THE EFFICACY OF A 1500G MAGNETIC BREATHING DEVICE IN OPTIMIZING CARDIO-RESPIRATORY FUNCTION IN ENDURANCE ATHLETES DURING MAXIMAL EXERCISE TESTING

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DECLARATION

I, Robyn-Jenna Turton, student number 15080595, declare the work on which this project is based is original and my own work (except where acknowledgements indicate to the contrary) and that neither the whole work nor part thereof has been, is presently or is to be submitted for another degree at this or any other university.

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ABSTRACT

Introduction: The O_2 Gold magnetic device is a non-medicinal inhaler containing a magnetic coil that has been designed to improve cardio-respiratory function. Oxygen (O_2) in the inhaled air passes through the magnetic coil in this breathing device and acquires a magnetic charge. Former studies (Ryan, 2007; Roberts, 2007) have reported improvements in peak power output and post-exercise recovery, supporting anecdotal reports of improved peak power output in world-class endurance athletes following regular use of this device. The mechanisms by which this improved peak power output may occur, are however unknown.

Objectives: The primary objectives of this study were to determine the effects of 28 days of regular use of the magnetic breathing device on the cardio-respiratory function of well-trained endurance athletes during an incremental exercise test to exhaustion. Secondary objectives included the determination of lung function and red blood cell status at rest, and maximal exercise performance and O_2 uptake ($\dot{V}O_2$) as well as heart rate (HR) and blood pressure (BP) response to a maximal exercise test. Finally the possible role of systemic concentrations of erythropoietin (EPO) and interleukin-3 (IL-3) as mediators of the beneficial effects of the magnetic breathing device on red blood cell status, was investigated.

Study design and methods: The study was designed as a double blind, placebo controlled, cross-over trial. 18 Healthy male participants volunteered from running and triathlon clubs in the greater Durban area. The participants were particularly suited to a set of inclusion criteria which included a specific age range (>18 and <45 years), were recreational or professional runners that were willing to maintain a training schedule of at least three times per week for the three months leading up to, and during the study period. The participants were required to use both the magnetic and placebo breathing devices, 30 times a day for 28 days each. Each participant acted as their own control and the sequence of the trials was determined by the manufacturers of the pre-coded devices. At baseline and after active/placebo intervention, anthropometric characteristics and lung function were assessed and venous blood samples were collected for later determination of full blood count (FBC), serum EPO and plasma IL-3 concentration. Metabolic and respiratory responses to an incremental exercise protocol were determined during an incremental maximal exercise test. Selected cardiovascular parameters including BP and HR were also measured before, during and for the first two minutes following the exercise test.

Results: Ten participants, aged between 27 and 40 (mean: 32.3±4.9 yr) with a mean stature (cm) of 175.8±7.7 reported compliance with all aspects of the study. Analysis of the physical characteristics, including mass, % body fat, resting HR and blood pressure in this sample (*n=10*), revealed no significant difference (*p>0.05*) between mean (±SD) at baseline and after placebo or active trials.

Six participants (60%) recorded a statistically significant (*p<0.05*) improvement (vs. baseline) in forced vital capacity following the active and placebo trials. Maximal exercise test duration ranged between 8 to 17 minutes. Five participants (50%) recorded a statistically significant improvement (vs. placebo, *p=0.02*) in maximum treadmill workload and running time following the active trial.

Six of the sample presented with RBC count increases in (vs. placebo) and five with an increase in Hb concentration (vs. placebo) following the active trial. The mean (±SD) increases in this subsample of positive responders were both significant (*p=0.02; 0.047*) and corresponded with increases in $\dot{V}O_2$ maximum in each of these individuals. However no significant differences (*p>0.05*) were obtained in the means (±SD) of the circulating concentration of the hormone EPO and the haematopoietic growth factor, IL-3, between active and placebo trials. The association between pre-post change in serum EPO concentration and plasma IL-3 concentration and changes in RBC count were also not significant (*p>0.05*).

Mean (±SD) and range of recovery HR, both 60 and 120 seconds post-test, showed no statistically significant improvement (*n=10, p>0.05*). Upon analysis of individual results, four of the participants showed an improvement in 120 second post maximal exercise test HR recovery when using the active device. The mean (±SD) of the improvement in this subsample was statistically significant (*p=0.03*). Although mean (± SD) post-test diastolic BP was not significantly lower in the full sample (*n=10*), there was a significant drop in this parameter in five individual participants following the active trial (*p<0.03*).

Conclusion: Only 50% of this subsample presented with significantly improved performance during the treadmill running test and 40% with significantly improved Hb concentration, HR at 120 seconds post exercise and post exercise DBP. 60% of the sample presented with a significant improvement in RBC, but this was not related to an associated increase in $\dot{V}O_2$ maximum. Serum IL-3 and plasma EPO concentrations do not appear to be the mechanisms by which the beneficial effects on RBC count are mediated.

The possibility of the existence of responders and non-responders to this intervention and factors which influence this potential response, require further examination. Further studies examining the benefits of the magnetic breathing device, also need to consider the possibility of under-acknowledged reduced compliance in the frequency of the device usage by human participants.

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LIST OF ABBREVIATIONS

SaO_2	Arterial blood oxygen saturation
$(a\text{-}v)O_2$	Arterio-venous oxygen difference
BP	Blood Pressure
bpm	Beats per minute
BHT	Breath holding time
BF	Breathing frequency
CO_2	Carbon dioxide
Q	Cardiac output
DBP	Diastolic blood pressure
EPO	Erythropoietin
FEV_1	Forced expiratory volume
FIVC	Forced Inspiratory Capacity
FVC	Forced vital capacity
FVC/FEV_1	Forced vital capacity: Forced expiratory volume
G	Gauss
Hb	Haemoglobin
Hct	Haematocrit
HR	Heart rate
H^+	Hydrogen ion
IL-3	Interleukin-3
$\dot{V}E$ max	Maximum pulmonary ventilation
MCH	Mean cell haemoglobin
MCHC	Mean cell haemoglobin concentration

MCV	Mean cell volume
mT	Micro-Tesla
mU/mL	Milliunits per milliliter
NO	Nitric oxide
NOS	Nitric oxide synthase
O_2	Oxygen
PO_2	Partial pressure in oxygen
HCO_3^-	Plasma bicarbonate
PEH	Post-exercise hypotension
RPE	Rating of perceived exertion
RER	Respiratory exchange ratio
RHR	Resting heart rate
RBC	Red blood cell
RDW	Red cell distribution width
SMF	Static magnetic field
SBP	Systolic blood pressure
T	Tesla
Ts	Training index
TV	Tidal volume
$\dot{V}O_2$	Volume of oxygen consumption per unit of time

CHAPTER ONE

INTRODUCTION TO THE STUDY

1.1 Background

Magnetic therapy, the use of magnetic fields to treat a range of medical conditions, has in recent years accumulated a great following. It has been observed that magnetic fields have the ability to alter water solubility, enzyme activity, gene expression, ion transport, membrane permeability and mitochondrial function (George *et al.*, 1996). It has also been shown that magnetic therapy is beneficial in arthritis and pain relief (Mizushima, 1975), and that it enhances neurological and endocrine function (Hong, 1987).

The Therahaler® O_2 Gold is a magnetic breathing device that was originally invented by Bryan Speight of the Royal Pharmaceutical Society of Great Britain in 1998 and is currently being marketed as the "O_2 Gold" by a South African company, Rexi Pharmaceuticals CC. A magnetic coil of strength 1500 or 3000 Gauss (G) is the active component of the inhaler and inspired air is drawn directly through it. The manufacturers currently recommend that it is used over a period of 4-8 weeks, with a minimum of 25-30 inhalations to be taken daily at any stage or interval period throughout the day.

When air is inhaled through this device, it passes through a magnetic field at which point the inhaled oxygen (O_2) is ionized and develops a magnetic charge. The magnetized O_2 is then drawn into the lungs and onto the iron binding sites of the haemoglobin (Hb). O_2 transport to alveolar capillaries is thought to be accelerated and binding to Hb improved (Chater *et al.*, 2006; Roberts *et al.*, 2008). The manufacturers claim that the magnetic charge is then imparted onto a number of different molecular and biological systems as the blood circulates through the body.

The magnetic breathing device was first designed to assist with asthmatic patients' integration into a normal, functional lifestyle. Rexi Pharmaceuticals CC claims that the O_2 Gold is non-medicative and beneficial to athletes of all ages. These marketers of the O_2 Gold magnetic inhaler also suggest that athletic performance may be enhanced by magnetic fields, possibly by accelerating cell membrane substrate transport systems, elevating enzyme activity and ATP production. Further claims following magnetic induction and use of a

magnetic breathing device are an elevation in haematocrit (Hct) and Hb concentration (Chater *et al.*, 2006), improvement in immune response (Jankovic *et al.*, 1991), improved respiratory muscle function (Roberts, 2008), a lower resting heart rate (HR; Ryan, 2010), as well as post-exercise HR recovery (Ryan, 2007), collagen deposition (Zhang *et al.*, 2000) leading to accelerated muscle repair (Zhang *et al.*, 2000), and increased bone mineral density (Costantino *et al.*, 2007).

For athletes, international attention and the rise in popularity of sport has been partnered with a tremendous amount of pressure to excel and maintain high performance levels. This has led to many athletes opting for performance-enhancing substances which are often illegal and potentially detrimental to their long-term health (Krcik, 2001). The magnetic breathing device may serve as a viable substitute for illegal performance enhancers if it yields the results claimed by the former marketers, Magnetic Air Health Products, and Rexi Pharmaceuticals.

In the initial two unpublished pilot studies examining the effects of regular use of the Therahaler® O_2 Gold on athletic performance over a four week-period, first described by Roberts (2004), heart rate recovery in 14 triathletes after completing a 15 minute cycle ergometer test as well as changes in endurance capacity in rugby players, were examined. In the triathletes using an active device (n=10), a significant reduction in resting heart rate, immediate post-exercise as well as recovery heart rate, one and three minutes after completing the cycle test was reported compared to those using a placebo device without a magnetic coil (n=4), while the rugby players using the Therahaler® O_2 Gold (n=8) showed a 10.15% increase in performance in the sprint bleep test when compared to that of a control group (n=20).

A large scale double-blind placebo-controlled clinical maximal cycle trial was thereafter conducted to determine if the Therahaler® O_2 Gold improved peak power output and exercise time to exhaustion after four weeks of use. Roberts (2007) reported that there was a significant 6.88% increase in the peak power output as well as a significant improvement ($p < 0.05$) in recovery heart rate and rate of perceived exertion (RPE) in the active group on a 1500G magnetic device (n=44) compared to that of the placebo group (n=59) and a group on a 3000G magnetic device (n=35).

As the evidence of the efficacy of this magnetic breathing device in optimizing athletic performance, is however presently primarily based on unpublished and anecdotal reports with only one extensive double–blind placebo-controlled trial having been conducted (Roberts, 2007), a further double blind, placebo-controlled, cross-over study was designed to confirm these reports of performance benefits and begin an investigation into possible mechanisms which could explain the possible improvements in cardio-respiratory function in endurance athletes using this device.

1.2 Primary Aim

To determine the effects of 28 days of regular O_2 Gold usage, according to the current specifications of the manufacturers, on the cardio-respiratory function of well-trained endurance athletes during a maximal exercise test.

1.3 Secondary Objectives

1. To determine the effects of regular use of the magnetic inhaler on the following parameters during and following an incremental treadmill exercise test to exhaustion:

- peak power output and maximal running time on the treadmill
- absolute and relative maximum oxygen consumption ($\dot{V}O_2$ max)
- RPE, HR, $\dot{V}_E$, respiratory exchange ratio (RER) and O_2 saturation at the workload at which $\dot{V}O_2$ max was reached
    a. submaximal minute ventilation ($\dot{V}_E$, $L.min^{-1}$), absolute O_2 uptake ($\dot{V}O_2$, $L.min^{-1}$), heart rate (HR), rating of perceived exertion (RPE), and O_2 saturation
- HR recovery during the first two minutes post exercise

2. To determine the effects of regular use of the magnetic inhaler on pre-exercise forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FVC/FEV_1 and forced inspiratory volume (FIV_1).

3. To determine the effects of regular use of the magnetic inhaler on red blood cell indices, serum erythropoietin (EPO) and plasma interleukin-3 (IL-3) concentrations in pre-exercise venous blood as well as exercise-induced elevations in nitric oxide in plasma

1.4 Hypotheses

In view of the apparent consensus in the literature, albeit by a limited number of published studies, regarding a performance enhancing effect following regular use of the magnetic inhaler, a positive alternative hypothesis was set for the objectives relating to this effect, namely,

Twenty-eight days of regular use of the 1500G O_2 Gold magnetic breathing device will improve

- *peak power output and maximal running time on the treadmill*
- *pre-exercise test respiratory function, RBC and Hb concentrations and Hct of endurance athletes*

In view of the lack of published research findings and consensus regarding the objectives concerning possible mechanisms for this, null hypotheses were set of the remainder of the study objectives, namely,

Twenty-eight days of regular use of the 1500G O_2 Gold magnetic breathing device will not affect

- *absolute and relative maximum oxygen consumption ($\dot{V}O_2$ max)*
- *RPE, HR, $\dot{V}_E$, respiratory exchange ratio (RER) and O_2 saturation at the workload at which $\dot{V}O_2$ max was reached*
- *submaximal minute ventilation ($\dot{V}_E$,), absolute O_2 uptake ($\dot{V}O_2$,), heart rate (HR), rating of perceived exertion (RPE), and O_2 saturation*
- *resting circulating IL-3 and EPO concentrations*
- *exercise-induced increases in systemic concentrations of nitric oxide*

CHAPTER TWO

REVIEW OF THE RELATED LITERATURE

2.1 Magnetism and Magnetic Therapy

Magnetism is created primarily by the motion of electrically charged particles (Durney *et al*., 1999). A magnetic field is a force field generated by these moving electrical charges (Saini *et al*., 1988). Figure 2.1 below represents how electrical charges behave in the absence and presence of a magnetic field. In permanent magnets, this is created by the quantum mechanical motion of electrons in the atoms, each of which produces a magnetic moment (Jackson, 1988). The strength of a magnetic field is its magnetic flux density, with the SI unit of measurement being the Tesla (T) (Nave, 2007). For a magnetic flux density of one Tesla, a force of one Newton must act on a one meter length of wire carrying one ampere of one current (Nave, 2007). One Newton of force is a very large force. Therefore a smaller unit of magnetic flux density is often used: Gauss (G) (1 Gauss = 1/10000 Tesla) (Nave, 2007). The earth's magnetic flux is 0.5 Gauss, whereas the strength of the magnetic field of a fridge magnet is about 10 Gauss (Crowell, 2006).

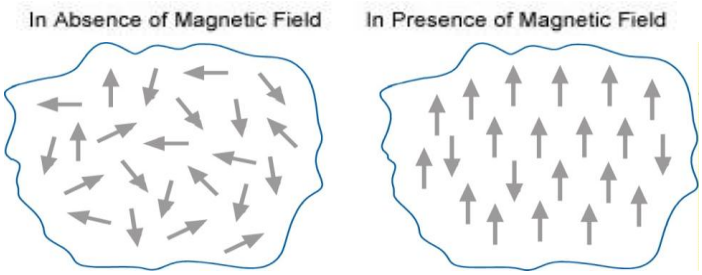

Figure 2.1 Moving electrical charges in the presence of a magnetic field.
Adapted from: www.themagnetguide.com/magnetic-materials.html

Many civilizations throughout history have used magnets and the magnetic field they create, to treat illness and enhance the lives of human beings (Roberts, 2008). Magnetic therapy has also been reported to be useful in treating ailments such as fractures (Sharrard, 1990), wound healing (Lee *et al*., 1993; Man *et al*., 1999), chronic pain (Valbona *et al*., 1997) and psychiatric disorders, including depression (Baker-Price and Persinger, 1996).

For example, more recently the effect of static magnetic fields on cutaneous wound healing in an animal model was analysed by Henry *et al*. (2008). Standardized wounds were created on the backs of 33 Sprague-Dawley rats, which were divided into three groups to which a 23

gauss magnet, a sham magnet, or no magnet was positioned over the wound. Wounds in the magnet group healed in an average of 15.3 days, significantly faster than those in either the sham group (20.9 days, $p=0.006$) or control group (20.3 days, $p<0.0001$). Localized inflammation was induced via injection of inflammatory agents into rat hind paws (Morris and Skalak, 2008). Application of a 10 or 70 mT magnet for 15 or 30 minutes immediately following histamine induced oedema, resulted in a significant, 20–50% reduction in oedema formation. Costantino *et al*. (2007) studied 40 patients with wrist fractures after applying a magnet of 12,500 G directly over the fracture in the plaster cast of the participants. This resulted in bone callus formation that produced a 35% improvement in healing rates compared to standard time. The pain-relieving efficacy of static magnetic fields produced by 200 G magnets compared with 50 G magnets were also examined in a double-blind, randomized, two-phase crossover study in patients with chronic lumbar radicular pain. Pain was rated on a scale of 1-10. A greater increase in pain was observed with use of the 200 G magnet (Khoromi *et al*., 2007). Laszlo *et al*. (2009) examined antinociceptive activity in the writhing test in mice and concluded that a 3 T homogeneous static magnetic field of a clinical magnetic resonance system induces a significant pain-inhibitory effect and Butariu *et al*. (2009) confirmed improved neural function when they investigated the application of pulsed magnetic fields in the rehabilitation treatment of 20 participants with peripheral nerve lesions of the hand and reported an 11.1% improvement in peripheral nerve function.

There is, however, limited information relating the use of magnetic therapy to enhance athletic performance (Roberts, 2004; 2007; Roberts *et al*., 2008). Bassett and Howley (1997) proposed that athletic performance may be enhanced by magnetic fields possibly by accelerating cell membrane substrate transport systems, elevating enzyme activity and ATP production. It has been found to enhance nerve excitability (Hong, 1987), Hct and Hb concentration (Chater *et al.,* 2006), collagen deposition (Zhang *et al*., 2000) and immune response (Jankovic *et al*., 1991). Further claims of an improved isometric exercise benefit for the inspiratory muscles (Roberts, 2004; 2007), a lower resting heart rate (HR; Ryan, 2007), improved muscle repair (Zhang *et al*., 2000), bone mineral density (Costantino *et al*., 2007), post-exercise HR recovery (Ryan, 2007), vascular tone and tissue perfusion and general nervous system function have been made (Hong, 1987).

Little is however known of the exact mechanisms which are responsible for the reported elevation of RBC count, Hct and Hb concentrations, which may affect endurance capacity (Chater *et al.*, 2006). Whether regular exposure to magnetic fields, for example, enhances RBC concentrations by affecting blood erythropoietin hormone concentrations or haematopoeitic growth factors, is unknown.

Oxygen (O_2) is the only gas that exhibits paramagnetic properties with molecular attraction and orientation in the presence of a magnetic field. This is caused by the electrons in motion in atoms forming microscopic current loops that are capable of forming magnetic fields of their own, a phenomenon that is recognised and utilised in Magnetic Resonance Imaging (Griffith *et al.*, 1984). Figure 2.2 is an enlarged diagrammatic representation of an oxygen molecule showing the configuration of electrons surrounding the nucleus.

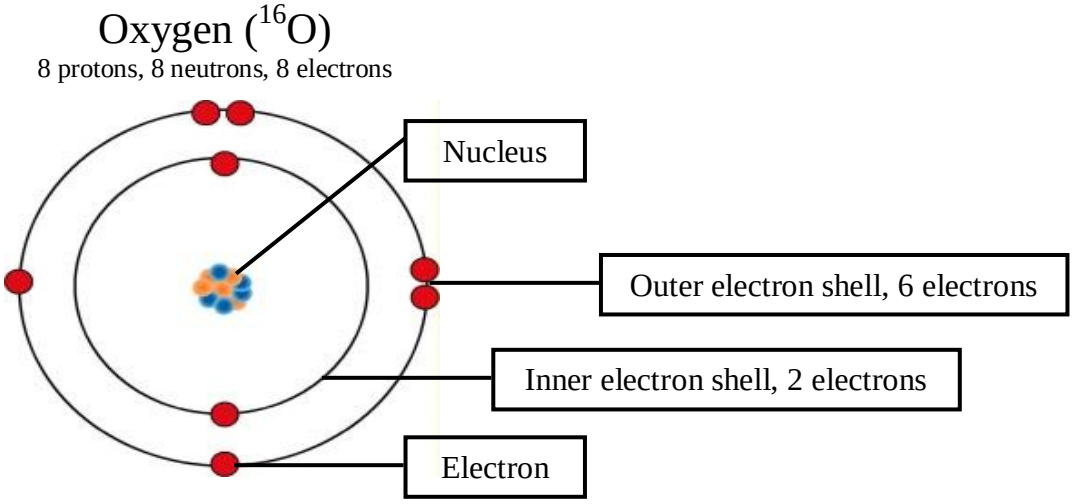

Figure 2.2 Diagrammatic representation of an oxygen molecule.
Adapted from: www.google.co.za/imgres?imgurl=&imgrefurl=http%3A%2F%2Fmontessorimuddle.org%2F2013%2F01%2F13%2Fdrawing-atoms%2F&h=0&w=0&sz=1&tbnid=0zjpV8agojJf_M&tbnh=226&tbnw=223&zoom=1&docid=uEEwRm7Fe2ucqM&hl=en&ei=bg9RUpnqOsGJ7Aav74DICA&ved=0CAIQsCU

In the case of recently designed breathing devices containing magnets varying in strength from 1800 to 3000 Gauss, atmospheric O_2 inhaled through the device, is thus ionized. The charged O_2 then passes through the lungs and onto the iron binding sites of Hb within the red blood cells. Miller (1977) found that magnetic fields reduce water surface tension, possibly by altering characteristics of hydrogen bonding equilibrium and may hold this charge for 24 hours. The surface tension of water (Gerber, 2001) is affected as hydrogen bonding occurs when a negative O_2 atom of one water molecule is attracted to the positive hydrogen atom of another water molecule. Water makes up the majority of blood therefore it is proposed that the charge may affect nutrient solubility and athletic performance (Miller, 1977).

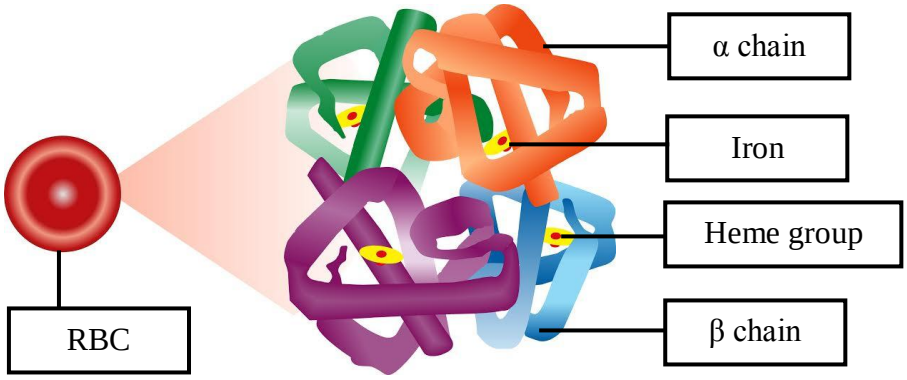

Figure 2.3 Diagrammatic representation of a haemoglobin molecule.
Adapted from: http://gassama.myweb.uga.edu/

Hb is a molecule comprising an iron atom surrounded by a ring of hydrogen, O_2 and carbon atoms which make up four polypeptide chains and the globin portion of the Hb molecule, as can be seen in Figure 2.3 above. Under conditions of neutral or alkaline pH, iron is found in the Ferric state (Fe^{3+}) state and at acidic pH, the Ferrous state (Fe^{2+}) state is favoured. The Fe^{3+} state is not readily soluble and the Fe^{2+} state favours O_2 binding (Sakurai *et al*., 2000). It is suggested that O_2 reduces haeme iron from its Fe^{3+} to its Fe^{2+} therefore gaining an electron and an O_2 molecule. Thereby oxyhaemoglobin levels and active tissue O_2 perfusion are increased (Sakurai *et al*., 2000).

Zhernovoi *et al*. (2001) found that in some Hb molecules exposed to a magnetic field, the bond between nitrogen and iron atoms are disrupted, causing Hb activation. O_2 may then be added to the free bond of the iron atom of activated Hb. The enhanced O_2 carrying capacity of blood may be explained by the binding of two O_2 molecules to the iron atom of Hb in the presence of a magnetic field, forming bioxyhaemoglobin. Bioxyhaemoglobin however, is dependent on a constant magnetic field, and decomposes when the magnetic field is removed. Formation of bioxyhaemoglobin also depends on the plasma concentration of dissolved O_2 (Zhernovoi *et al*., 2001).

2.2 Magnetic Breathing Device

The O_2 Gold magnetic breathing device, previously marketed as the Therahaler® O_2 Gold, is a non-medicative magnetic breathing device that was initially developed by Bryan Speight, a member of the Royal Pharmaceutical Society of Great Britain in 1998, as an aid to treat asthma and in response to the results of research on the magnetic effects of O_2 and O_2 transport. This early work was conducted by Prof Botiko of Moscow University and Dr B Shapiro, assistant professor, Department of Anaesthesiology from North-western Medical School (Shapiro, 1973).

The generally accepted procedure for use of the device, which is schematically represented in Figure 2.4 below, is that patients/athletes are required to breathe in through the O_2 Gold containing a solid magnet and fill their lungs to full capacity. Thereafter, are required to hold their breath for as long as reasonably possible, and then exhale. It is suggested that athletes should do this 25 to 30 times a day for the initial 4 weeks, whereas an asthmatic person is required to complete an 8 week period. Subsequently a maintenance program of twice a day is sufficient.

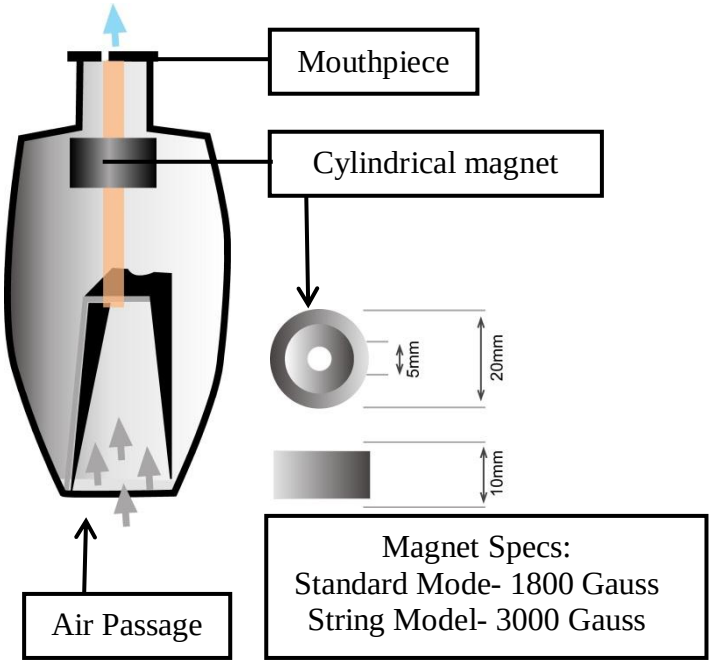

Figure 2.4 Schematic representation of the O_2 Gold magnetic breathing device.
Adapted from: www.ammhealth.co.za/therahaler/effects.htm.

2.3 Studies on the Effects of the O_2 Gold on Athletic Performance

The O_2 Gold magnetic breathing device is firstly believed to help condition the inspiratory respiratory muscles. When air is inhaled through the device, it is designed to create slight resistance to such airflow. This increases the work of the respiratory muscles during the inhalation. Several different studies have indicated that exercise does induce respiratory muscle fatigue (Johnson *et al*., 1993; Mador *et al*., 1993) and that respiratory muscle fatigue can limit exercise performance (Mador *et al*., 1991). Respiratory muscle training, particularly inspiratory muscle training is therefore thought to enhance endurance exercise performance in both trained and untrained individuals (Boutellier *et al*., 1992; Splenger *et al*., 1998; Splenge, 1999). The potential inspiratory muscle training provided by regular use of the O_2 Gold may therefore be more directly responsible as a benefit than the magnetism of

the device itself and it is acknowledged by the author that such alternate factors do exist in contributing to improved endurance performance.

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Two initial pilot studies that were conducted using the magnetic breathing device were done on asthmatic patients by Drs Giereke and van der Linde, pulmonologists from Durban in 1999 and 2001, respectively (Roberts, 2007). In the first trial, Giereke found a significant reduction in the use of asthma medication as well as a reduction in the number and severity of asthma attacks (Geireke, 1999). In the second study by van der Linde, 45 asthmatics were assessed according to quality of life. The use of the Therahaler® O_2 Gold resulted in a reported improvement in the quality of life and a 71% reduction in the use of reliever medication, with no side effects reported (van der Linde, 2001). There are also anecdotal reports of a number of the active trial patients that indicate an improvement in their physical performance and a few athletes reported running their personal best times while using the Therahaler® O_2 Gold (Roberts 2004).

In terms of the effect of regular prolonged usage of the Therahaler® O_2 Gold on athletic performance, the first pilot trial was conducted by Angus Ryan, a Biokinetisist, on 14 triathletes in 2003. As described by Roberts (2004; 2007), a heart rate recovery test was conducted on 10 athletes who were given an active Therahaler® O_2 Gold device and four who were given placebo devices (identical breathing devices without a magnetic coil). A 15 minute cycle ergometer test was completed and heart rate responses were analysed, both

before and after the standardized cycle ergometer test at the commencement of the study and again after 4 weeks. As is shown in Table 2.1, the O_2 Gold group showed a significant reduction in resting heart rate immediately after completing the 15 minute cycle, as well as recovery heart rate one and three minutes after completing the test, when compared to the placebo group (Ryan, 2007). Table 2.1 details the findings of his study.

Table 2.1 Heart rate response to regular use of the Therahaler® O_2 Gold.
Adapted from: Ryan (2007).

Test Parameter	**Athletes using O_2 Gold (n=10)**			**Athletes using Placebo (n=4)**		
	At Start	After 4 weeks	% Change	At Start	After 4 Weeks	% Change
Ave resting heart rate (bpm)	66.14	61.80	-7.35	64.75	66.50	+1.02
Ave resting heart rate after 15 min exercise (bpm)	160.20	150.50	-6.00	163.75	165.00	-0.91
Ave resting heart rate after 1 minute rest (bpm)	122.70	105.60	-13.90	123.00	124.25	+1.00
Ave resting heart rate after 3 minute rest (bpm)	91.30	81.10	-11.70	92.25	98.25	+6.25

In the same year (2003), Roberts also conducted controlled testing on a 28-man rugby squad over a four week exercise regime during which the sprint bleep-test was used to measure endurance levels. At the end of the four weeks the Therahaler® O_2 Gold users (n=8) showed a 24.44% increase in performance in the bleep test whilst the control group (n=20) showed a 14.29% increase (Roberts, 2004; 2007).

In a further unpublished local pilot study described in Roberts (2004), blood gas, Hb and oxyhaemoglobin levels were assessed in seven participants using the Therahaler® O_2 Gold for four weeks. Following extraction of baseline arterial blood samples, participants were required to use the Therahaler® O_2 Gold according to the manufacturer's recommendations at 30 minute intervals during waking hours and again report for arterial blood sampling after two and four weeks. Although the average oxyhaemoglobin levels rose over the four weeks from 93.69 to 94.75%, this increase only reached borderline statistical significance (p = 0.0516) and it is not certain whether the mean increase confirms a clinically significant

therapeutic effect of improved bonding of the oxygen to the Hb. Interestingly, the PCO_2 levels were not significantly disturbed (p=.3184), ruling out the possibility of a possible improvement in mean oxyhaemoglobin concentrations being the result of hyperventilation.

In a subsequent double-blind baseline maximal cycle trial undertaken to determine if the Therahaler® O_2 Gold improved peak power output and exercise time to exhaustion after four weeks of use, 131 healthy participants were recruited from running, cycling, swimming, triathlon, hockey and rugby clubs (Roberts, 2007; Roberts *et al.*, 2007). Following baseline maximal cycling tests, the participants were divided into three groups, a placebo group (n=52) and two active groups, on a 1500G (n=44) and on a 3000G Therahaler® O_2 Gold (n=35). The participants were requested to use the device every 30 minutes throughout the day while awake, and to record their daily use as well as training volume and intensity. They were then retested two and four weeks after device use. Roberts (2007) found that after two weeks there was no significant difference in the peak power output and in exercise time to exhaustion in the three groups ($p>0.05$). However, after four weeks of use there was a significant 13.78% increase in the peak power output in the 1500G group ($p=0.0004$) compared with a 6.90% increase in the placebo group ($p=0.0122$), but no significant change in the 3000G group ($p=0.1$). After four weeks there was also a significant improvement in the mean exercise time to exhaustion in all three groups; the mean improvement in the 1500G group was 85 seconds ($p<0.0001$), in the 3000G group, 53 seconds ($p=0.027$) and in the placebo group, 53 seconds ($p<0.001$).

Although there was also no significant difference in the HR response to exercise in the placebo and 3000G group ($p>0.1$), in the 1500G group after four weeks of usage, there was a significant reduction in the heart rate after four and a half minutes and after seven minutes of exercise ($p<0.05$). After two weeks there was a significant reduction in the rating of perceived exertion (RPE) after four and a half minutes of exercise in the 1500G group ($p<0.05$), and after four weeks there was a significant reduction in the RPE after four and a half minutes in the 1500G and 3000G group ($p<0.05;$ Roberts, 2007).

The author acknowledges that the above reviewed literature relies primarily on unpublished, anecdotal and often small-scale works, with only one extensive double blind placebo-controlled trial (also unpublished), having been conducted to date. It can therefore be concluded that further work in which major extraneous confounders such as changes in training status, compliance and diet are controlled, is necessary in order to confirm the

findings of the above-mentioned studies. Furthermore, to the author's knowledge, no work examining possible mechanisms which may contribute to the reported apparent benefits of magnetic therapy on athletic performance, has yet been published.

2.4 $\dot{V}O_2max$

The term "maximal oxygen consumption" ($\dot{V}O_2max$) was first coined and defined by Hill and Herbst in the 1920s (Warpeha, 2003). In 1923 Hill and Lupton postulated that (i) there is an upper limit to O_2 uptake, (ii) there are inter-individual differences in $\dot{V}O_2max$ and (iii) a. high $\dot{V}O_2max$ is a prerequisite for success in middle and long distance running with $\dot{V}O_2max$ being limited by the ability of cardiorespiratory system to transport O_2 to the muscles

Traditionalists supporting these early theories of a physiological upper limit to the body's ability to consume O_2, claim that $\dot{V}O_2max$, the highest rate at which one can transport and utilise oxygen, is the most widely accepted determinant of ability in endurance sports (Bassett and Howley, 1999). $\dot{V}O_2max$ thus remains one of the most commonly measured parameters in the basic and applied physiological sciences.

Absolute values of $\dot{V}O_2max$ are typically 40-60% higher in men than in women (Hyde *et al*., 2007). The average untrained healthy male will have a $\dot{V}O_2max$ of approximately 35–40 $mL.kg.^{-1}min^{-1}$ whereas the average untrained healthy female will score a $\dot{V}O_2max$ of approximately 27–31 $ml.kg^{-1}.min^{-1}$ (Heywood, 1998; Guyton and Hall, 2011). These scores can improve with training and decrease with age, although the degree of trainability also varies very widely. Conditioning has been reported to double $\dot{V}O_2max$ in previously untrained individuals, and to only marginally improve it in others (Kolata, 2992; Claude *et al*., 2007). In sports in which endurance is an important component in performance, such as cycling, rowing, cross-country skiing, swimming and running, world class athletes typically have $\dot{V}O_2$ maxima in excess of 70 $mL.kg^{-1}.min^{-1}$. Elite male runners can consume up to 85 $mL.kg^{-1}.min^{-1}$, and female elite runners can consume about 77 $mL.kg^{-1}.min^{-1}$ (Noakes, 2001).

According to the classical, traditional premise, the capacity of the heart, lungs and blood to transport oxygen to the working muscles, as well as the muscles' ability to utilize that oxygen during exercise determine $\dot{V}O_2max$ (Bassett and Howley, 1990). $\dot{V}O_2max$ is therefore, also defined as the product of Q_{max} and ($C_aO_2 - C_vO_2$) where Q_{max} is the maximum cardiac output, C_aO_2 is the arterial oxygen content, and C_vO_2 is the venous oxygen content. $C_aO_2 - C_vO_2$ is also known as the arteriovenous (a-v) oxygen difference. Limiting

physiological factors would therefore include the inspiratory capacity of the lungs, pulmonary diffusing capacity of O_2 into the pulmonary circulation, O_2 transport to the active muscles which is dependent on maximal cardiac output and the O_2 carrying capacity of the blood and skeletal muscle characteristics including diffusion capacity, mitochondrial enzymes, and capillary density (Bassett and Howley, 1990). These limiting physiological factors are represented in Figure 2.5.

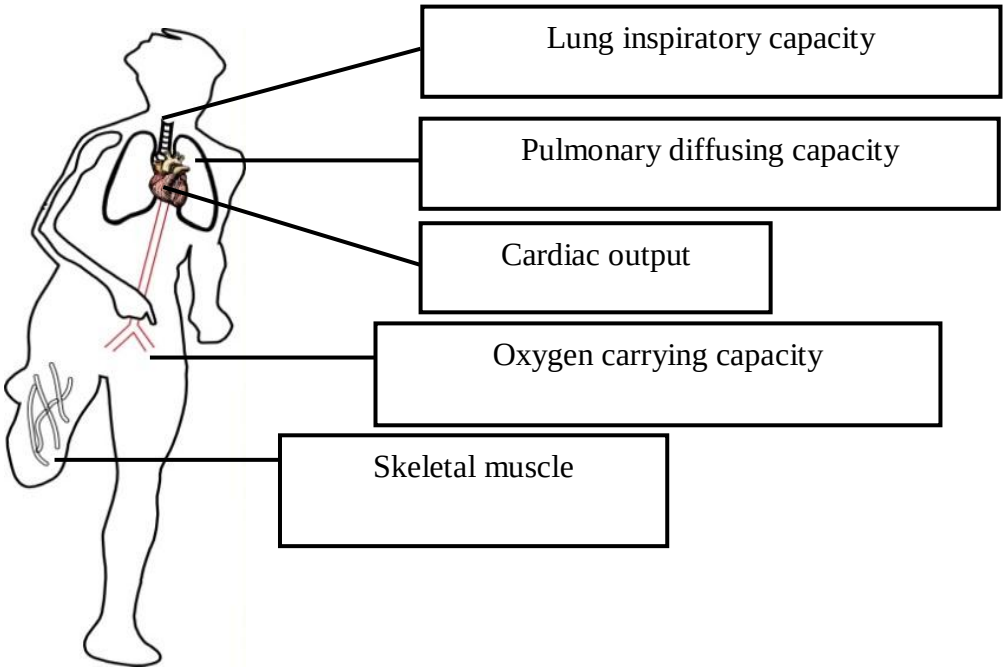

Figure 2.5 Physiological factors that potentially limit maximal oxygen uptake in exercising humans. Adapted from: Bassett and Howley (1999).

The first four of these factors are commonly classified as the "central" factors, while those relating to uptake of oxygen by skeletal muscle are termed the "peripheral" factors. Although both sets of factors suggest that availability of O_2 limits muscle fiber oxidative ATP production, traditionally, exercise physiologists that support the traditional/ classical theory of the determinants of $\dot{V}O_2max$ are divided into proponents of the "central" and "peripheral" perspectives.

2.4.1 Central Factors

The pulmonary system consists of the lungs, responsible for saturating the arterial blood with O_2. It is well accepted that healthy lungs are able to saturate the arterial blood with O_2 extremely well (Guyton and Hall, 2011). Hill *et al*., however, predicted that a significant drop in arterial saturation does not occur based on the appearance of their participants in the early 1920's and modern researchers have verified that the pulmonary system may indeed

limit VO_2max under certain circumstances (Bassett and Howley, 1999). Dempsey *et al*. (1984) showed that elite athletes are more likely to undergo arterial O_2 desaturation during maximal work compared with normal individuals. The reason for this has been related to the fact that trained individuals have a higher cardiac output than untrained individuals, and this therefore leads to a decreased transit time of the red blood cells in the pulmonary capillary. Consequently there may not be enough time to saturate the blood with O_2 before it exits the pulmonary capillary. However this pulmonary limitation in highly trained athletes can be overcome with O_2-enriched air (Dempsey *et al*., 1984), a fact which may be of great significance in terms of the potential effect of usage of a magnetically charged breathing device.

In 1923 Hill *et al*. proposed that cardiac output, the product of the stroke volume and heart rate, was the primary factor explaining individual differences in $\dot{V}O_2$max. Today it is known that the normal range of $\dot{V}O_2$max values observed in sedentary and trained men and women of the same age is due primarily to variations in maximal stroke volume, given that considerably less variation exists in the maximal heart rate which also decreases with age, although to a much lesser extent (Hill *et al*., 1923; Bassett and Howley, 1999).

It has been estimated that 70-85% of the limitations in $\dot{V}O_2$max are linked to the maximum cardiac output (Cerretelli and Prampero, 1987). Longitudinal studies have shown that the training induced increases in $\dot{V}O_2$max result primarily from an increase in maximal cardiac output, rather than a widening of the systemic (a-v) O_2 difference, which is regarded as a peripheral factor and will be discussed below (Bassett and Howley, 1999).

Another "central" factor involved in oxygen delivery is the muscle blood flow. During exercise there is a redistribution of cardiac output so that muscle blood flow can increase from a resting volume of ±1L.min^{-1} (20% of cardiac output) to around 20L.min^{-1} (80% of cardiac output) during maximal exercise. However vasodilation of the periphery cannot be unlimited as this would cause a drop in blood pressure. Increasing the demand for peripheral blood flow to an additional vascular bed by adding arm exercise to high intensity leg exercise will cause a reduction in leg blood flow, despite an unchanged work rate. This therefore indicates that the capacity of the periphery to vasodilate is actually greater than that elicited near exhaustion under normal physiological conditions. Muscle blood flow can also be increased without compromising peripheral resistance by increased muscle capillarity.

Since endurance training increases both muscle capillarity and $\dot{V}O_2$max, it is possible that inadequate muscle capillarity could limit the $\dot{V}O_2$max of untrained individuals, although an increase in muscle bulk alone would show an increase in $\dot{V}O_2$max independent of any increases in muscle capillarity.

The next step in the physiological chain would then be the extraction of oxygen from the blood by the working muscles. The finding that femoral venous oxygen content is not close to zero at maximal exercise implies that oxygen delivery is adequate, but the muscle capacity for oxygen extraction may be exceeded. The mechanism of oxygen extraction includes its dissociation from Hb, diffusion from the red blood cells into the muscle cells and finally diffusion and transport within the muscle cells to the mitochondria.

It would therefore be interesting to establish whether an improvement in central factors which govern the maximum O_2 carrying capacity of the blood, including increased respiratory function (resulting in improved pulmonary ventilation), erythrocyte production, Hct, Hb and oxyhemoglobin concentration are related to increases in maximum O_2 uptake during intense bouts of endurance exercise involving the large muscle groups.

2.4.2 Peripheral Factors

While O_2 transport to the active muscles is dependent on central factors including the pulmonary diffusing capacity, maximal cardiac output and O_2 saturation or O_2 carrying capacity of the blood, peripheral factors including O_2 diffusion into the muscle and mitochondrial oxidative capacity have also been considered as possible limitations of $\dot{V}O_2$max, particularly during exercise with small muscle groups (Ferretti *et al.*, 1997).

Systemic O_2 extraction is a possible peripheral factor that can affect the amount of O_2 transported to the active muscles (Bassett and Howley, 1999). During maximum exercise almost all of the available O_2 is extracted from the blood perusing the active muscles. The O_2 content of arterial blood is approximately 200mL $O_2.L^{-1}$ whereas in venous blood draining maximally working muscles it falls to about 20-30 mL $O_2.\ L^{-1}$. This therefore indicates that there is little O_2 left to be extracted out of the blood during heavy exercise.

Honig *et al*. (1992) however presented evidence for a peripheral O_2 diffusion limitation in red canine muscles. According to their experiments and a mathematical model, the principle

site of resistance to O_2 diffusion occurs between the surface of the red blood cells and the sarcolemma. They reported a large drop in PO_2 over this short distance. They therefore concluded that O_2 delivery is not the limiting factor. Without a peripheral diffusion gradient, O_2 uptake will not increase. Within the muscle fibers the mitochondria are the site where O_2 is consumed in the final step of the electron transport chain. In theory, doubling the number of mitochondria should double the number of sites for O_2 uptake in the muscle (Bassett and Howley, 1999). However human studies show that there is only a modest increase in $\dot{V}O_2$max (20-40%) despite a 2.2-fold increase in mitochondrial enzymes (Saltin *et al*., 1977).

Proponents of the classical traditional theory therefore maintain that "$\dot{V}O_2$max sets the upper limit for performance in endurance events" rather than being "the best predictor of athletic ability" (Basset and Howley, 1997). $\dot{V}O_2$max is directly linked to the rate of ATP generation that can be maintained during a distance race, although distance races are not run at 100% $\dot{V}O_2$max. The rate of ATP generation is dependent on the $\dot{V}O_2$ ($mL.kg^{-1}.min^{-1}$) that can be maintained during the run, which is determined by the participants $\dot{V}O_2$max and the percent of $\dot{V}O_2$max at which the subject can perform. For example, to complete a 2:15 marathon, a $\dot{V}O_2$ of about $60mL.kg.min^{-1}$ must be maintained throughout the run. Therefore even if a marathon could be run at 100% $\dot{V}O_2$max, the runner would need a $\dot{V}O_2$max of 60 $mL.kg^{-1}.min^{-1}$ for the above performance. However, since the marathon is typically run at about 80–85% of $\dot{V}O_2$max, the $\dot{V}O_2$max values needed for that performance would be 70.5–75 $mL.kg^{-1}.min^{-1}$. Hence $\dot{V}O_2$max is thought to set the upper limit for energy production in endurance events, but does not determine the final performance.

2.4.3 An Alternative Perspective

Recently a school of thought has emerged which proposes that local muscle factors independent of O_2 delivery may limit the $\dot{V}O_2$max test by halting maximal exercise before the O_2 delivery systems are taken to their maximal capacity (Hawley *et al*., 1995). This muscular limitation could be due to the ability of the mitochondria to utilize O_2. Hawley *et al*.(1995), also thought that the proposed muscular limitation may be independent of O_2 - supply and utilization and dependent rather on the proper function of the muscle fiber excitation and acto-myosin interaction and relaxation.

Factors determining the maximal work rate achieved during the maximal exercise test are therefore multiple and may also be related to skeletal muscle contractile function in the

fatigued state. Under conditions in which the products of high rates of ATP utilizations begin to accumulation, the rate of cross-bridge cycling is reduced by a decrease in myosin-ATPase activity. The subsequent decrease in the rate of ATP hydrolysis spares intracellular ATP concentrations. Accordingly, muscle ATP concentrations will always be maintained above the critical value at which irreversible energy depletion could develop. It may be that maximum high intensity exercise in humans is terminated by a regulated process that specifically presents the development of ATP depletion in the active muscles. However muscle ATP concentrations are preserved in normal individuals even during maximal exercise under ischemic condition. Therefore even in participants with mitochondrial myopathies who lack the oxidative capacity to produce ATP at very high rates, exercise terminates well before the onset of ATP depletion (Bassett and Howley, 1999).

Muscle work rate or power output is not only a function of the myosin ATPase activity and myofibrillar cross-bridge turnover rate, but also the number of interacting cross-bridges and the force produced by each. The metabolites which accumulate during high rates if ATP utilization, such as hydrogen ions and phosphate, also decrease the force produced per cross-bridge and thus a potential decreased maximal power output of the muscles. These metabolites may also decrease the rate of sarcoplasmic reticulum ATPase activity with the result that production of calcium from the intracellular space is less efficient and relaxation is impaired. Hawley *et al*. (1995) therefore concluded that exercise tests that are designed to elicit a $\dot{V}O_2$max may potentially be inhibited by these intramuscular factors before the classical "central" and "peripheral" factors of O_2 utilization have reached an upper limit.

2.4.4 $\dot{V}O_2$ max Versus "Running Economy"

Mechanical efficiency is the ratio of work done to energy expended. The term "running economy" is used to express the oxygen uptake needed to run at a given velocity. This can be shown by plotting oxygen uptake ($mL.kg.^{-1}min^{-1}$) versus running velocity ($m.min^{-1}$) or by simply expressing economy as the energy required per unit mass to cover a horizontal distance ($mL.kg.^{-1}min^{-1}$; Bassett and Howley, 1999). As was pointed out in the rebuttal to this (Noakes, 1998), when one examines the fastest four runners (10 km in 30.5–31 min) there was considerable variability in the economy of running (45–49 $mL.kg^{-1}.min^{-1}$ at 268 $m.min^{-1}$), suggesting a lack of association between the variables. A comprehensive explanation of how $\dot{V}O_2$max and running economy interact to affect running velocity was provided by Daniels (1985) in his description of "velocity at $\dot{V}O_2$max" ($v\dot{V}O_2$max). Figure

2.6 presents a plot of male and female runners equal in terms of $\dot{V}O_2max$, but differing in running economy (Daniels and Daniels, 1992). A line was drawn through the series of points used to construct an economy-of-running line, and was extrapolated to the subject's $\dot{V}O_2max$. A perpendicular line was then drawn from the $\dot{V}O_2max$ value to the x-axis to estimate the velocity that subject would have achieved at $\dot{V}O_2max$. This is an estimate of the maximal speed that can be maintained by oxidative phosphorylation. In this example, the difference in running economy resulted in a clear difference in the speed that could be achieved if that race were run at $\dot{V}O_2max$.

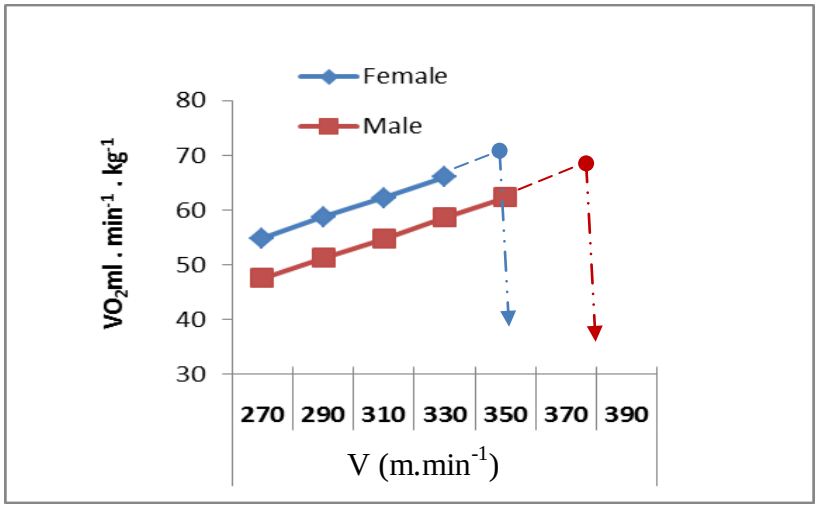

Figure 2.6 Comparison of male and female runners of equal VO_2max where males are significantly favoured in economy and VO_2max. Adapted from: Daniels and Daniels (1991).

2.5 Blood Cell Status and its Regulation

2.5.1 The Role of Erythropoietin

Oxygen carrying capacity is an important component of the 'central' factors which determine $\dot{V}O_2max$. This is dependent on the RBC and Hb concentrations. A factor to be examined would therefore include the possibility that previously shown increased erythrocyte and Hct levels are related to increases renal production of the hormone, erythropoietin (EPO). Erythropoietin, also known as erythropoetin or erthropoyetin or EPO, is a glycoprotein hormone that controls erythropoiesis, or red blood cell production. This would assist in clarifying the currently opposing theories that exist regarding the actions of magnetic fields, which have on the one hand, suggested increased O_2 availability (Saini *et al.*, 1988), but on the other hand, enhanced hormonal activity (George *et al.*, 1996).

The adult human kidney is the main organ for production and release of EPO, which stimulates the proliferation, differentiation and maturation of the erythroid precursors in bone marrow (Jelkmann, 2003), therefore increasing the production of red blood cells. About 120 million erythrocytes are destroyed every minute in the adult human body. This occurs mainly in the spleen, liver and bone marrow (Ratcliffe *et al*., 1996).

To avoid anaemia, equilibrium between the destruction and production of new red blood cells has to be maintained. Under conditions of constant O_2 availability the glycoprotein EPO is the main humoral factor responsible for maintaining a normal blood erythrocyte count (Gunga *et al*., 2007).

EPO concentrations are expressed as milliunits per milliliter ($mU.mL^{-1}$). The normal range of EPO levels in human serum or plasma is in the order of 5-25 $mU.mL^{-1}$, but EPO levels can be increased 100- to 1000-fold in response to hypoxia or blood loss. In healthy individuals and patients with various types of anemia (e.g. caused by blood loss, hemolysis, iron deficiency, aplastic bone marrow or by nutritional deficiencies), EPO levels are inversely correlated with hematocrit and hemoglobin levels, and reflect the reciprocal relation between oxygen supply and EPO production rate (Wognum, 2011).

As endogenous renal EPO production occurs mainly in response to hypoxia, it is under hypoxic conditions, such as training at altitude or with O_2 depleted gas and living in O_2 depleted tents, that athletes have been able to increase their production of EPO and thus in return increase their red blood cell count. This therefore results in an increase in Hb concentrations, which will ultimately result in the fundamental increase in O_2 carrying capacity and availability of O_2 to the active skeletal muscle. It would therefore be interesting to ascertain whether the mechanism by which the reported increases in Hct levels are related to magnetically induced increases in endogenous production of EPO despite the apparently contradictory findings that magnetic therapy has been shown to increase O_2 availability.

2.5.2 Interleukin-3

Another potential mediator of the regulation of red blood cell production is via systemic concentrations of interleukin-3 (IL-3). This is a cytokine protein signaling molecule produced by T cells and mast cells, which acts as a broad spectrum haematopoeitic growth factor, regulating the differentiation of myeloid stem cells into red blood cells, thrombocytes

and granulocytes (Guyton, 2011). It is therefore of interest to ascertain whether regular exposure to a magnetic field over a 28 day period, will increase systemic concentrations of this cytokine, and thereby account for the previously described increase in RBC count reported by Chater *et al. (*2006).

2.6 Criteria used to determine the endpoint of a maximal exercise test

A phenomenon sometimes encountered in elite endurance athletes is the VO_2max plateau as opposed to a peak $\dot{V}O_2$ which is commonly encountered in less well trained athletes. When an athlete is challenged to progressively increasing workloads, with sufficient time for recovery between each increment of work, a linear relation between workload and oxygen intake occurs. Ultimately, maximal oxygen intake per unit of time is reached. Beyond this point the workload can usually be increased even further, but oxygen intake levels off or declines. This is commonly referred to as the $\dot{V}O_2$max plateau (Mitchell *et al.*, 1957).

Considerable variation in the achievement of a plateau in $\dot{V}O_2$ has been reported in literature. For example the percentage of participants who achieve a plateau has been reported at 90-100% (Taylor *et al.*, 1955), 60-80% (Sidney *et al.*, 1977) and ≤50% (Froelicher *et al.*, 1974). Therefore a variety of factors must be considered when making a judgement about each individual case or difficulties encountered in achieving a plateau in oxygen uptake. These include the population being studied, as children, unfit and elderly people are more likely to only reach $\dot{V}O_2$ peak when the test needs to be stopped due to exhaustion before they have reached their true $\dot{V}O_2$max. Trained and untrained people also display varied oxygen uptake, as represented by Figure 2.7.

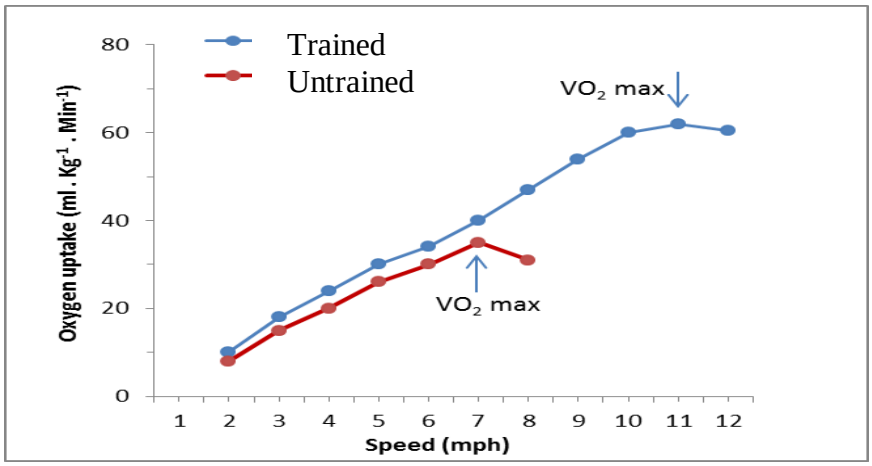

Figure 2.7 The comparison in $\dot{V}O_2$ peak reached in trained and untrained individuals. Adapted from: Bassett and Howley (1999).

Pulmonary respiratory gas-exchange ratios (RER) defined as CO_2 production/O_2 consumption is used as a secondary criterion for having reached $\dot{V}O_2max$. It is based on the reaction between a rise in plasma hydrogen ion (H^+) concentration and plasma bicarbonate (HCO_3^-). As the CO_2 is generated ventilation increases thus increasing the RER (ACSM, 9th edition). The use of an RER value ≥1.15 as a criterion for achieving $\dot{V}O_2max$ can be traced back to a study by Issekutz *et al.* (1961).

Niekamp *et al*. (2012) conducted a study to assess whether diet affects RER changes during exercise. 57 sedentary individuals between 47 and 63 were used. The study concluded that a diet which promotes systemic alkalinity would cause an RER of 1.10 to be more easily achieved therefore resulting in a peak maximal oxygen uptake elicited in an incremental exercise test. RER is heavily influenced by CO_2 production from acid buffering by the bicarbonate buffer system during maximal exercise. Therefore an RER of greater than 1.15 in the most commonly accented value for termination of a test whereby a "true" $\dot{V}O_2max$ will be reached.

The achievement of a percentage of the age adjusted maximal heart rate is the most problematic criterion for the termination of a maximal exercise test. The standard deviation associated with the estimate is approximately ±11b.min^{-1} therefore making it a very difficult standard to justify (Londeree and Moeschberger, 1984). Participants in the lower half of this distribution would therefore not be able to achieve their heart rate standard, even when working maximally. While those at the other end of the distribution would achieve the estimate while working at submaximal work rates. It is for this reason that the American College of Sports Medicine states that predicted maximal heart rate should not be used for an absolute end point in the termination of a maximal exercise test (Howley *et al.*, 1995).

RPE is another frequently used criterion to end the test. As a measure of general fatigue that the person feels, it is measured on a scale of 1-10 or 4-20 (Borg, 1982). Perceived exertion can be defined as "the act of detecting and interpreting sensations arising from the body during physical exertion". A persons' perception of physical exertion allows them to monitor feelings of exercise intensity by sensory feedback; such internal feedback allows an individual to pace themselves appropriately during a specific bout of exercise or physical activity (Borg, 1982).

In conclusion a combination of the presence of at least three of the abovementioned criteria, is therefore generally used to determine the point at which the test should be terminated (Bassett and Howley, 1999).

2.7 Blood Pressure

It is well accepted that arterial blood pressure (BP), the pressure exerted against walls of the arteries, is dependent on cardiac output and total peripheral resistance (Guyton, 2011). One of the most frequently reported health benefits of regular participation in endurance exercise is lower resting BP, with the greatest effects seen in those with borderline hypertension (Fagard, 1993; 1999). Fagard (1993) noted that 'aerobic' exercise training decreased BP along a continuum with systolic (SBP) and diastolic (DBP) BP lowered by an average of 3mmHg in individuals with normal BP, 6 and 7mmHg in those with high normal BP, respectively.

Dynamic aerobic training including cycling, walking, jogging and running at a relatively low intensity e.g. 50% $\dot{V}O_2$ max, for an average of 30 minutes per day on five days in a week, can promote the lowering of clinical blood pressure during the post-exercise period in both hypertensive and normotensive participants. This phenomenon has been called post-exercise hypotension (PEH) and is characterized by a sustained decrease in blood pressure after a single episode of exercise (Pescatello *et al*., 2004).

Several mechanisms have been proposed for the hypotensive efficacy of regular exercise. Studies by Japanese investigators suggest that the blood pressure reduction is initiated by volume depletion, induced by activation of the renal kinin system, dopamine, and prostaglandin systems. A subsequent reduction in sympathetic activity might be involved in the maintenance of the blood pressure reduction (Miura, 1994). Jennings (1997) on the other hand, suggests that in Caucasians the primary events are an improvement of endothelium-mediated vasodilatation (via release of dilatory agents including nitric oxide) and an increase in systemic arterial compliance in large vessels, although increases in arterial compliance are not always found. This changes the afferent input to the arterial baroreceptors. The result could be a reduced sympathetic outflow to the renal bed which could counterbalance any tendency to an increase in blood volume and thus blood pressure. It is quite possible that the antihypertensive mechanism of exercise training differs among populations depending on the underlying hypertensive mechanism (Pescatello *et al*., 2004). Kouamé *et al*. (1991) suggest

that an attenuation of the cardiopulmonary baroreflex control of skeletal muscle vascular resistance after training at 70% $\dot{V}O_2$max compared with training at 50% $\dot{V}O_2$max may contribute to the less pronounced hypotensive efficacy of higher intensity exercise compared with lower intensity exercise.

Microcirculation is the flow of blood through the microvasculature, including the arterioles, capillaries, and venules. It is these vessels that nourish the body's tissues and organs. Two important functions of this circulatory system are to alter blood flow according to the varying metabolic requirements of the tissues it serves and to stabilize blood flow and pressure by making local regulatory adjustments (Zweifach, 1977). Several attempts have been made to explore the parameters of microcirculation and microvasculature when tissue and/or blood vessels have been exposed to a magnetic field (MF) (McKay *et al*., 2007). As previously mentioned many of the health benefits of magnets have been associated with the polarity of the static magnetic field (SMF). The negative and positive poles of magnets are believed to produce opposite physiological effects.

The biological effects of MFs have often been linked to nitric oxide (NO). It is believed that NO may also be the molecule responsible for the changes in vessel diameter following MF exposure (McKay *et al*., 2007). In an experiment by Okano and Ohkubo (2001), blood pressure changes associated with SMF exposure were investigated in conscious rabbits. When blood pressure was increased using a nitric oxide synthase (NOS) inhibitor which resulted in vasoconstriction, exposure to a SMF caused a significant decrease in blood pressure during and post-exposure. This led to a significant increase in blood flow, measured using microphotoelectric plethysmography, after 10 minutes of exposure through to 40 minutes post-exposure (Okano and Ohkubo, 2001), and was attributed to the vasodilatory effect of SMF exposure, it was therefore suggested that this may be related to the endothelial release of NO.

This magnetic effect was again tested by Okano and Ohkubo (2003) on genetically hypertensive rats. At seven weeks of age, the rats were continuously exposed to a SMF (10 or 25 mT) for 12 weeks. Throughout the 3rd to 5th weeks of SMF exposure, significant antipressor effects on mean blood pressure were found using the tail-cuff method. No differences in mean blood pressure were found between the two MF intensities that were tested. Hormone analysis revealed that the 10mT SMF (at five weeks of exposure) reduced

angiotensin II by 65.3% and aldosterone by 39.6%. The 25mT SMF (at five weeks of exposure) reduced angiotensin II by 63.8% and aldosterone by 36.6%. These reductions disappeared at 12 weeks of exposure.

Okano and Ohkubo (2005) did further research into the effect of a stronger SMF (180 mT) implanted in the neck of spontaneously hypertensive rats. Hypertensive rats that were exposed to the SMF (14 weeks) had a mean blood pressure reduction (tail-cuff measurements) of 3.8% in comparison to controls during the 5^{th} –8^{th} weeks of exposure. The SMF also inhibited the decrease in baroreflex sensitivity that was observed in sham animals during the 5th–8th weeks of exposure. When nicardipine (Ca^{2+} channel blocker) was administered to decrease blood pressure, the application of the SMF further enhanced this decrease in mean blood pressure by 6.9% during weeks 1–8 of exposure. These results suggested that the SMF synergistically antagonized Ca^{2+} influx through Ca^{2+} channels.

The investigation by Okano and Ohkubo (2005) indicates that the homeostatic effect of MFs might influence NO pathways. When genetically hypertensive rats were exposed to a SMF (1 or 5 mT) for 12 weeks, blood pressure, the concentration of NO metabolites, angiotensin II, and aldosterone were reduced. Specifically, exposure to the SMF reduced blood pressure during weeks 3–6. Hypertensive rats are known to have increased levels of NO metabolites, most likely due to the upregulation of NOS. Exposure to the 5 mT SMF for 6 weeks significantly reduced the concentration of NO metabolites by 73.2%. The 1 mT SMF did not have an effect on the NO metabolites. At three weeks, the 5mTSMF reduced angiotensin II by 51.1% and aldosterone by 40.2%, and at six weeks reduced angiotensin II by 58.2% and aldosterone by 72.2%. Similar significant reductions in angiotensin II and aldosterone were seen with the 1mT field. At 12 weeks, all effects on the NO metabolites, angiotensin II, and aldosterone disappeared.

2.8 Heart Rate

As previously mentioned, a study conducted by the Ryan (2007) on the effect of using the Thrahaler® O_2 Gold to improve the heart rate response during exercise in 14 triathletes was performed. In this study, the group using the magnetic breathing device showed a significant reduction in resting heart rate, heart rate immediately after completing the 15 minute cycle, as well as recovery heart rate one and three minutes after completing the test compared to the placebo group

According to Colbert *et al*. (2009), fifty six studies have been conducted on the effects of static magnetic field therapy, in both patient populations and in healthy volunteers. In the 56 studies, 39 different physiological or pathological conditions were represented. The physiological outcomes measured included improvement in muscle strength, muscle soreness post exercise, postural sway, fine touch, blood flow and heart rate and blood pressure.

A study by Hinman (2002) compared HR and BP responses among healthy participants as they rested on pads containing magnets of negative polarity, magnets of positive polarity or placebo magnets. These physiological measures were selected because Philpott (1998) claimed that the heart is the most responsive tissue to the stress or anti-stress fields created by magnets. He stated that a significant (10 point) decrease in HR will occur within a few minutes of exposure to a negative SMF. Another further study by Jehenson *et al*. (1998) confirmed this as they reported a significant increase in cardiac cycle length (i.e. decrease in HR) following exposure to a high-intensity SMF (20 000 gauss) in a magnetic resonance chamber. However, other participants who were exposed to a weaker SMF (10 000 gauss) experienced no changes in HR or rhythm.

Hinman (2002) therefore concluded that the changes in HR and BP that occurred in the participants within the study did not differ in relation to the type of pad on which they lay, and none of these changes were more than one might expect to find in a normal individual at rest. All participants experienced a slight reduction in both HR and BP that was most likely due to a general relaxation response. Thus, these findings do not support Philpott's assertion that exposure to a negative SMF will gradually slow the HR by 10 bpm. Overall Hinman's findings suggest that healthy people who lie on either positive or negative magnetic pads, experience no significant deviations in their HR or BP.

2.9 Pulse Oximetry

A pulse oximeter is a device intended for the non-invasive measurement of arterial blood oxygen saturation (SaO_2) and pulse rate. Pulse oximeters use a light source and photodiode light detector to measure the amount of light passing through an arteriolar bed. SaO_2 can be estimated noninvasively because the light-absorbing characteristics of haemoglobin differ between oxyhemoglobin and deoxyhemoglobin.

Pulse oximeters are commonly used during exercise in clinical and research settings to provide a noninvasive, continuous estimate of the oxyhemoglobin saturation of arterial blood. Arterial oxyhemoglobin saturation indicates the degree of arterial blood oxygenation (Mengelkoch *et al*., 1994). However, although well accepted for use in resting participants, using pulse oximetry during exercise for accurate measurement of SaO_2 has been problematic for several reasons. First, depending on the sensor site, sensors are subjected to varying degrees of motion resulting in signal corruption and thus inaccurate estimations of saturation (Plummer, 1995). Furthermore, sensors placed on the digits are even more susceptible to this problem especially during cycle because gripping the handlebars results in weakening or even complete loss of signals (Plummer, 1995).

2.10 Conclusion

This review of the literature indicates that there is evidence in favour of possible therapeutic benefits when the human body is exposed to static magnetic fields. As much of the evidence however remains inconclusive and in some cases contradictory, confirmation in further well controlled studies on athletes is required. The exact mechanisms by which a magnetic breathing device may affect endurance performance and associated physiological responses including improved endurance capacity, enhanced RBC and Hb cell concentrations, O_2 – carrying capacity, $\dot{V}O_2max$ and lowered heart rate and blood pressure responses to exercise also remain open areas for further research.

CHAPTER THREE

METHODOLOGY

3.1 Ethical Clearance and Study Design

The study was designed as a double blind, placebo-controlled, cross-over laboratory trial preceded by a baseline assessment.

Full ethical clearance for this study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (Ethics Clearance No: BFC 82/012) (Appendix A).

In order to implement the double-blind nature of the study, devices were coded by the manufacturer so that the researchers as well as participants were not aware which devices were the placebos and which were the active. Only after completion if the trial were the devices decoded.

3.2 Participants

All volunteers from three sporting clubs who met inclusion criteria (n= 18) were included in the original sample. Clubs were contacted and informed about the study via information meetings as well as visual representation. Participants then volunteered to participate in the study, and were only included if inclusion and exclusion criteria were met.

The inclusion and exclusion criteria for the participants were as follows:

INCLUSION CRITERIA	EXCLUSION CRITERIA
• **Healthy males**	Women
• **Aged >18 and <45 years old**	Age <18 and >45 years old
• **Willing participants who consent to participate in the entirety of the trial, which included regular prescriptive O_2 Gold use, three maximal exercise tests on a treadmill, and provision of small venous blood samples at baseline and after the active and placebo**	Any contraindications to exercise as per Physical Activity Readiness Questionnaire (PAR-Q) Regular or chronic use of medication Smoking or excessive alcohol consumption

trials	Implanted metal or medical devices
Recreational or professional endurance runners who were prepared to maintain their weekly training distance during the 3 months prior to the study	Use of performance enhancing agents Consumption of any drug, caffeine or alcohol on test days Any bleeding disorders Vegetarians Regular consumption of any form of nutritional supplementation (e.g. multivitamins, calcium, magnesium)

After completing baseline assessments eighteen athletes were assigned the O_2 Gold breathing device that had been pre-coded by the manufacturer prior to the study; 50% assigned to the active trial first, and 50% assigned to the placebo trial first. The cross-over design of the study is clarified in the schematic representation given in Table 3.1.

Table 3.1 Schematic representation of the cross-over design used during the trial

Baseline Assessment	**1st 28-day intervention period**	**7-14 day interval**	**2nd 28-day intervention period**	
TEST 1	Group A Active trial	**TEST 2**	Group B Active trial	**TEST 3**
	Group B Inactive trial		Group A Inactive trial	

3.3 Testing Procedure

On three occasions participants were required to present themselves to the Exercise Laboratory in the Division of Human Physiology at the University of KwaZulu-Natal, Westville Campus. Before the first 28-day intervention period participants reported to the laboratory. After studying the information sheet (Appendix B), consent forms were completed by each athlete (Appendix C). Thereafter a medical questionnaire (Appendix D) as well as baseline questionnaires (Appendix E) which provided information regarding their training history, their dietary intakes, mileage/racing experience as well as other sporting endeavours) were completed. Basic anthropometric measures including stature (cm), body

mass (kg; in running shorts without shoes), waist circumference (measured at the mid-point between the lowest rib and the top of the illiac crest) and seven-site skinfold measurements including the triceps, chest, mid axilla, suprailiac, subscapular, abdominal and thigh skinfold thickness, were taken. Percentage subcutaneous body fat was calculated using the Jackson and Pollock (1978) formula.

Dynamic resting lung function including FVC, FEV_1, FVC/FEV_1 and FIV_1 was determined using a Jaeger Mastercope Flowmate Spirometer (Wuerzburg, Germany), as seen in Figure 3.1 below. All participants underwent medical screening conducted by a general practitioner in order to assess their general health, musculo-skeletal status and to rule out the presence of any clinical condition/s that may have prevented full participation in the trial. A 4mL venous blood sample was then taken.

Figure 3.1 Lung Function Testing using a Jaeger Mastercope Flowmate Spirometer

The Oxygen Pro Analyser (Cardinal Health, Hoechberg, Germany) was used to measure metabolic and respiratory responses before and during exercise. After verification of ambient air conditions as determined by the integrated Ambient Unit, automatic calibration of the volume sensor was conducted according to manufacturer's recommendations (Cardinal Health, Hoechberg, Germany). Gas analysers were calibrated using room air and a 2-litre gas cylinder containing 16% O_2 and 5% CO_2 in nitrogen (Cardinal Health, Hoechberg, Germany).

After entering the participant details (including body mass) into the computer, a heart rate monitor belt (Polar Electro OY, Finland) and a disinfected connector facemask which was

connected to a disinfected triple V transducer and twin tube, were fitted. Exhaled respiratory gas analysis was then performed using Triple V sensors to detect the volume of expired air, and an aliqout thereof was fed into the gas analysers. A pulse oximeter (Oxypal, OLV-2700, Nihon Kohden, Japan) was used to provide a continuous non-invasive measurement of O_2 saturation of the arterial blood before and during the test.

Prior to starting the exercise trials, baseline data (including heart rate, blood pressure, oxygen saturation, VE and $\dot{V}O_2$) were recorded while the participant was comfortably seated on a chair, shown clearly in Figure 3.2.

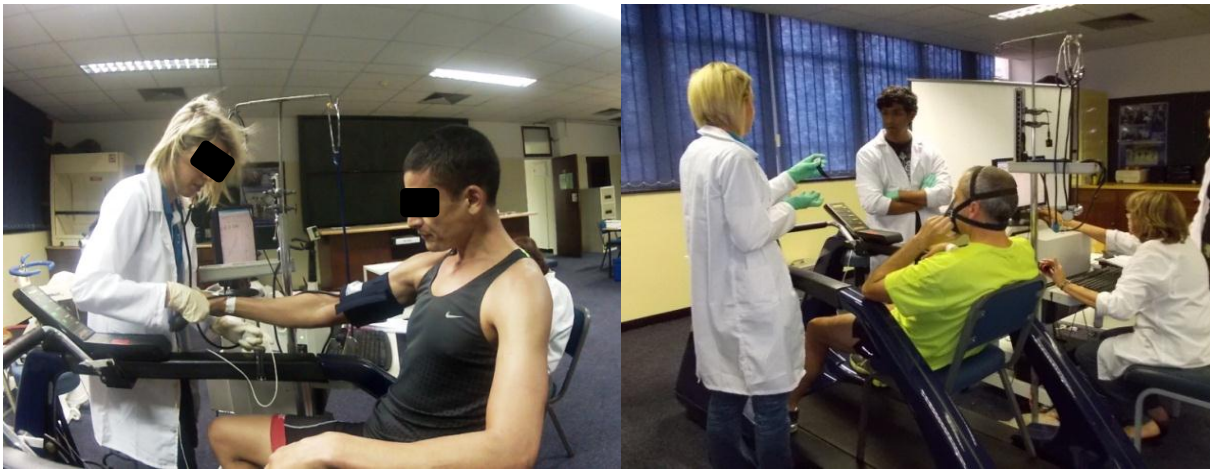

Figure 3.2 Baseline Measures Conducted before the start of the Maximal Exercise Test

Figure 3.3 The Maximal Exercise Test

Participants were then introduced to the motor driven treadmill (Powerjog GX100, Sport Engineering Limited, Birmingham, England) on which all $\dot{V}O_2$max testing was conducted. They completed a five minute warm-up at a speed of 12 km.hr^{-1} with no incline. Thereafter the speed remained constant (at 12 km.hr^{-1}) while the gradient increased to an initial 2% in the first minute and a further 1% each minute until the test was terminated.

Continuous monitoring of heart rate and oxygen saturation occurred throughout the test, as depicted in Figure 3.3 above, and a 10 point Borg scale was used to quantify subjective rate of perceived exertion (Borg. 1982).

The test was terminated when participants had reached three of the following: (i) RPE of > 8.0 (ii) an RER of 1.15 or greater (iii) estimated heart rate maximum (iv) an apparent $\dot{V}O_2$ plateau despite a further increase in workload on the treadmill.

Immediately post-test systolic and diastolic blood pressure was measured, as well as a 60 second and 120 second post exercise HR recording, while participants were seated on a chair, as can be seen in Figure 3.4 below.

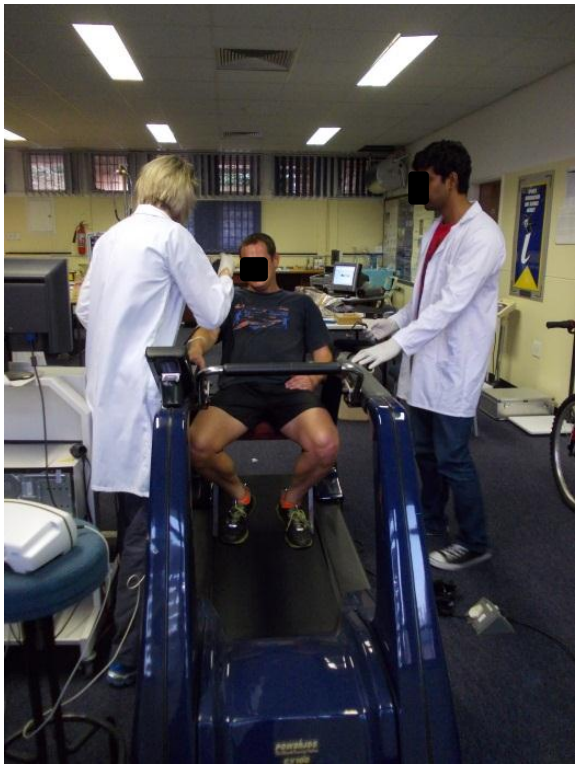

Figure 3.4 Post Test Recovery Recordings

3.4 Active and Placebo Interventions

Participants were required to use each of the magnetic breathing devices a minimum of 30 times daily for the 28-day duration of each intervention. Inhalations were to be taken daily, either at half-hour intervals or at the end of the day with two minute breaks between inhalations, as stipulated by the manufacturer of the device. Figure 3.5 presents a detailed description of the current recommendations for the use of the device.

Figure 3.5 Manufacturer's recommendations for use of the O_2 Gold device

3.5 Quantification of Training Status

Participants were requested to record their daily usage of the device, training volume and intensity on a daily basis (Appendix F). An index of their training status (Ts index) based on the total amount of training that was done during each of the 28 day trials was computed. This was determined from the sum of the number of minutes spent training at high (0.8), medium (0.5) and low (0.2) intensity for each day of the week and then averaged over the 4 weeks.

$$\text{Ts index} = \sum \text{time}\,(0.2) + \sum \text{time}\,(0.5) + \sum \text{time}\,(0.8)/4$$

Examples of Ts index, ranging from 1.42 - 26.73, are provided in Appendix G

3.6 Processing of Blood Samples

Four mL of whole venous blood was collected in vacutainer tubes containing K_3 - ethylene diaminetetra-acetic acid (EDTA) and transported to a commercial pathology laboratory (Ampath Laboratories, Westridge, Durban) for the assessment of full blood count (FBC). FBC and differential leukocyte and platelet counts were determined on the EDTA treated specimens using standard haematological procedures on an automated STKS model (Coulter Electronics Inc., Hialeah, Florida, USA).

A further 4mL sample was collected in pre-cooled EDTA tubes and immediately centrifuged at 3000rpm for five minutes, while serum collection vacutainer tubes were used for the collection of the third 4mL sample which was allowed to clot at ambient temperature after which the serum was separated by centrifugation at 3000 rpm for four minutes. Aliquots of 0.5mL of plasma and serum were snap-frozen in liquid nitrogen until transferred to an ultra-freezer at -80^{o} Celsius for storage in the Department of Human Physiology for later ELISA analysis of the concentration of plasma IL-3, determination of serum EPO concentrations and serum osmolality.

After noting a trend of decreased post-exercise blood pressure following numerous trials during the study, additional post-exercise samples were collected into pre-cooled EDTA tubes from the last few participants tested. They were immediately centrifuged at 3000rpm for five minutes. Aliquots of 0.5mL of plasma were snap-frozen in liquid nitrogen until transferred to an ultra-freezer at -80^{o}C for later indirect determination of nitric oxide from the concentration of nitrate and nitrite in these samples as well as the pre-exercise-samples obtained before the exercise-test at baseline.

3.7 Biochemical Analysis of Blood Samples

3.7.1 Plasma IL-3 Concentration

An *in vitro* enzyme-linked immunosorbent assay for the quantitative measurement of human IL-3 in serum, plasma and cell culture supernatants was conducted using IL-3 human ELISA kit (Abcam, UK, USA, Japan, Hong Kong).

The stock standard was prepared by adding 400µl assay diluent into a vial containing IL-3 standard. Seven serial dilutions were prepared by adding assay diluent to the stock standard as shown in Figure 3.5.

Figure 3.6 Serial Dilution of Standard

A 96- well plate was coated with an antibody specific for human IL-3 standards and blood plasma samples were pipetted into wells and IL-3 present in the samples was bound to the wells by the immobilized antibody. The wells were washed and biotinylated anti-Human IL-3 antibody was added. After washing away unbound biotinylated antibody, HRP-conjugated Streptavidin was pipetted to the wells. The wells were again washed. A TMB substrate solution was added to the wells and colour developed in proportion to the amount of IL-3 bound. The stop solution changed the colour from blue to yellow and the intensity of the colour was measured at 450nm.

3.7.2 Erythopoietin Concentration

Serum samples were selected from a subsample of athletes for the assessment of EPO. A Pathology Laboratory (Ampath Laboratories, Westridge, Durban) determined serum EPO concentration using a commercial radioimmunoassay.

3.7.3 Nitric Oxide Determination

The principle of this assay was reduction of nitrate by vanadium (III) combined with detection by the acidic Griess reaction. NO has a short half life and exists at low concentrations thus detection is impractical. The stable metabolites, nitrites and nitrates can be used as a measure. Thus NO concentration is indirectly determined by nitrites, formed by auto-oxidation of NO in aqueous solutions and nitrates, formed by reaction of NO with superoxide or oxyhaemoglobin. This assay was sensitive to 0.5µM NO_3. Standards were prepared by dissolving 6.06mg of sodium nitrate in dH_2O. Eight serial dilutions were prepared from 0-200µM. 50µl of serum blood sample was pipetted into a well of a 96 well

plate in triplicate and 50µl of VCl_3 followed by 25µl of sulfanilamide and N-1-napthyl ethylenediamine dihydrochloride were rapidly added to each well. The plate was then was then incubated for 30-45min (in the dark). Absorbance was measured at 540nm with a reference of 690nm.

3.8 Uncoding and Final Feedback

After all testing procedures for both trials were completed by the participants, the coding of the devices was revealed to the researchers by the manufacturer. A comprehensive feedback report was compiled for each participant (examples given in Appendix H). After the device compliance was established and training status during the two separate 28-day trial periods was calculated using the Ts index, described on page 33, the necessary exclusion of additional non-compliant participants took place and the final sample size (n=10) was confirmed.

3.9 Statistical Analyses

Data were expressed as mean (±SD and were analysed with GraphPad Prism 5 Software (Version 5.01, 2007). Level of significance was set at p=0.05.

Paired *t*-tests were used when comparisons of the post-active and post-placebo trials was required. One-way analysis of variance (ANOVA) with a Bonferroni correction to establish the exact location of the differences, was used to determine whether the difference between the means of baseline, post-active and post-placebo trials were significant or not.

Pearson's Product Moment Co-efficient of Correlation was used to determine whether the relationship between EPO concentration and red blood cell count was statistically significant or not.

CHAPTER FOUR

RESULTS

Eighteen athletes who met all inclusion criteria initially enrolled for the trial and completed the baseline assessment. Of these only thirteen completed both active and placebo trials. Five participants withdrew, three due to personal reasons, one due to medical reasons and another due to a knee injury.

When analysing the training records and the compliance of the participants' use of the magnetic breathing device (Appendix F), an additional three participants who had completed both sets of post-trial tests needed to be excluded from the study. This was necessary as variation in training status, as revealed by computation of their Ts index (Appendix G) and irregular/inadequate use of the magnetic device, may have confounded their results.

According to the data provided by participants, ten participants therefore complied with all aspects of the study. Uncoding of the devices of the fully compliant participants revealed that seven of the final sample (*n=10*) completed the active trial first and three completed the placebo trial first.

4.1 Participants' Characteristics

The ten participants who complied with all aspects of the study were aged between 27 and 40 (mean: 32.3±4.9 yr) with a mean stature (cm) of 175.8±7.7. They included elite endurance athletes who participated in a variety of endurance events including a combination of running, paddling and cycling e.g. Dusi Canoe Marathon (*n=8*) as well as a serious participant in gymnasium training (*n=1*) and a recreational runner (*n=1*).

No participants reported deviation from usual regular dietary practices, vegetarianism, or acknowledgement of the use of iron supplementation or any form of ergogenic aid, during the course of the 10 week study.

Further mean (± SD) baseline physical characteristics of these participants are provided in Table 4.1. No statistically significant difference was found in mean (±SD) data recorded between baseline data and after the active and placebo trials ($p>0.05$).

Table 4.1 Mean (± SD) and range of baseline characteristics of the participants who complied with all aspects of the trial (*n =10*)

Characteristic	Baseline Mean (SD); Range	After placebo trial Mean (SD); Range	After active trial Mean (SD); Range
Mass (kg)	74.7 (4.7); 65.6-82.7	74.6 (4.3); 67.3-81.5	74.6 (3.9); 67.3-80.9
% body fat *	13.3 (5.6); 6.1-24.1	12.7 (5.6); 6.4-24.6	12.8 (5.4); 6.0-23.7
RHR (bpm)	56.0 (5.8); 48-66	49.4 (4.9); 40-61	52.4 (12.8); 40-84
SBP (mmHg)	124.2 (8.1); 112-142	122.0 (5.3); 112-128	123.6 (5.8); 114-132
DBP (mmHg)	68.0 (8.7); 50-80	69.8 (7.9); 60-86	65.0 (5.8); 60-78

** Derived from the sum of triceps, chest, mid axilla, suprailiac, subscapular, abdominal and thigh skinfold thickness; RHR: Resting heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure*

Results of the quantification of the training status index (Ts) while using the active and placebo devices are shown in Table 4.2. The mean (±SD) was not statistical significant between the two trials (paired t test; $p > 0.05$).

Table 4.2 Mean ± SD training status index (Ts) while on active and placebo devices

Characteristic	After placebo trial	After active trial
Mean	9.94	11.51
SD	±6.07	±6.66

4.2 Lung Function

With regard to the mean (± SD) and range of lung function shown in Table 4.3, FVC was consistently in excess of the reference range for non-athletic individuals of the specified age, gender and height. Only one participant presented with an F_EV1/FVC ratio of <0.80, indicating the presence of possible minor obstruction to air flow.

Table 4.3 Mean (± SD) and range of lung function of the participants who complied with all aspects of the trial (*n =10*)

Characteristic	Baseline Mean (SD); Range	After placebo trial Mean (SD); Range	After active trial Mean (SD); Range
FVC (L/min)	5.3 (0.7); 4.0-6.5	5.5 (0.8); 4.2-6.7	5.4 (0.7); 4.0-6.3
FEV1 (L/min)	4.4 (0.5); 3.5-5.1	4.3 (0.5); 3.5-5.1	4.4 (0.5); 3.4-5.1
F_EV1/FVC	0.8 (0.1); 0.7-1.0	0.8 (0.1); 0.7-0.9	0.8 (0.1); 0.7-0.9
FIVC (L/min)	5.4 (0.7); 4.4-6.6	5.6 (0.8); 4.3-6.9	5.5 (0.6); 4.2-6.3
BHT	77.4 (28.6); 48-132	91.4 (29.8); 45-144	93.3 (31.6); 60-148

FVC: Forced Vital Capacity, FEV_1: Forced Expiratory Volume in 1 Sec, FVC/FEV1: Forced Expiratory Volume: Forced Vital Capacity in 1 Sec, FIVC: Forced Inspiratory Capacity, BHT: Breath holding Time

Although one-way ANOVA revealed that the difference between the mean (±SD) of the tests of dynamic lung function conducted at the three trials, was not statistically significant (*p>0.05*), six (60%) participants recorded an improvement (vs. baseline) in FVC and five (50%) in FIVC following the active trial. The mean (±SD) of the FVC of the six positive responders was significantly greater than baseline (*p = 0.038*). These results are graphically presented in Figure 4.1.

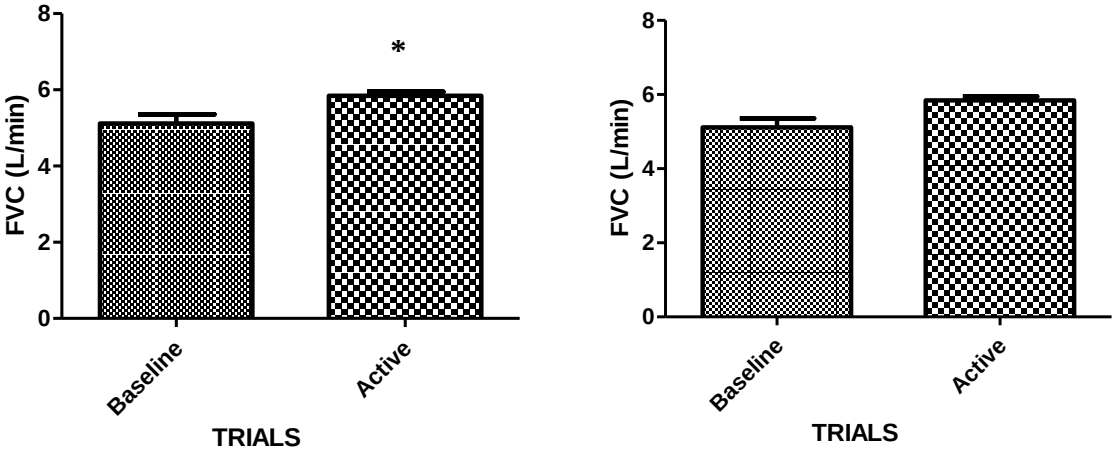

Figure 4.1 Graphical representation of results of lung spirometry in the positive responders (FVC, *n=6* and FIVC, *n=5*) Data presented as mean (±SD) * *p<0.05*, paired students *t* test

4.3 Maximal Exercise Test

The mean (± SD) and range of the selected data obtained from the maximal exercise test, is provided in Table 4.4. The tests ranged in duration from 8 to 17 minutes. It was confirmed by one-way ANOVA that use of the magnetic breathing device did not optimize mean workload on the treadmill or final mean running time obtained in the test, during active and/or placebo trials (*p>0.05*). However five (50%) participants recorded an improvement (vs. placebo) in maximum running time and hence peak power output following the active trial. The mean (± SD) improvements of this subsample of positive responders (*n=5*) was statistically significant (*p = 0.018*)

Table 4.4 Mean (± SD) and range of results of maximal exercise test of the participants who complied with all aspects of the trial (*n =10*)

Characteristic	Baseline	After placebo trial	After active trial
	Mean (SD); Range	**Mean (SD); Range**	**Mean (SD); Range**
	SUBMAXIMAL (During the last 15 seconds 8th minute of the exercise test)		
HR (bpm)	165.4 (12.9); 144-188	160.7 (12.1); 144-180	161.4 (14.5); 138-182
O_2 saturation (%)	94.3 (2.0); 92-96	94.4 (1.8); 92-97	94.6 (2.2); 90-98
	MAXIMUM		
Workload (% gradient)	9.5 (2.9); 4.0-13	9.6 (3.1); 5-14	9.8 (3.1); 5-13
Running Time (min)	8.6 (2.8); 3.3-12	8.6 (3.0); 3.7-12.1	7.8 (4.1); 3.6-12.1
HR (bpm)	184.0 (9.0); 169-194	183.4 (6.6); 168-191	182.4 (9.1); 164-195
O_2 saturation (%)	90.4 (2.2); 87-93	91.0 (2.9); 85-95	90.1 (3.4); 85-95
RPE	8.8 (1.4); 6-10	9.1 (1.7); 5-10	9.5 (1.0); 7-10
VE ($L.min^{-1}$)	150.7 (18.5); 130-192	155.4 (16.7); 128-189	154.8 (15.1); 133-186
TV (L)	3.1 (0.4); 2.6-3.7	3.2 (0.4); 2.6-4.0	3.2 (0.4); 2.6-3..8
BF ($breaths.min^{-1}$)	50.1 (8.0); 39-61	50.1 (8.0); 41-62	50.1 (7.9); 40-64
VO_2 ($mL.min^{-1}$)	4861 (561.8); 3983-5716	5009 (538.9); 4248-5760	4915 (587.1); 4044-5728
VO_2 ($L.min^{-1}.kg^{-1}$)	65.3 (8.1); 55-78.5	67.3 (7.8); 58-80.4	66.1 (9.1); 55.6-81.5
	POST TEST		
60 sec HR (bpm)	149.2 (10.9); 130-162	143.9 (10.8); 130-162	145.6 (11.2); 128-165
120sec HR (bpm)*	126.3 (10.3): 109-139	116.4 (10.7); 101-131	119.3 (13.3); 102-144
SBP (mmHg)	171.4 (17.9); 140-200	185.2 (12.4); 162-202	179.3 (9.3); 164-192
DBP (mmHg)	64.7 (5.8); 58-72	58.4 (7.2); 48-70	61.5 (5.8); 52-72

HR: Heart rate, VE: Minute ventilation, RPE: Rating of perceived exertion, TV: Tidal volume, BF: Breathing frequency, RER: Respiratory exchange ratio; n=8,*

In terms of submaximal physiological response during the last 15 seconds of the 8th minute of the incremental protocol used in the maximal exercise test, an improvement (vs. placebo) in submaximal heart rate and O_2 saturation was documented in four (40%) and three (30%) of the participants, respectively. One-way ANOVA however revealed no difference in terms of mean (± SD) submaximal heart rate and O_2 saturation during this stage of the test in the complete sample (*n=10, p= 0.69; 0.94*). This lack of significance in the differences between trials was also apparent in the positive responders (*n= 4,3*; *p = 0.098,* 0.12)

No significant improvements in mean or individual maximum minute ventilation, tidal volume and breathing frequency (*p>0.05*) were noted use of the active device. Although one-way ANOVA did not show a significant increase in mean absolute $\dot{V}O_2$ max (*p>0.05*)

after use of the active or placebo devices, when compared to baseline testing, five (50%) participants recorded small improvements (vs. placebo) in absolute $\dot{V}O_2$ max following the active trial. These improvements which averaged 6.5% were however not great enough to create a statistically significant difference in the mean (*p = 0.37*).

Regarding post test recovery, neither mean (± SD) post-test heart rate recovery at the 60 and 120 second time-points or post-test diastolic blood pressure, were significantly lower in the entire sample (*n=10*). There was however a significant drop in HR recovery at the 120 second time point in four (40%) of the sample (*p = 0.033*) and in DBP in five (50%) individual participants following the active trial (*p = 0.086*). As is shown in Table 4.5, pre-post treadmill running blood samples were obtained from two of these participants and showed an increase nitric oxide concentration in both when on the active device.

Table 4.5 Individual and mean serum Nitric Oxide concentrations (μM) determined from plasma nitrate and nitrite concentration in a subsample (*n=2*) in whom lower post-trial diastolic blood pressure was recorded after being on the active device.

Participant	**Placebo**	**Active**
11	58.74	92.12
14	67.63	94.94
Mean	63.18	93.53
SD	± 6.28	± 1.99

SD: Standard deviation

4.4 Red Blood Cell Indices

Mean (± SD) and range of red blood cell indices of the participants who complied with all aspects of the trial (*n =10*), are shown in Table 4.6. The findings of a lack of significance in the difference between mean Hct and Hb concentration were paralleled by an absence of changes in the mean cell volume of the red blood cells. One-way ANOVA confirmed the absence of a statistical significance in both mean RBC and Hb (*p>0.05*). However when data from individual participants were analysed, six (60%) of the sample presented with significant increases in RBC count (vs. placebo; *p = 0.029*) and five (50%) with a significant increase in Hb concentration following the active trial (vs. placebo; *p = 0.047*).

Table 4.6 Mean (± SD) and range of red blood cell indices of the participants who complied with all aspects of the trial (*n =10*)

Characteristic	Baseline Mean (SD); Range	After placebo trial Mean (SD); Range	After active trial Mean (SD); Range
Hb (g/dl)	16.6 (0.3); 15.2-16.1	15.1 (0.8); 13.9-16.4	15.5 (0.8); 13.9-16.6
RBC(10^{12}/L)	5.0 (0.1); 4.9-5.2	4.9 (0.3); 4.6-5.4	5.0 (0.3); 4.7-5.3
Hct (%)	46.1 (1.0); 44.4-47.4	44.3 (2.1); 41.1-47.7	45.5 (2.0); 42.1-48.4
MCV (fL)	91.5 (2.5); 88.6-96.3	91.3 (2.2); 89.1-96.5	91.1 (2.5); 88.6-96.6
MCH (pg)	30.2 (3.0); 21.8-32.5	31.1 (1.2); 29.8-33.8	30.9 (1.2); 29.5-33.5
MCHC (g/dL)	33.9 (0.5); 33.0-34.3	34.1 (0.7); 33.2-35.2	33.9 (0.6); 32.9-34.7
RDW (%)	13.0 (0.3); 12.7-13.6	13.1 (0.3); 12.5-13.6	13.0 (0.3); 12.6-13.5

Hb: Haemoglobin, RBC: Red blood cell, Hct: Haematocrit, MCV: Mean cell volume, MCH: Mean cell haemoglobin, MCHC: Mean cell haemoglobin concentration RDW: Red cell distribution width

4.5 $\dot{V}O_2$ Max vs. Red Blood Cell Count

The relationship between the change in absolute $\dot{V}O_2$max and change in RBC in each participant following placebo and active trials is presented in Figure 4.2. This revealed positive, linear correlation (r = 0.68) which is statistically significant (*p = 0.029*).

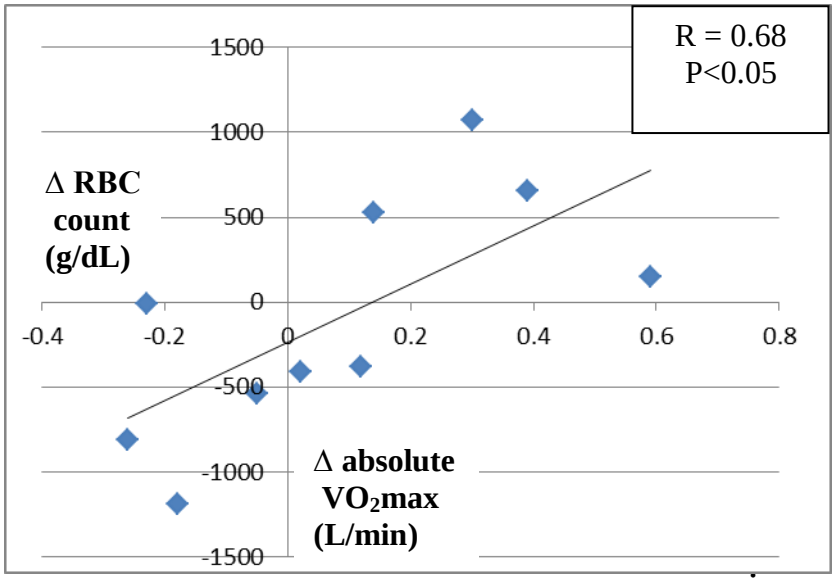

Figure 4.2 The association between change in absolute $\dot{V}O_2$max and change in RBC count following active and placebo trials in the complete sample (*n=10*). * Pearson's Product Moment Co-efficient of Correlation

4.6 Serum EPO

The individual serum EPO concentration following active and placebo trials for a subsample of 7 participants, is given in Table 4.7. The mean (±SD) was not significantly improved (*p=0.13*; paired students t-test) with the use of the active breathing device in this subsample. As is shown in Figure 4.3, Pearson's product moment co-efficient of correlation also did not

confirm a statistically significant correlation between the change in serum EPO concentration and the change in red blood cell count (r = 0.69; *p<0.05*) following active and placebo trials.

Table 4.7 Individual and mean (± SD) serum EPO (mLU.mL^{-1}) concentration following active and placebo trials, taken from a subsample of participants (*n=7*)

Participant No.	After placebo trial	After active trial
1	45.5	58.9
5	12.9	11.8
6	39.1	64.0
8	10.2	5.7
10	2.3	5.4
11	114	136
13	2.9	0.7
Mean	24.2	29.8
SD	39.8	49.8

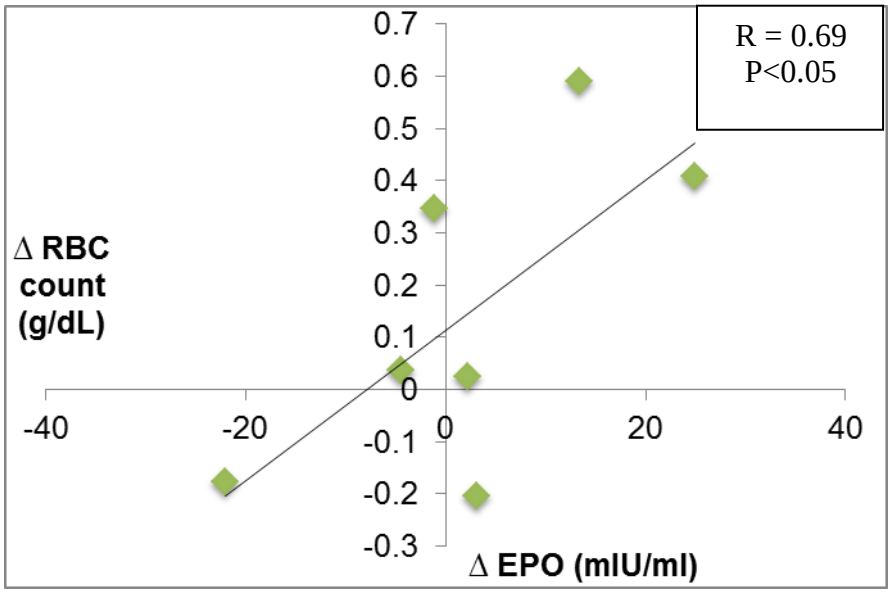

Figure 4.3 The association between change in serum EPO concentration and change in RBC count following active and placebo trials. * Pearson's Product Moment Co-efficient of Correlation

4.7 Plasma IL-3 Concentrations

Although individual plasma IL-3 concentrations increased following the active trial in four (40%) of the study sample, one-way ANOVA revealed that there was no significant difference in plasma IL-3 concentration between baseline and active and placebo interventions (*p>0.05*). Mean (± SD) plasma IL-3 concentrations at baseline and following active and placebo trials (*n=10*) are shown in Figure 4.4

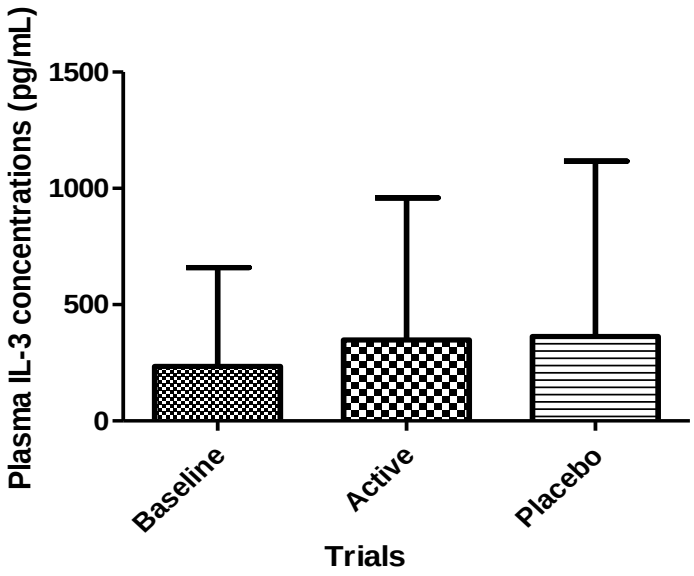

Figure 4.4 Mean (±SD) plasma IL-3 concentration ($pg.mL^{-1}$), at baseline and following active and placebo trials (*n=10*)

4.8 Integrated Physiological Profile of Positive Responders

When the individual profile of each of the five participants in whom either an improvement in absolute $\dot{V}O_2$max or peak power output on the treadmill was achieved during the maximal exercise test following the active trial, is analysed, this corresponds with an increase in RBC concentration in 100% of the group and an increase in HB concentration in 80% of the group. Furthermore, submaximal heart rate in the last 15 seconds of the 8th minute of the test as well as 2 minute post-test HR , also improved in 80% (*n=4*) of the sample. The overall profile of these positive responders (*n=5*) is presented in Table 4.8.

Table 4.8 Overall profile of positive responders to improvement in absolute $\dot{V}O_2$max or peak power output on the treadmill (*n=5*)

Participant No.	$\dot{V}O_2$max L/min	Running time (min)	FVC (L/min)	FIVC (L/min)	RBC 10^{12}/L	Hb (g/dL)	HR Submax (bpm)	HR 120 sec post (bpm)	DBP (mmHg)
1	+	-	+	+	+	+	-	-	+
5	+	+	+	+	+	+	+	+	-
6	+	+	-	-	+	+	+	+	+
8	-	+	+	+	+	+	+	+	-
12	+	+	+	+	+	=	+	+	+

+ : positive improvement on active , - : No improvement on active, = : Same results

4.9 Conclusion

Statistically significant differences between the active, placebo and baseline trials were not apparent in any of the reported measures when expressed as mean ± SD of the completed sample (*n=10*). However following 28 days of use of the magnetic device, 60% of the sample presented with a statistically significant improvement in mean ± SD FVC and RBC count (*p = 0.038*; 0.029)and 40% with significantly improved mean ± SD peak power output (*p = 0.018*), Hb concentration (*p = 0.047*), and HR at 120 seconds post exercise (*p = 0.033*).

CHAPTER FIVE

DISCUSSION OF RESULTS

5.1 Introduction

While the restricted sample size may be regarded as a limitation of this work, this study required an exceptional amount of commitment from each participant. They were expected to use the device 30 times a day, maintain their usual dietary intake and keep their training status consistent over the course of the study. This led to the decrease in sample size from eighteen to ten participants over the 10 week duration of the study.

Only thirteen participants completed both active and placebo trials as well as the three assessments. Four athletes presented with influenza and/or upper respiratory tract infection symptoms. In addition the time of year was not optimal for the majority of these participants who were endurance athletes as it is generally their off season/ base training period over the winter months. Therefore it was difficult encouraging them to maintain their initial high training volume. After the computation of the Ts index of the participants (Table 4.2), three additional participants therefore had to be excluded from the study as their training was inconsistent or they had been ill for an extended period of time, thus decreasing both training and compliance in using the device. The final sample (*n=10*), although limited in size, was therefore restricted only to individuals who had reported adequate compliance with the inclusion criteria of the study. It is felt that this stringent attention to control possible confounding influences was an important strength of the study.

Another strength of the study was the cross-over design (Table 3.1) which was preceded by baseline testing. This resulted in each athlete acting as their own control and the sequence of trials varying equally within the original sample (*n=18*). The intention was that any possible carry-over effect in those who first used the active device would have been apparent when placebo trial results were compared to the results of the baseline testing. Provision was made for this by the use of a one-way ANOVA followed by a Bonferroni *post hoc* test in the statistical analyses of the results.

5.2 Participant Characteristics and Quantification of Training

The mean ± SD percentage body fat (12.8 ± 5.4), resting heart rates (52.4 ± 12.8 bpm) and diastolic blood pressures (65.0 ± 5.8 mmHg) of the participants (Table 4.1) confirmed that they were in elite sporting condition throughout the entire duration of the study. The athletes had above normal lung function with a mean ± SD FVC of 5.4 ± 0.7 $L.min^{-1}$ and FIVC 5.5 ± 0.6 $L.min^{-1}$. Statistical analysis also revealed that this condition did not change significantly over the 10 week period of the two trials.

As this study focused on cardio-respiratory function, change in training status was one of the most important potential confounders of the results of this study. As discussed on page 33, a method was therefore devised in order to quantify the participants specific Ts while using the active and placebo devices. This showed lack of statistical significance in the difference between the amount of training done by the athletes during active and placebo trials ($p>0.05$), hence eliminating the possibility of changes in the fitness level of the athletes significantly confounding the results of the study.

5.3 Lung Function

The purpose of including a lung function test in the pre-post trial assessment was not to assess a possible effect of the magnetic influences of the device, but as a means of confirming compliance in the use of the device. It is well known that when air is inhaled through the device, resistance to airflow is created. This resistance is believed to increase the work of the diaphragm, the external intercostal and the interchondral part of the internal intercostal muscles during the inhalation and has been shown to enhance endurance exercise performance in both trained and untrained individuals (Boutellier *et al.,* 1992; Splenger *et al.,* 1998; Roberts, 2004; 2007). Although no significant pre-post trial difference was found in mean (±SD) FVC, F_EV1 or FIVC of the sample ($n=10; p>0.05$), when individual results of the participants were studied independently of the mean (±SD), only 50% of the final sample ($n=5$) showed a significant improvement in FVC and FIVC ($p = 0.038; p = 0.095$) when using the active magnetic inhaler. This does not confirm the compliance of these athletes with device use throughout the entire duration of both trials, and raises a question regarding the 'reported' compliance in the remaining participants. For this reason, it was regarded as prudent to also focus on individual results and conduct statistical analyses of the improvements recorded in the positive responders as detailed in Table 4.8.

5.4 Red Blood Cell Indices

Although not yet proven, it has been hypothesised that the magnetic effect on erythrocytes, Hct and Hb concentrations could influence athletic performance by increasing the oxygen-carrying capacity of the blood (Roberts *et al.*, 2008). Zhernovoi *et al.* (2001) found that in some Hb molecules exposed to a magnetic field, the bond between nitrogen and iron atoms are disrupted, causing Hb activation. O_2 may then be added to the free bond of the iron atom of activated Hb. The enhanced O_2 carrying capacity of blood may be explained by the binding of two O_2 molecules to the iron atom of Hb in the presence of a magnetic field, forming bioxyhaemoglobin. Although this was confirmed in an unpublished pilot study conducted on 7 participants by Drs Craig Roberts and Bruce Biccard (Roberts, 2004), which showed a 0.9% improvement in the oxyhaemoglobin concentration from an average of 94.4% to 95.3% after four weeks using the Therahaler magnetic breathing device (p = 0.0516), the findings of this study did not lend support to this possibility.

As the non-invasive measurement of oxyhaemoglobin concentration using pulse-oximetry has many limitations (Plummer, 1995) and the use of an arterial blood sample was regarded as too invasive a procedure to use on the athletes prior to a maximal exercise test, no specific, sensitive measure of oxyhaemoglobin concentration was obtained in this trial and the haematological assessment in this trial was restricted to venous blood sampling.

The mean (±SD) and range of both RBC and Hb concentrations showed no statistically significant improvement following the active trial. Although this finding which did not confirm previous findings of Chater *et al*. (2003), all of the positive responders in terms of $\dot{V}O_2$max and peak power output ($n=5$), did however present with statistically significant increases in RBC count ($p=0.029$) and Hb concentration ($p=0.047$). As these individuals also had improved lung function which confirmed their use of the device, the alternative hypothesis set at the onset of the study, that RBC indices would improve following use of the magnetic breathing device, cannot be rejected. The possibility of unacknowledged under-compliance in usage of the device and the existence of non-responders in whom venous blood RBC and Hb concentrations do not rise with a small rise in oxyhaemoglobin concentrations, does however need to be acknowledged.

In view of previous findings that RBC counts are increased following use of the device, focus was also placed on possible mechanisms in this trial. Therefore the circulating

concentration of the hormone EPO and the haematopoietic growth factor, IL-3, were investigated. However no significant differences were obtained in the means (±SD) between active and placebo trials or the association between pre-post change in serum EPO concentration and change in RBC count. Mean plasma IL-3 concentration also did not change, therefore a direct effect on the circulating concentration of EPO and IL-3 can be excluded as possible mechanism by which the O_2 Gold may improve blood cell status.

5.5 Maximal Exercise Test

5.5.1 Peak Power Output and Exercise Time to Exhaustion

One of the primary findings of the study was that although statistically significant improvement in mean peak power output (% gradient on the treadmill) and exercise time to exhaustion, as described previously by Roberts *et al.*, (2008), was not confirmed in the complete sample (*n=10*), there were however five positive responders. Four of the five participants who showed a statistically significant increase in both peak power output and exercise time to exhaustion were the elite endurance athletes, thus suggesting that well trained endurance athletes are perhaps more responsive.

A possible overriding confounder which cannot be overlooked, was the competitive nature of the participants and their intrinsic motivation to 'push themselves' to maximum capacity and better their performance during each consecutive test. While this may have played a part in their maximal performance, the cross-over design of the study was aimed at compensating for this possibility. Of further interest was the finding shown in Table 4.4, that there was no benefit associated with use of the magnetic breathing device ($p > 0.05$) in terms of their perception of effort at the same work load, as RPE was not reduced after using the active breathing device.

5.5.2 Response to Submaximal Exercise

Submaximal heart rate, recorded in the eighth minute on the maximal exercise test, also showed an improved in 40% of the participants when using the active devices, but the mean mean (±SD) of this subgroup did not reach statistical significance ($p = 0.098$). The finding of this study does therefore not confirm the early pilot work conducted by Ryan in 2003 (Roberts, 2004).

Higher submaximal O_2 saturation, based on pulse oximetry, was only documented in 30% of the participants. The insignificant difference in users of the active breathing device obtained from both the results of the ANOVA analyses and analysis of the individual positive responders, therefore do not support those of Biccard (2005). Although a special effort was made to overcome the limitation of considerable variability with hand movements during treadmill running (Plummer, 1995) by only recording stable readings during the last 15 seconds of each workload, pulse oximetry does also provide a relatively gross estimation of saturation of Hb with O_2 (percentages in whole numbers). Sole reliance on this technique for the measurement of O_2 saturation must therefore be acknowledged as a limitation of the study.

5.5.3 $\dot{V}O_2$ max

As $\dot{V}O_2$ max is a function of numerous cardio-respiratory processes including lung inspiratory and pulmonary diffusing capacity, cardiac output, oxygen carrying capacity as well as uptake of oxygen at the level of skeletal muscle (Bassett and Howley, 1999), this assessment was a major focus of this study. Interpretation of the findings were only based on absolute $\dot{V}O_2$ max recordings ($L.min^{-1}$) as the relative $\dot{V}O_2$ max is reliant on a change in body mass over the 10 week period of the trial.

One of the most important findings of this study was that absolute $\dot{V}O_2$ max only improved in 40% of the sample. The magnitude of the mean improvement (6.5%) in this subsample (*n=4*) was however not sufficient to result in a statistically significant change at the 0.05 level of significance. Furthermore, as is seen in Table 4.8, this was not accompanied by an improved peak power output and running time on the treadmill in the each of the participants. The practical significance of these findings for endurance athletes is therefore to be questioned.

A further interesting and important observation is that in the four positive responders, the improvement in absolute $\dot{V}O_2$ max was accompanied by an increase in RBC count in each of the participants and in Hb concentration in four of the participants (Table 4.8). This was also supported by the positive correlation between $\dot{V}O_2$ max and RBC in the complete sample (Table 4.2). The findings therefore lend support to the premise that central factors may affect absolute $\dot{V}O_2$ max via an improvement in oxygen carrying capacity of the blood.

5.5.4 Post Maximal Exercise Test Heart Rate and DBP

In this study mean (±SD) and range of recovery heart rate, both 60 and 120 seconds post-test however showed no statistically significant improvement in both active and placebo trials. Upon analysis of individual results, 40% of the participants showed an improvement in 120 second post maximal exercise test HR recovery when using the active device. The mean (±SD) improvement was significant and confirms the hypothesis of Philpott (1998) and the findings of Jehenson *et al*. (1998) following the exposure to the high intensity SMF, as well as those of Ryan (2007). On the other hand, the absence in improvement in non-responders, although possibly due to lesser compliance in use of the device, may lend support to the findings of Hipman (2002). As the sample size in this study was small, further work is therefore required in order to clarify this question.

Five participants presented with a lower post-test DBP following use of the active device confirming the findings of Okan and Ohkubo (2001). It is well accepted that the synthesis of nitric oxide by vascular endothelium is responsible for the vasodilator tone that is essential for the regulation of blood pressure (Moncada and Higgs, 1993). Pre-post treadmill running venous blood samples were taken and analysed for nitric oxide concentration from two of the participants during the later phases of the study. Interestingly in both of these participants who also presented with lower post-test DBP, an increase in nitric oxide concentration was found in the post exercise test samples following the use of the active device (Table 4.5). This once again confirms the findings of Okan and Ohkubo (2001; 2003; 2005) and presents a direction for further research on humans. Whether the well described post exercise hypotension (Noakes, 2001) is exacerbated by the use of the magnetic breathing device, is an important question requiring further examination.

5.5.5 Conclusion

When individual profiles of the five participants who presented with either an improvement in absolute $\dot{V}O_2$max and/or peak power output on the treadmill are taken into account, a 100% presented with an improvement in RBC concentration and 80% with an improvement in Hb concentration after use of the active O_2 Gold device. The remaining 20% presented with an equal Hb concentration after both active and placebo trials (Table 4.8). Lack of compliance in device use may account for the remaining 20% of the results. Hence further investigation into other possible reasons for non-improvement warrants further study.

However the practical value of a 6.5 % improvement in absolute $\dot{V}O_2$ max to the athletes is to be questioned as this cannot compensate for or override the value of a well designed and implemented schedule of training which is known to increase $\dot{V}O_2$max and peak treadmill performance by a far greater percentage.

CHAPTER SIX

CONCLUSIONS AND DIRECTIONS FOR FURTHER RESEARCH

Every attempt was made to monitor participants throughout the entire duration of the trial in terms of their compliance with the device use, maintenance of a consistent training status and a balanced diet and refraining from the use of ergogenic aids. However in a study involving human participants which requires an intervention which is so reliant on the truthfulness of the participants in terms of their use of the devices over such a prolonged period, the possibility of latent under-compliance is always a reality. Hence a deeper look at the 'positive' responders was considered appropriate. Positive effects on cardio-respiratory function as a result of the constant use of a magnetic breathing device was verified in 50% of the participants.

According to the individual results of the five positive responders, the alternative hypothesis that the 1500G O_2 Gold magnetic breathing device will improve peak power output and maximal running time on the treadmill, pre-exercise test respiratory function, RBC and Hb concentrations and Hct of endurance athletes during a maximal exercise test, therefore cannot be rejected. The null hypothesis that twenty-eight days of regular use of the 1500G O_2 Gold magnetic breathing device will not affect absolute and relative maximum oxygen consumption ($\dot{V}O_2$ max) , RPE, HR, V_E, respiratory exchange ratio (RER) and O_2 saturation at the workload at which $\dot{V}O_2$ max was reached, submaximal minute ventilation (V_E, 1/min), absolute O_2 uptake ($\dot{V}O_2$, L/min), heart rate (HR), rating of perceived exertion (RPE), and O_2 saturation, resting circulating IL-3 and EPO, is accepted.

In order to exclude the possibility of Type 2 error, future research should include examining the effects of the O_2 Gold on a larger sample size. However because of the difficulty in ensuring device usage and maintenance of training status and other externally related practices including diet, this may not be practical. Therefore further work needs to firstly focus on validation of the device usage and control of all possible confounders. Furthermore the effect of the O_2 Gold should be determined in less well trained non-endurance athletes and the long term effects of the O_2 Gold should also be examined. Further investigation of the preliminary observation of changes in markers of nitric oxide concentration associated

with exacerbation of post-exercise reductions in DBP, is also an important direction for further research.

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APPENDICES

APPENDIX A

UNIVERSITY OF
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI
RESEARCH OFFICE
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
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Website: http://research.ukzn.ac.za/ResearchEthics/BiomedicalResearchEthics.aspx

07 May 2013

Prof Edith Peters-Futre
Department of Human Physiology
Westville Campus
University of KwaZulu-Natal

Dear Prof Edith Peters-Futre

PROTOCOL: The efficacy of a 1500G Therahaler magnetic breathing device in optimizing cardio- respiratory function during a maximal exercise test. REF:BFC082/12

Your correspondence dated 25 April 2013 in response to BREC letter dated 26 March 2013 was noted by the sub-committee of the Biomedical Research Ethics Committee.

BREC has granted final approval for the above study to be reactivated with Prof E Peter-Futre as PI and Mr A Naicker and Ms R Turton as Co-PI's. The study may commence as of today 07 May 2013.

This approval is valid for one year from **07 May 2013.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx. BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

PROFESSOR D R WASSENAAR
Chair: Biomedical Research Ethics Committee

APPENDIX B

PARTICIPANT INFORMATION FORM

UNIVERSITY OF KWAZULU-NATAL

DIVISION OF HUMAN PHYSIOLOGY
COLLEGE OF HEALTH SCIENCES

Dear participant,

Ms Robyn Turton, Mr Aroshen Naiker, Dr. Mike Marshall and Professor Edith Peters-Futre from the Division of Human Physiology in the School of Laboratory Medicine and Medical Sciences of the College of Health Sciences at the University of KwaZulu-Natal would like to conduct the following research project:

The efficacy of a Therahaler magnetic breathing device in optimizing cardio-respiratory function during a maximal exercise test.

You are being invited to consider participating in this study.

Background to the study:
Magnetic therapy, the use of magnetic fields to treat a range of medical conditions, has obtained great support in recent years. This non-medicinal breathing device is an inhaler containing a magnetic coil which is being marketed by Magnetic Air natural health products and has been successfully used in improving the oxygenation of blood in asthmatic subjects. Oxygen in the inhaled air passes through the magnetic coil in the Therahaler breathing device and acquires a magnetic charge. It is hypothesized that the magnetically charged oxygen is more highly attracted to the iron binding sites on haemoglobin, thus enhancing the oxyhaemoglobin concentration and oxygen carrying capacity. It is suggested that this will enhance O_2 uptake and may account for anectodatal reports of improved performance in world-class endurance athletes.
The aim and purpose of this research is to establish whether cardiorespiratory function, maximal oxygen uptake and maximal exercise performance during a maximal exercise test is enhanced by the use of a 1500G Therahaler. This trial may provide valuable insight into specific physiological responses to magnetic fields and inhalation of magnetically charged oxygen. It will also establish whether there is scientific verification for the anecdotal claims of endurance athletes that their performance and cardio-respiratory function is improved following regular inhalation of magnetically charged oxygen.

Who is eligible to participate in this study?
Male volunteer recreational endurance runners, healthy and relatively well trained,

- between 18-40 years old
- completing at least 60 km per week in training during the 3 months prior to the study,
- are not suffering from any ailment or chronic illness that will impede on the performance of the test

and do not

- use regular medication
- smoke or consume alcohol excessively
- have implanted metal or medical devices
- use any performance enhancing agents

What will be expected from volunteers in this study?

You will be asked to:

1. Use the Therahaler Device 1 and 2 for 28 days between three exercise tests in the laboratory.
2. Maintain your normal diet and training status throughout the study.
3. Provide a small (4ml) venous blood sample before and after each of the maximal exercise tests.

Outline of tests

As one of 30 healthy male runners who will be required to use the Therahaler Device 1 for 28 days after baseline test 1 and then Therahaler Device 2 for 28 days after test 2. This will involve inhaling through the little device a minimum of 25 times daily for the 28-day duration of each intervention.

At the start of the study, you will be required to visit the exercise laboratory for a basic familiarization session during which vital signs and basic anthropometric and lung function measures will be taken, you will be required to fill in a medical and training status questionnaire, and a medical doctor will conduct a basic examination of your health status. Thereafter you will be required to perform a maximal treadmill exercise test during which heart rate, blood pressure and non-invasive oxygen saturation will be measured. Before and after the treadmill tests a small blood sample will be taken for analysis of your red blood cell indices.

After using the Therahaler Device 1 and Therahaler Device 2, you will be asked to return to the laboratory for a repeat of the maximal exercise tests and provision of small blood samples before and after each treadmill test.

How can you benefit from participation in this study?

Following the study, you will be given the results of each of the laboratory tests and your haematocrit and haemoglobin concentrations. The magnetic strength of the two Therahaler devices that you have used, will then also be disclosed.

By participating you will establish whether a Therahaler is of benefit to your maximal running performance and your lung capacity and function, oxygen carrying capacity and cardiac response to exercise.

Will you be exposed to adverse effects of the study?

A minimal risk factor is involved in any physical test and all necessary precautions will be taken to ensure safe conditions.

As you are however a trained athlete, there is only a very slight risk of something unfortunate occurring while you are on the treadmill. There is also a very slight risk of complications from venipuncture (taking of blood), mainly infection at the site of puncture or inflammation (swelling) of the vein used.

In the unlikely event of a complication occurring, Dr. Mike Marshall will be present at all of the assessments and taking of the blood samples. He will ensure that procedures are performed according to the same standards that you would experience in a hospital environment.

Can you withdraw from the study?

As your participation is entirely voluntary, you may withdraw from the study at any time without penalty.

Will your individual results remain confidential?
Yes. The records identifying the participants will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Although the study is for degree purposes, the results of the study may be published. In all cases your identity will remain confidential.

Financial compensation
Any out-of-pocket expenses which you may incur as a result of your participation in this study (e.g. traveling expenses) will also be reimbursed by the research team.

Further queries
Should you have any queries or wish to obtain further details regarding this study, please do not hesitate to contact the following persons at the University of Kwa-Zulu-Natal:
Mr. Aroshen Naiker – 083-618 3478
Miss Robyn Turton_ 084-606-6987
Prof. Edith Peters-Futre - (031) 260 4237 (W); 0737597974

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APPENDIX C

SUBJECT CONSENT FORM

DIVISION OF HUMAN PHYSIOLOGY
COLLEGE OF HEALTH SCIENCES

THE EFFICACY OF A 1500G THERAHALER MAGNETIC BEATHING DEVICE IN OPTIMIZING CARDIO-RESPIRATORY FUNCTION DURING A MAXIMAL EXERCISE TEST.

I, …….. hereby agree to participate in a research study to be performed by Ms Robyn Turton, Mr Aroshen Naiker, Professor Edith Peters-Futre and Dr. Mike Marshall in the Division of Human Physiology in the College of Health Sciences of the University of KwaZulu-Natal. I have been informed about the study by the principal investigator, Mr. Muhammad Vahed.

I understand that the basic procedures to be carried out are to include:

1. Use of the Therahaler magnetic breathing device for 28 days after the first laboratory test and 28 days after the second laboratory test.

2. Completion of three maximal exercise tests on a treadmill.

3. Completion of a brief medical and training questionnaire before the trial and provision of 2ml blood samples before and after the treadmill tests.

The details of these procedures have been explained to me in full. I am aware that a certain level of discomfort may occur when the blood is taken and that this procedure may be accompanied by certain medical risks including infection and inflammation of the vein.

I understand that this study will form part of the Masters Degree of Ms. Robyn Turton and that the results may be published.

I understand that participation is entirely voluntary and that I may withdraw from the study at any time.

I may contact the principal investigator of the project, Ms Robyn Turton, Mr Aroshen Naiker at 0737861269 at any time if I have questions about the research or if I am injured as a result of the research.

_____ _____
Signature of Participant Date

_____ _____
Signature of Witness Date (Where applicable)

APPENDIX D

MEDICAL QUESTIONNAIRE

DIVISION OF HUMAN PHYSIOLOGY
COLLEGE OF HEALTH SCIENCES

The efficacy of a 1500G Therahaler magnetic breathing device in optimizing cardio-respiratory function during a maximal exercise test.

1. Name…… 2. Date of birth……

3. Are you currently in good health? (i.e. No illness within the last 3 months)
yes □ no □. If no, please specify
……

4. Do you suffer from any chronic medical conditions? (conditions diagnosed more than 3 months ago which affect your everyday life) e.g. diabetes, high blood pressure, asthma.
yes □ no □. If yes, please list
……..……..

5. Do you use anti-inflammatory tablets during a race of this nature?
yes □ no □. If yes, please specify the type and dosage
……

6. Are you using any other medication?
yes □ no□. If yes, please list
……

7. Do you suffer from a bleeding disorder e.g. haemophilia?
yes □ no □ If yes, please specify
……

8. Have you been admitted to hospital within the last year?
yes □ no □ If yes, please specify
……

9. Do you smoke? yes □ no □
If yes, please specify amount per day and for how many years
……

10. Are you presently or have you ever used performance enhancing drugs? (e.g. Erythropoeitin, anabolic steroids)
yes □ no □. If yes, please list
……

11. Do you have a cardiac pacemaker or any other implanted electromedical device?
yes □ no □

Thank you for your participation

APPENDIX E

PRE-TRIAL QUESTIONNAIRE

UNIVERSITY OF KWAZULU-NATAL

DIVISION OF HUMAN PHYSIOLOGY
COLLEGE OF HEALTH SCIENCE

The efficacy of a 1500G Therahaler magnetic breathing device in optimizing cardio-respiratory function during a maximal exercise test.

Name……..……
Device code (to be filled in by researchers)…….....

SECTION A: PLEASE ANSWER ALL QUESTIONS.

1. Date of birth: …… Age: …….....
2. Address: ……
3. Telephone numbers: Home: ……..
Work: ……...
Cell: ……..
4. Running club: …….
5. Occupation: ……....

Please tick one of the boxes in each of the following questions:

6. How many hours do you generally train per week?

- ☐ < 5
- ☐ 6 - 10
- ☐ 11 - 15
- ☐ 16 – 20

7. How would you classify your athletic ability?

- ☐ WEEK-END WARRIOR (only run on weekends)
- ☐ SERIOUS AMATEUR (> 5 races per year)
- ☐ ELITE (regular top 10% finisher)
- ☐ PROFESSIONAL (paid to run)
- ☐ OTHER – SPECIFY…….

8. Racing experience within last year?

- ☐ FUN RUNS
- ☐ < 5 x 21 km races) PER YEAR
- ☐ < 5 marathons (42km) PER YEAR
- ☐ > 2 ultra marathons (52 km or longer) PER YEAR
- ☐ PREVIOUS MULTISTAGE RACES e.g. Cape Odyssey, 3 Cranes
- ☐ OTHER -

9. Running history: Serious\social: …….
Age started running: ……..…….years
Level of training during these years: …….
Total number of running races: ……

10. Sports played in last 12 months (squash, rugby, soccer, etc)

……..

Dietary and fluid intake details

1. Are you on any specific diet? (Vegetarian, fish only, etc)

yes □ no□. If yes, please specify:

……

2. Are you presently using any supplements? (Multivit, Calmag, etc)

yes □ no □. If yes, please specify how much you are taking and how often:

……

3. Do you use water and/or a sports drink during training?……....

4. Please specify how much of each, how often and which product:

……

……

THANK YOU FOR YOUR PARTICIPATION

_____ _____

Participant's Signature Date

_____ _____

Principal Investigator's Signature Date

APPENDIX F

TRAINING DIARY

NAME	
DEVICE CODE	

DATE	NUMBER OF TIMES DEVICE WAS USED	TRAINING SCHEDULE			HAVE YOU TAKEN ALL SUPPLEMENTS/CURRENT MEDICATION
		DISTANCE	APPROXIMATE SPEED	INTENSITY HIGH/MODERATE/EASY	
06/26/13					
06/27/13					
06/28/13					
06/29/13					
06/30/13					
07/01/13					
07/02/13					
07/03/13					
07/04/13					
07/05/13					
07/06/13					
07/07/13					
07/08/13					
07/09/13					
07/10/13					
07/11/13					
07/12/13					
07/13/13					
07/14/13					
07/15/13					
07/16/13					

APPENDIX G

UANTIFICATION OF TRAINING STATUS

AN EXAMPLE

UNIVERSITY OF KWAZULU-NATAL

NAME:

	WEEK	DURATION OF TRAINING PER WEEK (hrs)	Time Fraction LOW INTENSITY	MODERATE INTESITY	HIGH INENSITY	FREQUENCY/WEEK	
ACTIVE	1	6.85	2.00	2.00	2.85	6.00	
	2	6.00	2.50	1.00	2.50	6.00	
	3	7.22	3.00	1.70	2.52	7.00	
	4	4.57	0.00	1.00	3.57	6.00	
	+3 DAYS	2.91	0.91	1.00	1.00	3.00	
		27.54	8.41	6.70	12.44	28.00	TOTALS PER MONTH
		6.22	1.90	1.51	2.81	6.32	AVERAGE PER WEEK
			9.50	3.03	3.51		
			16.03				
PLACEBO	5	6.11	2.00	2.00	2.11	6.00	
	6	6.17	1.84	1.40	2.93	6.00	
	7	5.00	2.50	1.50	1.00	5.00	
	+3 DAYS	1.34	0.67	0.00	0.67	2.00	
		18.62	7.01	4.90	6.71	19.00	TOTALS PER MONTH
		5.43	2.04	1.43	1.96	5.54	AVERAGE PER WEEK
			10.22	2.86	2.45		
			15.53				

APPENDIX H

PARTICIPANT FEEDBACK

AN EXAMPLE (PARTICIPANT EXCLUDED)

Physiology
y Medicine &Medical Sciences
iences
2013-07-30

THE EFFICACY OF A THERAHALER MAGNETIC BREATING DEVICE IN OPTIMIZING CARDIO-RESPIRATORY FUNCTION IN ATHLETES

Dear…….
Thank you very much for agreeing to take part in the above study. We are pleased to be able to provide you with the following feedback:
Uncoding of the devices has revealed that you were on an inactive placebo device for the first 4 week period; thereafter you were on an active device containing a 1500g magnet for the following 4 weeks.

TABLE 1: Your Physical and General Medical Characteristics

Physical Characteristic	Your value (PRE)	Your value (POST Device 2)	Predicted norm for active athlete of your age, gender and BMI/researcher's comment
Age	28		-
Medication	General vitamin		
Sporting Discipline	Running, Paddling, Diving		
Height (m)	1.71		
Cardiovascular status	Normal rhythm, heart sounds with no murmurs noted		
Respiratory status	No abnormalities detected		
Dermatological	No abnormalities/ dermatological lesions noted		
Musculoskeletal	No pain or limitation on range of motion of weight bearing joints		
Mass (kg)	65.6	67.3	Gained 1.7, 1.12% gain
BMI	22.4	23	Normal range:18.5-24.9
Triceps skinfold (mm)	5.8	5.4	
Chest Skinfold (mm)	4.6	4.9	
Midaxilla (mm)	4.8	5.4	
Subscapular(mm)	8.7	8.8	
Suprailliac(mm)	6.2	6.5	
Abdominal (mm)	6.3	6.2	
Thigh (mm)	9.3	7.8	
Body Fat % (determined from above skinfolds)	6.1	6.0	Elite Triathletes average between 5 and 12%
WAIST circumference (cm)	71	73	>95cm = central obesity
Hip Circumference(cm)	88	88	
Waist : Hip Ratio	0.81	0.83	< 0.90 =low risk
Resting Pulse Rate (bpm)	58	52	

Resting Blood Pressure (mmHg)			
Systolic	120	118	Within healthy range
Diastolic	50	64	

Reported Compliance in using Device:
Compliance with the use of the first inactive device did not reach the requirements of 30 inhalations per day. It was reported in your training diary that during this first period you used the device an average of 15-20 times per day. During the second period of the trial compliance with use of the device increased considerably to meet the studies requirements of 30 inhalations per day.

Training Status during the Experimental Period:
This was a very important confounder in the study which will affect the internal validity of the results. You were asked to keep your training status constant.

While using Active Device:
During this period of the trail you reported that you were decreasing your running mileage in order to focus on strength training on the water and gym. However you retained a consistent daily training status throughout this period

While using Placebo Device:
A consistent daily training status was reported during this first period of the trial. You did however report that during this time you were doing more running than when you moved onto the active device.

Other possible Confounders:
Illness: Nil
Use of medication: Nil
Use of performance enhancing agents:
USN carbohydrate racing juice

TABLE 2: Lung Function

	Unit	**Baseline**	**After use of Placebo Device**	**After Use of Active Device**	**NORMS for inactive person of your height, age and gender**	**Comment**
Forced Vital Capacity (FVC)	L/min	5.37	5.57	5.49	5.05	Excellent static and dynamic lung function
Forced Expiratory Volume in1 Sec ($F_E V1$)	L/min	4.46	4.5	4.44	4.15	
FVC/FEV1 ratio	%	0.83	0.81	0.81	>0.80 : no obstruction to air flow	
Forced Inspiratory Capacity(FIVC)	L/min	5.57	5.62	5.64	5.05	
Breath holding Time	Sec	98	114	125		
Maximum Expiratory Capacity (VE max) during Exercise Test	L/min	136	152	153	In elite category!	

TABLE 3: Performance in maximal running test

	Units	Baseline	After use of Active Device	After Use of Placebo Device	Comment
Pretest Data					
Body Mass	kg	65.6	67.3	67.3	Body mass gain, a confounder
After 8 minutes (12 km/hr, 4% gradient)					
Submaximal Heart Rate	bpm	167	153	156	Best after use of active device
Submaximal O_2 saturation	%	96	94	96	
At VO_2 max					
Workload	Km/hr, % Gradient	12Km/hr, 12% Gradient	12Km/hr, 13% Gradient	12Km/hr, 13% Gradient	Training /learning effect after initial baseline test?
Max Running Time	min: sec	11:00	12:00	12:03	
Heart Rate	bpm	194	191	195	
O_2 saturation	%	92	92	92	
RPE	Scale of 1-10	9	10	10	
VE (Minute ventilation)	L/min	136	152	153	
Tidal volume	L	2.6	2.8	2.8	
Breathing frequency	b/min	53	56	54	
O_2consumption (VO_2)	L/min	5144	5164	5489	Max achieved after placebo trial when you were doing more running. Outstanding capacity!
VO_2	ml/kg/min	78.5	76.7	81.5	
RER	Index ranging from 0.7-1.00 during "aerobic" exercise	1.04	1.10	1.08	Greatest reliance on CHO breakdown & tolerance of "anaerobic" metabolism after use of active device
Post Test					
Heart rate: 60 sec post	bpm	162	162	153	Greater endurance as tests progressed over the 8 weeks
Heart rate: 120 sec post	bpm	128	122	125	
Diastolic Blood	mmHg	58	58	54	Drop indicates dilation

Pressure					of blood vessels in response to intense exercise

TABLE 4: Results of Full Blood Count

	Units	Baseline	After use of Device 1	After Use of Device 2	Reference Range
Red Blood Cell Indices					
Hemoglobin(Hb)	g/dL	15.6	15.6	15.0	13.0-17.0
Red Blood Cell count (RBC)	1012 /L	5.03	5.0	4.77	4.5-5.5
Hematocrit(Hct)	%	45.8	45.5	43.3	40-50%
White Blood Cell Indices					
White Blood Cell Count (WBC)	109 /L		6.51		3.92-9.88
Neutrophills	109 /L		3.07		2.0-7.5
Lymphocytes	109 /L		2.65		1.0-4.0
Monocytes	109 /L		0.27		0.18-1.0
Eosinophils	109 /L		0.35		0-0.45
Basophils	109 /L		0.02		0-0.2
Platelets					
Platelets	109 /L		239		150-450

Conclusion:
You have an outstanding O_2 carrying and uptake capacity which is supported by your high red cell status in your blood and a good maximum ventilatory capacity. It is really a great pity that you changed over to doing less running and more strength training while on the active device. But this does show that there is no replacement for muscle specific training. To achieve max on the treadmill, you need to do running training; it improves capillarisation and oxidative capacity in the trained leg muscles, which are important determinants of VO_2 max when it is measured during treadmill running.

As the change in mode of training was a major confounder, the findings of this trial can unfortunately not be used to reveal how effective the magnetic device is for you.

We trust that you will find these results interesting and thank you for participating in this research project.

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Discipline of Human Physiology
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2013-08-30

THE EFFICACY OF A THERAHALER MAGNETIC BREATING DEVICE IN OPTIMIZING CARDIO-RESPIRATORY

Dear ……..

Thank you very much for agreeing to take part in the above study. We are pleased to be able to provide you with the following feedback:

Uncoding of the devices has revealed that you were on an active device containing a 1500g magnet for the first 4 week period; thereafter you were on an inactive placebo device for the following 4 weeks

TABLE 1: Your Physical and General Medical Characteristics

Physical Characteristic	Your value (PRE)	Your value (POST Device 2)	Predicted norm for active athlete of your age, gender and BMI/researcher's comment
Age	29 Years		
Medication	None reported		
Sporting Discipline	Hockey, elite trail runner and Mountain Biking		
Height (cm)	183		
Cardiovascular status	Normal rhythm, heart sounds with no murmurs noted		
Respiratory status	No abnormalities detected		
Dermatological	No abnormalities/ dermatological lesions noted		
Musculoskeletal	No musculoskeletal problems which will interfere with performance in treadmill running test or training		
Mass (kg)	72	71.6	Minimal loss
BMI	21.5	21.4	In lower section of normal range (18.5-24.9) despite added weight of muscle.
Triceps skinfold (mm)	7.3	8.4	
Chest Skinfold (mm)	6.9	5.3	
Midaxilla (mm)	6.2	6.3	
Subscapular(mm)	11.5	9.8	
Suprailliac(mm)	8.4	8.2	
Abdominal (mm)	8.3	8.0	
Thigh (mm)	7.1	7.4	
Body Fat % (determined from above skinfolds)	7.84	7.47	6-15% for elite cyclists; 5-12% for elite triathletes
WAIST circumference (cm)	72	74	>94cm = central obesity
Hip Circumference(cm)	88	93	
Waist : Hip Ratio	0.82	0.80	< 0.90 =low risk
Resting Pulse Rate (bpm)	49	40	Excellent! As expected for elite endurance athlete
Resting Blood Pressure (mmHg)			

Systolic **Diastolic**	126 78	116 68	Within healthy range

Reported Compliance in using Device:
The use of your initial active device was compliant with that of the studies requirements, averaging 30 inhalations every single day. During the use of the second (inactive) device compliance dropped a little as there were a few days on which less inhalations were reported.

Training Status during the Experimental Period:
This was a very important confounder in the study which will affect the internal validity of the results. You were asked to keep your training status constant.

While using Active Device:
A very consistent training history was reported throughout both trials. The mileage accumulated was also consistent at approximately 60km/wk. There is a range in distances between 10 and 20km of running per day, with a few rest days taken. The intensity of the exercise also remained consistent throughout the trial.

While using Placebo Device:
As above, a consistent training diary throughout the 8 weeks.

Other possible Confounders:
Illness: None reported
Use of medication: None reported
Use of performance enhancing agents: None reported

TABLE 2: Lung Function

	Unit	**Baseline**	**After use of Active Device**	**After use of Placebo Device**	**Predicted norms for your height, age and gender**	**Comment**
Forced Vital Capacity (FVC)	L/min	4.86	4.94	5.33	5.84	Appears not to have been maximal effort
Forced Expiratory Volume in1 Sec (F_EV1)	L/min	4.12	4.18	TD	4.75	
FVC/FEV1 ratio	%	0.85	0.85	TD	0.80	>0.80 absence of obstruction to air flow
Forced Inspiratory Capacity(FIVC)	L/min	4.76	5.08	5.07	5.84	Also appears not to have been maximal effort
Breathholding Time	Sec	52	N/A	45		
Maximum Expiratory Capacity (VE max) during Exercise Test	L/min	158	166	160		This places you into the elite category

N/A: not available; TD: Technical Difficulty

TABLE 3: Performance in maximal running test

	Units	Baseline	After use of Active Device	After Use of Placebo Device	Comment
Pretest Data					
Body Mass	kg	72.0	73.0	71.6	
After 8 minutes (12 km/hr, 4% gradient)					
Submaximal Heart Rate	bpm	160	152	152	No change in fitness status
Submaximal O_2 saturation	%	92	98	93	Far less of a drop in oxygen saturation of haemoglobin after being on active device
At VO_2 max					
Workload	Km/hr, % Gradient	12 km/hr; 13%	12 km/hr; 13%	12 km/hr; 14%	
Max Running Time	min: sec	12:00	12:00	12:04	
Heart Rate	bpm	193	186	187	Lower HR max compared to baseline, but little difference after use of the two devices
O_2 saturation	%	88	85	89	
RPE	Scale of 1-10	9	9	9	Perception of effort unchanged
Pulmonary Ventilation(VE)	L/min	158	166	160	Greatest after use of active device
Tv(Tidal Volume)	L	2.99	3.01	2.98	
Rf(respiratory Frequency)	b/min	54	56	54	
Absolute O_2consumption ($VO_{2\ max}$)	ml/min	5378	5728	5760	Improved VO_2max compared to baseline; excellent result! Active device usage did however not appear to improve this capacity.
VO_2	ml/kg/mi	74.7	78.5	80.4	
RER	Index ranging from 0.7-1.00 during "aerobic"	1.14	1.09	1.01	Reduced reliance on oxygen independent metabolism with time, appears to indicate improved endurance status.

	exercise				
Post Test					
Heart rate recovery: 60 sec post	bpm	147	138	134	Improved heart rate recovery. This again points to improved endurance status with time
Heart rate: 120 sec post	bpm	122	112	107	
Diastolic Blood Pressure	mmHg	72	70	60	Dilation of blood vessels in response to intense exercise improved with time (and fitness)

TABLE 4: Results of Full Blood Count

	Units	**Baseline**	**After use of Active Device**	**After use of Placebo Device**	**Reference Range**
Red Blood Cell Indices					
Hemoglobin(Hb)	g/dL	16	15.8	15.6	13.0-17.0
Red Blood Cell count (RBC)	10^{12}/L	4.92	4.73	4.61	4.5-5.5
Hematocrit(Hct)	%	47.4	45.7	44.5	40-50%
White Blood Cell Indices					
White Blood Cell Count (WBC)	10^{9}/L	6.23	6.19	5.43	3.92-9.88
Neutrophills	10^{9}/L	3.23	3.13	2.77	2.0-7.5
Lymphocytes	10^{9}/L	2.22	2.22	1.92	1.0-4.0
Monocytes	10^{9}/L	0.36	0.34	0.36	0.18-1.0
Eosinophils	10^{9}/L	0.27	0.36	0.27	0-0.45
Basophils	10^{9}/L	0.02	0,03	0.02	0-0.2
Platelets					
Platelets	10^{9}/L	214	182	209	150-450

Conclusion:
Congratulations on an outstanding VO_2 max! This places you into world class category!

Although you report that training status was constant, endurance levels do appear to have improved over the course of the study. This is particularly reflected in your heart rate recovery, lower RER, and greater vasodilatation (lower DBP) during the post-placebo device trial.

Red Blood indices remained relatively constant. We shall however be investigating your hydration status on test days to ensure that this remained constant.

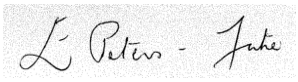
Your WBC counts appear to have been depressed following the placebo trial. Reasons for this could include suppressed immune defences following overtraining or high levels of stress and blood cortisol concentration.

In summary, the use of the active magnet device did not appear to be beneficial to you in terms of enhancing your performance at endurance events.

Robyn Turton
Masters Student in Sports Medicine

Aroshen Naicker
Post Grad student in Exercise Physiology

Dr Mike Marshall
Consulting Physician



Prof Peters-Futre
Research Supervisor