# Modelling and Control of Nitrogen Partial Pressure for Prophylaxis and Treatment of Air Embolism

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***Abstract*— This article describes a model for the absorption of a cerebral gas embolism. It is also shown that by controlling the ambient pressure and partial pressure of nitrogen, an air embolism can be absorbed at an accelerated rate. At ambient pressure, a breathing gas of 100% Oxygen will triple the rate of absorption. With an ambient pressure of 6 atmospheres, a 1-mm bubble is eliminated in 10 minutes instead of 12 hours.**

## I. INTRODUCTION

In Australia and Internationally, stroke is a leading cause of death and major disability. In 2010, stroke resulted in 8,300 deaths in Australia [1]. Of the 375,800 people that survived a stroke, 35 were left with a permanent disability [1]. Due to the the nature of stroke disabilities, 75,000 primary carers were required to provide assistance for stroke survivors. More than half of primary carers spend 40 hours or more each week in their caring role [1]. The total cost to Australia has been estimated at 367 Millon dollars a year [2].

In the last two decades, advances in neurovascular intervention have provided a number of effective interventions for the causes and consequences of stroke [3]. In particular, these interventions have dramatically reduced the risk of disability [3]. Despite the benefits, neurovascular intervention is associated with a number of risks and adverse outcomes [4]. Typically neurovascular intervention requires the entry of a system of tubes into an artery located in the groin. Due to complexity at the entry point, there is a non-zero risk of introducing an air bubble into the tube system. This bubble can be flushed into the brain resulting in an air embolism and stroke, which is uncommon, but has major consequences including disability or death [5].

Cardiac surgery can also result in microscopic cerebral arterial air embolisms and treatment plans have been developed. These treatment plans typically consist of hyperbaric oxygen therapy [6]. Hyperbaric oxygen therapy is commonly used to treat decompression sickness, which also involves the introduction and absorption of bubbles. To avoid oxygen toxicity at partial pressures above 1.6 atm, a helium-oxygen mix (heliox) can be employed [7].

In order to explore hyperbaric treatment plans in a safe environment, computer simulations have been preformed [8]. These simulations were based on the work of Hlastala and Van Liew investigating the absorption of *in vivo* gas bubbles in deep sea divers [9].

Throughout a stroke intervention, real-time x-ray imaging and intermittent computed tomography scans are used for guiding the tube system. These imaging modalities can also detect the formation of a bubble within the tube system. If detected, the tubes are immediately removed and the procedure is restarted. However, if the bubble is released and results in an embolism, x-ray imaging can determine the size of the embolism, which is critical for treatment planning and prognosis. As shown in Figure 1, this process can be viewed as a control loop where x-ray imaging provides feedback for a computer model which controls the ambient pressure and partial pressure of nitrogen.

## II. COMPUTER MODEL

In order to determine a treatment plan, the absorption mechanics of the embolism must be understood. The foundations for this analysis have been laid in previous work. For example, Hlastala and Van

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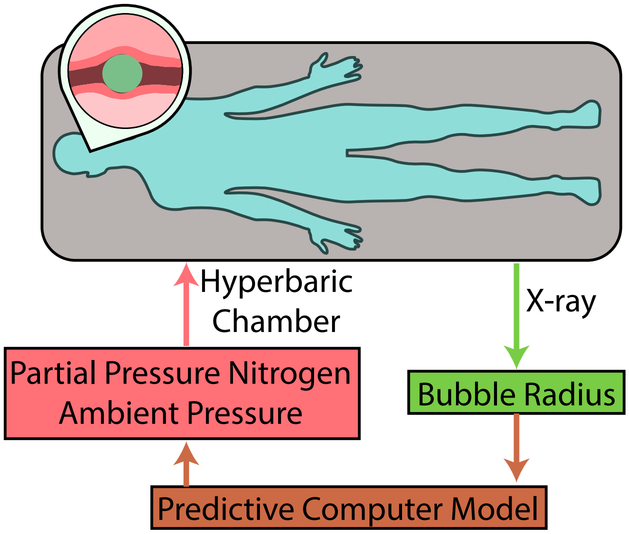


Fig. 1. Hyperbaric gas embolism treatment by controlling Nitrogen concentration and ambient pressure.

Liew developed a model to investigate the absorption of *in vivo* inert gas bubbles in deep sea divers [9]. Dexter, Bradley and Hindman later applied this work to cerebral arterial air embolisms as a result of complications of cardiac surgery [10]. Both of these studies investigated oxygen therapy to reduce the life time of air bubbles. The conclusions were that oxygen therapy can reduce the bubble life time by approximately two-thirds. These studies relied on solving equation 1, which describes the rate of change in the bubble radius. The derivation of equation 1 can be found in [9].

$$\frac{\mathrm{dR}}{\mathrm{dt}} = -\alpha_{\mathrm{t}}\mathrm{D}\mathrm{P}_{\mathrm{B}}\Big(1 - \frac{\mathrm{P_a}}{\mathrm{P_g}}\Big) \Big(\frac{1}{\mathrm{R}} + \frac{2\lambda}{\sqrt{\pi}}\int_0^{\lambda\sqrt{Dt}} \mathrm{e}^{-\mathrm{s}^2}\mathrm{ds} + \frac{\mathrm{e}^{-\lambda^2\mathrm{Dt}}}{\sqrt{\pi Dt}}\Big) \quad (1)$$

where

$$\lambda = \Big(\frac{\alpha_{\mathrm{b}}\mathrm{kQ}}{\alpha_{\mathrm{t}}\mathrm{D}}\Big)^{\frac{1}{2}} \quad (2)$$

In these equations, dR/dt is the rate of change (cm/s), $\alpha_{\mathrm{b}}$, $\alpha_{\mathrm{t}}$ are the solubilities of gas in blood and tissue respectively, D is the diffusivity of gas in tissue, $\mathrm{P_a}$ is the partial pressure of inert gas in the incoming arterial blood, $\mathrm{P_g}$ is the partial pressure of inert gas in the bubble, $\mathrm{P_B}$ is the absolute gas pressure surrounding the body and the product (kQ) is effective blood perfusion.

Equation 1 indicates that the dissolution rate (dR/dt) is dependent on the ratio of partial pressure of inert gas in the blood to the partial pressure of inert gas in the bubble. In this investigation it was assumed that the bubble consisted of only nitrogen, as equilibrium of metabolic gases ($O_2$ and $CO_2$) between the bubble and surrounding tissue occurs in only a few seconds [11]. Thus, the dissolution rate of the bubble can be increased by reducing the partial pressure of nitrogen in the surrounding tissue, which can be achieved by replacing the breathing gas of the patient with a nitrogen free gas mix.

Equation 1 also indicates that the dissolution rate is dependent on the absolute gas pressure surrounding the body, which can be increased in a hyperbaric chamber. In addition, increasing the pressure also result in an initial reduction of the volume due to the ideal gas law, shown below.

$$\mathrm{P_1V_1 = P_2V_2} \text{ assuming isothermal conditions} \quad (3)$$

This volume reduction will also increase the dissolution rate as this is proportional to the inverse of the bubble's radius. Equation 1 coupled with the ideal gas laws was solved computationally. Various treatment plans were tested for a for a variety of initial embolism radii.

## III. Results

Initially, three initial bubble radii were considered, 100 $\mu$m, 250 $\mu$m and 500 $\mu$m. The treatment plans included: 1) patient breathing room air, 2) patient breathing pure oxygen at ambient pressure, and 3) patient breathing a nitrogen free gas mix at 3 atm pressure. As shown in Figure 2, by removing the nitrogen from the patients tissue, the dissolution time is decreased by a factor of three, which is in agreement with [9], [10]. It also indicates that if the absolute gas pressure surrounding the body is increased to 3 atm the dissolution time is decreased by a factor of approximately 20.

As the key parameter for patient outcome is dissolution time, the next study focused on varying the absolute gas pressure surrounding the body and the initial bubble radius, then calculating the dissolution time. For this study, air and a nitrogen free mixture were used for breathing gas. Figure 3 and 4

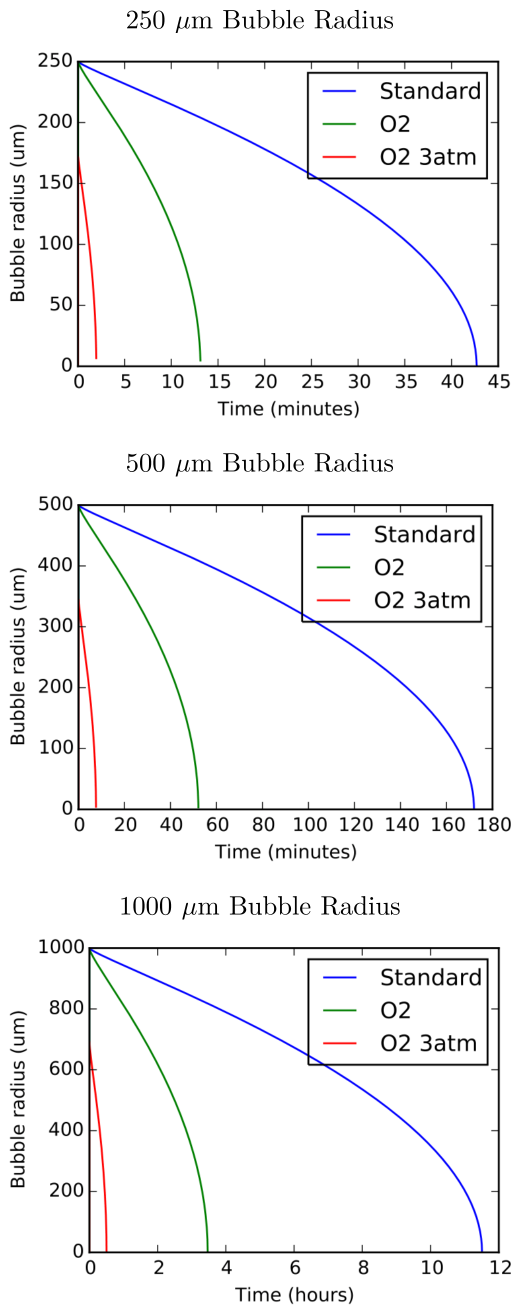


Fig. 2. Bubble radius versus time when breating air, 100% oxygen, and 0% nitrogen mix at 3 atm pressure.

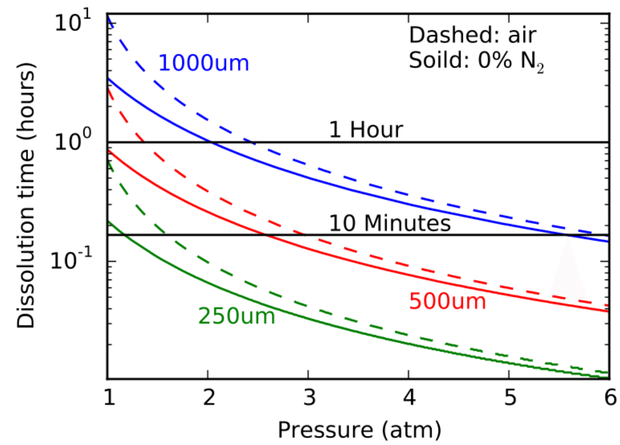


Fig. 3. Dissolution time versus pressure, for an initial bubble radius of 250 $\mu$m, 500 $\mu$m and 1000 $\mu$m.

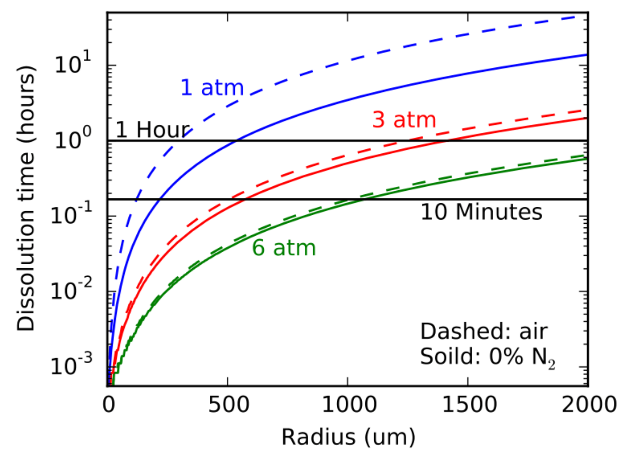


Fig. 4. Dissolution time versus the initial bubble radius, for an ambient pressure of 1 atm, 3 atm and 6 atm.

shows that increased ambient pressure dramatically deceases the dissolution time. For example, the dissolution time of a 1000-um bubble is reduced from 12 hours to under 10 minutes when the ambient pressure is increased to 6 atm.

A preliminary treatment aid in the form of a contour plot is shown in Figure 5. If the initial bubble radius is known, the required pressure to remove the bubble within a given time can be determined. For example, a 500-um bubble would require a pressure of at least 2.5 atm to remove the bubble within 10 minutes. However a more robust approach is to view the treatment plan as a slow control loop, as shown in Figure 1. Once a embolism is detected, the radius determines the required pressure of the hyperbaric chamber and recovery time.

Control over the partial pressure of nitrogen is obtained by changing the respiration gas mixture. However, the partial pressure of nitrogen in the body can only be estimated. Currently this estimation is simply the partial pressure of the respiration

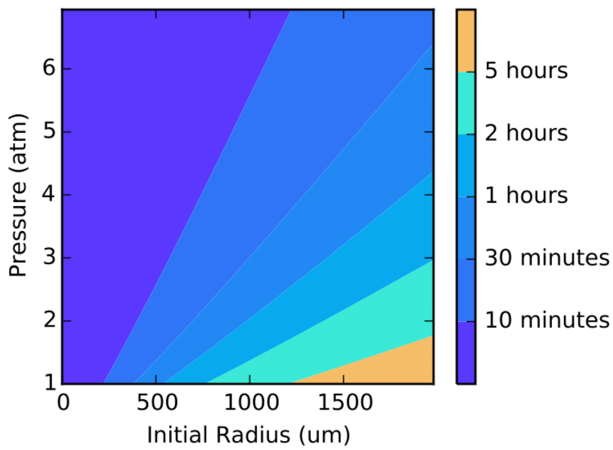


Fig. 5. Dissolution window, indicates what pressure is required to dissolve a bubble within a desired time window.

gas mixture. A far more robust estimation can be obtained by implementing the Varying Permeability Model (VPM) [12]. VPM is used by deep sea divers to calculate safe decompression plans. This would allow the control loop to be optimised for safe compression and decompression. However this has yet to be integrated into the current computer model.

## IV. CONCLUSIONS

A computer is described for predicting the absorption time of a cerebral air embolism as a function of initial radius, breathing gas, and ambient pressure. By using a breathing gas of 100% oxygen at atmospheric pressure, the rate of absorption is increased by a factor of three. The rate of absorption can be increased to twenty times by increasing the ambient pressure to three atmospheres, which is equivalent to a depth of 20 meters.

In future work, the partial pressure of physiological nitrogen will be modelled more accurately by combining the present work with a varying-permeability model (VPM). This will also allows the planning for safe decompression.

## References

[1] "Stroke and its management in Australia: an update (AIHW)." [Online]. Available: http://www.aihw.gov.au/publication-detail/?id=60129543613

[2] H. M. Dewey, A. G. Thrift, C. Mihalopoulos, R. Carter, R. A. L. Macdonell, J. J. McNeil, and G. A. Donnan, "Cost of Stroke in Australia From a Societal Perspective Results From the North East Melbourne Stroke Incidence Study (NEMESIS)," *Stroke*, vol. 32, no. 10, pp. 2409–2416, Oct. 2001. [Online]. Available: http://stroke.ahajournals.org/content/32/10/2409

[3] A. Cruz Culebras, A. Garcia-Pastor, G. Reig, B. Fuentes, P. Simal, J. C. Mendez-Cendnn, J. L. Caniego, E. Castro, R. Frutos, A. Gil, J. Vivancos, A. Gil-Nunez, E. Diez-Tejedor, J. A. Egido, M. Alonso de Lecimana, and J. Masjuan, "[Neurovascular intervention in the acute phase of cerebral infarction]," *Neurologia (Barcelona, Spain)*, vol. 25, no. 5, pp. 279–286, Jun. 2010.

[4] M. F. Lawson, G. J. Velat, K. M. Fargen, J. Mocco, and B. L. Hoh, "Interventional neurovascular disease: avoidance and management of complications and review of the current literature." *Journal of neurosurgical sciences*, vol. 55, no. 3, pp. 233–242, Sep. 2011. [Online]. Available: http://europepmc.org/abstract/med/21968586

[5] H. Sakai, N. Sakai, T. Higashi, K. Iihara, J. Takahashi, S. Kogure, R. Anei, N. Yamada, S. Imakita, and I. Nagata, "Embolic complications associated with neurovascular intervention: prospective evaluation by use of diffusion-weighted MR imaging," *No Shinkei Geka. Neurological Surgery*, vol. 30, no. 1, pp. 43–49, 2002.

[6] A. Ziser, Y. Adir, H. Lavon, and A. Shupak, "Hyperbaric oxygen therapy for massive arterial air embolism during cardiac operations," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 117, no. 4, pp. 818–821, Apr. 1999.

[7] O. Hyldegaard and J. Madsen, "Influence of heliox, oxygen, and n2-o2 breathing on n2 bubbles in adipose tissue." *Undersea biomedical research*, vol. 16, no. 3, pp. 185–193, 1989. [Online]. Available: http://europepmc.org/abstract/med/2741253

[8] A. B. Branger, C. J. Lambertsen, and D. M. Eckmann, "Cerebral gas embolism absorption during hyperbaric therapy: theory," *Journal of Applied Physiology (Bethesda, Md.: 1985)*, vol. 90, no. 2, pp. 593–600, Feb. 2001.

[9] M. P. Hlastala and H. D. Van Liew, "Absorption of in vivo inert gas bubbles," *Respiration Physiology*, vol. 24, no. 2, pp. 147–158, 1975.

[10] F. Dexter and B. J. Hindman, "Recommendations for hyperbaric oxygen therapy of cerebral air embolism based on a mathematical model of bubble absorption," *Anesthesia and Analgesia*, vol. 84, no. 6, pp. 1203–1207, Jun. 1997.

[11] H. C. Agrawal, J. M. Davis, and W. A. Himwich, "Water content of dog brain parts in relation to maturation of the brain," *The American Journal of Physiology*, vol. 215, no. 4, pp. 846–848, Oct. 1968.

[12] D. E. Yount and D. C. Hoffman, "On the use of a bubble formation model to calculate diving tables," *Aviation, Space, and Environmental Medicine*, vol. 57, no. 2, pp. 149–156, Feb. 1986.