

A Mathematical Modelling Study of the Effects of Air Expansion Inside the Brain on the Intracranial Pressure

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ABSTRACT

Pneumocephalus is a collection of intracranial air in the cranial cavity. Its presence can cause complications during air travel or post-surgery, altering intracranial pressure (ICP). The study presents a revision of the model proposed by Anderson et al. [9]. The effects of pneumocephalus on ICP during air travel and post-surgery are poorly understood. The proposed model first considered the absolute intracranial air pressure to depend on atmospheric pressure and ICP. The effects of varying ascension rates (exponential and logarithmic) on ICP were then investigated. Finally, the temperature effect on ICP post-craniotomy was explored. The proposed model simulated a maximum of 31% increase in intracranial air volume. The exponential function displayed a similar trend for intracranial volume but the ICP raised by larger increments. The logarithmic function showed a rise in ICP before dropping towards resting ICP near the maximum altitude (8000 ft). The temperature effects showed an increase of 8 mm Hg in ICP for a 6.3% intracranial air expansion, taking 15 s. The proposed model represents more accurately the hydrodynamics of the intracranial system in the presence of pneumocephalus. The change in ICP was also found to be dependent on ascension rates and more so on rates of temperature change. The article provides findings of a revised model by Anderson [9], incorporating also the temperature effects on pneumocephalus and ICP.

NOMENCLATURE

α	Numerical constant
β	Numerical constant
C	Cerebral compliance
CSF	Cerebrospinal fluid
dH/dt	Rate of ascension
dT/dt	Rate of temperature change
H	Altitude
I_a	CSF absorption rate into venous blood
I_f	CSF production rate
I_{IA}	Intracranial air expansion rate
I_r	Flow of fluid remaining in system

I_{tot}	Total fluid flow rate in system
ICP, P_{IC}	Intracranial pressure
K	Mathematical constant
P_{atm}	Atmospheric pressure
P_{atm0}	Atmospheric pressure at sea level
P_d	Dural sinus pressure
P_{IA}	Absolute intracranial air pressure
P_{IA0}	Intracranial air pressure at sea level
P_{ICr}	Resting intracranial pressure
PVI	Pressure-volume index
R	Outflow resistance of system
t	Time taken
T	Body temperature
T_i	Initial body temperature
V_{IA}	Intracranial air volume
V_{IA0}	Initial intracranial air volume
V_{IC}	Total volume of system

1. INTRODUCTION

Craniotomy is a critical and complicated process that involves operating on the cranium. However meticulously performed, it may leave trace amounts of air in the skull. This phenomenon of intracranial gas collection was first coined by Wolff [1] as pneumocephalus. Pneumocephalus may be present anywhere within the skull depending on the procedure but is usually harmless and spontaneously absorbed [2]. Although it is not harmful, patients are advised not to travel by air for a certain period. The timescales advised though, vary among surgeons. Timescales range from less than 2 to more than 8 weeks [3]. In 85% of patients, intracranial air was absorbed within a week [4] but may be present 3 weeks post-operation [5].

Pneumocephalus is a benign complication that can produce a mass effect (tension pneumocephalus (TP)) on the brain should the rate of intracranial air accumulation continuously increase [6]. TP is caused by the expansion of intracranial air following a decrease in ambient atmospheric pressure during air travel. Gas trapped in body cavities will expand when ambient pressure drops [7]. Owing to the rigidity of the skull, intracranial air cannot expand readily. This limitation in air expansion will result

in the compression of one or more of the intracranial components, thus, increasing intracranial pressure (ICP).

Also, during craniotomy, a patient's body temperature is cooled for operation. The cold is used to suspend life, giving surgeons enough time to complete the operation [8]. Once the surgery is completed, the patient is warmed to normal body temperature ($\sim 37^\circ\text{C}$). This change in temperature will cause a change in intracranial air volume which will affect ICP to some extent. However, the effects of temperature on pneumocephalus and ICP is not well known. There is a lack of literature exploring these effects.

Several models for the hydrodynamic relationships of the intracranial system have been investigated and proposed [9,10,11,12]. Experimental studies use invasive techniques to monitor ICP. These techniques may themselves alter ICP. Mathematical models offer an alternative, non-invasive method to study ICP. However, the validity of some of these models are still questioned and modified in various aspects. There are limited studies investigating the relationship between ICP and pneumocephalus during air travel. The present study will propose a model adopted from Anderson [9]. This model [9] made several assumptions which brought into question the findings. The study will propose a revision of this model [9] and will hopefully give a better understanding of pneumocephalus and its effects on ICP during air travel and post-craniotomy.

2. LITERATURE REVIEW

Pneumocephalus is usually caused by trauma to the head. It may result from a loss of fluid or meningitis from gas forming organisms [6]. Nontraumatic pneumocephalus may also arise from barotrauma, extracranial infections or by performing the Valsalva manoeuvres [13]. From 1996-2016 only 8 clinical cases of pneumocephalus had been reported [14], portraying the rarity and limited knowledge of this pathogen. However, this phenomenon may possibly cause herniation of the brain.

Craniotomy is a process involving the surgical removal of a section of the skull to access the intracranial compartment. During this process, body temperature is cooled to $18\text{--}24^\circ\text{C}$ [8]. Once the neurosurgeon has repaired the damage, the bone flap is secured back in its initial

position on the skull with plates and screws, and the patient is warmed with blankets to $\sim 37^\circ\text{C}$. Neurosurgeons take extra care to not trap air while closing the cranial cavity. However, this process often leaves traces of trapped air in the cranium [15]. Clinical studies have confirmed the presence of intracranial air post-operation. There have also been several reported cases of the complication arising from intracranial air following air travel in even pilots and soldiers who are frequent flyers [16,17,18].

Below pressures of 1500 mm Hg (200 kPa), air can be treated as an ideal gas. As ambient atmospheric pressure decreases or ambient temperature increases, intracranial air volume will increase to maintain equilibrium. Following the Boyle-Mariotte's law for ideal gases ($P_1V_1=P_2V_2$), the trapped air is expected to expand to increase in volume and compensate for the fall in pressure. Likewise, according to Charles' law for ideal gases ($V_1/T_1=V_2/T_2$), temperature and volume are directly proportional [19]. However, due to the skull rigidity, the trapped air cannot readily expand, and thus, compresses the brain, raising ICP.

Pneumocephalus and its effects on the intracranial system are poorly understood. This field lacks sufficient research and evidence. This information is useful to neurosurgeons and responders to medical air evacuation. Standard procedures have been modified and updated following published medical literature. Several authors have pointed out the paucity in the field [3,20]. There has also been much controversy from the multiple published studies. In a simulated study by Peterson [21] it was found that altitude alone had little effect on ICP which contradicts findings of other authors [22,23]. In a study by Donovan [24], pneumocephalus was not found to cause any contraindication during air travel, contrary to the findings of Reasoner [5] and Anderson [9].

From the lack of evidence and contradiction of multiple studies, there is much controversy on the effects of pneumocephalus on ICP. It also known that volume, pressure and temperature are inter-dependent. As far as this paper is concerned, no research has investigated temperature effects on pneumocephalus and ICP. The proposed model will be designed to help shed some light on the contradictions and fill the porosity in the literature.

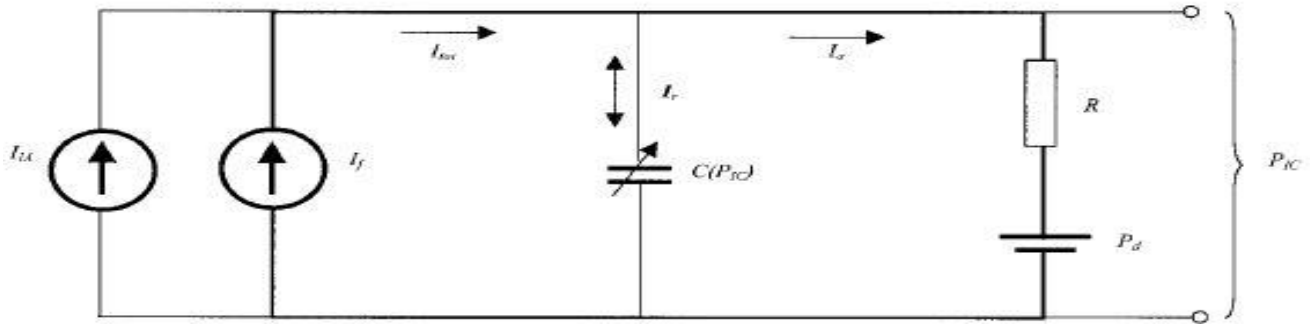


Figure 1: The analogous electrical system proposed by Anderson [9] which was an extension of that by Marmarou [10]

3. METHODOLOGY

3.1 Mathematical Formulation of System

The schematics of the model proposed is shown in Figure 1. The system consists of the cerebrospinal fluid (CSF), blood volume and tissue, and the intracranial air. A state of hydrodynamic equilibrium is always assumed. The total inflow/expansion of the system (I_{tot}) is given by the sum of CSF formation (I_f) and expansion of intracranial air (I_{IA}). The model assumed the rates of re-absorption of air and fluid accumulation due to tissue swelling, to be negligible compared to I_f and I_{IA} . The outflow resistance R and dural sinus pressure P_d will influence the change in I_a , the CSF absorption rate into the venous blood.

$$I_{tot} = I_{IA} + I_f = I_a + I_r \quad (1)$$

$$I_a = \frac{P_{IC} - P_d}{R} \quad (2)$$

Compliance, C is defined as the ratio of change in brain blood volume to change in brain tissue pressure [10].

$$C = \frac{dV_{IC}}{dP_{IC}} \quad (3)$$

Another mathematical expression to determine compliance is the Pressure Volume Index (PVI). PVI is clinically defined as the volume of fluid (in millimetres) needed to raise the ICP ten-fold [26].

$$PVI = \frac{P_{IC}}{0.4343} C \quad (4)$$

Marmarou [10] found that due to the exponential nature of the volume-pressure relationship, the compliance will decrease as ICP increases and can be expressed by:

$$C = \frac{1}{KP_{IC}} \quad (5)$$

where K is a mathematical constant given by $K = 1/(0.4343PVI)$. Combining Equations (3) and (5) will yield an expression for the system's rate of pressure change:

$$\frac{dP_{IC}}{dt} = \frac{dP_{IC}}{dV_{IC}} \frac{dV_{IC}}{dt} = KP_{IC} \frac{dV_{IC}}{dt} \quad (6)$$

The model considered the volume variation to occur only in the CSF, i.e., blood volume remains constant, then dV_{IC}/t is represented by I_r . With this assumption, and Equations (1) and (6), the rate of pressure change is:

$$\frac{dP_{IC}}{dt} = KP_{IC}I_r = KP_{IC}(I_{tot} - I_a) \quad (7)$$

When the rates of formation and absorption of CSF are in equilibrium, the system is in steady state. The pressure difference is dependent on I_f and R . P_d is thus, thought to regulate the steady state ICP (P_{ICr}), on the ground at equilibrium ($P_{ICr} = P_d + I_f R$). I_f , R , and P_d can be assumed to be independent of ICP within the interesting pressure range and so were approximated as constants in the model [27]. From this relationship and Equation (2), Equation (7) can be rearranged to set up the following differential equation:

$$\frac{dP_{IC}}{dt} = \frac{KP_{IC}}{R} \left(R \frac{dV_{IA}}{dt} + P_{ICr} - P_{IC} \right) \quad (8)$$

In Anderson's model [9], a linear approximation was used to solve Equation (8). In this study, this equation was solved

numerically in MATLAB using the ode45 solver.

3.2 Intracranial Air Expansion

3.2.1 Pressure Relationship

The expression found for V_{IA} makes use of the Boyle-Mariotte's law, since the intracranial air can be treated as an ideal gas. The intracranial air pressure was found to vary with atmospheric pressure and ICP, and thus, derived the following expression using the hydrostatic equation for the standard atmosphere [9]:

$$P_{IA}(t) = P_{atm} + P_{IC} = P_{atm_0} \left(1 - \alpha \frac{dH}{dt} t \right)^\beta + P_{IC}(t) \quad (9)$$

$$V_{IA}(t) = \frac{V_{IA_0} P_{IA_0}}{P_{IA}(t)} \quad (10)$$

where P_{atm_0} is the atmospheric pressure at sea level, $\alpha = 2257 \times 10^{-8}$ and $\beta = 5.264$ are numerical constants, dH/dt is the constant or varying rate of ascension, t is the time travelled, V_{IA_0} is the initial intracranial air volume present and P_{IA_0} is the initial absolute pressure, approximated by P_{atm_0} . Combining Equations (9) and (10) will yield an expression for intracranial air volume as a function of time in terms of ICP and rate of altitude change. This expression is differentiated and inserted in Equation (8) which is solved in MATLAB.

3.2.2 Temperature Relationship

Following Charles' law, a relationship between the body temperature and intracranial air volume can be found. It was assumed that the intracranial air is isolated from the ambient and so is dependent only on body temperature.

$$V_{IA}(t) = \frac{V_{IA_0}}{T_i} T(t) \quad (11)$$

$$\frac{dV_{IA}}{dt} = \frac{V_{IA_0}}{T_i} \frac{dT}{dt} \quad (12)$$

where T_i is the initial body temperature after surgery and T is the change in body temperature as a function of time. dT/dt is the rate of change of temperature to reach 37 °C. Equation (12) is inserted in Equation (8) and the expression is solved in MATLAB.

3.3 Parameter Selection

The parameters used in the model are shown in Table 1. All ICP simulations were done for 10 mm Hg (normal P_{ICr}) and 20 mm Hg (high P_{ICr}). The worst-case scenarios were chosen and so PVI was assumed to be 12.6 ml and 16.1 mm Hg·ml⁻¹·min⁻¹ for R . The amount of intracranial air present was estimated at volumes 10, 20 and 30 ml to cover a considerable scope. To study the effect of dH/dt , constant ascension rates of 250, 500 and 1000 ft·min⁻¹ were assumed. For varying ascension rates, two additional cases were analyzed: a logarithmic change in altitude:

$$H = X \ln(t + 1) \quad (13)$$

and an exponential change in altitude:

$$H = Y e^{(Zt-1)} \quad (14)$$

where X , Y and Z are numerical constants that were found. H is the change in altitude. The model simulated results

until a maximum altitude of 8000 ft for all dH/dt . X , Y and Z were estimated to take the same amount of time as dH/dt as shown in Figure 2. T_i based on literature ranged from 18-24 °C. dT/dt was found by evaluating the slope to reach 37 °C (Figure 3).

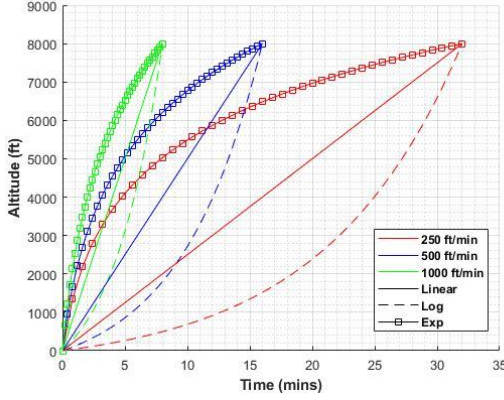


Figure 2: Linear, logarithmic and exponential functions of altitude with time

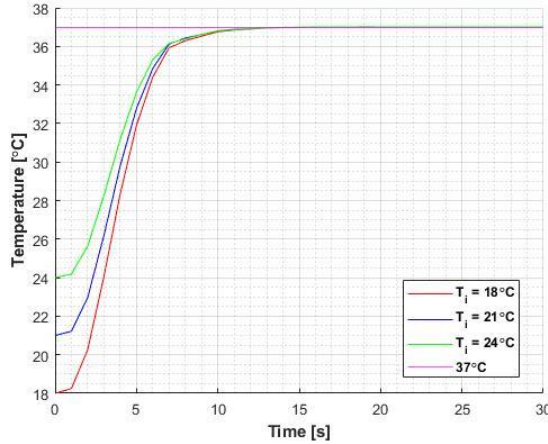


Figure 3: Change in body temperature with time for three initial temperatures and 30 ml initial intracranial volume

Table 1: Parameter Selection for Model

Parameter	Value
P_{ICr}	10 and 20 mm Hg
PVI	12.6 ml
R	16.1 mm Hg·ml ⁻¹ ·min ⁻¹
V_{IA0}	10, 20 and 30 ml
dH/dt	250, 500 and 1000 ft·min ⁻¹
T_i	18, 21 and 24 °C
dT/dt^*	2.99 ± 0.4 , 1.95 ± 0.3 and 1.05 ± 0.2 K·s ⁻¹
X	2288, 2824 and 3641
Y	141.49, 223.04 and 375.23
Z	0.0015, 0.0026 and 0.0042

*Temperature change depends on initial air volumes (found using COMSOL Multiphysics Simulation Software) [25]

4. RESULTS

4.1 Change in Ambient Pressure

4.1.1 Constant Ascension Rate

The results were simulated in MATLAB to study the effects of altitude on intracranial air volume (Figure 4) and ICP (Figure 5). In Anderson's model [9], intracranial volume increased by almost 35% whereas in the proposed model it was found to increase by 31%.

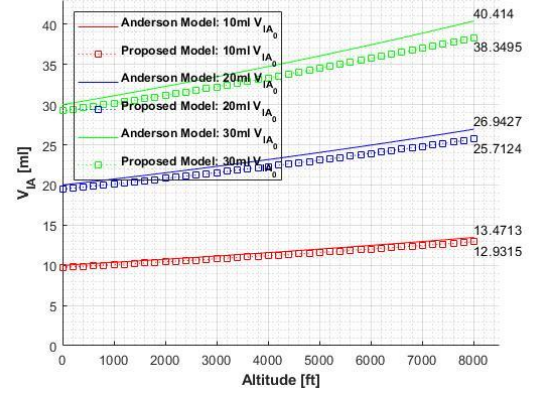


Figure 4: Change in intracranial volume during ascent at 500 ft·min⁻¹, simulated for three initial volumes

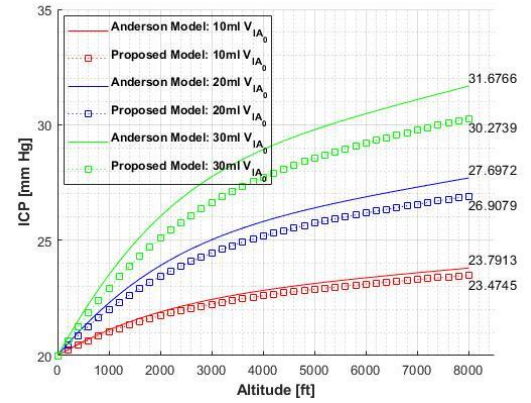


Figure 5: Change in ICP during ascent at 500 ft·min⁻¹ simulated for three initial volumes and 20 mm Hg P_{ICr}

4.1.2 Varying Ascension Rate

Equations (8) and (14), and parameters from Table 1 were used to simulate the results presented in Figure 6 and Figure 7. Anderson's model [9] still predicts an increase of 35% in intracranial volume. The proposed model simulated an increase of nearly 30% in intracranial volume.

Equations (8) and (13) were used to simulate the change in intracranial volume (Figure 8) and change in ICP (Figure 9) during a logarithmic ascension. In Anderson's model [9], intracranial volume increased by 4.5% compared to a 1.5% increase in the proposed model. It was also found that after around 3000 ft, ICP decreased to the P_{ICr}

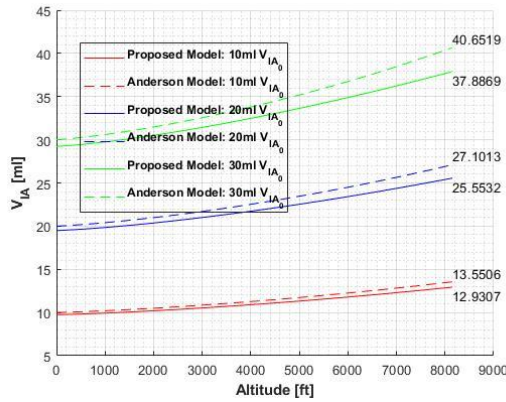


Figure 6: Change in intracranial volume during exponential ascension simulated with three initial volumes

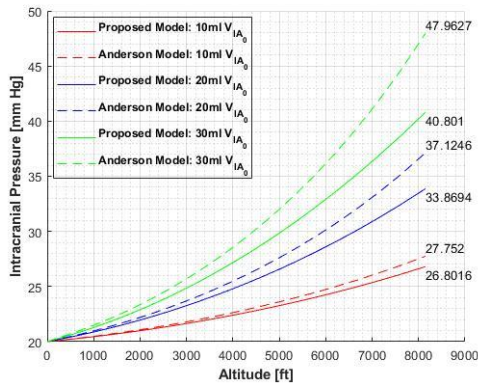


Figure 7: Change in ICP during exponential ascension simulated with three initial volumes and 20 mm Hg P_{ICr}

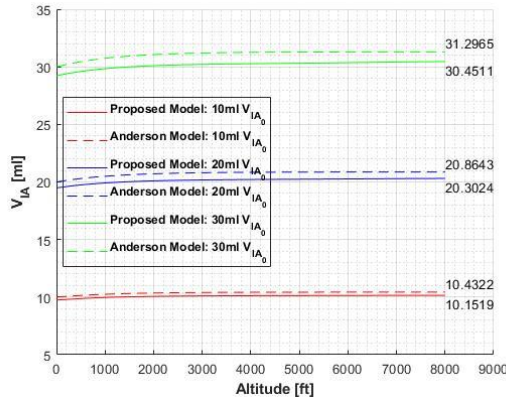


Figure 8: Change in intracranial volume during logarithmic ascension simulated with three initial volumes

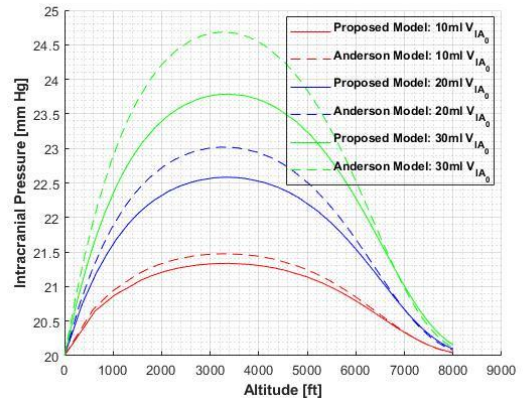


Figure 9: Change in ICP during logarithmic ascension with three initial volumes and 20 mm Hg P_{ICr}

4.3 Change in Ambient Temperature

Equations (8) and (12) and parameters from Table 1 were used to simulate the temperature effect on intracranial volume (Figure 10) and ICP (Figure 11). The model simulated an increase of 6.3% in intracranial volume which corresponded to a rise of roughly 8 mm Hg in ICP when 30 ml intracranial air was initially present.

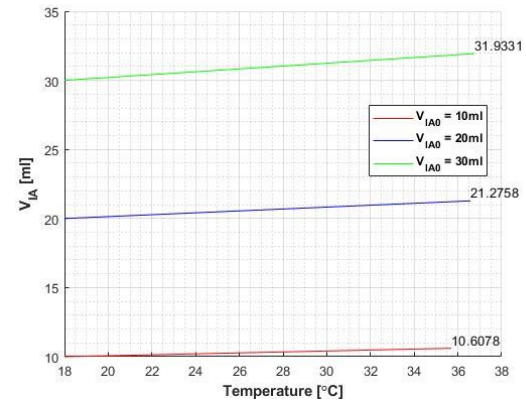


Figure 10: Change in intracranial volume with change in temperature simulated with three initial volumes

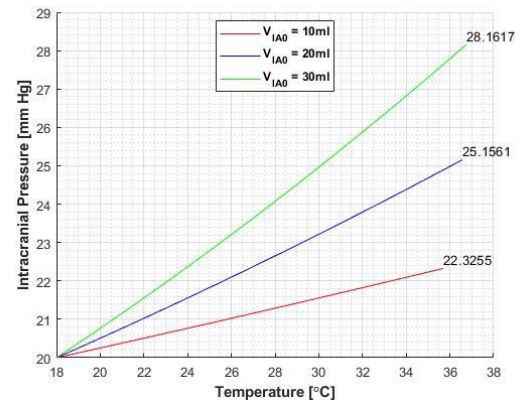


Figure 11: Change in ICP with temperature simulated with three initial volumes, 20 mm Hg P_{ICr} and 18 °C T_i

5. DISCUSSION

Prior to 2003, no mathematical study concerning the effects of altitude on ICP in the presence of pneumocephalus had been conducted [9]. A study on the influence of intraocular gas on the intraocular pressure found that the presence of gas increased intraocular pressure as ambient pressure reduced [28]. The fluid mechanics of the eye and brain are similar and so can be hydrodynamically characterized by the outflow resistance, formation rate, and compliance. This supports the findings of the calculations [9].

For pressures below 1500 mm Hg (200 kPa), air can be treated as an ideal gas [19]. The Boyle-Mariotte's law can be used to characterize the volume expansion during air travel and Charles' law for the volume expansion post-craniotomy. Since the location of intracranial air depends on the patient's position and no large pressure gradients are expected in the brain, intracranial air will expand similarly irrespective of its geometry and location [9].

From Equations (9) and (10), $V_{IA}(t)$ clearly depends on dH/dt and Equations (9) and (11) show $V_{IA}(t)$ dependence on $T(t)$. The hydrodynamic system works in such a way that the timeframe for spatial compensation depends on the rate of change of ambient pressure or temperature [29]. Also, cerebral perfusion pressure (CPP) was only considered for the temperature effect despite findings that compliance (used to regulate ICP) is dependent on CPP [30].

For the simulations conducted by Anderson [9], it was assumed that because P_{atm} ranged between 75-100 kPa and P_{IC} fell between 1-3 kPa, Equation (9) could be approximated to $P_{IA}=P_{atm}$. In the proposed model, Equation (9) was used in the simulation for ICP. There was up to a 4% difference in intracranial air volume between the proposed model and Anderson's model [9]. The final ICP was also found to differ by up to 6% between the models.

Although extreme changes like rapid compression and decompression rates were not accounted for, this paper reports the findings of the effects of an accelerating and decelerating dH/dt on ICP (Figure 7 & Figure 9). The exponential increase in ICP regarding the exponential rate of climb was of no surprise owing to the nature of Equation (14). The reason for the decrease in ICP using the logarithmic Equation (13) is again due to the nature of the expression. The slope is always decreasing, and so, until the maximum altitude of 8000 ft is reached, ICP has time to decrease to P_{ICr} [29,31]. From Equation (8), the dV_{IA}/dt term is causing an increase in dP_{IC}/dt until 3000 ft, after which the $-P_{IC}$ term becomes more significant. Thus, with a logarithmic ascension the ICP drops back towards P_{ICr} after 3000 ft.

It was found that for the worst-case scenario for the warming process of patients post-craniotomy was for 18 °C T_i , 30 ml V_{IA0} and 20 mm Hg P_{ICr} . From Figure 10, intracranial air increased by 6.3% compared to Figure 4 or Figure 6 where it expanded by almost 35% in size. The

temperature response of pneumocephalus caused ICP to raise by 8 mm Hg whereas with the exponential ascension ICP increased by 20.80 mm Hg and 10.27 mm Hg for a constant 500 ft·min⁻¹ dH/dt . It has been established through invasive studies, that a relationship exists between temperature (governed by metabolic heat generation and blood flow through capillaries) and brain activity [32]. The findings suggest that temperature has a greater impact than pressure on ICP. However, it should be noted that the ambient pressure change took 16 mins for 500 ft·min⁻¹ whereas the temperature change from 18-37 °C for 30 ml V_{IA0} (worst-case scenario) was 15 s, compared to 5-6 and 8 s for 10 and 20 ml V_{IA0} respectively.

The results of this study show that the important factors influencing ICP are initial intracranial air volume and initial temperature. The change becomes more significant with higher initial volumes and lower initial temperature. This difference was also more significant when higher initial volumes were used to compare the proposed model with Anderson's model [9].

6. CONCLUSION

The present study provides a revision to the model proposed by Anderson [9]. The proposed model did not make the same assumption regarding absolute intracranial pressure as Anderson [9]. It was found that there was a difference between the two models, which became more significant with increasing initial intracranial air volumes. The effects of temperature post-craniotomy on pneumocephalus and ICP are also presented in this paper. The model's behavior agrees with physical expectations and the simulated results shows the dependence of ICP on dH/dt and even more so on dT/dt . ICP can reach high levels for high initial volumes, high P_{ICr} and low initial temperatures. The model should be further examined to provide more useful information to neurosurgeons and air ambulances to avoid serious complications.

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