



A Novel Mathematical Equation for a Noninvasive Determination of the Number of Alveoli of the Human Lung

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Background: There had always been a spirited effort in understanding the transport of air or molecular oxygen plus other gases from alveolar air space into the pulmonary capillaries and from the latter back into the former using mathematical models; the determination of the number of alveoli using cadaver and invasive and partially noninvasive methods have been made. There is a need for a noninvasive method of mathematical nature, with evaluative, diagnostic, and prognostic application.

Objectives: The objectives of this research were to derive a mathematical equation for the noninvasive determination of the number of alveoli during rest and physical activity and elucidate the usefulness and advantage of the model over known methods.

Methods: Theoretical and computational (calculational) methods; data in the literature were substituted into the model mathematical equation for the computation of the number of alveoli in the human lungs.

Results and Discussion: The computed number (N_{alv}) of alveoli differed from one country or subcontinental region to another. The N_{alv} for the male were expectedly larger than for the female subjects.

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Conclusion: The mathematical equation for totally noninvasive determination by computation is derivable and was derived. The total number (N_{alv}) of alveoli mobilised for function is a function of the width (d) of the nares ($d^{22/15}$), rate (R_v) of gas flow ($R_v^{3/5}$), and radius (r_{alv}) of a functional alveolus ($r_{alv}^{2/3}$). The equation has the potential to be of diagnostic, evaluative and prognostic value in medical practice. This new computational approach could be faster than other known approaches for the determination of the N_{alv} . A noninvasive approach by computation, relying on other noninvasively determined respiratory parameters, can eliminate the possibility of tissue damage.

Keywords: Derivation of mathematical equation; computation; number of alveolar at rest and exercise; width of nares; air; molecular oxygen.

1. INTRODUCTION

The lung is comprised of bifurcating hollow branches that carry air to the terminal airways (alveoli) where gas exchange takes place [1]. Mathematical models of gas exchange, that have focused on different aspects of the process of gas transfer and distribution between ambient air and blood, including distribution of ventilation, transport between alveolar air space and pulmonary capillaries, hemoglobin dynamics and acid-base physiology can be found in the literature [2]. There is also an age-long model for the computation of the total number of alveoli which requires cadaver [3]. Though not too familiar, the flow system in the exchange of gas between blood and alveolar has been described in terms of higher level mathematics, the continuity and Navier-Stokes equations in the cylindrical coordinate [4].

According to Wagner [5], the lungs are a collection of some 300 million very small gas-filled polyhedrons (alveoli), the walls of which are made up of little more than a rich capillary network supported by a very thin interstitial matrix. Each alveolus expands with fresh gas (high in O_2 and low in CO_2) that has flowed down the bronchial tree from the nasal cavity during inspiration. The alveoli then reduce in volume during expiration, returning gas (lower in O_2 and higher in CO_2) up the bronchial tree to the nostril. This process is of course called ventilation [5].

Many other researchers have attempted to determine the number of alveoli in human beings in particular [1, 3, 6] and lower mammals [7]. Some methods are invasive while others are not. The invasive methods may present minor but significant complication and distress to the patient. Formalin-based cadaver fixation, preparatory to counting with microscopy in line with histological method cannot be applied to human subject. With reference to pieces of

information in the literature Leong *et al.* [1] noted that previous investigation of lung structure at the alveolar scale have been done using imaging techniques that include; optical coherence tomography (OPCT), confocal laser scanning microscopy (CLSM) and endoscopy microscopy [8-10]. Endoscopy microscopy is relatively non-invasive as it places an endoscope in the pleura visceralis [1]. However, that was shown to alter the intrapleural pressure, which artificially changes the alveolar morphology [11]. However, the working definition for noninvasive method in this research is the total absence of entry of any tool to point beneath the skin. To this end, a non-invasive phase contrast x-ray (PCX) imaging technique to measure the size and population of alveoli *in situ* has been investigated [1]. Thus, the objectives of this research as a modest contribution to the fight against respiratory disease occasioned by covid-19 are to derive a mathematical equation for the noninvasive determination of the number of alveoli during rest and physical activity and elucidate the usefulness and advantage of the model over known methods.

2. THEORETICAL DEVELOPMENT

2.1 Background

To begin this section it is very important to re-state the equation often cited in the literature for many years. For instance Angus and Thurlbeck [3] gave the equation below.

$$N_v = J^2 \sqrt{N_A^3} / \beta V_v^{1/2} \quad (1a)$$

Where, N_v , N_A , V_v , J , and β are the number of alveoli per unit volume of the lung, the number of alveoli per square centimetre of tissue slice, the percentage of alveolar air, a distribution variable equal to 1, and a shape constant which relates average cross-sectional area to volume.

The total number of alveoli, N_a is given as

$$N_a = 0.885 N_v V_L \quad (1b)$$

Where, V_L is the total lung volume.

Although it is not clear how V_v can be calculated, the real concern is about the need for tissue slice which may definitely be derived from a cadaver. The mathematical model proposed here may be applied without such requirement. Thus, it is necessary to state that the first objective of this section is to derive a general equation which contains variables such as nares' width (or the diameter of the trachea which is for the feature). This implies that the number of alveoli to be calculated may be a function of the size of entire nares, a positive non-integer (a decimal number >1) multiple of twice the nostril's diameter (either left or right), and non-integer (>1) multiple of the internal tracheal diameter.

It is not just the pressure gradient alone that promotes rapid flow or diffusion of air (which may be only oxygen if respirator coupled to oxygen cylinder is the case as in this era of covid-19 pandemic) into and in the lung airways but the structural aspect of the airways-the tracheal system of decreasing diameter. The issue of tapering diameter and its effect is for feature consideration. The rate of gas flow is expressed as:

$$R_v = \frac{\pi \xi^2 R_A}{r^2} \quad (2)$$

Where, R_v and R_A are the rate of diffusion measured in unit of volume per unit time and rate of diffusion measured in unit of volume per unit cross-sectional area per unit time; r is the number of times the total radial distance (ξ), covered in random motion is $>$ the real radius of the airway at any generation of the respiratory tract. The parameter R_A has the unit of velocity. However,

$$R_A = \frac{v}{\phi} \quad (3)$$

Where, the "reduction factor" (ϕ) i.e. the number of times the root mean square velocity (v) of the gas molecule is larger than R_A . The factor ϕ is expressed as:

$$\phi = \sqrt[3]{\frac{3k_B \theta \xi}{v h}} \quad \text{or} \quad \sqrt[3]{\frac{m v \xi}{h}} \quad (\text{Because } 3k_B \theta = m v^2) \quad (4)$$

Where, k_B and θ are the Boltzmann constant and thermodynamic temperature; h and m are the

Planck constant and the mass of oxygen or a gas in general. The alternatives to Eq. (4) are determined as follows:

$$\phi^2 = \frac{3k_B \theta}{m R_A^2} \quad (\text{Because } v > R_A) \quad (5)$$

But, the equation for R_A as determine elsewhere [12] is

$$R_A = \sqrt[3]{\frac{v h}{m t}} \quad (6)$$

Where, t is the time spent in covering the total radial distance in different direction. Equation (5) can be restated. Thus,

$$\phi^2 = \frac{v^2}{R_A^2}, \quad \text{because } \frac{3k_B \theta}{m} = v^2 \quad (7)$$

Substitution of the square of Eq. (6) into Eq. (7) gives:

$$\begin{aligned} \phi^2 &= \frac{v^2 (\sqrt[3]{m t})^2}{\sqrt[3]{v^2} \cdot \sqrt[3]{h^2}} \\ &= \left(\sqrt[3]{v^2} \cdot \sqrt[3]{\frac{m t}{h}} \right)^2 \end{aligned} \quad (8)$$

Meanwhile, given a distance (ξ) covered in random motion, t should be ξ / v . Thus,

$$\begin{aligned} \phi &= \sqrt[3]{v^2} \cdot \sqrt[3]{\frac{m \xi}{h v}} \\ &= \sqrt[3]{\frac{m v \xi}{h}} \quad \text{or} \quad \sqrt[3]{\left(\frac{\sqrt[2]{3} m k_B \theta}{h} \xi \right)} \end{aligned} \quad (9)$$

Substitution of Eq. (3) into Eq. (2) gives:

$$R_v = \frac{\pi \xi^2 v}{r^2 \phi} \quad (10a)$$

Substitution of Eq. (9) into Eq. (10a) gives:

$$\begin{aligned} R_v &= \frac{\pi \xi^2 v}{r^2 (\sqrt[3]{v})^2} \sqrt[3]{\frac{h v}{m \xi}} \\ &= \frac{\pi \xi^2}{r^2} \sqrt[3]{\frac{h v^2}{m \xi}} \\ &= \frac{\pi (\sqrt[3]{v})^2}{r^2} \sqrt[3]{\frac{h \xi^5}{m}} \end{aligned} \quad (10b)$$

Making ξ subject of the formula gives:

$$\xi = \left(\frac{R_V^3 m r^6}{\pi^3 h v^2} \right)^{1/5} \quad (11)$$

The number of times the original velocity is reduced is re-expressed as:

$$\phi = \left(\frac{m v}{h} \left(\frac{R_V^3 m r^6}{\pi^3 h v^2} \right)^{1/5} \right)^{1/3} \quad (12)$$

Therefore, the new velocity due to the effect of random motion is given as:

$$u = v \left(\frac{h}{m v} \left(\frac{\pi^3 h v^2}{R_V^3 m r^6} \right)^{1/5} \right)^{1/3} \quad (13a)$$

Simplification of Eq. (13a) gives

$$u = \left(\frac{\pi}{R_V} \right)^{1/5} \left(\frac{h v^2}{m r} \right)^{2/5} \quad (13b)$$

Due to pressure gradient - < atmospheric pressure within the lung and respiratory tracts – an initial near-total absence of randomness may be the case. Re-writing u as $R_{A(\text{tract})}$ the rate of gas flow in volume per unit time per cross-sectional area of each tract is given as:

$$R_{A(\text{tract})} = R_V / \varepsilon \pi r^2 \quad (14)$$

Substituting Eq. (14) into Eq. (13b) gives

$$R_V / \varepsilon \pi r^2 = \left(\frac{\pi}{R_V} \right)^{1/5} \left(\frac{h v^2}{m r} \right)^{2/5} \quad (15)$$

Where, ε is the number of respiratory tracts, and for the purpose of this research, r is re-defined as:

$$r = \left(\frac{m v}{h} \left(\frac{\pi}{R_V} \right)^3 \left(\frac{d}{2} \right)^6 \frac{h v^2}{m} \right)^{1/2} = \left(\frac{\pi v}{R_V} \right)^{3/2} \frac{d^3}{8} \quad (16)$$

Where, d is the width of the nares for the purpose of this research. Other relationship in which the diameter of the nostril and trachea may be the case awaits future investigation.

2.2 Mathematical Model with Which to Calculate the Number of Alveoli at a Given Respiratory Rate

Rearranging Eq. (15) gives

$$\varepsilon = \left(\frac{R_V^5}{\pi^6 r_{alv}^{10}} \right)^{1/5} \left(\frac{r m}{h v^2} \right)^{2/5} \quad (17)$$

Where, ε for the purpose of this section, is re-designated as the number of alveoli and, r_{alv} which is used in place of r , is the radius of an

alveolus. Within the lumen of the respiratory tract, it is suggested that there may be further reduction in the velocity of directional motion as the pressure gradient decreases. Hence, v in Eq. (17) is re-designated as v_x and expressed as

$$\left(\sqrt[3]{\frac{h}{m v d}} \right) v \text{ or } \left(\sqrt[3]{\frac{h}{m d}} \cdot \sqrt[3]{v^2} \right).$$

Substitution of this and Eq. (16) into Eq. (17) gives after a complicated simplification and rearrangement processes the following.

$$\varepsilon = \sqrt[15]{v d^{22}} \left(\frac{R_V}{4 \pi} \right)^{3/5} \left(\frac{m}{h} \right)^{2/5} / r_{alv}^2 \quad (18)$$

3. MATERIALS AND METHODS

3.1 Materials

Since no experiment was carried out, experimentally generated data in the literature [13, 14] were used for computation. There were no human subjects and no forms of chemicals were needed.

3.2 Methods

The research is purely theoretical and computational which entailed formulation of mathematical models (Eq. (18) in particular, in its finality in this research) which needs to be tested using data available in the literature. The parameter ε is calculated based on the observation that there may be a relationship between anatomical parts of a subject: It is known in the literature that certain respiratory parameter may be dependent on or could be a function of certain anatomical feature [15]. The value of R_V used for resting subjects is $12 \times (750 - 150) / \text{minute}$ for a male and $12 \times 450 / \text{minute}$ for a female having taken into account the fact that whatever volume in a female is about 25% less than the volume in a male. The value of R_V used for excising subjects is $(40 - 60) \times (1923 - 150) / \text{minute}$ for the males and $(40 - 60) \times 1329.75 / \text{minute}$ for the females having taken into account the fact that whatever volume in a female is about 25% less than the volume in a male.

4. RESULTS AND DISCUSSION

The results presented required *ab initio* the use of $1.165 \exp(-4)$ metres alveoli radius for the resting subjects and $1.365 \exp(-4)$ metres for the physically active subjects [14]. It is however,

proposed that such values cover both male and female adults and that they may not be totally generalisable to all races and corresponding demographic structure of a given race let alone on a global scale. There are differences between races in particular and between genders [13]. Thus the values of these variable used for computation should give a mere tentative result as a step before the use of determined variable across demographic structure between races and within races. The computed numbers of alveoli for subjects at rest and for subjects who are exercising, male and female adults, are shown in Table 1 for adult subjects of West African origin, Table 2 for adult subjects of East Asian origin, Table 3 for adult subjects of South Asian origin, and Table 4 for adult subjects of South Asian origin. A clear general feature of all the results across racial divide is that the number of alveoli for males is larger than for the females. This is not unexpected given the fact that the width of the nares for the males is longer than for the females [13]. In the same vein, a comparison of the number of alveoli between subjects from different locations is in the order: West Africa > East Asia > South Asia > North Europe.

However, pieces of information available in the literature [3, 6] do not indicate the characteristic of the population studied. The average number of alveoli for 6 subjects/samples only is 480 million with a range of 274–790 million; perhaps if the population covered was much larger, the magnitude of the lower part of the range may be much lower; 212–605 million was reported for a number of subjects/samples equal to 32 [3]. This validates the claim that larger samples could have given broader range. The fact is that the lungs from cadavers were used by all researchers. Therefore, no question of whether or not the lungs were for resting or dead subject. This is unlike this research in which the numbers of alveoli as a function of respiratory rate and other parameters Eq. ((18)) for either the resting (breathing rate (BR) = 12 / minute) or exercising (BR = 40-60 / minute) living subjects were computed. Thus Tables 1, 2, 3, and 4 for subjects from different regions of the globe, male and female, also show results for exercising and resting subjects. The number of alveoli computed for the exercising case is larger than for the resting subjects. This simply means that not all the alveoli are mobilised during rest and while exercising, most other alveoli are mobilised. Perhaps, this view is similar to the claim that in healthy human subjects the lung inflates primarily by alveolar recruitment and, to a lesser extent, by

anisotropic expansion of alveolar ducts [16]. Recruitment, in this context, may imply the participation of other alveoli in the accommodation of incoming air/O₂. Thus, taking measurement of tidal volume and respiratory rate under condition similar to fight–or–flight condition can yield values that enable the computation of the total number of alveoli. One may not ignore not just the existence of a few, but significant numbers of alveoli, in other parts of the acinus, respiratory bronchiole for instance, but also the subpleural alveoli [11] which can add to the overall population of the pulmonary alveoli.

Going by the observation in the literature [10] that the total intranasal volume is positively correlated with the size of the nostril opening thus indicating that nostril size can be used as a substitute in the absence of measures of intranasal volume, it became instructive to investigate mathematically if the number of alveoli can be determined based on its relationship with the width of the nares. Therefore, the fact that the width of subjects may differ due to racial and continental differences led to the observed differences in the computed number of alveoli (Tables 1 – 4). This is clearly consequent upon the observation that the total number of alveoli mobilised for function is a function of the width (d) of the nares ($d^{22/15}$), rate (R_v) of gas flow ($R_v^{3/5}$), and radius (r_{alv}) of a functional alveolus ($r_{alv}^{2/3}$). The parameters, d , R_v , and r_{alv} differ from one subject to another, from one race to another, and from one continent to another [13].

The results from this research are based mainly on Eq. (18). Therefore, it is important one realises that the values of R_v while resting and during exercise used were obtained from the literature [14] and there is a need to discuss such values that gave different results when used. The values of the nares' width and the diameter of the alveolus were also obtained from the literature, respectively from the works of Zaide *et al.* [13] and Balásházy *et al.* [14]. The values at rest are totally different from the values during any form of physical exertion, walking, jogging, sprinting, intense labour *etc.* Meanwhile, normal resting alveolar ventilation is about 5 L/min [5]. During exercise, ventilation might increase from resting values of around 5-6 litres /min to > 100 litre per min [17]. With the understanding that minute ventilation (R_v) is given as ventilatory rate, breaths per minute (BPM) multiplied by tidal volume less dead space volume, the rate of gas flow in volume per unit time is calculated.

The miniature nature of human alveolus has been observed as exemplified with 100-300 μm diameters in humans [9] though how such value was arrived at is not certain; another example is 75–300 μm (www.sciencedirect.com/alveolus). This is against the backdrop of other value such as 125 μm in the resting state with a minimum average of 116.5 μm on the basis of a tidal volume (T_v) equal to 750 mL per breath [14]. Substitution of any of the shorter radii into Eq. (18) for the resting subject should give result that

would have meant that larger number of alveoli is applicable to subjects with shorter alveolar radius. This may not be the case because the T_v and the respiratory rate (R_r) may be much lower for such subjects. On the basis of such argument, the maximum length of an alveolar radius equal to 136.5 μm given a T_v equal to 1923 mL per breath [14] during exercise is different from what is obtainable when at rest as may be applicable to different subjects be it either at rest or while exercising.

Table 1. Computed numbers of alveoli for adult subjects of West African origin

BPM	Male		Female	
	ϵ (in atmosphere)	ϵ (in oxygen gas)	ϵ (in atmosphere)	ϵ (in oxygen gas)
12	206,371,029.3	215,436,166.1	141,766,653.3	147,993,950.2
60	756,400,440.4	789,626,388.3	519,609,555.2	542,434,125.6
50	678,020,812.9	707,803,826.0	465,766,641.8	486,226,087.6
40	593,057,793.7	619,108,687.3	407,401,265.2	425,296,930.8

Respiratory rate (R_r) is the number of breaths per minute (BPM). BPM =12 is the R_r at rest while 40–60 are values of R_r during moderate to intense exercise. The tidal volume (T_v) for male while at rest is 750 mL [14]. The dead space volume used is 150 mL. The T_v while exercising is taken generally to be 1923 mL [14]. The equivalent values for the female subjects were calculated to be 0.25 (25%) < the male values. The width of nares for the male and female are 45.36 (2.74) and 39.50 (2.95) mm respectively [13]; the figures in parenthesis are the SD and ϵ is the number of alveoli

Table 2. Computed numbers of alveoli for adult subjects of East Asian origin

BPM	Male		Female	
	ϵ (in atmosphere)	ϵ (in oxygen gas)	ϵ (in atmosphere)	ϵ (in oxygen gas)
12	162,566,364.2	169,707,334.3	115,502,371.4	120,575,982.2
60	595,845,597.2	622,019,004.0	430,594,488.1	430,594,488.1
50	534,102,962.6	557,564,232.1	385,975,482.4	385,975,482.4
40	467,174,338.3	487,695,668.1	337,608,763.1	337,608,763.1

Respiratory rate (R_r) is the number of breaths per minute (BPM). BPM =12 is the R_r at rest while 40–60 are values of R_r during moderate to intense exercise. The tidal volume (T_v) for male while at rest is 750 mL [14]. The dead space volume used is 150 mL. The T_v while exercising is taken generally to be 1923 mL [14]. The equivalent values for the female subjects were calculated to be 0.25 (25%) < the male values. The width of nares for the male and female are 38.55 (2.28) and 34.35(2.02) mm respectively [13]; the figures in parenthesis are the SD and ϵ is the number of alveoli

Table 3. Computed numbers of alveoli for adult subjects of South Asian origin

BPM	Male		Female	
	ϵ (in atmosphere)	ϵ (in oxygen gas)	ϵ (in atmosphere)	ϵ (in oxygen gas)
12	155,930,476.9	162,779,947.7	109,875,501.9	114,701,936.4
60	571,523,442.6	626,420,183.3	402,713,514.9	420,410,729.8
50	512,301,115.0	561,509,353.0	360,983,587.6	376,846,984.1
40	448,104,487.7	491,146,424.6	315,748,611.2	329,624,160.1

Respiratory rate (R_r) is the number of breaths per minute (BPM). BPM =12 is the R_r at rest while 40–60 are values of R_r during moderate to intense exercise. The tidal volume (T_v) for male while at rest is 750 mL [14]. The dead space volume used is 150 mL. The T_v while exercising is taken generally to be 1923 mL [14]. The equivalent values for the female subjects were calculated to be 0.25 (25%) < the male values. The width of nares for the male and female are 37.47 (2.59) and 33.20(1.92) mm [13]; the figures in parenthesis are the SD and ϵ is the number of alveoli

Table 4. Computed numbers of alveoli for adult subjects of North European origin

BPM	Male		Female	
	ϵ (in atmosphere)	ϵ (in oxygen gas)	ϵ (in atmosphere)	ϵ (in oxygen gas)
12	136,911,704.0	142,925,745.9	98,941,141.87	103,287,274.7
60	501,814,975.3	523,857,913.9	362,643,552.0	378,573,194.9
50	449,815,969.6	469,574,777.7	325,065,749.3	339,344,732.8
40	393,449,377.1	410,732,202.3	284,331,649.5	296,821,328.7

Respiratory rate (R_r) is the number of breaths per minute (BPM). BPM =12 is the R_r at rest while 40–60 are values of R_r during moderate to intense exercise. The tidal volume (T_v) for male while at rest is 750 mL [14]. The dead space volume used is 150 mL. The T_v while exercising is taken generally to be 1923 mL [14]. The equivalent values for the female subjects were calculated to be 0.25 (25%) < the male values. The width of nares for the male and female are 34.29 (2.42) and 30.91 (2.07) mm [13]; the figures in parenthesis are the SD and ϵ is the number of alveoli

The occurrence of alveoli is not for the natural function only but it has been found useful in civil and criminal investigation. A method that accurately describes the interaction of alcohol with the airways and predicts the effects of variable ventilation parameters have been investigated [18]. By far the most studied high blood- and water-soluble gas is gaseous ethanol. This is useful in investigating the level of ethanol in drunken driving cases. For instance, in the United States each year, there are 1.5 million arrests for driving while intoxicated. The alcohol breath test is based on the assumption that end-exhaled breath ethanol concentration is always equal to alveolar ethanol concentration (which is presumed to be in equilibrium with mixed venous blood) [19]. Someone who has taken too much alcohol may not speculatively exhibit the same respiratory rate. As such, the number of alveoli computed for the specified age, height, gender, and race (tribe) may be different from the range established for subjects that possess such general characteristics within a group. The issues raised highlight the biological and investigative importance or usefulness of the alveoli. The direction of diffusion across barrier is made possible by partial pressure gradient between compartments [20].

“Lung diffusing capacity for carbon monoxide (DLCO) is a valuable clinical tool in the assessment of pulmonary diseases. It measures the ability of the lungs to transfer gas from the alveolar space to the red blood cells in the pulmonary vessels [21]. Measurement of DL is informative for pathophysiologic diagnoses of lung diseases and serial measurements are used to follow the course of disease [22]. It must be made clear that carbon (II) oxide, though, used in a safe way for pathophysiologic diagnoses of any lung, it is nevertheless, a deadly silent killer. Therefore, the practicable theoretical model

proposed in this research offers a very good alternative, being noninvasively applicable to the subjects in good and ill health.

With reference to pieces of information in the literature [23–27], Liu *et al* [11] observed that drops or aerosols have been delivered to the nasal cavity in the treatment of allergies and congestion; there is also interest in the possibility that vaccines, insulin, and other medications can be delivered to treat blood disorders, migraine headaches *etc*: The challenge however, is that pharmaceutical industries do not have standard nasal replicas in the face of individualised replicas that lack universality or generalisability. However, this challenge notwithstanding, there is a need to realise that transit into the alveoli provides the most effective way of delivering massively vaporised therapeutic agents into the blood stream, particularly at temperatures above body temperature; besides, breathing rate is higher during exercise and shortly after exercise coupled with associated rise in body temperature. So, for a subject undergoing treatment, and who is not physically fit, for any mild exercise, very warm therapeutics can be delivered into the blood stream via the alveoli. The broader distribution of air/O₂ laden therapeutics can easily be achieved at higher temperature as a result of increased thermal energy.

The importance of alveoli cannot be overemphasised. The exchange of gas between the alveoli and the pulmonary vasculature makes the alveoli the most important part of the pulmonary organ. This is against the backdrop of the need for respirators in this unfortunate era of covi-19 pandemic that has regrettably claimed human lives. The respiratory apparatus may be effective and efficient, but “the end may justify the means”. This means that, where the alveolar

dead space is significantly large, the gas (O_2) delivered across the alveolar-capillary wall barrier to the blood may be grossly insufficient to meet the great demand of the brain. Such may lead to neurologically based complication such as stroke. Equally disturbing is the racially based murders via asphyxiation. However, “the functional inhomogeneity of lungs, due to unequal distribution of ventilation, perfusion, and diffusing capacity to lung volume leading to local diversity of alveolar P_{CO_2} and P_o , is generally recognised to be one of the major obstacles to an accurate assessment of alveolar-capillary diffusion” [28]. This current mathematical approach may be a panacea to such challenge.

The advantage of current mathematical approach is not farfetched. The most important interest in this research is the possibility of creating a means of calculating the number of alveoli in healthy and unhealthy subjects. It is not unlikely that ill health characterised by respiratory disease as in the current pandemic occasioned by covid-19 may have created more alveolar dead space. This may not be too speculative; otherwise, the sophisticated state-of-the-art medical equipment available in highly advanced countries could have made substantial positive impact in drastically reducing fatalities. Information about the hike in the number of alveolar dead space should therefore, call for other medication methodology. A noninvasive computational approach as shown in this research offers such possibility. It is likely to be very fast given that with appropriate equipment without invasion one can measure respiratory rate and tidal volume for any subject. This should be an overwhelming advantage over other known methods. It is known that investigation of lung structure at the alveolar scale have been done using imaging techniques that include; optical coherence tomography (OPCT), confocal laser scanning microscopy (CLSM) and endoscopy microscopy during respiration [8–10]. The disadvantage of the techniques is that they have short penetrative depth even after invasive manoeuvres to bypass the skin. Endoscopy microscopy (EM) which is said to be relatively noninvasive as it places an endoscope in the pleura visceralis alters the intrapleural pressure, which artificially changes the alveolar morphology [11]. Still, EM is seen to be relatively noninvasive as it places an endoscope in the pleura viscera. The concern in this research is total noninvasive approach which has been demonstrated via computation based on derived equation. Support for noninvasiveness can be

found in the work of Leong *et al* [1] who applied a noninvasive phase contrast x-ray imaging technique to measure the size and population of alveoli *in situ*. A noninvasive method offers opportunity for the avoidance of tissue injury. Using the Euler characteristic with fractionators sampling is according to Hyde *et al* [7], very efficient and does not require knowledge of tissue shrinkage in the estimation of total alveolar number in the lung. Nonetheless, this technique can best be understood by specialist and after capacity building and needs cadaver. Death may result from the occurrence of dysfunctional alveoli despite life-supporting respirator in this era of global pandemic in particular. This raises the question as to whether or not covid-19 affects the structural and functional integrity of the alveoli considering the implication of a compromised function of the surfactant if available. Preservation of life should be the overriding goal in this era of global pandemic with urgency in the advancement of needed knowledge.

5. CONCLUSION

The mathematical equation for totally noninvasive determination by computation (calculation) is derivable and was derived. The total number of alveoli mobilised for function is a function of the width (d) of the nares ($d^{22/15}$), rate (R_v) of gas flow ($R_v^{3/5}$), and radius (r_{alv}) of a functional alveolus ($1/r_{alv}^2$). The equation has the potential to be of diagnostic, evaluative and prognostic value in medical practice. This new computational approach could be faster than other known approaches for the determination of the N_{alv} . A noninvasive approach by computation, relying on other noninvasively determined respiratory parameters, can eliminate the possibility of tissue damage. Feature research will attempt to determine the radius of alveoli for subjects from different nation and (sub) continents.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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