7 weeks, this period may vary depending on the type of tumor and its response to radiation.

Curative radiochemotherapy can be applied in different ways. This treatment is performed in 3 different types. One of them is called adjuvant therapy. This treatment is a form of treatment that is combined with chemotherapy after surgery. This treatment is aimed at reducing the local recurrence rate of cancer. Adjuvant therapy is mostly preferred in brain tumors, breast, rectum, larynx, endometrium, stomach and cervix cancers. One of these treatments is neoadjuvant therapy. The main goal of this treatment is to reduce the tumor size by targeting it, to make the surgical intervention more effective and thus to ensure more effective regional control. Neoadjuvant therapy is preferred in lung, rectum and soft tissue cancers. The third is the definitive treatment. This treatment, on the other hand, is the preferred treatment when radiotherapy is used alone or simultaneously with chemotherapy. In definitive treatment, patients are not treated surgically. If the disease recurs, surgery is considered. Definitive treatment is applied to prostate, cervix, lung, nasopharynx, and early-stage glottic larynx cancers. [6–8] The main purpose of radiotherapy is to the water molecules in the cells, where free radicals are produced that cause damage to DNA. Hypoxic cells formed due to decreased oxygen levels are more resistant to radiotherapy. The majority of the tumor structure has less oxygen content. Radiotherapy is a form of treatment in which more than one dose is usually administered in weekly periods. The main purpose of radiotherapy is to cause maximum damage to the tumor cells with the radiation dose given while ensuring that the healthy cells are minimally affected by the radiation dose. Radiation therapy works best when the oxygen levels in the cells are highest, as the hypoxic environment allows the cells to become more oxygenated and more sensitive to radiation. [9,10]

No studies have investigated SMO2 changes as assessed by the moxy oxygen monitor before and after curative radiochemotherapy in individuals diagnosed with locally advanced lung cancer. This study aimed to examine the possible effects of curative radiochemotherapy on muscle oxygen saturation dynamics with moxy oxygen monitor in individuals with locally advanced lung cancer.

2. MATERIAL AND METHOD

The study was conducted prospectively at Atatürk University Sports Sciences Application and Research Center. In the Radiation Oncology Clinic of Erzurum Regional Training and Research Hospital, male patients with locally advanced lung cancer who met our criteria had normal blood values and volunteered were included in the study. For these patients, planning was done for local oxygen saturation and total hemoglobin evaluations with near-infrared spectroscopy method using a 10-minute low-intensity acute aerobic walking exercise protocol using a treadmill (treadmill) twice, before and after curative radiochemotherapy and after curative radiochemotherapy.

In addition, similar studies in the literature were used to calculate the sample size of this study. [1,3] Similar studies' mean and standard deviation values were inserted into the G*Power 3.1.9.4 analysis program [Bidirectional, α= 0.05, Power (1-β)= 0.95, Effect size=1.43]. According to the calculation result, this study's minimum number of samples was 9. The study is planned to be conducted in 10 patients with locally advanced lung cancer.

Inclusion criteria for the study:

1. Male patients aged 30-70 years diagnosed with locally advanced lung cancer
2. Stable patients who do not interfere with treadmill exercise
3. Those who voluntarily agreed to participate in the study

Exclusion criteria:

1. Those who do not agree to participate in the study
2. Being under 30 years old and over 70 years old and being a woman
3. Cardiologically unstable patients with recent MI
4. Oxygen saturation ≤85% in room air
5. Patient group with unstable severe lung cancer diagnosis
6. Presence of diseases such as diabetes, hypertension, cardiovascular disorder, neurodegenerative disease, head trauma, alcohol and drug addiction, epilepsy

7. Patients with treadmill exercise contraindications (acute muscle spasm, limitation in joint range of motion, joint effusion, severe osteoporosis around the joint, just after surgical procedures)

In our study, all kinds of explanations and information about the study were made before the volunteer patient group signed an informed consent form.

This research is experimental research with pre-test and post-test designs. The height, body weight and body mass index of 10 patients participating in the study were calculated. Before and after curative radiochemotherapy, patients were walked on a treadmill for 10 minutes by the low-intensity acute aerobic walking exercise protocol, and muscle oxygen saturation and total hemoglobin levels were monitored in the rectus femoris muscle with near-infrared spectroscopy, both during and after the test, with a Moxy monitor device. After resting in a sitting position for five minutes, SmO2 and THb resting measurements were recorded. Rectus femoris muscle oxygenation (SmO2 rest, %SmO2min, %SmO2 recovery) and total hemoglobin level (Thbirest, Thbmin, Thbrecovery) were measured with a Moxy monitor during and after the rest and low-intensity acute aerobic walking exercise.

Test Protocol

Based on evidence from the American Cancer Society (ACS) and American Sports Medicine (ACSM), a moderate aerobic exercise program is recommended for cancer patients. For 3-4 days a week, 30-60 minutes of maximal oxygen uptake or 40%-80% of the heart rate reserve, more walking, brisk walking, cycling or swimming exercises are recommended [11].

The patient volunteers in this study applied low-intensity acute aerobic walking on the treadmill for 10 minutes at the exercise intensity recommended by the ACSM (heart rate reserve or pulse range corresponding to 50-60% of the target heart rate). This exercise measured muscle oxygen saturation only twice, before and after curative radiochemotherapy. Against any health problem that may be experienced during the test protocol, the researchers involved in the study were personally present and necessary precautions were taken. Before starting the

walking exercise, the exercise intensity was calculated by the Karvonen method for the walking exercise patients would do.[12]

Karvonen Formula

Maximum Heart Rate = 220- Age

Heart Rate Reserve or Target Heart Rate = (Maximal Heart Rate - Resting Heart Rate) x Exercise Intensity + Resting Heart Rate

The specified calculations were calculated with the above formula and the heart rate of the patients was followed on the treadmill screen during walking.

Placing Moxy

Before Moxy is placed, the area should be shaved with an electric shaver and cleaned with alcohol wipes. The device must be secured with a light shield and athletic tape to prevent the near-infrared light from interfering with the detectors while recording. Moxy can be placed on the rectus femoris or vastus lateralis muscles of both the dominant and non-dominant leg. During our study, we planned to record using the rectus femoris muscle. The rectus femoris is involved in flexion of the thigh concerning the pelvis and provides flexion of the pelvis concerning the thigh when the thigh is fixed; therefore, it is chosen as the location of Moxy both because it is a part of the knee extensor group that makes the primary contribution to strength formation and because it is easier to place. [1,3] Considering these details, we placed the Moxy and took the measurements (Figure 1). Taking measurements on the treadmill with the near-infrared spectroscopy method using the Moxy oxygen monitor is also shown in Figure 2.

Planning will be done so that the total process time will be approximately 15-20 minutes.

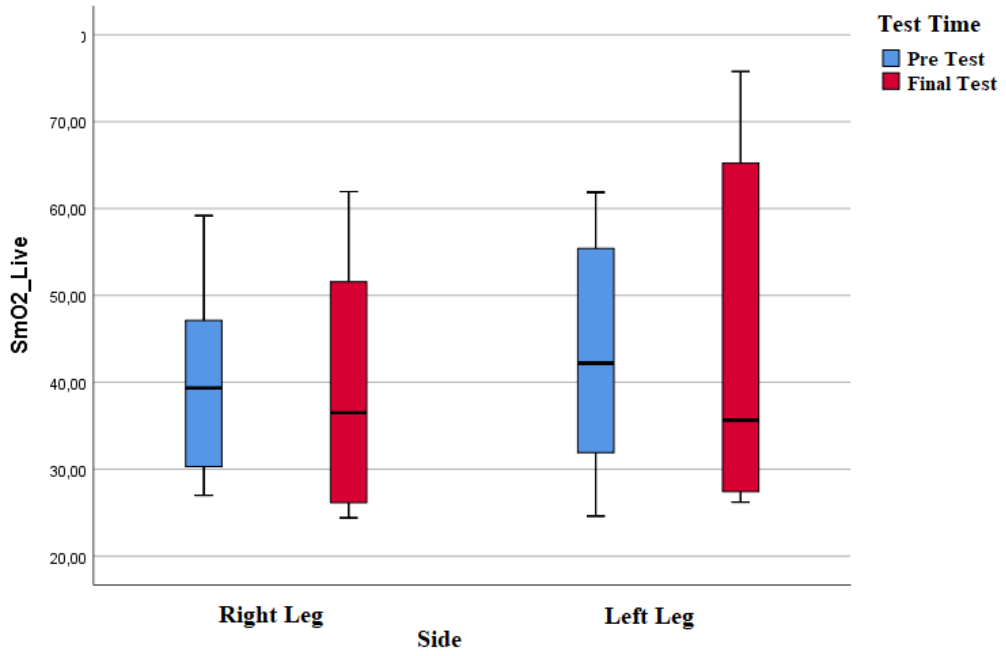
Figure 1: Placement of moxy in the rectus femoris muscle

Figure 2: SmO2 and THb monitoring and recording with the moxy device during low-intensity acute aerobic walking exercise on the treadmill

3. FINDINGS

Table 1. Dependent groups t-test results of pre-test and post-test results of SmO2 Live right and left legs

Parameter	N	Side	Test Time	X±S.S	t	*P*
SmO_2 Live	10	Right Leg	Pre Test	39.96±11.21	0.253	0.807
	10		Final Test	39.35±14.20		
	10	Left Leg	Pre Test	43.19±13.48	-0.244	0.815
	10		Final Test	44.82±21.17		



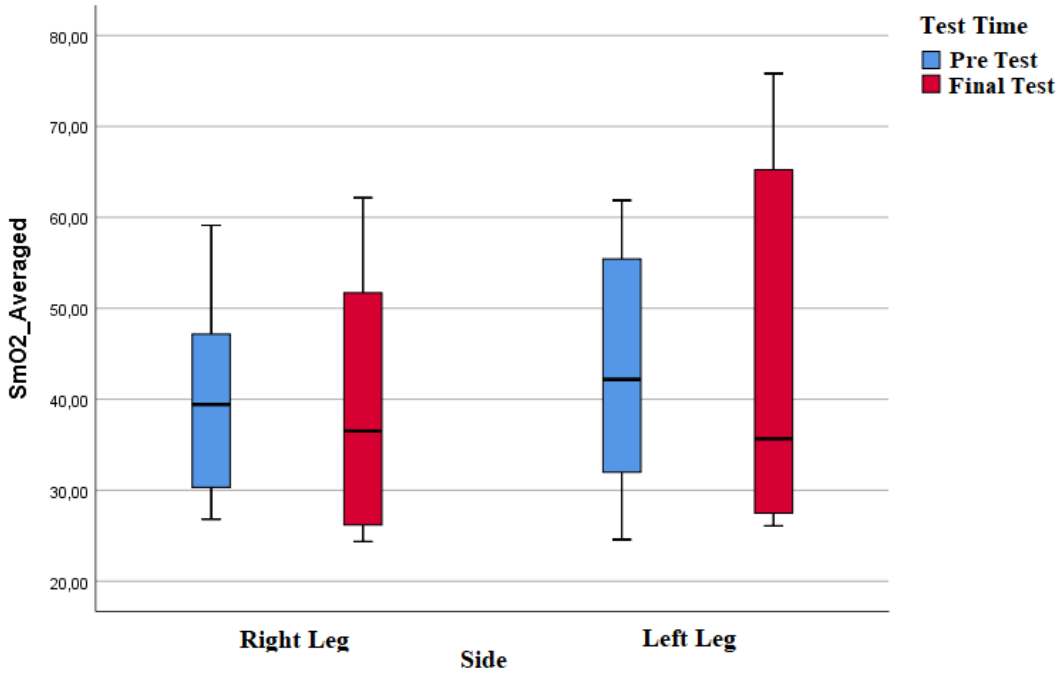
Graph 1. All group and individual changes for SmO2 Live right and left leg

Considering the SmO2 Live parameter, the right leg pre-test average is 39.96, and the post-test average is 39.35. The t-value calculated on the scores of the two tests is 0.253. The p=0.807 value obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether there is any

difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level. Considering the SmO2 Live parameter, the left leg pre-test average is 43.19, and the post-test average is 44.82. The t value calculated on the scores of the two tests is -0.244. The p=0.815 value obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether there is any difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level (Table 1 and Graph 1).

Table 2. Dependent groups t-test results regarding SmO2 Averaged pre-test and post-test results of right and left legs

Parameter	N	Side	Test Time	X±S.S	t	*P*
SmO_2 Averaged	10	Right Leg	Pre Test	39.97±11.23	0.226	0.828
	10		Final Test	39.42±14.28		
	10	Left Leg	Pre Test	43.21±13.46	-0.243	0.815
	10		Final Test	44.83±21.18		

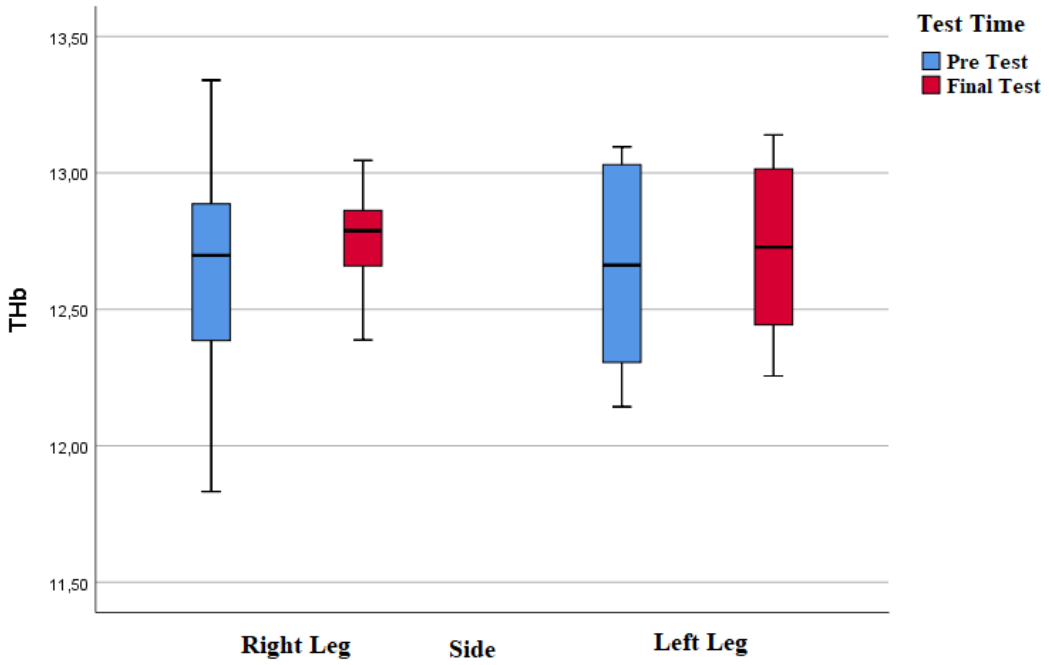


Graph 2. SmO2 Averaged all group and individual changes for right and left legs

Considering the SmO2 Averaged parameter, the right leg pre-test average is 39.97, and the post-test average is 39.42. The t-value calculated on the scores of the two tests is 0.226. The p=0.828 value obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether there is any difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level. Considering the SmO2 Averaged parameter, the left leg pre-test average is 43.21, and the post-test average is 44.83. The t value calculated on the scores of the two tests is -0.243. The p=0.815 value obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether there is any difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level (Table 2 and Graph 2).

Table 3. Dependent groups t-test results regarding the pre-test and post-test results of THb right and left legs

Parameter	N	Side	Test Time	X±S.S	t	*P*
THb	10	Right Leg	Pre Test	12.64±0.46	0.062	0.952
	10		Final Test	12.63±0.42		
	10	Left Leg	Pre Test	12.65±0.38	-0.308	0.767
	10		Final Test	12.72±0.33		



Graph 3. All group and individual changes for THb right and left legs

Considering the THb parameter, the right leg pre-test average is 12.64, and the post-test average is 12.63. The t-value calculated on the scores of the two tests is 0.062. The p=0.952 value obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether there is any difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level. Considering the THb parameter, the left leg pre-test average is 12.65, and the post-test average is 12.72. The t-value calculated on the scores of the two tests is -0.308. The p=0.767 value was obtained as a result of the dependent groups (Paired sample t-test) t-test performed to determine whether any difference between the pre-test and the post-test indicates no difference between the tests at the 0.05 significance level (Table 3 and Graph 3).

4. DISCUSSION

Fort he first time, we described changes in skeletal muscle O2 saturation induced by a moxy oxygen monitor with a 10-minute low-intensity acute aerobic walking exercise protocol using a treadmill twice, before and after curative

radiochemotherapy, in a population diagnosed with locally advanced lung cancer. In lung cancers, it is inevitable to increase shortness of breath and hypoxemia due to the size of the tumoral mass and pressure on the respiratory tract [4,5]. Curative radiochemotherapy is a treatment whose primary goal is to cure the tumor or reduce the local recurrence rate. [6–8]

In addition to the results of rectus femoris, trunk strength, and large muscle mass, the patella and patellar tendon is a special structure that performs movement and fixation of the joints. The rectus femoris is a dynamic muscle that flexes and extends the knee joints. [13–15] It also plays a role in the expectation of posture. For the rectus femoris to perform these objects, the capillary vascular system network that feeds these regions must also be well-developed and have vasodilator use. Oxygenation of the muscle, the ability to use the incoming oxygen, and the amount of incoming oxygen to the muscle are extremely important for the volume of the muscle. [15–18]

There is hypoxia in lung cancers and when the mass of the tumor increases, blood supply is impaired because it stays away from the blood vessels. [4,5]

Considering that curative radiochemotherapy can reduce tumor size with multiple imaging studies during treatment in individuals with advanced lung cancer, they predicted this might be the most effective adaptive control method. [19,20]

Although studies have shown that there is a decrease in muscle strength due to toxicities in the musculoskeletal system of cancer patients, and the decrease in muscle strength becomes more evident as the dosage of treatments and the number of cures increase [21–27], studies investigating the relationship between muscle strength and quality of life are insufficient in the literature. In 2007, an 18-week combined exercise (aerobic, resistant) program was applied to cancer patients whose treatments were completed in the Netherlands. It has been shown that these patients have improvements in their muscle strength and cardiovascular capacity, and accordingly, the quality of life, functional performance, symptoms and general health score parameters. [28] The findings from this study support our

research. In our study, although there was no statistically significant difference (p>0.05) between the SmO2 Live, SmO2 Averaged and THb parameters of the participants after curative radiochemotherapy application, a higher increase was found in the left leg compared to the right leg.

According to the findings of the study, Sig. Although there was no significant difference since the (2-tailed) values were higher than 0.05, it was determined that the participants' right and left leg total hemoglobin values increased after curative radiochemotherapy application.

5. CONCLUSION AND RECOMMENDATIONS

As a result, curative radiochemotherapy has shown an improved effect on muscle oxygen saturation and total hemoglobin.

As a result of our study, we have analyzed the skeletal muscle O2 saturation with moxy oxygen monitor with scientific data in individuals diagnosed with locally advanced lung cancer. We believe that providing adequate muscle oxygen saturation while establishing a treatment protocol in individuals with locally advanced lung cancer who have received or will receive curative radiochemotherapy will benefit the treatment's success and the patient's survival.

Finding patients was tough since our study was voluntary and conducted in a specific patient group. A study can be conducted in which the low-intensity exercise program recommended by the ACS and ACSM is applied simultaneously as the number of patients is kept higher and/or curative radiochemotherapy is received.

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Conflict of Interests

The authors approved that they have no conflict of interest. Financial Support The authors approved that this study has received no financial support from any institution.

Ethical Approval

The ethics committee permission required was obtained from the Faculty of Medicine Clinical Research Ethics Committee with the decision numbered B.30.2.AT**.0.01.00/2.

Data sharing statement

None

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REFERENCES

1. Crum EM, O'Connor WJ, Van Loo L, Valckx M, Stannard SR. Validity and reliability of the Moxy oxygen monitor during incremental cycling exercise. *Eur J Sport Sci*. 2017;17(8):1037-1043. doi:10.1080/17461391.2017.1330899
2. Miranda-Fuentes C, Chirosa-Ríos LJ, Guisado-Requena IM, Delgado-Floody P, Jerez-Mayorga D. Changes in Muscle Oxygen Saturation Measured Using Wireless Near-Infrared Spectroscopy in Resistance Training: A Systematic Review. *Int J Environ Res Public Health*.

2021;18(8):4293. doi:10.3390/ijerph18084293

3. Takagi S, Murase N, Kime R, Niwayama M, Osada T, Katsumura T. Muscle Oxygen Dynamics During Cycling Exercise in Angina Pectoris Patients. *Adv Exp Med Biol*. 2016;923:291-297. doi:10.1007/978-3-319-38810-6_39
4. David S, Lokesh V. Peripheral Blood Oxygen Saturation: A Non-invasive Prognostic Marker in Cancer Patients Treated with Radiation Therapy- A Pilot Study. *Open Cancer Immunol J*. 2020;8(1):1-7. doi:10.2174/1874601002008010001
5. Airley RE, Mobasheri A. Hypoxic Regulation of Glucose Transport, Anaerobic Metabolism and Angiogenesis in Cancer: Novel Pathways and Targets for Anticancer Therapeutics. *Chemotherapy*. 2007;53(4):233-256. doi:10.1159/000104457
6. Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and Radiation Therapy: Current Advances and Future Directions. *Int J Med Sci*. 2012;9(3):193-199. doi:10.7150/ijms.3635
7. Falkson CB, Vella ET, Yu E, et al. Guideline for Radiotherapy with Curative Intent in Patients with Early-Stage Medically Inoperable Non-Small-Cell Lung Cancer. *Curr Oncol*. 2017;24(1):44-49. doi:10.3747/co.24.3358
8. Spitz DR, Hauer-Jensen M. Ionizing Radiation-Induced Responses: Where Free Radical Chemistry Meets Redox Biology and Medicine. *Antioxid Redox Signal*. 2014;20(9):1407-1409. doi:10.1089/ars.2013.5769
9. Cui J, Mao X, Olman V, Hastings PJ, Xu Y. Hypoxia and miscoupling between reduced energy efficiency and signaling to cell proliferation drive cancer to grow increasingly faster. *J Mol Cell Biol*. 2012;4(3):174-176. doi:10.1093/jmcb/mjs017
10. Stewart RD, Yu VK, Georgakilas AG, Koumenis C, Park JH, Carlson DJ. Effects of radiation quality and oxygen on clustered DNA lesions and cell death. *Radiat Res*. 2011;176(5):587-602. doi:10.1667/rr2663.1
11. Thompson WR, Gordon NF, Pescatello LS. *ACSM's Guidelines for*

Exercise Testing and Prescription. 8th ed. (Lippincott Williams &Wilkins, ed.).; 2010.

12. KARVONEN MJ, KENTALA E, MUSTALA O. The effects of training on heart rate; a longitudinal study. *Ann Med Exp Biol Fenn*. 1957;35(3):307-315.
13. Kopydlowski NJ, Weber AE, Sekiya JK. Functional Anatomy of the Hamstrings and Quadriceps. In: *Hamstring and Quadriceps Injuries in Athletes*. Springer US; 2014:1-14. doi:10.1007/978-1-4899-7510-2_1
14. Bordoni B, Varacallo M. *Anatomy, Bony Pelvis and Lower Limb: Thigh Quadriceps Muscle*.; 2023.
15. Soames R. W, Atha J. The role of the antigravity musculature during quiet standing in man. *Eur J Appl Physiol Occup Physiol*. 1981;20:159-167.
16. Çelenk Ç., Marangoz İ., Aktug Z.B. The effect of quadriceps femoris and hamstring muscular force on static and dynamic balance performance. *Int J Phys Educ*. 2015;2(2):323-325.
17. Abbiss CR, Laursen PB. Models to Explain Fatigue during Prolonged Endurance Cycling. *Sport Med*. 2005;35(10):865-898. doi:10.2165/00007256-200535100-00004
18. Allen DG, Lamb GD, Westerblad H. Skeletal muscle fatigue: cellular mechanisms. *Physiol Rev*. 2008;88(1):287-332. doi:10.1152/physrev.00015.2007
19. Yan D, Lockman D, Martinez A, et al. Computed tomography guided management of interfractional patient variation. *Semin Radiat Oncol*. 2005;15(3):168-179. doi:10.1016/j.semradonc.2005.01.007
20. van Zwienen M, van Beek S, Belderbos J, et al. Anatomical Changes during Radiotherapy of Lung Cancer Patients. *Int J Radiat Oncol*. 2008;72(1):S111. doi:10.1016/j.ijrobp.2008.06.1018
21. Snyder CC. *Oncology Nursing*. Brown and Company; 1986.
22. Fischer DS, Knobf MT, Durivage HJ. *The Cancer Chemotherapy Handbook*. (St Louis: Mosby, ed.).; 1993.
23. Dimeo F. Exercise for cancer patients: a new challenge in sports medicine.

Br J Sports Med. 2000;34(3):160-161. doi:10.1136/bjsm.34.3.160

24. Greene D, Nail LM, Fieler VK, Dudgeon D, Jones LS. A comparison of patient-reported side effects among three chemotherapy regimens for breast cancer. *Cancer Pract*. 1994;2(1):57-62.

25. Caru M, Duhamel G, Marcil V, Sultan S, Meloche C, Bouchard I, Drouin S, Bertout L, Laverdiere C, Sinnett D, Curnier D. The VIE study: feasibility of a physical activity intervention in a multidisciplinary program in children with cancer. *Support Care Cancer*. 2020 Jun;28(6):2627-2636. doi: 10.1007/s00520-019-05085-5. Epub 2019 Oct 16. PMID: 31620924.

26. Braam KI, van der Torre P, Takken T, Veening MA, van Dulmen-den Broeder E, Kaspers GJ. Physical exercise training interventions for children and young adults during and after treatment for childhood cancer. *Cochrane Database Syst Rev*. 2013 Apr 30;(4):CD008796. doi: 10.1002/14651858.CD008796.pub2. Update in: Cochrane DatabaseSystRev. 2016 Mar 31;3:CD008796. doi: 10.1002/14651858.CD008796.pub3. PMID: 23633361.

27. Skotzke P, Schwindling S, Meyer T. Side differences and reproducibility of the Moxy muscle oximeter during cycling in trained men. *Eur J Appl Physiol*. 2024 Oct;124(10):3075-3083. doi: 10.1007/s00421-024-05514-2. Epub 2024 May 29. PMID: 38809481; PMCID: PMC11467065.

28. De Backer IC, Van Breda E, Vreugdenhil A, Nijziel MR, Kester AD, Schep G. High-intensity strength training improves quality of life in cancer survivors. *Acta Oncol*. 2007;46(8):1143-1151. doi:10.1080/02841860701418838