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Review Article

Partial pressure of oxygen in the human body: a general review

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Abstract: The human body is a highly aerobic organism, in which it is necessary to match oxygen supply at tissue levels to the metabolic demands. Along metazoan evolution, an exquisite control developed because although oxygen is required as the final acceptor of electron respiratory chain, an excessive level could be potentially harmful. Understanding the role of the main factors affecting oxygen availability, such as the gradient of pressure of oxygen during normal conditions, and during hypoxia is an important point. Several factors such as anaesthesia, hypoxia, and stress affect the regulation of the atmospheric, alveolar, arterial, capillary and tissue partial pressure of oxygen (PO_2). Our objective is to offer to the reader a summarized and practical appraisal of the mechanisms related to the oxygen's supply within the human body, including a facilitated description of the gradient of pressure from the atmosphere to the cells. This review also included the most relevant measuring methods of PO_2 as well as a practical overview of its reference values in several tissues.

Keywords: Hypoxia, gradient of pressure, pressure of oxygen, altitude acclimation, barometric pressure

Introduction

The human body is a highly aerobic organism that consumes oxygen according to its metabolic demand [1]. During aerobic respiration the presence of oxygen in addition to pyruvate, produces adenosine triphosphate (ATP), thus yielding energy to the entire organism [2]. To maintain homeostasis, the amount of oxygen within the tissues should respond to a gradient of pressure that pushes oxygen by diffusion throughout the membranes into the tissues [3]. The amount of dissolved oxygen within the tissues and the cells depends on several factors including: barometric pressure (BP), climatological conditions (temperature, relative humidity, latitude, altitude), as well as physiological, pathological, and physical-chemical processes within the organism itself [4, 5].

The composition of gases within the troposphere is constant at approximately the following ratio: 78.08% nitrogen, 20.95% oxygen, 0.93% argon and finally less than 0.038% for carbon dioxide and other gases [6].

Dalton's law establishes that within a combination of any given gases, the total pressure is the same as the sum of the partial pressures of each individual gas present in that mixture [7]. Thus, the partial pressure of oxygen (PO_2) depends mainly on the atmosphere's barometric pressure (BP) and its fractional concentration [8]. Geographical altitude is an important factor affecting BP, because as altitude increases, the amount of gas molecules in the air decreases, so the air becomes less dense than at sea level. At sea level BP is about 760 mmHg, although can be affected not only by altitude: latitude, humidity, temperature and even the season of the year may also affect BP [9, 10]. This changes are normally local, consequently, short-term temporal (time scale of minutes, hours, days and weeks) variations in BP in a same location usually range around 5-15 mmHg [9].

Partial pressure of oxygen

Within the troposphere (lowest region of the atmosphere), PO_2 depends on several vari-

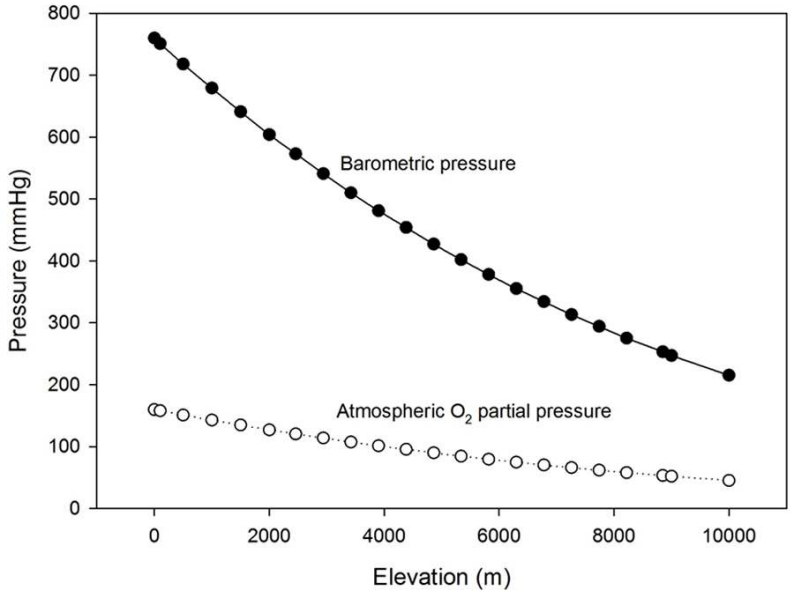

Figure 1. Relationship between elevation and Barometric Pressure (filled circles) and Atmospheric Partial Pressure of Oxygen (hollow circles). *Calculations were based on the standard atmosphere and were done by the authors.

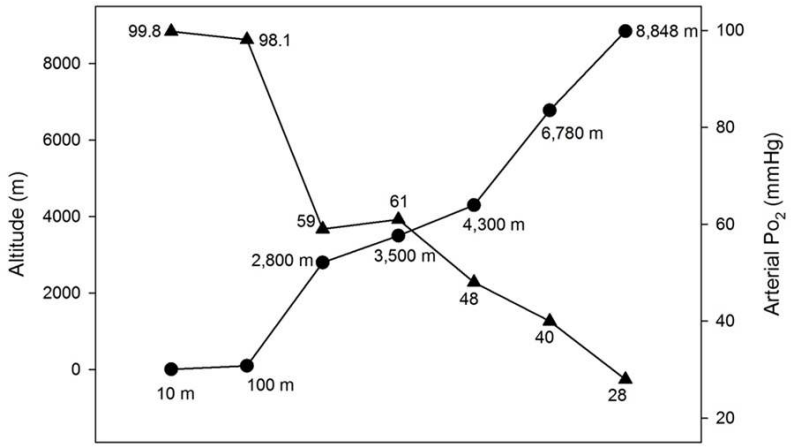

Figure 2. Arterial oxygen tension (PaO_2) at different altitudes in humans according to the values given in several reports [3, 4, 12, 17].

ables, but mainly on barometric pressure (**Figure 1**) [4]. Under physiological conditions, this relationship will be affected by any change in elevation or by modifying the fraction of inspired oxygen (FiO_2) under controlled circumstances [3, 11, 12].

Atmospheric partial pressure of oxygen ($_{Atm}PO_2$)

Humans depend on oxygen for survival, and this gas is acquired from the atmosphere where the partial pressure of oxygen ($_{Atm}PO_2$) within the troposphere depends on BP according to the Dalton's Law [13]:

$$_{Atm}PO_2 = 0.21 \cdot 760 \text{ mmHg} = 159 \text{ mmHg}$$

Humans are constantly exposed to changes in BP, either artificially or naturally, thus, pressure of inspired oxygen (as well as the other gasses) its inversely proportional reduced among those exposed to hypobaric or normobaric hypoxia [3, 14] (**Figure 1**).

Alveolar partial pressure of oxygen (PAO_2)

Once air is warmed and humidified in the nose and upper respiratory tract, the pressure of oxygen decreases while concentration of H_2O increases, thus altering effective PO_2 in this gas mixture. Therefore, oxygen partial pressure within the upper airway is noted inspired PO_2 (PiO_2) [15]. The reduction of pressure of oxygen is caused by the addition of water vapour (humidification) to the entire mixture of gases, thus reducing the pressure of the other gases [4]. The pressure of water vapour is constant at 47 mmHg at normal body temperature (37°C), and it is strongly temperature dependent [11]. This results in an effective reduction at the alveolar level in the partial pressure of oxygen (PAO_2) from 159 to 149 mmHg that is not likely to be physiologically relevant at sea level, because only represents about 6% of the total $_{Atm}PO_2$ [16]. However, when the BP is already low, such as at the summit of Mount Everest (altitude 8,848 m), a reduction of 47 mmHg (the water vapour pressure) represents almost 20% of the available $_{Atm}PO_2$, making this reduction life threatening [17, 18].

Moreover, once the inspired air has been humidified, there is an additional reduction in PO_2 from the trachea to the alveolus, due to the dead space and the mixing of inspired and expired gases [19]. This fall in the pressure of oxygen from the upper airways to the alveolus is almost all accounted for by the alveolar pressure of carbon dioxide ($PACO_2$) [10, 20]. Since inspired PCO_2 is zero and the $PACO_2$ is usually in the range of 40 mmHg, the partial pressure of oxygen must fall [21].

When oxygen is transported into the venous pulmonary capillary, an important gradient of pressure from the upcoming arterial blood pushes the CO_2 out to the alveoli [22].

The alveolar partial pressure of oxygen (PAO_2) in the alveoli-capillary barrier at sea level is calculated based on the fraction of inspired oxygen (FiO_2). At least in the troposphere, air contains a standard 20.95% of oxygen, thus the in order to estimate the alveolar PO_2 the following equation is used:

$$PAO_2 = FiO_2 (PB-47) - 1/R (PACO_2)$$

Where R is the respiratory exchange ratio and equals 0.8 most of the time and the 47 correspond to the water vapour pressure at normal body temperature (37°) [4].

Arterial partial pressure of oxygen (PaO_2)

Once in the lungs, oxygen diffuses across the alveolar-capillary barrier from the alveoli into the arterial circulation. The initial diffusion gradient of pressures in the microcirculation arises when arterial partial pressure of oxygen (PaO_2) with a higher pressure is mixed with the pressure of oxygen within the veins (PVO_2) [23].

The rate of oxygen diffusion across the alveoli-capillary membrane in addition to a faster and easier elimination of CO_2, assures that capillary PaO_2 is almost equal to the alveolar PAO_2 and during normal conditions (at sea level) it correspond to 75 to 100 mmHg [24].

At sea level, during normal conditions, the partial pressure of oxygen in the arteries is high enough to satisfy the oxygen demands for the entire organism [10]. However, during high altitude exposure (hypobaric hypoxia), as barometric pressure descends, the pressure of oxygen in the arterial circulation is inversely proportion reduced [25, 26]. This reduction attributes to the significant reduction in $_{Atm}PO_2$ and determines the actual pressure of oxygen available for tissue and cellular requirements [27, 28] (**Figure 2**).

Tissue partial pressure of oxygen (PtO_2)

Once oxygen has reached the arteries, the difference in pressures (gradient of pressure) between the capillary to the cytosol of surrounding cells results in a steep diffusion gradient, the greatest in the body reaching more than 42% [4]. The average partial pressure in the tissue is called the tissue partial pressure of oxygen (PtO_2) [10].

The transport of oxygen from the atmosphere into the entire body is mediated by the rate diffusion as well as the rate of consumption between physiological barriers [29]. Diffusion is based on the kinetic theory that encompasses the rapid movement of molecules, causing a self-generated energy source to rapidly cross membranes [30]. Whereas convective transport refers to the heat transferred and energy-consuming combination of molecules to cause the movement of oxygen in the trachea and the bronchial tree with the surrounding alveoli-capillary circulation [31]. The diffusive transport is the passive movement of oxygen across several barriers, such as the endothelium, the alveolus and the mitochondrial membrane [32]. The amount of diffusive oxygen movement depends on the gradient of partial pressure of oxygen, the available surface area to diffusion, the permeability and thickness of diffusion barriers and the local metabolic demand [33, 34].

Tissue partial pressure of oxygen (PtO_2) is regulated by the blood flow, the availability of oxygen and the consumption rate from one region to another [3, 24, 35, 36]. The Bohr effect allows that hemoglobin releases more oxygen in response to the metabolic rate of that tissue in highly aerobic tissues [37]. For instance, neurons and cardiac myocytes are largely aerobic and depend on the presence of oxygen for their survival, although some lactate can be produced within the brain, most of them depended on the metabolic rate of oxygen consumption [36, 38]. Other cells, such as the bladder myocytes or the skeletal myocytes are more tolerant to hypoxia, and are able to obtain energy without the presence of oxygen for longer periods of time than can neurons in the brain [10].

Table 1. References values of PtO_2 measurements using different techniques

PtO_2 (mmHg)	Organ and Tissue	Reference	Methods	Species
30-48	Brain	Meixensberger [51], Hoffman [52], Ortiz-Prado [3]	Positron emission tomography (PET)	Human And rats
104-108	Alveoulus	Guyton [4]	Polarographic measurements of tissue oxygen tension using gold microelectrodes	Human
8	Skin epidermis	Wang [35], Carreau [53]	Microelectrodes	Human
24	Dermal papillae			
35.2	Sub-papillary plexus			
61.2	Small bowel	Müller [54, 55], Carreau [53]	Electron paramagnetic resonance oximetry (EPR)	Human
57.6	Large bowel	Müller [54, 55], Carreau [53]	Electron paramagnetic resonance oximetry (EPR)	Human
55.5 ± 21.3	Liver	Leary [56]	Electron paramagnetic resonance oximetry (EPR) with Indian ink.	Human
72 ± 20	Superficial cortex of the kidney	Muller [57], Carreau [53]	Phosphorescence lifetime technique	Human
28.9 ± 3.4	Muscle fibers	Beerthuizen [58], Carreau [53]	Proton NMR spectra of myoglobin	Human
29.6 ± 1.8				
51.8 ± 14.5	Bone Marrow	Carreau [53]	The technique of aspiration in a syringe	Human
34 ± 1.6	Femur Bone	Maurer [59]	Technique of radioactive microspheres in interosseous blood samples and blood flow in the bone	Human
71.4	Mandibule			
55	Suprarenal Gland	Bloom [60]	Phosphorescence lifetime technique	Calf
88	Ovaries	Fraser [61]	Clark electrode for pO_2	Human
18	Umbilical Arteries	Gluckman [62], Carreau [53]	Umbilical cord blood gas	Human
29.2	Umbilical Vein	Guyton [4], Gluckman [62], Carreau [53]	Umbilical cord blood gas	Human
90 ± 5	Arterial PO_2	Mah and Cheng [20], Guyton [4]	Gasometry	Human
40 ± 5	Venous PO_2	Mah and Cheng [20], Guyton [4]	Gasometry	Human
48.2 ± 3.1	Synovial Fluid	Richman [63]	Routine macroscopic and microscopic examination	Human
30.6 ± 3.1	Cornea	Bonanno [64]	Oxygen sensitive dye, Pd-meso-tetra (4-carboxyphenyl) porphine, bound to bovine serum albumin, was incubated with contact lenses	Human
22	The Eye	Bonanno [64]	The T1 mapping method was applied	Human

Intracellular partial pressure of oxygen

Once oxygen reaches the cells, the metabolic demand must to be satisfied. The gradient of partial pressure of oxygen, from the extracellular space into the cell determines the availability of oxygen to the mitochondria [39, 40].

In highly aerobic cells, such as the neurons, energy production depends largely on the availability of oxygen supplied to the mitochondria [41]. Inside this organelle, a series of enzyme-catalysed chemical reactions occur, converting metabolites into carbon dioxide and water to generate a form of usable energy in the form of high energy phosphates [42].

Although it has long been reported that the intracellular partial pressure of oxygen (iPO_2) drops around the oxygen-consuming organelle, the mitochondrion PO_2 must be very small [39]. Various attempts to determine the gradient of oxygen between the mitochondria and the extracellular fluids have led to some incongruous results [40, 43, 44]. Reported values range from one type of cell to another and ranges from below 1 mmHg measured by indirect methods to 1 to 10 mmHg by intracellular direct methods [45]. The classic insensitivity of mitochondrial respiration to local PO_2 has been challenged recently by in vivo [46] and in vitro [47] studies, in which mitochondrial oxygen consumption is dependent on PO_2 over the full physiological range.

Partial pressure of oxygen in different tissues

Once the arteries bring O_2 to the cells, the difference in pressure between the arterial vascular lumen and the tissue will cause that gases that are at higher pressures diffuse to those tissues with lower pressure, exchanging oxygen and carbon dioxide (CO_2) in both directions [29]. The average partial pressure in the tissue along this diffusion gradient is called the tissue partial pressure of oxygen (PtO_2) and varies according with oxygen consumption, capillary density, metabolic rate and blood flow [10, 48].

While under normal circumstances alveolar PO_2 is equal to 104 mmHg, the lungs will transfer this oxygen through the alveolar-capillary barrier, reaching the same PO_2 (104 mmHg), however, before reaching the left atria, the pulmonary shunt blood coming from the bronchial veins (40 mmHg) will mix with blood from pulmonary veins, reaching the atria with an arterial PO_2 of 95 mmHg. This is known as "pulmonary venous admixture" [10, 49].

From the aorta, the amount of oxygen that is released from the hemoglobin will depend upon the metabolic demands from that specific organ, that are usually matched to the arterial oxygen supply and vasomotor sensitivity [50].

In the following section we summarized the range of PO_2 according to the type of tissue, describing in more depth those which have more available data in humans. It is important to point out that due to the lack of studies in controlled environments, an specific range mean value is hard to be provided, therefore, we state the reference value according to the lowest-highest range described (**Table 1**).

Partial pressure of oxygen in the brain

The brain is an organ with one of the highest oxygen and glucose requirements, although it is not able to store metabolic products for further use, its blood supply is highly dependent of vasoactive substances, arterial blood gases and metabolic demand allowing the availability of these nutrients [3, 65, 66].

Changes in tissue brain Partial Pressure of Oxygen depends on the cerebral metabolic rate (CMR), the local cerebral blood flow (CBF) and the systemic exposure of hypoxia [3, 36, 67, 68]. Brain PtO_2 can change due to several factors like CMR, hypoxia, exercise, angiogenesis, stress and Anesthesia [3]. In general and considering that humans are in constant activity and many cofounders cannot be controlled, the available evidence suggest that cortical PtO_2 ranges from 20-25 mmHg in rest and low altitude and reach up to 48 mmHg in high altitudes or intense physical activity [51, 52, 69].

Partial pressure of oxygen in the liver

The liver receives more than 6% of the cardiac output per minute and more than 26% of the cardiac output when considering the portal venous system [10]. This organ seems to be highly oxygenated, however, during sympathetic vascular tone changes, anesthesia, restraining and also depending of the method of measurement, liver tissue PO_2 fluctuates [56]. The

Table 2. Adapted from Harold M. Swartz; Jeff F. Dunn * Minimum Volume Sampled

Method	Parameter measured	Mechanism of measurement	Site of measurement	*Volume sampled
Microelectrode	pO_2	Current generated by the electrolytic decomposition of dioxygen	Interstitial volume in contact with the tip	µl
Near infrared monitoring of haemoglobin and myoglobin	Physiological parameter relative or absolute changes in saturation	Amount or fraction of haemoglobin (Hb) or myoglobin (Mb) and its relative oxygen saturation	Location of the proteins. In the vascular system by non-linear weighting of Hb related to vessel diameter. Idem in muscle for Mb.	ml's
Near infrared monitoring or cytochromes	Physiological parameter relative changes in cytochrome oxidation	Redox state of cytochoromes	Intracellular cytochromes	5 ml's
Phosphorescent and fluorescent methods based on redox states of intermediates	Physiological parameter based on redox potential	Ratio of reduced and oxidized states of redox couples	Sites of the redox intermediates (usually intracellular)	µl's
Phosphorescent and fluorescent methods based on quenching by oxygen	O_2	Change in lifetimes of the excited states	Sites of the introduced probe molecules, intravascular or at a catheter tip	µl's
NMR perfluorocarbon relaxation	O_2	Effect on relaxation rates of fluonne nuclei	Sites of the introduced emulsion	µl-ml's
Substances that localize in hypoxic areas	Physiological parameter	Amount of material that localizes in the tissue, related to perfusion and O_2 at time of administration	Tissues where substances localize	<10 µ in biopsy
EPR oximetry based on soluble materials	pO_2	Effect on linewidth of EPR spectrum	Sites of the particles (usually interstitial)	100 µl
EPR oximetry based on soluble materials	O_2	Effect on linewidth of EPR spectrum or relaxation rates	Sites of the soluble molecules (usually throughout the tissues)	-1 ml
NMR spectroscopy	Physiological parameter metabolic correlates with oxygen	Concentrations of metabolites which change with oxidative status of cells	Sites of metabolites	-1 ml 25 µl-ml's
Proton NMR spectra of myoglobin	Physiological parameter relative or absolute change in oxymyoglobin	Relative concentrations of deoxy and oxymyoglobin	Muscle (myoglobin)	-1 ml µl-ml's
NMR overhauser effect	O_2	Relaxation rates of protons that couple to free radicals	Sites of the soluble free radicals (usually throughout the tissues)	Potential resolution of MRI
NMR bold effect	Physiological parameter	Amount of deoxyhemoglobin in the voxels	Vascular system with a non-uniform weighting to vascular diameters	<0.2 ml µl-ml's

*The minimum volume of tissue that was sampled for theoretical rather than practical interest.

liver can survive with less than 60% of the total liver blood supply due to sympathetic electric nerve stimulation, resulting in an important reduction of tissue PO_2, however under normal conditions the very few reports available in humans refer that PO_2 ranges from 50-55 mmHg [56, 70].

Partial pressure of oxygen in skeletal muscle

The muscle is a highly effective oxygen consuming tissue that responds to blood flow requirements and oxygen availability [71]. The local tissue oxygenation of the skeletal muscle is highly variable, being skeletal muscle one of the most tolerant tissues to hypoxia and metabolic acidosis [72]. Tissue oxygenation level depends on the rate of oxygen supply and the rate of oxygen consumption per tissue [73]. The critical level in which the muscle will suffer ischemia has not been explored, however, muscle PO_2 and its relationship with systemic factors such as sepsis and infections have been reported several times [58, 74]. Considering the reports available, skeletal muscle oxygenation ranges from 7.5 to 31 mmHg [74].

Partial pressure of oxygen in the skin

The skin is one of the most vasoactive tissue within the body, reacting strongly to sympathetic, thermic and metabolic changes [10]. At rest and in neutral thermal conditions, less than 2% of the total cardiac output goes to the skin [75], however, fluctuations in skin blood flow are always occurring due to sympathomimetic variability [76]. The oxygen availability measured locally depends on the influence of the microcirculation and the skin PtO_2 ranges according to the skin layers. The more external layer ranges from 3.2 to 8 mmHg, the papillary dermis from 6.4 to 24 mmHg and below the subcutaneous fat, the skin PtO_2 ranges from 8 to 38 mmHg [53, 75].

Methods to measure tissue partial pressure of oxygen

Several methods have been used to measure the availability of oxygen within the tissues (PtO_2). In **Table 2** we summarize the methods that are available nowadays with some technical specifications such as the mechanism of measurement, the site of data collection and minimum sample volume needed (**Table 2**).

Qualitative methods to measure tissue PtO_2

The most common qualitative methods available to measure brain PtO_2 include, but are not limited, to positron emission tomography (PET), near-infrared spectroscopy (NIR) and magnetic resonance imaging (MRI) or nuclear magnetic resonance (NMR) [77, 78].

Positron emission tomography (PET)

Positron emission tomography (PET) is an imaging technique that uses positron emitting isotopes which are injected into the tissue to provide a three-dimensional image or picture of functional processes in the body [79]. The parameters used to measure brain oxygenation are based on the oxygen extraction fraction (OEF) or the cerebral metabolic rate for oxygen ($CMRO_2$). The use of PET in brain oxygenation studies has been reported several times, although its use is reduced in the clinical setting due to its high cost and technical complexity [77, 80].

Near infrared spectroscopy (NIR)

Near infrared spectroscopy (NIR) is a technology based on light absorption in the near infrared spectrum (700-1000 nm) [81]. It is characterized for its ability to scatter through skin, bone and other tissues, thus detecting low resolution but real time changes in regional hemoglobin content and rarely with brain cerebral perfusion [82, 83].

Blood oxygenation level dependent MRI (BOLD MRI)

Oxyhemoglobin has diamagnetic properties whereas deoxyhemoglobin is a paramagnetic molecule [84]. These magnetic properties can be used as an endogenous source of contrast to visualize tissue oxygenation [85-87]. This technology can be used to measure brain oxygenation based on the concept that changes in deoxyhemoglobin modulate the MRI signal intensity. For example, an increase in regional cerebral blood flow caused by neural activity is accompanied by a local reduction in deoxyhemoglobin content [88].

Quantitative methods to measure brain PtO_2

The physical and chemical characteristics of oxygen can be measured according to its spe-

cific interaction with determined oxygen-reactive molecules [89]. The measurement of tissue partial pressure of oxygen (PtO_2) is expressed in mmHg, kPa or Torr and is one of the main "direct" measurements of oxygenation in the tissue [77].

Polarographic microelectrodes

Molecules of oxygen are electron acceptors and this oxidative reaction can be measured using microelectrodes [90]. This oxygen reduction reaction allows a signal that creates a potential difference which is recorded by the electrode [91]. The use of this type of electrodes has allowed the measurement of brain PtO_2 during various conditions, including head trauma, brain surgery, hypothermia and hibernation [92-96].

Electron paramagnetic resonance oximetry

Electron paramagnetic resonance oximetry (EPR) is a spectroscopic technique that detects chemical species that have unpaired electrons [97]. EPR oximetry is a relatively non-invasive method for monitoring tissue partial pressure of oxygen (PtO_2) using paramagnetic oxygen sensitive materials including perchlorotriphenylmethyl molecules or lithium phthalocyanine (LiPc) crystals [85, 97-100].

The fundamental mechanism of this technique is the detection of unpaired electron species which react with the implanted materials (i.e. LiPc crystals) [101]. The identification of these chemical species co-existing in the determined paramagnetic spectrum can be observed and interpreted as oxygen tensions [100, 102-104].

The use of EPR oximetry for the study of tissue oxygenation allows multiple measurements to be performed through the use of crystals that are highly sensitive to low PtO_2 [98]. The advantages of this method are stable calibration and relative unresponsiveness to changes in pH or redox reactions [104, 105].

Mass spectrometry and brain PtO_2 measurements

Mass spectrometry (MS) is a technique that make it possible to obtain analytical information of the molecular mass and its elemental composition of a sample or molecule [106]. For this it is necessary to ionize molecules using different techniques such as chromatographic separation in order to measure the mass to charge ratio caused by external electric and magnetic fields [83, 106].

Mass spectrometry is a complicated technology to use, Atoms are very reactive and they have a short live, thus, manipulation must be performed in a vacuum environment, with very low barometric pressures that ranges from ~10^{-5} to 10^{-8} Torr [106]. These factors, plus the greater degree of invasively, and the response time and delay of mass spectrometers, make mass spectrometry less favourable as a method [83].

Fluorescence and phosphorescence-based probes

The optical methods of oxygen detection are based on the recognition of an atom or molecule which has been electronically excited by the absorption of a photon [3]. This excitation facilitates the transitions of a species from high excitation state or activation, to a ground or low excitation state, this molecular reaction involves the emission of a photon of light [3].

Fiber optic optodes can be used to measure brain PtO_2 in awake and unanesthetized subjects, however its availability in human studies is limited. This technology is based on short pulses of light that are transmitted along a fiber optic sensor, exciting the platinum (new version) or ruthenium (older version) based tip, producing a photon-molecular reaction that is quenched by the presence of oxygen [3, 45, 107, 108].

One of the most important physiological advantages of this optical technique is that it is very sensitive during hypoxia [3]. This feature is clinically relevant when studying tumour growth which depends on oxygenation as well as when studying ischemia or brain injuries [109]. Another important feature of this technology is its insensitivity to magnetic fields. This technology allows us to measure brain PtO_2 while applying simultaneously other exploration or imaging techniques, such as MRI or EPR. This feature can be used to validate two or more methods [110].

The effects of acute and chronic hypoxia on Tissue PO_2

The effects of hypoxia (acute or chronic) and the presence of oxygen deprivation in different tissues have been reported as early as the 1950's [111]. The hypoxic environment was simulated using different fractions of inspired oxygen (normobaric hypoxia) or by exposing the subject to lower barometric pressure (hypobaric hypoxia), either by using low pressure chambers, or taking the subject to high altitude [8, 112].

Although oxygen levels are critical parameters in order to asses tissue survival, monitoring the level of oxygen at a tisular level remains a challenge [3, 52, 68, 110]. Real time, *in vivo* measurements during acute inflammation, hypoxia or hyperoxia have been done very few times and is not widely available [80].

Measuring tissue oxygenation during acute or chronic is a difficult task, especially due to the presence of cofounders like exercise, anesthesia, time of exposure or restraining the animal model [113, 114]. In humans, acclimation to high altitude exposure or controlled normobaric hypoxia will cause different readings in terms of PtO_2 [68]. Adaption on the other hand will cause differences between populations, making extrapolation a difficult task [115]. Obtaining reference values in such conditions is very difficult due to the implications of such a challenge and the ethical limitations of these type of technologies in humans.

Discussion

This practical review of the available literature about the gradient of pressure of oxygen revealed complex, varied and often not conclusive results. We tried to summarize the most relevant information to present it as friendly as possible for educational purposes. A more profound analysis of cellular and molecular hypoxia and normoxia signalling we recommend Keeley and Mann review [116].

The usefulness of understanding the gradient of PO_2 among healthcare providers is essential. Understanding how the gradient of pressure works and how oxygen is delivered is related to an entire spectrum of clinical uses. Some of the most important results come from athletes performance [117], forecasting mortality due to prevalent diseases [118], wound healing evaluation [119], treatment effectiveness in ulcers, burns, cancer or cerebral and cardio vascular disease [120-125].

In this sense, we have exposed the physiological mechanisms, the methods for measuring and the pressures values reported in different organs from the atmosphere to the mitochondria. Tissue partial pressure of oxygen reflects a balance between arterial blood flow and tissue oxygen consumption rate [92]. Due to technical limitations and confounding factors such as anesthesia, inflammation, restraint and hypoxia, an appraisal of partial pressure of oxygen during normal conditions is very difficult. However, *in vivo* and clinical data available have been included to offer the reader a better perspective of how partial pressure of oxygen behaves within the human body.

Conclusions

The human body is a complex living organism, which has developed mechanisms to keep oxygen levels in a suitable level as to cover the metabolic demand, while avoiding excessive oxygen pressure.

The partial pressure of oxygen varies in the different structures of the organism. Each organ and tissue have its own requirements in order to correctly function. For example, the partial pressure of oxygen in the lungs for carrying out the gas exchange is different from the partial pressure of oxygen within the pulmonary tissue. We have emphasized that the organism has been able to develop physiological mechanisms that allow it to respond to short-term and long-term changes not only of the oxygen partial pressure, but also of the different gases in the atmosphere. This fascinating response capacity is responsible of how the human body manages to function correctly when it finds itself in different climates and altitudes.

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