Journal of Regenerative Biology and Medicine

ISSN: 2582-385X
Slater G, et al., 2022- J Regn Bio Med
Review Article

Hyperbaric Oxygen Therapy: An Overview

Gordon Slater[1*], Martin O'Malley[2], Tayla Slater[3] and Tandose Sambo[4]

Abstract

Hyperbaric Oxygen Therapy (HBOT) has been a recognised treatment for a multitude of injuries for decades and presents significant opportunities for the improvement of wound healing, blood vessel restoration, reduction in recovery time after surgery, treatment of neurological and neurodegenerative disorders, improvement of memory and cognition, sports injury rehabilitation, cartilage regeneration, and overall quality of life. This paper aims to investigate HBOT and its indications for use, both as an adjuvant with other established treatments and independently, in order to provide an overview of treatment avenues with immense possibilities and versatility.

Keywords: Hyperbaric oxygen therapy; Cartilage repair; Sports injury; Regenerative medicine; Diabetes.

"Wellness is not a 'medical fix' but a way of living-a lifestyle sensitive and responsive to all the dimensions of body, mind, and spirit, an approach to life we each design to achieve our highest potential for well-being now and forever"-Greg Anderson.

[1]MBBS FRACS FA OrthoA, Clinical Private Practice, Double Bay NSW Sydney, Australia

[2]Sport Foot Ankle, New York

[3]BEng (Hon)/MBiomedEng, Clinical Private Practice, Double Bay NSW Sydney, Australia

[4]Clinical Private Practice, Double Bay NSW Sydney, Australia

[*]**Corresponding Author:** Slater G, MBBS FRACS FA OrthoA, Clinical Private Practice, Double Bay NSW Sydney, Australia.

Received Date: 05-23-2022

Accepted Date: 05-28-2022

Published Date: 06-22-2022

Introduction

Hyperbaric Oxygen Therapy (HBOT) is a non-invasive solution for, among other things, rehabilitation from physical injury, recovery from fatigue, and treatment for neurological and neurogenerative disorders [1-3]. Over the past decade, competitive sports injuries have reached a new high, not only in support from the general public and sponsors, but in recorded injuries to athletes [4].

New and better treatments are required to aid in returning athletes to the game faster as well as improving overall health. While HBOT presents a first-class option for professional athletes, HBOT also has significant benefits for the general population. Additionally, HBOT has been linked to cartilage repair [5-8]. The potential benefits of HBOT are extensive and whether used as an adjuvant

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

with other treatments, or separately, HBOT presents a state-of-the-art solution with an extensive range of indications from musculoskeletal and neurologic to recovery and sports performance.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) can be classified as the administration of 100% oxygen at atmospheric pressures greater than ambient barometric pressure at sea level, usually between 1 to 3 standard atmospheres [4,9,10]. Treatment can be carried out in either a monoplace or multiplace chamber. A monoplace chamber (Figure 1) accommodates a single patient and historically, is entirely pressurized with 100% O_2 in which the patient breathes ambient oxygen without the need for a mask. A multiplace chamber is pressurized with compressed air. It can accommodate two or more people, such as patients, medical professionals, and support personnel, in which patients will breathe close to 100% oxygen through masks or endotracheal tubes [11]. Most new monoplace chambers are similar to traditional multiplace chambers in that they constitute pressurized ambient air and a mask providing 100% O_2. This configuration is considerably safer in terms of combustibility. While soft chambers made of fabric, instead of steel or polymer, do exist and are increasing in popularity, they are not capable of reaching above 1.4 ATA, and will not be the main focus of this overview [12,13]. Due to the higher cost of multiplace chambers, monoplace chambers are the most common [14].

Figure 1: Fortius420® from Oxyhealth, a monoplace hyperbaric chamber capable of reaching up to 3.0AT [15].

The concept of using compressed air at higher pressures than sea level has an extensive history and is closely tied to diving medicine. It was observed that people living at higher altitudes took longer to heal than those spending time in high pressure environments, like deep sea divers [4].

The first recorded hyperbaric oxygen treatment was performed by British physiologist Nathaniel Henshaw in 1662, who created an airtight room called a 'domicilium'. Henshaw was able to manipulate the pressure in the room using large bellows [16,17].

HBOT and its role in healing

Oxygen inherently plays an essential role in recovery from injury and fatigue. HBOT acts to increase the amount of oxygen dissolved in plasma, allowing more oxygen to reach the

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

peripheral tissues [16]. It follows Henry's law, which can be summarised as "gas solubility in a solution depends on the partial pressure applied to it but does not change the affinity of haemoglobin for oxygen" [18]. When an injury occurs, cells and blood vessels are disrupted, resulting in hypoxia [4]. Ultimately, molecular oxygen plays a significant role in all three phases of tissue healing: inflammatory, proliferative, and remodelling [19]. According to Lew et al [20], "Collagen synthesis, matrix deposition, angiogenesis, epithelialisation, and bacterial killing all require molecular oxygen during the reparative process." Exposure to HBOT increases oxygen content available in tissues, and this accelerates the process of healing [19].

When patients are exposed to 2 atmospheres absolute (ATA) and 100% oxygen, the oxygen content in plasma can be up to "10 times higher than breathing regular air at sea level"[14]. The effects of this increased oxygen content include vasoconstriction which acts to reduce oedema and improve neutrophil phagocytic function to mitigate infection, phagocytosis activation, neovascularization, neoangiogenesis, collagen production and inhibition of anaerobic organisms [1,11,14].

Indications for HBOT

The healing mechanisms of HBOT make it an effective treatment option for various conditions and injuries, including, but not limited to, difficult wounds like diabetic ulcers, decompression sickness, gas embolism, fractures, muscle damage, ischemia, carbon monoxide poisoning, radiation injury, skin grafts and flaps, nerve healing, and smoke inhalation [2,5,19]. Interestingly, there are only 13 FDA approved indications for HBOT as seen in Table 1 [21].

1	Air and gas bubbles in blood vessels
2	Anaemia (severe anaemia when blood transfusions cannot be used)
3	Burns (severe and large burns treated at a specialised burn center)
4	Carbon monoxide poisoning
5	Crush injury
6	Decompression sickness (diving risk)
7	Gas gangrene
8	Hearing loss (complete hearing loss that occurs suddenly and without any known cause)
9	Infection of the skin and bone (severe)
10	Radiation injury
11	Skin graft flap at risk of tissue death
12	Vision loss (when sudden and painless in one eye due to blockage of blood flow)
13	Wounds (non-healing, diabetic foot ulcers)

Table 1: FDA Approved Indications for Hyperbaric Oxygen Therapy [21]. While there are limited approved applications for HBOT, there are still a number of growing "off-label" indications such as treatment of patients with Alzheimer's disease, stroke, and COVID-19 [2].

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

Stem cells and wound healing

In 2018, Peña-Villalobos et al analysed the effects of HBOT on tissue growth, maintenance, and regeneration by using HBOT in conjunction with Wharton Jelly mesenchymal stem cells (WJ-MSCs) [18]. They discovered the ability of HBOT to influence the proliferation rate of stem cells in the small intestines of mice, increase angiogenesis in the chorio-allantoic membranes of chicken embryos, and improve tissue regeneration in diabetic mice. HBOT most likely immobilises stem cells to enhance homing, engraftment, and more organised proliferation. This in conjunction with increased oxygen content in tissues results in a faster rate of wound healing, similar to that observed when using commercially available wound dressing scaffolds [18].

Stem cells, spinal cord injury (sci) and nerve regeneration

Spinal cord injury (SCI) threatens the quality of life of patients with potential paralysis, however, transplantation of bone marrow-derived stem cells (BMSCs) can be utilized to regenerate a damaged nervous system via immunoregulatory macromolecules which act to repair injury. Geng, et al. studied this effect enhanced by HBOT in rats and observed that the combination of BMSC transplantation and HBOT encourage an environment advantageous to stem cell survival and thus can restore neurological function [22]. Additionally, HBOT when applied to neurological disorders, such as crush injury, is capable of generating "endogenous neurogenesis either through direct effects, anti-inflammatory effects, or immunomodulation" [23]. This study by Pan, et al. concluded that the addition of HBO to transplanted amniotic fluid mesenchymal stem cells (AFS) lessened stem cell death and further promoted the peripheral nerve repair already seen with AFS transplantation alone. Thus, it is possible to use HBO as an adjuvant therapy to stem cell transplantation in peripheral nerve injury.[23].

Erectile disfunction

As defined by Hadanny et al, angiogenesis is "the sprouting of new blood vessels using vasculogenic stem cells which differentiate into endothelial cells, as well as other supporting structures" [24]. Since hyperbaric oxygen therapy can induce angiogenesis, it was hypothesised that it could reverse the microvascular insufficiency commonly causing erectile dysfunction (ED). After treating patients to a total of 40 daily 90min sessions of HBOT at 100% oxygen and 2 ATA, 5 days per week, Hadanny et al [24] observed an 88% improvement in ED. Unlike PDE5 inhibitors and other penile interventions which offer short-term relief from symptoms, HBO works to reinstate the basic vascular pathology and returns the possibility of spontaneity. Patients can see improvement even after years of ED or subsequent to trying PDE5s, or similar, without result. However, like most regenerative approaches, HBOT requires a significant amount of time and commitment [24].

Recovery after coronary artery bypass graft surgery

In 2010, Yogaratnam, et al. published a study examining the effects of HBO preconditioning on patients undergoing coronary artery bypass graft (CABG) surgery

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

[13]. Patients were preconditioned for two 30min intervals, separated at 5min apart, at 100% oxygen and 2.4 ATA 4h prior to surgery. Patients preconditioned with HBO had an 18% reduction in ICU stay and 57% reduction in intraoperative blood loss. It is thought that the oxidative stress induced by HBOT increases reactive oxygen species (ROS), which initiates a cascade of events leading to myocardial protection. The researchers concluded that while the results were encouraging, at the time of the study, limited availability of sufficient HBO facilities to treat ill post cardiac ICU patients meant an uncertain future for HBO preconditioning.

Stroke, traumatic brain injury (TBI) and neurological disorder

Debilitating diseases such as stroke, traumatic brain injury (TBI) and other neurodegenerative disorders constitute a substantial burden on health systems and economies worldwide [25]. In 2012 approximately, 3.1 billion people were living with TBI, surmounting to US $76.5 billion in health care costs [26,27]. Additionally, in a 2017 update, the American heart Association determined stroke as the number one cause for long-term disability in the United States [28]. Thus, management and effective treatment of these neurodegenerative diseases not only prevents death and exorbitant health costs but improves quality of life for billions of people. While HBOT has been used for over 50 years, only in recent years has it been applied to improving cognition, memory loss, language and comprehension deficits after brain trauma and stroke, offering an alternative treatment to more invasive procedures like cell transplants [2,29]. HBOT has been shown to increase oxygen supply and hence reduce ischemia injury caused by stroke, minimizing neurological damage [30].

Moreover, Gottfried, et al. conducted literary research and concluded that HBOT elevates cerebral blood flow (CBF), increases neuronal stem cell proliferation and migration to damaged areas, reduces neuroinflammation, inhibits apoptosis, improves mitochondrial function, and enhances antioxidant defence activity [2]. They discovered neurological improvements have been observed in stroke patients and improvement in cognitive function in patients suffering from Alzheimer's Disease and Vascular Dementia. While the possibilities for HBOT treatment of neurodegenerative and neurological disorders are numerous and growing, it is believed that it cannot revert major neuron loss in severe cases and thus should be considered early after diagnosis.

Improving cognition

The human brain is the most metabolically active organ in the body, consuming up to 25% of blood oxygen supply [31]. While HBOT has been proven to improve cognitive function after stroke and brain injury, HBOT also has the ability to increase cognitive performance in healthy, young people.

In a study conducted in 2017 by Vadas, et. al. motor task, multitask, and memory performance was greatly increased under hyperbaric conditions compared to normobaric, thus they concluded that oxygen is a "rate limiting factor for brain activity" [32]. Additionally, Yu, et. al. highlighted HBO causes "increases in spatial working memory and memory quotient", affecting the

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

"functional connectivity of several subcortical regions" [31].

Also, Moss and Scholey established improved memory consolidation as a result of heightened cerebral oxygen, Scholey, et. al. confirmed improved word recall, and Moss, et. al. showed improved attention and vigilance. Increased activation of the right frontal, left temporal, and left fusiform gyri was demonstrated by Chung et al when patients were treated with higher oxygen concentrations than in air [3,33-35].

Most of these studies were performed while patients were undergoing treatment, so little is known about the long-term effects of HBOT on cognitive performance. However, it can still be concluded that HBOT has a significant impact on multiple facets of memory and cognition.

Diabetes: insulin sensitivity and foot ulcers

Diabetes mellitus is a serious and growing concern. It is projected that over 12% of the population will be diagnosed with diabetes by 2045, with health costs expected to reach 1,054 billion USD in the same year [36]. HBOT could offer relief for patients affected by insulin resistance and diabetic foot ulcers. Insulin resistance is the diminished ability for insulin to effect glucose metabolism and is a good predictor of future development of diabetes [37]. A study conducted by Wilkinson, et al. examined patients with type 2 diabetes which demonstrated an increase in insulin sensitivity during the third and thirteenth HBOT sessions. The effect was conserved for at least 30 minutes after cessation of treatment [38].

Persistent foot ulcers affect 15% of diabetes sufferers and represent 85% of diabetes related amputations [39-41]. HBOT has the potential to decrease the risk of amputation from 30.07% to 13.63% via bacterial death by production of oxygen free radicals and enhanced leukocyte activity [42,43]. Additionally, increased limb salvage rates for infected diabetic wounds have been reported with more than 10 HBO treatments [44]. As such, HBOT presents a possible treatment avenue for insulin resistance observed in type 2 diabetics and for the treatment and prevention of amputation of unhealing ulcers**.**

Sports injury

In the past decade, competitive sports have gained in popularity with fierce competition between athletes who work hard to be the best in their field [4]. Such competitiveness pushes athletes to their limit, often resulting in injuries such as muscle strains and contusions, muscle stretch injuries, ankle sprains, ACL ruptures, and fractures [14]. The teams of professional athletes must continue paying their players even while injured and unable to participate. As such, it is a constant challenge for physicians to provide treatments which promote a faster rate of recovery. HBOT is one avenue which accelerates rehabilitation to allow athletes to return to competition faster vs traditional therapies [4, 11]. The first recorded application of HBOT for a sports injury was in the late 1980s in Scotland in which James, et al. reported that the average saving in injury time due to HBOT was 70% (Figure 2) [45].

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

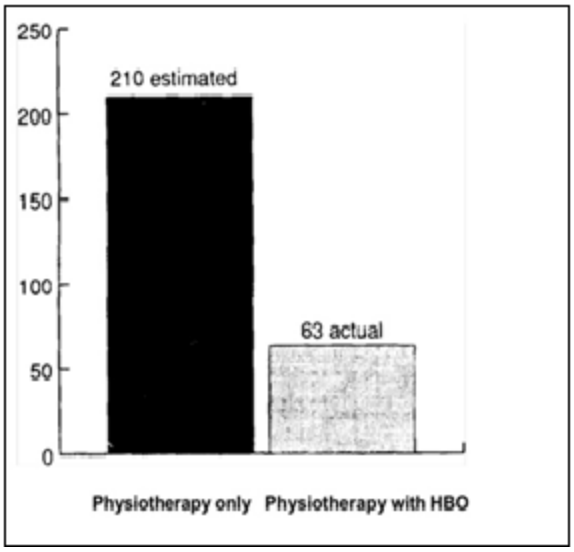

Figure 2: Comparison by James, et. al. of physiotherapy alone and physiotherapy with hyperbaric oxygen in recovery from 20 minor sports injuries [45].

In case studies, they reported a patient with Achilles tendonitis expected to take four days to recover. After a single session of HBOT, he was able to resume full training activities after one day. Similarly, another patient with a severe ankle sprain estimated to take 3 weeks to recover was, after 2 sessions of HBOT, able to return to training after 4 days.

While the study showed promising results, limitations include a lack of a control group or proper classification of injuries based on their severity. As such, it is difficult to accurately predict and compare the effectiveness of HBOT.

In addition to physical injury, HBOT has been effective in recovery from fatigue and improvement of endurance. One example is the use of HBOT for competitors at the Nagano Winter Olympics to combat fatigue and allow players to return to the games with a better performance than without HBOT [16]. Also, Fischer et al reported use of HBOT between tennis games improved recovery from fatigue by removing ammonia from the blood. Ishii et al confirmed HBOT aids in removal of lactic acid. After 45mins of 100% oxygen at 1.3 ATA, lactic acid removal was 14% higher than inhaling regular air (76% vs 61%). [46,47].

Whilst there is little evidence of HBOT effecting recovery from delayed onset muscle soreness (DOMS), a study by Shimoda et al examined muscle fatigue after plantar flexion exercise and concluded HBO treatment at 2 ATA and 100% oxygen for 60mins improved plantar flexion torque and suppressed muscle fatigue progression, thus sustaining force production. [48-51].

Regarding endurance, after 3 weeks of under HBO conditions of 100% O2 at 2 ATA, Burgos, et al. observed improved endurance capacity without an increase in oxidative stress markers when compared to normoxic training of young soccer players. Those players who trained under HBO achieved and sustained notable increases in VO_2max. As such, they concluded that injured athletes who need a swift return to competition could

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

train under HBO conditions. Basic science studies have also shown that quality of repair tissue from MCL tear and Achilles tear is improved over controls in laboratory rats and a clinical study in Japanese rugby players showed expedited recovery over controls [52-55]. These results indicate HBOT is not only beneficial for external injuries, but also for enhancing training and conditioning for athletes [16].

Platelet rich plasma in hamstring injury

HBOT as an adjuvant therapy has been discussed previously in this paper. In the cases discussed, HBOT works to enhance the effects of another treatment. The same can be said for HBOT used in conjunction with blood platelet injection therapy. In a case series report completed by Botha, et al. in 2015, platelet rich plasma (PRP) was examined in conjunction with HBOT in their effectiveness in treating hamstring injuries in professional rugby players.

PRP is reported to contain a large concentration of growth factors (including vascular endothelial growth factors VEGF) and insulin-like growth factor-1 (IGF-1) and is obtained from the blood of the patient in which it will be injected. As a result of the hyperoxia induced by HBOT, VEGF is stimulated resulting in more rapid development of capillary budding, arborisation, and granulation tissue formation in the wound bed. Players exposed to 100% oxygen at 2.4 ATA for 60mins exhibited a 46% acceleration in healing of a Grade two muscle injury (classified as "a significant number of muscle fibres are torn. Active contraction of the muscle would cause pain. Localised swelling and a palpable depression would present in the muscle belly, and the patient would have a limited range of motion and muscle strength on contraction due to pain,") and a 0% reinjury rate [56,57]. Such a significant reduction in rehabilitation time means less time off the field, and more time earning for the club.

Cartilage regeneration

Articular cartilage is an avascular, aneural, alymphatic tissue highly specialized to support immense compressive loads and virtually eliminate friction in diarthrodial joints [58]. The limited healing capacity of cartilage and high incidence of cartilage disorders like osteoarthritis means the development of treatments for regeneration and repair is imperative in maintaining mobility and quality of life [59].

As previously mentioned, oxygen plays an important role in tissue regeneration. Mature articular cartilage receives limited oxygen via diffusion from synovial fluid. Oxygen partial pressure decreases from 10% in the superficial (tangential) zone (STZ) to as little as 1% near the subchondral bone. HBO may act to increase oxygen in even the deepest layers of cartilage, promoting chondrocyte proliferation and collagen production [19,58].

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

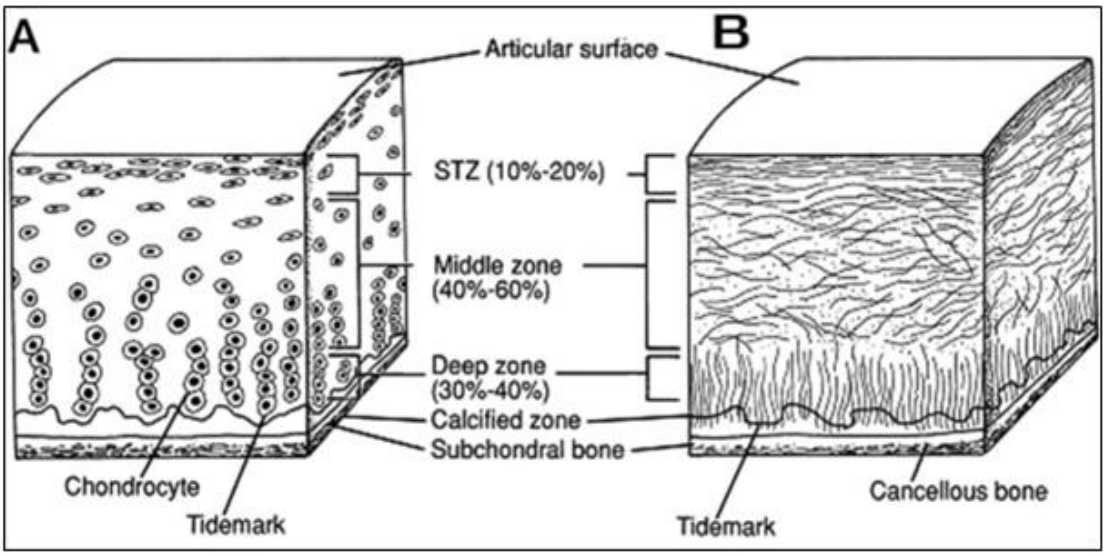

Figure 3: The Structure of Articular Cartilage; A: organization of zones; B: Collagen fiber alignment [60].

Ueng, et al. confirmed oxygen's role in the production of the extracellular matrix and osteochondral regeneration after cartilage damage. Yuan, et al. demonstrated the ability of HBOT to reduce apoptosis and enhance proteoglycan synthesis by suppression of nitric oxide (NO) production in rabbits, which may inhibit the progression of osteoarthritis (OA). Figure 4 demonstrates the increase in oxygen tension in the joint cavity after treatment with HBOT [61,62].

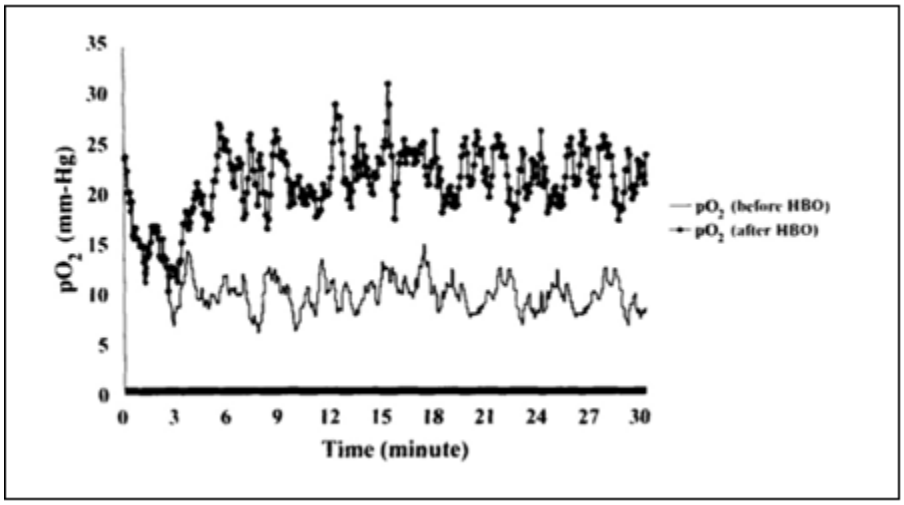

Figure 4: Oxygen sensor tracings of the partial pressure of oxygen obtained in one of the animals in the study conducted by Yuan et al [62].

A 2020 study conducted by Korucu et al examined damaged cartilage treated with hyperbaric oxygen (HBO), which regenerated "significantly better" than the control group. Moreover, Chen et al concluded HBOT treatment is an effective, non-invasive treatment for cartilage repair by acting to improve neovascularization which facilitates

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

osteochondral healing, promote angiogenesis and enhance collagen synthesis. They added, however, that the strength of the repaired cartilage had not been investigated. [63,9].

Whilst HBOT has promising results regarding cartilage regeneration in vivo, it can also be applied to enhance cartilage tissue engineering in vitro. Cherng et al demonstrated that when using a scaffold material, such as collagen or hyaluronic acid (among others) for seeding of chondrocytes or mesenchymal stem cells (MSCs), HBO proved successful in improving chondrocyte differentiation of human adipose-derived stem cells (HASC), with chondrogenesis remaining elevated even 15 days after treatment. [7].

The possibilities of HBOT for cartilage regeneration both in vivo and in vitro are extensive, however, more research needs to be conducted on human cartilage to thoroughly confirm the processes by which HBOT regenerates the complex tissue.

Pressure, oxygen concentration and number of treatments required

The recommended pressure, oxygen concentration and number of treatments required for hyperbaric oxygen treatment is varied and depends largely on the injury being treated. Typically, treatment is performed daily for between 1 to 1.5 hours at 100% oxygen and 1.5 to 2.2 ATA but should be at above 1.4 ATA in order to be classified as true hyperbaric and not mild [11].

Lew, et al. examined cell response to HBOT and found that 2.4 ATA effectively stimulates cell proliferation. In the case of the Nagano Winter Olympians, athletes were exposed to 30–40-minute sessions at 1.3 ATA for a maximum of 6 times after physical activity, resulting in a return to competition without difficulty even after muscle pain and anterior knee pain [20,47]. Uhl et al believed in the improvement of re-epithelisation in normal and ischaemic skin tissue after twice daily treatments at 100% oxygen, 2 ATA for 45 minutes [64]. Return to almost normal elasticity and fracture intensity of a ligament was reported by Webster et al after 4 weeks of HBOT at 2.8 ATA for 1.5hrs. 2 to 3 ATA is equivalent to being 13 to 20 metres under water [4,65]. According to Schaefer enough oxygen can be dissolved into plasma at 3 ATA to sustain life temporarily without red blood cells. [66].

Figure 5 shows data compiled by Peña-Villalobos et al which demonstrates the variability in HBOT sessions used from 2001 to 2017**.**

Since the indications for HBOT are so diverse, so are the pressure, oxygen concentration, and number/frequency of treatments. More research is required on specific indications for a greater understanding of the exact requirements suited to each injury.

Adverse effects

Hyperbaric Oxygen Therapy has a multitude of benefits for wound healing, recovery from fatigue, and cognitive improvement, however, there are some risks involved. A high standard of safety is required for HBOT, especially when using highly flammable pure oxygen [16]. The monoplace chamber and multiplace chambers which employ 100% oxygen through a face mask are generally safer than the monoplace chambers which pressurize the entire chamber with 100% oxygen. This is because the percentage of O_2 in the chambers employing a face mask rarely exceed 24% and thus the fire risk is much less

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

when releasing the air from chamber. A common complication is barotrauma or inability to pressurize ears which we have found to be more likely in older patients and usually can be avoided by a slow descent during the patients' initial sessions until it can be determined what depth they can comfortably manage. In addition, complications like oxygen toxicity and claustrophobia are possible complications associated with HBOT [11, 45]. Some patients also report symptoms of nausea, tooth and sinus pain, and blurred vision. While it is possible for implications to occur at high pressures for extended periods of time, most treatments outside of decompression sickness rarely exceed 2.2 ATA for 60-90 minutes are thus very safe [4].

Organism	Pressure (ATA)	Session duration (h)	Sessions	Reference
Rat	2	1	1	Lin and Wan, 2008
	2.8	1	1	Yang et al., 2010
	2.5	2	5	Takeyama et al., 2007
	2.8	0.75	2/day, 1 day	Palzur et al., 2008
	3	2	5 days, 4 weeks	Kurt et al., 2008
	2.5	1	2/day, 3 days	Liu et al., 2008
	~6	0.08	1	Li et al., 2008
	3	1	2/day, 28 days	Gregorevic et al., 2001
	2	1	1	Imperatore et al., 2006
	3	1.5	1	Chu et al., 2007
	2	1	7	Wang et al., 2008
Mice	2	1	1/day, 30 days	Dave et al., 2003
	3	1	1/day, 14 days	Asano et al., 2007
	2.5	1	2/day, 3 days	Sakata et al., 2010
	2.5	1.5	1/day, 2 weeks	Chen et al., 2003
	2.5	2	2/day, 5 days	Gajendrareddy et al., 2005
	3	1	1	Veltkamp et al., 2005
	1.5 to 2.4	1	4 days/week	Verma et al., 2015
	2.5	1.5	Three times weekly	Poff et al., 2015
	2	1	4 days	Baratz-Goldstein et al., 2017
	2.5	1.5	1/day, 21 days	Lu et al., 2016
	2.5	1.5	6	Sletta et al., 2017
Rabbit	2.4	1.5	5 days/ 4 weeks	Jan et al., 2009
	2.5	2	20	Altesalp et al., 2009
Human	2	1.5	1/day, 20 days	Boykin and Baylis, 2007
	3	2.08	30 sessions, 5 or 6/week	Hulshof et al., 2002
	2.4	1.5	2/day, 6 days	Kaya et al., 2009
	2	1.5	1/day	Safra et al., 2008
	2	2	10 to 20	Thom et al., 2006
	2.5	0.33	30 sessions, 5/week	Gerlach et al., 2008
	2 to 3	1.5	1/day, 30 days	Duzgun et al., 2008

The pressure parameters, the duration, and the number of sessions administered to the different vertebrate models are indicated.

Figure 5: Variability of selected HBOT sessions between 2001 and 2017, as compiled by Peña-Villalobos, et. al. [18].

Conclusion

Hyperbaric Oxygen Therapy presents incredible opportunities for healing and recovery, not just for professional athletes, but also for the general population. The ability for HBOT to increase the oxygen pressure and concentration in plasma allows for significant healing and repair in all body tissues. While there are some risks involved with HBOT, proper safety procedures, pressures, and treatment lengths reduce adverse effects to almost zero. More research

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

required to determine appropriate oxygen concentration, pressure, and number of treatments for various injuries, and the comprehensive effects of HBOT on human tissues, and overall well-being.

Disclaimer

Dr Gordon Slater is a medical director of Integrant Pty Ltd, an orthobiologics company. He also has a pecuniary interest in Regen-U and MD Hyperbaric Australia.

Dr Martin O'Malley, MD is the Medical Director of MD Hyperbaric. Associate Professor of Orthopaedics Surgery at The Hospital for Special Surgery, and Team Physician for the Brooklyn Nets and USA Basketball.

References

1. B Çelik, M Kefeli, HK Çelik, and EK Gülen, "Effects of hyperbaric oxygen treatment on cartilage regeneration: an experimental study," Turkish Journal of Thoracic and Cardiovascular Surgery. 2015;23:112-18. CrossRef
2. Gottfried I, Schottlender N, Ashery U. Hyperbaric Oxygen Treatment—From Mechanisms to Cognitive Improvement. Biomolecules. 2021;11(10):1520. PubMed | CrossRef
3. Moss MC, Scholey AB, Wesnes K. Oxygen administration selectively enhances cognitive performance in healthy young adults: a placebo-controlled double-blind crossover study. Psychopharmacology. 1998;138(1):27-33. PubMed | CrossRef
4. Babul S, Rhodes EC. The role of hyperbaric oxygen therapy in sports medicine. Sports Med. 2000;30(6):395-403. PubMed | CrossRef
5. Yılmaz O, Bilge A, Erken HY, Kuru T. The effects of systemic ozone application and hyperbaric oxygen therapy on knee osteoarthritis: an experimental study in rats. Int Orthop. 2021;45(2):489-96. PubMed | CrossRef
6. Levin D, Norman D, Zinman C, Rubinstein L, Sabo E, Misselevich I,et al. Treatment of experimental avascular necrosis of the femoral head with hyperbaric oxygen in rats: histological evaluation of the femoral heads during the early phase of the reparative process. Exp Mol Pathol. 1999;67(2):99-108. PubMed | CrossRef
7. Cherng JH, Chang SC, Chen SG, Hsu ML, Hong PD, Teng SC, et al. The effect of hyperbaric oxygen and air on cartilage tissue engineering. Ann Plast Surg. 2012;69(6):650-5. PubMed | CrossRef
8. Mardones R, Jofré CM, Minguell JJ. Cell therapy and tissue engineering approaches for cartilage repair and/or regeneration. Int J Stem Cells. 2015;8(1):48-53. PubMed | CrossRef
9. Chen AC, Lee MS, Lin SS, Pan LC, Ueng SW. Augmentation of osteochondral repair with hyperbaric oxygenation: a rabbit study. J Orthop Surg Res. 2010;5(1):1-9. PubMed | CrossRef
10. Nagatomo F, Gu N, Fujino H, Okiura T, Morimatsu F, Takeda I, et al. Effects of exposure to hyperbaric oxygen on oxidative stress in rats with type II collagen-induced arthritis. Clin Exp Med. 2010;10(1):7-13. PubMed | CrossRef
11. Moghadam N, Hieda M, Ramey L, Levine BD, Guilliod R. Hyperbaric Oxygen Therapy in Sports Musculoskeletal Injuries. Med Sci Sports Exerc. 2020;52(6):1420-6. PubMed | CrossRef
12. Burman F. Low-pressure fabric hyperbaric chambers. S Afr Med J. 2019;109(4):200. PubMed | CrossRef
13. Yogaratnam JZ, Laden G, Guvendik L, Cowen M, Cale A, Griffin S. Hyperbaric oxygen preconditioning improves myocardial function, reduces length of intensive care stay, and limits complications post coronary artery bypass graft surgery. Cardiovasc Revasc Med. 2010;11(1):8-19. PubMed | CrossRef
14. Barata P, Cervaens M, Resende R, Camacho Ó, Marques F. Hyperbaric oxygen effects on sports injuries. Ther Adv Musculoskelet Dis. 2011;3(2):111-21. PubMed | CrossRef
15. https://www.oxyhealth.com/fortius-420.html
16. Ishii Y, Deie M, Adachi N, Yasunaga Y, Sharman P, Miyanaga Y,et al. Hyperbaric oxygen as an adjuvant for athletes. Sports Med. 2005;35(9):739-46. PubMed | CrossRef
17. Jain KK, Baydin SA. Textbook of hyperbaric medicine. Basel, Switzerland: Springer International Publishing. 2017:589-92. CrossRef

18. Peña-Villalobos I, Casanova-Maldonado I, Lois P, Prieto C, Pizarro C, Lattus J, et al. Hyperbaric oxygen increases stem cell proliferation, angiogenesis and wound-healing ability of WJ-MSCs in diabetic mice. Front Physiol. 2018;9:995. CrossRef
19. Melcher C, Sievers B, Höchsmann N, Düren F, Jansson V, Müller PE. Effect of hyperbaric oxygen on proliferation and gene expression of human chondrocytes: An in vitro study. Cartilage. 2019;10(4):459-66. PubMed | CrossRef
20. Lew D, Stoll JL. Cell response to hyperbaric oxygen treatment. Int J Oral Maxillofac Surg. 1997;26(2):82-6. PubMed | CrossRef
21. https://www.fda.gov/consumers/consumer-updates/hyperbaric-oxygen-therapy-get-facts
22. Geng CK, Cao HH, Ying X, Yu HL. Effect of mesenchymal stem cells transplantation combining with hyperbaric oxygen therapy on rehabilitation of rat spinal cord injury. Asian Pac J Trop Med. 2015;8(6):468-73. PubMed | CrossRef
23. Pan HC, Chin CS, Yang DY, Ho SP, Chen CJ, Hwang SM, et al. Human amniotic fluid mesenchymal stem cells in combination with hyperbaric oxygen augment peripheral nerve regeneration. Neurochem Res. 2009;34(7):1304-16. PubMed | CrossRef
24. Hadanny A, Lang E, Copel L, Meir O, Bechor Y, Fishlev G, et al. Hyperbaric oxygen can induce angiogenesis and recover erectile function. Int J Impot Res. 2018;30(6):292-99. PubMed | CrossRef
25. Corey S, Bonsack B, Borlongan CV. Stem cell-based regenerative medicine for neurological disorders: A special tribute to Dr. Teng Ma. Brain Circ. 2019;5(3):97-100. PubMed | CrossRef
26. Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic brain injury–related emergency department visits, hospitalizations, and deaths—United States, 2007 and 2013. MMWR Surveill Summ. 2017;66(9):1-16. PubMed | CrossRef
27. Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. Arch Phys Med Rehabil. 2014;95(5):986-95. PubMed | CrossRef
28. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. circulation. 2017;135(10):146-603. PubMed | CrossRef
29. Gonzales-Portillo B, Lippert T, Nguyen H, Lee JY, Borlongan CV. Hyperbaric oxygen therapy: A new look on treating stroke and traumatic brain injury. Brain Circ. 2019;5(3):101. PubMed | CrossRef
30. Chandra A, Stone CR, Du X, Li WA, Huber M, Bremer R, et al. The cerebral circulation and cerebrovascular disease III: Stroke. Brain Circ. 2017;3(2):66. CrossRef
31. Yu R, Wang B, Li S, Wang J, Zhou F, Chu S, et al. Cognitive enhancement of healthy young adults with hyperbaric oxygen: a preliminary resting-state fMRI study. Clin Neurophysiols. 2015;126(11):2058-67. PubMed | CrossRef
32. Vadas D, Kalichman L, Hadanny A, Efrati S. Hyperbaric oxygen environment can enhance brain activity and multitasking performance. Front Integr Neurosci. 2017;11:25. PubMed | CrossRef
33. Moss MC, Scholey AB. Oxygen administration enhances memory formation in healthy young adults. Psychopharmacology. 1996;124(3):255-60. PubMed | CrossRef
34. Scholey AB, Moss MC, Wesnes K. Oxygen and cognitive performance: the temporal relationship between hyperoxia and enhanced memory. Psychopharmacology. 1998;140(1):123-6. PubMed | CrossRef
35. Chung SC, Sohn JH, Lee B, Tack GR, Yi JH, You JH, et al. The effect of transient increase in oxygen level on brain activation and verbal performance. Int J Psychophysiol. 2006;62(1):103-8. PubMed | CrossRef
36. un H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;1(183):109119. PubMed | CrossRef
37. Wilkinson D, Nolting M, Mahadi MK, Chapman I, Heilbronn L. Hyperbaric oxygen therapy increases insulin sensitivity in overweight men with and without type 2 diabetes. Diving Hyperb Med. 2015;45(1):30-6. PubMed | CrossRef
38. Wilkinson D, Chapman IM, Heilbronn LK. Hyperbaric oxygen therapy improves peripheral insulin sensitivity in humans. Diabet Med. 2012;29(8):986-9. PubMed | CrossRef

39. Slater G, Slater T. Current Concepts Review: Orthotics in Post-operative Foot and Ankle Surgery. J Regen Biol Med. 2022;4(1):1-4.
40. Boulton AJ. The diabetic foot: from art to science. The 18th Camillo Golgi lecture. Diabetologia. 2004;47(8):1343-53. PubMed | CrossRef
41. Larsson J, Agardh CD, Apelqvist J, Stenström A. Long-term prognosis after healed amputation in patients with diabetes. Clin Orthop Relat Res. 1998;(350):149-58. PubMed | CrossRef
42. Liu R, Li L, Yang M, Boden G, Yang G. Systematic review of the effectiveness of hyperbaric oxygenation therapy in the management of chronic diabetic foot ulcers. Mayo Clin Proc. 2013;88(2):166-175. PubMed | CrossRef
43. Çimşit M, Uzun G, Yıldız Ş. Hyperbaric oxygen therapy as an anti-infective agent. Expert Rev Anti Infect Ther. 2009;7(8):1015-26. PubMed | CrossRef
44. Chen CE, Ko JY, Fong CY, Juhn RJ. Treatment of diabetic foot infection with hyperbaric oxygen therapy. Foot Ankle Surg. 2010;16(2):91-5. PubMed | CrossRef
45. James PB, Scott B, Allen MW. Hyperbaric oxygen therapy in sports injuries. PHYSIOTHERAPY-LONDON. 1993;79:571. CrossRef
46. Fischer B, Jain KK, Braun E, Lehrl S. Handbook of hyperbaric oxygen therapy. Springer. 1988.
47. Ishii Y, Miyanaga Y, Shimojo H. The effect of hyperbaric oxygen therapy on the lactate concentration after maximal exercise. The Japanese Journal of Hyperbaric Medicine. 1995;30:109-14.
48. Harrison BC, Robinson DW, Davison BJ, Foley B, Seda E, Byrnes WC. Treatment of exercise-induced muscle injury via hyperbaric oxygen therapy. Med Sci Sports Exerc. 2001;33(1):36-42. PubMed | CrossRef
49. Mekjavic IB, Exner JA, Tesch PA, Eiken O. Hyperbaric oxygen therapy does not affect recovery from delayed onset muscle soreness. Med Sci Sports Exerc. 2000;32(3):558-63. PubMed | CrossRef
50. Babul S, Rhodes EC, Taunton JE, Lepawsky M. Effects of intermittent exposure to hyperbaric oxygen for the treatment of an acute soft tissue injury. Clin J Sport Med. 2003;13(3):138-47. PubMed | CrossRef
51. Shimoda M, Enomoto M, Horie M, Miyakawa S, Yagishita K. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise. J Strength Cond Res. 2015;29(6):1648-56. PubMed | CrossRef
52. Burgos C, Henríquez-Olguín C, Andrade DC, Ramírez-Campillo R, Araneda OF, White A, et al. Effects of exercise training under hyperbaric oxygen on oxidative stress markers and endurance performance in young soccer players: A pilot study. J Nutr Metab. 2016:5647407. PubMed | CrossRef
53. Kuran F, Pekedis M, Yildiz H, Aydin F, Eliyatkin N. Effect of hyperbaric oxygen treatment on tendon healing after Achilles tendon repair: an experimental study on rats. Acta Orthop Traumatol Turc. 2012;46(4):293-300. PubMed | CrossRef
54. Ueng SW, Lee MS, Tai CL, Hsu KY, Lin SS, Chan YS, et al. Hyperbaric oxygen therapy improves medial collateral ligament healing in a rabbit model. J Formos Musculoskeletal Dis. 2011;2(1):7-11. CrossRef
55. Yagishita K, Enomoto M, Takazawa Y, Fukuda J, Koga H. Effects of hyperbaric oxygen therapy on recovery acceleration in Japanese professional or semi-professional rugby players with grade 2 medial collateral ligament injury of the knee: A comparative non-randomized study. Undersea Hyperb Med. 2019;46(5):647-54. PubMed | CrossRef
56. Botha DM, Coopoo Y, Lynch E, Botha MK, Collins R, Van Niekerk RL. The effect of hyperbaric oxygen and blood platelet injection therapy on the healing of hamstring injuries in rugby players: a case series report. Afr J Phys Health Educ Recreat Dance. 2015:29-39.
57. Slater G, Slater T. Articular Cartilage-A Literature Review. J Regen Biol Med. 2022;4(1):1-0. CrossRef
58. Slater G, Slater T. Articular Cartilage-A Literature Review. J Regen Biol Med. 2022;4(1):1-0. CrossRef
59. Slater G, Richardson L. Biologics that increase Chondrocyte Number and/or Matrix. J Stem Cell Res. 2021;2(2):1-5. CrossRef
60. Buckwalter JA, Mow VC, Ratcliffe A. Restoration of injured or degenerated articular cartilage. J Am Acad Orthop Surg. 1994;2(4):192-201. PubMed | CrossRef
61. Ueng SW, Yuan LJ, Lin SS, Niu CC, Chan YS, Wang IC, et al. Hyperbaric oxygen treatment prevents nitric oxide-induced apoptosis in articular cartilage injury via enhancement of the expression of heat shock protein 70. J Orthop Res. 2013;31(3):376-84. PubMed | CrossRef

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111

62. Yuan LJ, Ueng SW, Lin SS, Yeh WL, Yang CY, Lin PY. Attenuation of apoptosis and enhancement of proteoglycan synthesis in rabbit cartilage defects by hyperbaric oxygen treatment are related to the suppression of nitric oxide production. J Orthop Res. 2004;22(5):1126-34. PubMed | CrossRef
63. Korucu İH, Kekeç AF, Arslan A, Oltulu P, Korucu EN, Özer M. Regenerative effects of hyperbaric oxygen therapy and platelet-rich plasma on the osteochondral defects of rats. Jt Dis Relat Surg. 2020;31(2):260. PubMed | CrossRef
64. Uhl E, Sirsjö A, Haapaniemi T, Nilsson G, Nylander G. Hyperbaric oxygen improves wound healing in normal and ischemic skin tissue. Plast Reconstr Surg. 1994;93(4):835-41.PubMed | CrossRef
65. Webster DA, Horn P, Amin HM, Weissbrich O, Mascia MF, Werner FW. Effect of hyperbaric oxygen on ligament healing in a rat model. Clin Orthop Relat Res. 1999;(360):238-42 PubMed | CrossRef
66. Schaefer SE. Fundamentals of hyperbaric oxygen therapy. Orthop Nurs. 1992;11(6):9-15. PubMed | CrossRef

Citation: Slater G, Malley MO, Slater T, Sambo T. Hyperbaric Oxygen Therapy: An Overview. J Regen Biol Med. 2022; 4(3):1-15.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-4(3)-111