Physical and Computational Modeling of Ventilation of the Maxillary Sinus

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Abstract

Objective. Sinus ventilation is often associated with sinusitis, a common condition causing significant pain and reduced quality of life. Clinical implications of the diverse anatomy of ostia connecting sinus to nose and the efficacy of surgical intervention in chronic sinusitis are poorly understood. This study aimed to measure sinus ventilation and explore variables in physical and mathematical models.

Study Design. \(^{81m}\text{Kr}\)-scintigraphy of krypton \(^{81m}\text{Kr}\) was carried out in a stylized physical model of a human maxillary sinus. Computational simulations matched this model for validation and extrapolated to combinations of variables not possible experimentally for evaluation of transport mechanisms.

Setting. Research laboratory in Department of Aeronautics, Imperial College London, and Department of Nuclear Medicine, Hammersmith Hospital, London.

Methods. \(^{81m}\text{Kr}\) distribution was measured with both single- and double-ostia sinuses. Computational simulations matched and extended the physical measurements and enabled separate identification and evaluation of transport mechanisms.

Results. The presence of an additional ostium resulted in a 50-fold increase in the effective volume flow rate of gas replacement in the sinus. In the case of a single ostium, doubling the ostial diameter doubled the effective volume flow rate of gas exchange.

Conclusion. \(\gamma\)-Scintigraphy of \(^{81m}\text{Kr}\) enables quantitative assessment of effective volume flow rate in physical model sinuses. These flow rates obtained experimentally for single- and double-ostium sinuses match the computational predictions of matching geometries. The increased ventilation seen with an additional ostium or increased ostial diameters may not be clinically beneficial, because it could reduce nitric oxide concentration in the sinus.

Keywords

krypton, \(\gamma\)-scintigraphy, sinus ventilation, maxillary sinus, nitric oxide

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Rhinosinusitis is a common condition affecting \(\sim15\%\) of the population and is a major reason for medical consultation worldwide.\textsuperscript{1} It is ranked in the top 10 most expensive diagnoses because of medical costs and reduced productivity.\textsuperscript{2} Despite the huge health impact of sinusitis, the causes are not well understood. Important factors in the pathogenesis of sinusitis are reduced sinus ventilation and impaired mucociliary transport.\textsuperscript{3}

Improved sinus ventilation is often a goal of clinical interventions; however, the links among sinus geometry, ventilation, and clinical outcomes are still poorly understood. The physiological value of sinus ventilation, except in adjusting to significant external pressure variations (such as deep-sea diving or moving to high altitudes), is also unclear, as the nasal mucosa has a rich blood supply\textsuperscript{4} and should not need supplementary gas exchange directly from the air. However, low levels of sinus ventilation and the
resulting reduced sinus oxygen concentration have been shown to decrease nitric oxide production \(^5\)\(^6\) and impair mucociliary transport. \(^7\) An improved insight into normal sinus function is critical to furthering our understanding of the pathophysiologic processes that mediate sinus disease.

Sinus gas transport has previously been investigated both in vivo and in vitro. Early experiments were carried out by Aust and Drettner, \(^8\) who investigated the recovery of oxygen concentration in sinuses where air had been replaced by pure nitrogen. Two isotopes of xenon have also been used in conjunction with imaging: xenon 133 is a \(\beta\)- and \(\gamma\)-emitter that can be detected by single photon emission computed tomography (SPECT) cameras, used, for example, by Zippel and Streckenbach \(^9\) and Paulsson et al. \(^10\)\(^11\) whereas xenon 129 is radiodense rather than radioactive and has been used with computed tomography (CT) imaging, for example, by Leopold et al. \(^12\) and Marcucci et al. \(^13\) Recently, Möller et al. \(^14\) used krypton 81m \((^{81m}\text{Kr})\) to image human sinuses and investigate the effects of pulsating airflow but did not quantify the ventilation of the sinuses under normal breathing conditions. No experimental investigations of the effects of the existence of an additional ostium on ventilation are known.

An additional ostium can occur due to either a natural accessory ostium or surgical antrostomy, for example, an inferior meatal antrostomy. The proportion of the population who have accessory ostia is controversial, with rates between 5% and 44% reported in the literature. \(^15\)\(^16\)\(^17\)\(^18\) Measurements of ostial size and the presence of accessory ostia are hampered by the inaccessibility and complex geometry of the sinuses, and as a result many studies have been performed in cadavers where the thin fontanelle membranes (in which the majority of accessory ostia are found) could easily be damaged when drying out. \(^19\) A relationship between rhinosinusitis and the presence of accessory ostia has been reported in the literature but the causal link is unclear. It has been proposed that infections may damage the fontanelle membranes and create accessory ostia \(^20\) and that accessory ostia disrupt mucociliary clearance pathways and result in sinusitis. \(^21\) Inferior meatal antrostomies were designed to aerate the maxillary antrum and drain the sinus by gravity; however, we know that dependent drainage does not occur as the cilia continue to transport secretions to the natural ostium. \(^22\) Inferior meatal antrostomies have now been largely abandoned given the low rate of long-term patency and high rate of failure. \(^23\)

\(^{81m}\text{Kr}\) is a \(\gamma\)-emitter with a half-life of 13 seconds that is currently used clinically in ventilation–perfusion imaging of the lungs. \(^24\) The short half-life means that little time is needed for the counts in the model to reduce to background between experimental runs, and minimal radiation protection is required. The short half-life can, however, be a disadvantage when investigating slow sinus transport processes, as dynamic imaging is not useful for processes lasting longer than around 40 seconds (~3 half lives) and ventilation rates can only be assessed from count ratios in static imaging. In contrast to xenon, which is lipophilic and anesthetic and can cause complications for both in vitro and in vivo investigations, krypton is chemically inert and does not interact with the materials of a physical model or with biological tissues. Technetium aerosols are also commonly used as a contrast agent for respiratory imaging but are less appropriate for physiological transport measurements, because aerosols follow different transport processes to gases.

Previous work by our group has used computational modeling to investigate gas transport in idealized sinus geometries with 1 or 2 ostia, \(^25\) but no physical experiments were carried out to verify the results obtained. In this study we aimed to extend the earlier computational modeling with the use of experiments in a physical model and numerical simulation in matching geometries.

**Methods**

The physical model geometry (Figure 1) represents a human middle meatus, maxillary sinus, and 2 ostia that join the sinus to the meatus. The dimensions are based on measurements from a preexisting CT scan. These dimensions fall within the normal range of values, although the sinus volume of 10 mL is at the lower end of the range. \(^8\) The top plate of the model was removable to allow the ostium configuration to be changed. Adhesive tape was used to cover each ostium in turn for single-ostium tests and removed for the double-ostium tests. The use of idealized physical models has allowed the ostium geometry to be varied in a controlled manner. The known volume of the model sinus also allows the effective volume flow rate to be calculated from the images, whereas for real sinuses with unknown volume, only ventilation per unit volume can be obtained. The flow rate of 5 L/min for a channel caliber of 2 mm and a model span of 50 mm corresponds to a peak velocity of 1.2 m/s, which is representative of middle meatal flow as deduced from the computational fluid dynamics (CFD) results of Doorly et al. \(^26\)

Both the physical experiments and the computational modeling used steady flow through the nose to drive gas transport in the sinus. Bidirectional flow in breathing has 2 possible flow effects for the sinus, both of which have previously been shown to be minor. During the breathing cycle, there is a pressure variation in the nose and sinuses of around 10 mm H\(_2\)O (100 Pa), and it has been suggested, based on unpublished results, that this pressure variation could drive flow to the sinuses. \(^27\) Möller et al. \(^14\)\(^28\) also asserted that pressure gradients had been found to drive flow to the sinuses. However, earlier publications reported that the pressure in the sinuses was exactly equal to the pressure in the nasal cavity during normal breathing, implying that there is no pressure gradient and no flow is driven. \(^29\)\(^30\) There will be a small movement of air due to the volume change associated with the pressure change, but the volume moved is very small relative to the volume of the sinus. As initially calculated by Proetz, \(^31\) it took about an hour to replace all the air in a typical sinus. There may be some additional mixing caused by the reversal of flow...
between each half-cycle. Aust and Drettner\(^8\) used bidirectional flow in their experiments, the results of which were well-matched by earlier computational simulations in comparable idealized sinus geometries with steady flow through the nose,\(^25\) suggesting that the effect of flow-reversal mixing is small.

\(^{81}\)mKr was obtained from a rubidium generator, as used for clinical tests.\(^32\) The flow rate from the generator was around 1 L/min, with compressed air added to increase the flow rate. The model was viewed through parallel \(\gamma\)-cameras, which detected the \(\gamma\) decays emitted by the model. Images of cumulative count number were recorded for times ranging from 2 to 10 minutes. Dynamic imaging sequences, with 2-second collection times, were used to assess the time taken for the counts to reach steady state.

The \(\gamma\) images were processed by identifying 2 regions of interest, containing the sinus and channel, respectively, and assessing the number of counts in each region. Further analysis follows Amis and Jones,\(^24\) who considered the steady-state balance between the transport and decay of krypton to find relationships between activity and ventilation per unit volume in lung images. The effective ventilation flow rate through the sinus can thus be found according to the following equation:

\[
Q_{\text{eff}} = \beta Q_c \lambda / (Q_c / V_c + \lambda - \beta Q_c / V_s),
\]

where \(Q_{\text{eff}}\) is the effective volume flow rate of gas replacement in the sinus, \(\beta\) is the ratio of counts found in the sinus to those in the channel at steady state, \(Q_c\) is the flow rate through the channel representing the middle meatus (converted from L/min to m\(^3\)/s), \(\lambda\) is the decay constant for \(^{81}\)mKr (0.0533/s), \(V_c\) is the volume of the region of interest in the channel, and \(V_s\) is the volume of the sinus (converted from mL to m\(^3\)). \(Q_{\text{eff}}\) is thus the only unknown variable in the equation, and its value can be found.

A computational geometry and mesh were created in Gambit 2.4.6 (Fluent Inc, Lebanon, New Hampshire) to match each physical model configuration. To reduce computational expense, the vertical sections at each end of the physical model channel were not included in the computational geometry, because they did not affect the flow profile approaching the ostia. Different volume cell geometries were used in different regions of the model to improve computational efficiency. Hence, anisotropic hexahedral cells were used in the channel, with the highest mesh density across the thickness of the channel where the gradients of flow variables are expected to be steepest and with increased mesh density close to the ostia. The irregular shapes of the ostia and sinus did not allow for hexahedral meshing, so tetrahedral cells were used in these components. Nonconformal surface meshes at the interface of the different types of volume mesh were avoided by using triangular prism cells in the projections of the ostia across the channel.

Flow simulations were run in Fluent 6.3.26, initially only modeling steady velocity and pressure for convective transport and later adding unsteady transport of an inert species to allow for diffusion. Convective-only volume flow rates for single-ostium sinuses are upper-bound estimates and were determined by finding the integral of positive \(z\)-velocities across a surface of constant \(z\) (perpendicular to the ostium axis) just below the curved ostium–sinus interface. For the double-ostium sinuses, the volume flow rate through each ostium could be obtained directly from Fluent.

Effective volume flow rates for combined convection and diffusion simulations were calculated based on the concentration of Kr in the sinus relative to that in the nose (ratio \(\alpha\), based on the assumption that the sinus is a well-mixed cavity, so \(Q_{\text{eff}} = V_s \ln(1 - \alpha) / T\alpha\), where \(V_s\) is the volume of the sinus and \(T\alpha\) is the time at which the ratio of
concentration in the sinus to that in the nose is \( \alpha \). For the single-ostium geometries, where transport is expected to be dominated by diffusion, first-order estimates of \( Q_{\text{eff}} \), based on Fick’s law of 1-dimensional diffusion, were also made as \( Q_{\text{eff}} = DA/L \), where \( D \) is the diffusion coefficient of Kr in air (1.578 \( \times \) 10\(^{-5}\) m\(^2\)/s), \( A \) is the cross-sectional area of the ostium, and \( L \) is the ostium length.

**Ethical Approval**

This research was carried out in accordance with protocols at Imperial College London. No ethical approval was required for this study because no patients were involved.

**Results**

The results from the krypton experiments show increased levels of radioactivity in the sinus with the presence of an additional ostium (Figure 2). This translates to an approximately 50-fold increase in the effective volume flow rate of gas replacement in the sinus with an additional ostium. The measurements in Table 1 show that the actual increase is from 1.5 \( \times \) 10\(^{-8}\) m\(^3\)/s (standard deviation = 2.7 \( \times \) 10\(^{-10}\) m\(^3\)/s) to 7.4 \( \times \) 10\(^{-7}\) m\(^3\)/s (standard deviation = 2.3 \( \times \) 10\(^{-8}\) m\(^3\)/s); hence, the increase is more precisely estimated as 49.3 \( \pm \) 1.5. Increased levels of radioactivity were also seen when the ostial diameter was increased (Table 1). In the case of a single ostium, doubling the ostial diameter doubles the effective volume flow rate of gas exchange. The 90% exchange time for the single large ostia is 45 minutes yet with the 2 ostia is only 36 seconds, showing that the natural ventilation rate of a sinus with a single ostium is extremely slow.

The computational results clearly demonstrate the different flow patterns in the sinus for different ostial geometries, as shown by the streamlines in Figure 3. When there is only a single ostium, there can be no net flow across the ostium so exchange is limited to diffusion and is very slow. In the presence of an additional ostium, there is a net flow through the sinus and convective gas transport is dominant.

The computational results closely match the experimental findings, giving us increased confidence in both methods. A comparison of the experimental and computational results can be seen in Table 1.

**Discussion**

Imaging using \(^{81m}\)Kr and \( \gamma \)-camera has been shown to enable a quantitative assessment of effective volume flow rate in physical model sinuses. The effective volume flow rates obtained experimentally for single- and double-ostium sinuses match the computational predictions of matching geometries, whereas velocity fields follow the patterns found in simplified sinus geometries\(^{33,34}\) and topologically similar geometries.\(^{33,34}\) The combined use of computational simulations and physical experiments provides valuable cross-checking of results. Once matching has been established with a few sets of variables with results from both methods, there is increased confidence in results from each method alone; for example, it is not always possible to obtain clear images with very low flow rates, but computational simulations are still possible. This demonstration of the use of \(^{81m}\)Kr to assess ventilation in model sinuses is seen as a first step to using \(^{81m}\)Kr to investigate sinus ventilation in vivo in a clinical setting.

The computational and experimental effective flow rates depend on the ostium geometry. Sinuses with 2 ostia have much faster transport than sinuses with a single ostium. Sinuses with a single ostium also have diffusion-dominated gas transport, whereas sinuses with 2 ostia are convection-dominated. In the convection-dominated nature of the 2-ostia flow, there is an increase in effective flow rate of 8% when the effect of diffusion is included in the computational model. The differences in both transport mechanism and transport rate between single- and double-ostium configurations are due to a qualitative difference in flow, as a sinus with a single ostium acts as a reservoir of fluid attached to the nose but a sinus with 2 ostia forms an alternative flow path to the nose. Increasing the diameter or reducing the length of the ostia is also seen to increase sinus ventilation but not to the extent of an additional ostium unless the ostium is very large (eg, a middle meatal antrostomy).

The results of this study suggest that the natural single-ostium sinus ventilation is remarkably slow. This limited ventilation may be protective for the sinus, preventing mucosal drying, maintaining sterility with high nitric oxide (NO) concentrations, and minimizing entry of pathogens.

Previous work has shown that modeling of mucociliary velocities on the mucosal surfaces had no effect on convective or diffusive exchange times.\(^{25}\) Mucus plugging can prevent gaseous exchange, but this was not modeled in this study. Mucociliary transport is, however, essential in maintaining healthy sinuses because it is required to remove pathogens that enter the sinus. Additional ostia are associated with disrupted mucociliary transport,\(^{21}\) possibly leading to delay or prevention of the removal of any pathogens entering the sinus and to recirculation of mucus, which can introduce pathogens from other parts of the nasal cavity.

Whereas ventilation is necessary, excessive ventilation due to an additional ostium or very large ostium may not be clinically beneficial, because it could (1) increase washout of NO, which is excreted by the mucosa of the paranasal sinuses and is thought to have bacteriostatic and mucociliary regulating properties\(^{35}\); (2) increase access of pathogens to the sinus, which could have compound effects with NO reduction; and (3) cause mucosal drying, particularly if the

Figure 2. Raw \( \gamma \)-camera images for (A) single large ostium and (B) double-ostium configurations, 10 mL sinus, flow rate 5 L/min.
upstream ostium is near the nostril and thus exposed to less well-conditioned air.

Rapid sinonasal gas exchange and the resulting reduction in NO levels could arguably contribute to the development of rhinosinusitis. More research is needed to clarify the role of an additional ostium in sinonasal exchange processes and the effects of changing NO concentrations on sinonasal pathology.

$^{81m}$Kr was recently used to image sinuses in vivo by Möller et al., but they have not made a quantitative assessment of sinus ventilation under normal breathing conditions. This study represents the first step in quantitatively analyzing sinus ventilation. The use of krypton imaging for quantitative assessment is successfully demonstrated and corroborated by comparison with computational modeling. Further work will look at the changes of sinus ventilation with variation of flow rate and sinus volume—expanding the verification of computations and testing the flexibility of the experimental method. The authors are currently in the process of obtaining ethical approval to use $^{81m}$Kr to assess sinus ventilation in vivo.

### Conclusions

In this study, earlier computational simulations have been extended and verified with matching physical model experiments. The following conclusions were made:

- Diffusive transport is dominant for sinuses with a single ostium, whereas convection is more important for sinuses with 2 ostia, which also have much faster gas replacement.
- Natural single-ostium sinus ventilation is extremely slow but is enhanced by increasing ostial diameter. An additional ostium can increase the effective volume flow rate of gas replacement in the sinus by an order of magnitude that may not be clinically beneficial.

$^{81m}$Kr and $\gamma$-scintigraphy may be of use for in vivo investigations of sinus ventilation.

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### Author Contributions

Catherine E. Rennie, major part in designing the study, acquired all experimental data, analyzed data, wrote significant part of paper, revised and approved final draft; Christina M. Hood, large part in the design of the study, performed all computations, analyzed results, wrote a major portion of the paper, revised drafts and approved final draft; Esther J. S. M. Blenke, large part in the design of the study, performed some early pilot work, wrote and revised paper; Robert S. Schroter, a great help in the design and planning of the study, provided advice throughout data analysis and critically reviewed the paper; Denis J. Doorly, provided a substantial contribution to the conception and design of the study, provided advice on data analysis, critically revised the paper and approved the final draft; Hazel Jones, key in the conception and design of the study, provided excellent advice and guidance on nuclear medicine techniques, refined the experimental process, wrote and critically reviewed the paper; David Towey, involved throughout the study, instrumental in determining the experimental design and acquiring experimental results, provided a critical review on all phases of writing and contributing significantly particularly on nuclear medicine techniques; Neil S. Tolley, involved in the conception and design of the study, provided an overview throughout and kept us in touch with the clinical implications of the work, critically reviewed the paper.

### Disclosures

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