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RESEARCH NOTE

REVISED **The impact of fresh gas flow on wash-in, wash-out time and gas consumption for sevoflurane and desflurane, comparing two anaesthesia machines, a test-lung study. [version 2; referees: 3 approved]**

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Abstract
Low-flow anaesthesia is considered beneficial for the patient and the environment, and it is cost reducing due to reduced anaesthetic gas consumption. An initial high-flow to saturate the circle system (*wash-in*) is desirable from a clinical point of view. We measured the wash-in and wash-out times (time to saturate and to eliminate the anaesthetic agent, AA), for sevoflurane and desflurane, in a test-lung with fixed 3 MAC vaporizer setting at different fresh gas flow (FGF) and calculated the consumption of AA. We tried to find an optimal flow rate for speed and gas consumption, comparing two anaesthesia machines (AMs): Aisys and Flow-i. Time to reach 1 minimal alveolar concentration (MAC) (wash-in) decreased (p<0.05) at higher flow rates (1 – 2 – 4) but plateaued at 4-4.8 l/min. The consumption of AA was at its lowest around 4-4.8 l/min (optimal flow) for all but the Aisys /desflurane group. Wash-out times decreased as FGF increased, until reaching plateau at FGF of 4-6 l/min. Aisys had generally shorter wash-in times at flow rates < 4 l/min as well as lower consumption of AA. At higher flow rates there were little difference between the AMs. The "optimal FGF" for wash-out, elimination of gas from the test-lung and circle system, plateaued with no increase in speed beyond 6 l/min. A fresh gas flow of 4 l/min. seems "optimal" taking speed to reach a 1 MAC ET and gas consumption into account during wash-in with a fixed 3 MAC vaporizer setting, and increasing fresh gas flow beyond 6 l/min does not seem to confirm major benefit during wash-out.

Open Peer Review

Referee Status: ✓ ✓ ✓

	Invited Referees		
	1	**2**	**3**
REVISED **version 2** published 22 Dec 2017	✓ report	✓ report	✓ report
	↑	↑	↑
version 1 published 13 Nov 2017	? report	? report	? report

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First published: 13 Nov 2017, **6**:1997 (doi: 10.12688/f1000research.13064.1)

Introduction
Low flow anaesthesia is associated with several benefits, reducing the heat loss caused by cold gases and improving humidification in the airways[1]. It is also environmentally friendly, reducing the release of anaesthetic agents into the atmosphere, and lastly, it also reduces costs. The initial period needed to achieve a steady state is dependent on fresh gas flow and the vaporizer setting[2]. Many different FGF schemes have been described for the wash-in[3,4]. The wash-out of the inhaled anaesthetic from the lungs and circle is also of importance, to facilitate a rapid awakening and recommencement of protective reflexes.

The aim of the present study was to measure the time required to reach stable end tidal 1 MAC anaesthetic (*wash-in*), to measure gas consumption during wash-in and the time needed to eliminate the anaesthetic agent (*wash-out*) for sevoflurane and desflurane in the entire gas reservoir in the machine, circle system and in an lung model representing a 4 litre functional lung capacity and a test lung with a maximal capacity of 1 litre, and to compare the impact of different fresh gas flows and anaesthesia machines.

Methods
This study used a test-lung setup. It was conducted in the operating room with proper scavenging equipment and central gas supply at Danderyds hospital, Sweden.

Two standard anaesthesia machines were used: Flow-i[R] (Maquet Critical Care AB, Solna, Sweden) and Aisys[R] (GE Healthcare, Madison, WI, USA), and two anaesthetic agents: sevoflurane and desflurane, making up a total of four test groups. All standard safety measures were followed, including checking each machine for performance and leakage before every session, in accordance with the Instruction for use (IFU), to ensure a safe working environment.

A standard disposable adult circle system was used (GE patient circuit, adult, disposable, 1.8 m and 1.5 litre volume), including a Y-piece at the end of the tube. A humidity-filter (Humid-vent, filter compact A) was fitted on the Y-piece. The circle system also included a standard CO_2 absorber (soda lime canister) even though no carbon dioxide was used in the experiments, because some of the anaesthetic agent (AA) may also be absorbed and therefore mimic clinical conditions better.

A test lung was assembled using the following equipment: The Maquet test-lung 190 (Maquet Critical Care AB, Solna, Sweden), tidal volume max 1 litre and internal volume of 0, was mounted on one of the tubes of another Y-piece. Two 2-liter Intersurgical reservoir bags were connected to a T-tube to the other tube of the Y-piece.

Measurements of FiAA and EtAA of sevoflurane and desflurane were done with a mainstream sensor (instead of the AM sidestream sensors). IRMA AX +, (Masimo Sweden AB, Danderyd, Sweden) with an accuracy of 0.15 vol. % was used. This allowed us to get more exact measurements without any delay or dilution of gases. The mainstream sensor was connected to an external computer via a USB port and the Gasmaster® (Masimo Sweden AB, Danderyd, Sweden) program was used to record our measurements.

During the entire experiment a fixed respiratory rate and tidal volume was used, set at 12/min and 400 ml respectively. The positive end-expiratory pressure (PEEP) was set at 5 cm H_2O and the inspiratory/expiratory rate was set two 1:2.

Two direct injection vaporizers were used for the Flow-i (one for each AA) and two variable bypass vaporizers for the Aisys (one for each AA). The AAs were released at fixed vaporizer settings of $3 \times$ MAC-value (6 % and 18 % for sevoflurane and desflurane respectively).

Wash-in
The timer/data log was started at the same time as when the vaporizer was turned on. The wash-in time to reach 1 MAC (i.e. increasing the EtAA concentration from 0 to 1 MAC), adjusted for a 40-year-old, 70 kg male (2% for sevoflurane and 6% for desflurane), was measured three consecutive times for each fresh gas flow (FGF). MAC values taken from the companies' summary of product characteristics[1]. The FGF tested included 1, 2, 4, 4.8, 6 and 8 l/min, with a composition of 80% oxygen and 20% air for each of the AAs and anaesthesia machines.

Wash-out
Wash-out (reducing EtAA to 0 MAC) was performed after each wash-in session of the test-lung/circle. This was done by turning off the vaporizer and setting the FGF to one of 5 (2, 4, 6, 8 and 10 l/min) on each anaesthesia machine (AM) and AA.

[1] www.baxterhealthcare.com.au/downloads/...pi/suprane_pi.pdf
www.baxterhealthcare.com.au/downloads/.../sevoflurane_pi.pdf

The same protocol was used for sevoflurane and desflurane as well as for Flow-i and Aisys and the results for each wash-in session were presented as a mean of 3.

Gas consumption

Gas consumption was calculated using the known wash-in time, FGF, vaporizer settings (VA concentration) and the vapour/liquid quote for each AA: vapour (ml)/liquid (ml) = 184 and vapour (ml)/liquid (ml) = 210 for sevoflurane and desflurane respectively. It means that 1ml of liquid AA equals 184ml and 210ml of vaporized sevoflurane and desflurane, respectively[5].

This gives the equation: AA consumption $= \dfrac{\frac{time(s) \times FGF \, x1000}{60} \times VA \, conc \, (vol\%)}{(vapor/liquid \, quote) \times 100 \, (vol\%)}$

Statistical analysis

SPSS 24 (IBM, Armonk, NY, USA) was used for statistical analysis. All wash-in data was presented as mean of 3 measurements with standard deviation (SD) calculated. The mean time to reach 1 MAC for the different FGF was compared among the Flow-i and Aisys AM using analysis of variance (ANOVA). To determine which of the mean FGFs differed significantly from each other, we also performed Tukey's post hoc test. A $p < 0.05$ was considered statistically significant.

Ethical statement

This is a test model study. The research does not involve human participants and/or animals, and thus no informed consent has been requested. The set-up is entirely experimental and no human or animals have been exposed to anaesthetics, and thus no ethical review board assessment has been considered necessary, according to Swedish research regulations.

Results

Wash-in times were significantly faster with higher flow rates for FGF spanning from 1, 2 and 4 l/min ($p < 0.05$) for all 4 groups (Figure 1 and Figure 2). There was however a plateau starting at FGF 4–4.8 l/min, where increasing the FGF further up to 6 or 8 l/min did not shorten the time to reach 1 MAC significantly; similar patterns could be observed in all 4 groups. With Flow-i that plateau started at 4 and 4.8 l/min for sevoflurane and desflurane, respectively. With Aisys this plateau started at 4 l/min, for both the sevoflurane and desflurane group. Aisys had generally shorter wash-in times for both sevoflurane and desflurane at flow rates < 4 l/min. For flow rates of 4 l/min and above the difference was very small but somewhat more pronounced for desflurane wash-in, with Flow-i having shorter wash-in times than Aisys (Figure 2 a–d).

Anaesthetic agent consumption showed a somewhat different pattern (Figure 2 a–d). The lowest consumption differed between sevoflurane and desflurane and also between the Aisys and Flow-i. The lowest consumption of AA per wash-in for Flow-i sevoflurane and Flow-i/desflurane, 1.4 ml and 3.9 ml respectively, was calculated at FGF equal to minute ventilation (4.8 l/min). The lowest consumption of AA for Aisys /sevoflurane, 1.3 ml, was calculated at a FGF at 4 l/min. The lowest consumption of AA for Aisys /desflurane, 3 ml, was calculated at the lowest FGF (1 l/min), in difference to the other 3 groups, followed by FGF 2 and 4 l/min with a calculated consumption of AA of 3.3 ml and 3.9 ml respectively. This was unique for Aisys /desflurane (Figure 2 a–d).

Wash-out times were faster at higher FGF until a plateau was reached at around FGF 4–6 l/min. Increasing the FGF further did not lead to faster wash-out times, except for the Aisys / sevoflurane
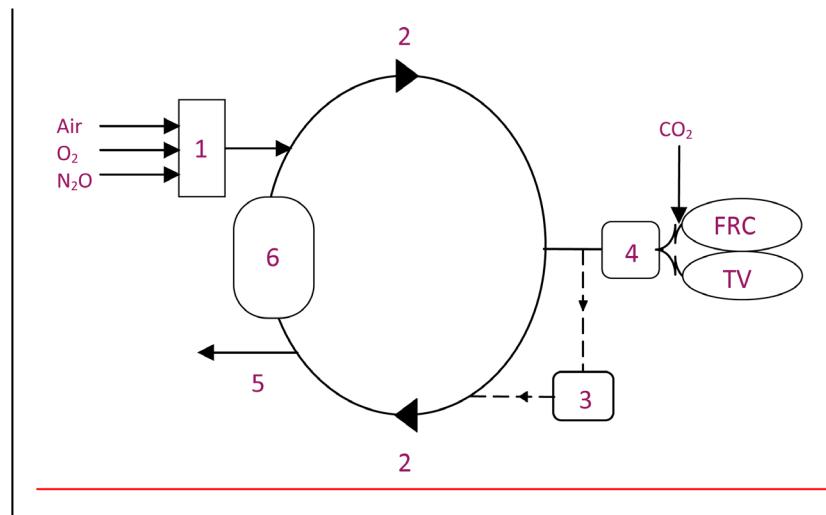
Figure 1. Schematic view of the experimental set-up. The fresh-gas flow is defined in this project as the gas-mixture introduced to the circle i.e. after the vaporizer. The functional residual capacity (FRC) consisted of two reservoir bags. The tidal volume (TV) consisted of one self-deflating bag. A small volume of gas gets diverted through the sidestream sensor but is reintroduced into the circle afterwards. 1. Vaporizer; 2. One-way valves; 3. Sidestream sensor; 4. Mainstream sensor; 5. Spill-valve; 6. CO_2 Absorber.

(a)

(b)

(c)

(d)
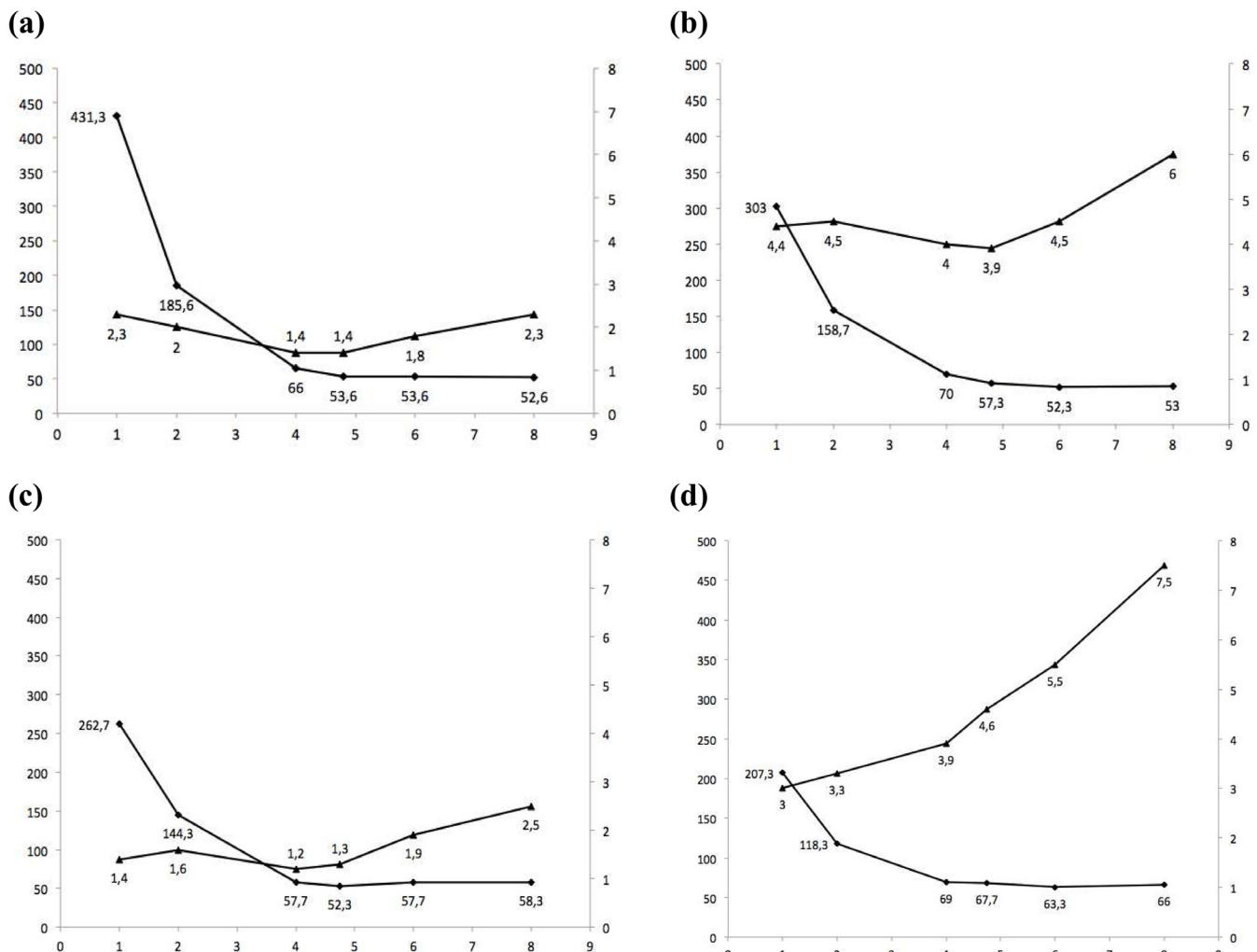
Figure 2. Time to reach 1 MAC and the calculated AA consumption for each fresh gas flows. (**a**) Flow-i /sevoflurane. (**b**) Flow-i / desflurane. (**c**) Aisys /sevoflurane. (**d**) Aisys/desflurane. Time(s) is on the Y-axis. FGF (l/min) is on the X-axis. AA (ml) is on the secondary Y-axis.

group. The fastest wash-out time with Flow-i /sevoflurane, 349s, was recorded at FGF 6 l/min where it also plateaued. Wash-out times for Flow-i /desflurane plateaued at FGF 4 l/min and 1013s, which differed a few seconds from the fastest wash-out time, 1007s, recorded at FGF 8 l/min. Wash-out times for Aisys /sevoflurane had a plateau that was not as distinct as the other groups with the fastest wash-out time, 303s, recorded at FGF 10 l/min. The fastest wash-out time for Aisys /desflurane, 797s, was recorded at FGF 6 l/min, where it reached a clear plateau (Table 1). There

was minor difference in elimination, Aisys being marginally faster (Figure 3 a–b). No statistical analysis was performed on the wash-out data.

Table 1. Times at which wash-out plateaued, and fastest wash-out times at optimal flow rate.

	Flow-i	Aisys	All (mean)
Sevoflurane	349 s	317 s	333 s
Desflurane	1013 s	797 s	905 s
All (mean)	681 s	557 s	

(a)

(b)
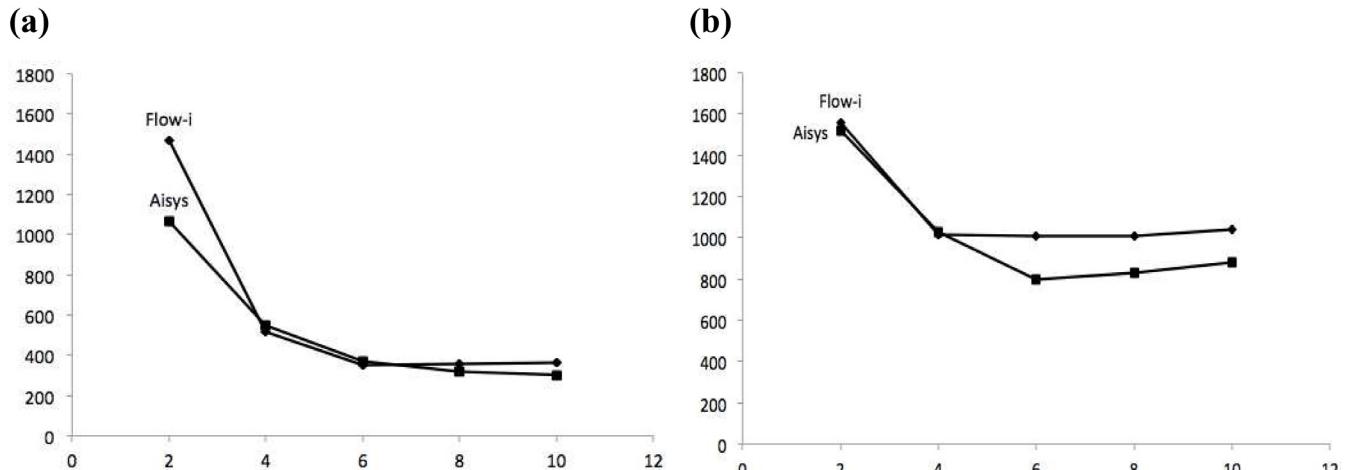
Figure 3. Wash-out times comparing Flow-i and Aisys AMs. (**a**) sevoflurane (**b**) desflurane. Time (s) is on the Y-axis and FGF (l/min) is on the X-axis.

Discussion

The present study was set up to gain insight to whether two modern anaesthetic workstations with different vaporizer technologies and different internal volumes differed in time needed to saturate internal and externa gas reservoirs; circle system, CO2-absorber and further including an anticipated normal adult lung volume. We found, in this test-lung setup, that it is possible to increase the anaesthetic agent concentration from 0 to 1 MAC value in around one minute by using a FGF of 4–4.8 l/min on both AMs, but raising the FGF further did not result in shorter wash-in times. These flow rates were also the most efficient, in terms of both speed and gas consumption for both anaesthetic agents (sevoflurane and desflurane) and anaesthetic machines (Aisys and Flow-i) except when using Aisys and desflurane. Aisys had generally shorter wash-in times when using lower flow rates (< 4 l/min). For flow rates of 4 l/min and above, the difference was very small between the two machines tested. Anaesthetic agent consumption showed different patterns, but Aisys had generally lower gas consumption than Flow-i for both AAs. The shortest wash-out times were found at FGFs of 4–6 l/min; raising the FGF further did not result in shorter wash-out times. Wash-out of desflurane from the test-lung was more than twice as time-consuming as the sevoflurane wash-out.

This is merely a test-lung study and it was expected that there would be more rapid wash-in with increased fresh gas flow, but it

is important to acknowledge the plateau at around 4–5 l/min FGF. Our results also show that Maplesons mathematical calculations of a theoretical optimal FGF at around 4 l/min were accurate[6]. The result is also in line with what Shin *et al.* found in their study: increasing the FGF from low flow to moderately high flow will decrease the wash-in time[7]. However, our results show that there seem to be no benefits to raising the FGF to levels of 6 l/min and above while performing a wash-in. This is an experimental test-lung set-up and we cannot comment to what extent the human uptake and elimination, e.g. the impact of the different blood gas solubility for the agents tested, would have on the time events studied.

Likewise the finding of increased AA consumption at both low and high FGFs is of interest, minimising the consumption of anaesthetic vapour is of economical as well as ecological importance. There was a difference between the AMs in terms of which FGF was most effective. We noted that the most effective FGF for the Flow-i, in terms of both consumption of AA and shortest wash-in time, was equal to the minute volume – 4.8 l/min. This applied to both sevoflurane and desflurane wash-in.

The small difference in wash-in between the AMs at lower fresh gas flows are in line with our previous study with a simpler test setup with sevoflurane[8]. We used a more "physiologic" test-lung setup in the present study, which we believe mimics functional

residual capacity and tidal volume for a 70 kg male. Our test-lung was constructed to represent both tidal volume (the volume of a normal breath) and the FRC in our test-lung setting, making the measurements more realistic. The Maquet test-lung 190 was representing the tidal volume and the two reservoir bags were representing a normal FRC (4 litre) in a 40-year-old male[9]. We used an external main stream multi gas sensor in the present study, possibly reducing the difference in monitor performance. The difference in wash-in could of course be associated to the differences in vaporiser technology and algorithms for introduction of gas, a continuous influx or an intermittent – during inspiration only.

The finding that gas consumption is higher with desflurane than with sevoflurane may not be surprising, when taking the difference in MAC gas concentration into account. Whether there is any material absorption of desflurane in the Flow-i cannot be assessed. The huge difference, the twice as long time to eliminating desflurane as compared to sevoflurane, is to us also unexpected.

There are several limitations to this study, indeed this is merely a test-lung experiment and one may of course argue about its clinical application. The vaporizer setting was fixed at 3 MAC. We believe that our findings have clinical implications; we know that high fresh gas flows do not provide major benefits during wash-in or wash-out and there is the possibility to wash-in to a 1 MAC concentration within about a minute, 4 – 5 l/min FGF being the "optimal" time for wash-in. We used the AMC values presented on the product information sheet. There are slightly lower values suggested. Our study provides information around the machines, how the workstations performs during wash-in and wash-out of the gaseous phases. The uptake, blood solubility and likewise elimination must of course be taken into account. Both Aisys and Flow-i have built-in techniques for target end-tidal MAC, were fresh gas and vaporizers are automatically set to reach the target value[10]. The Flow-i automatic gas control provides also the option to reach goal concentrations with different speed, possibly avoiding inappropriate heamodynamic response. We did study only high flow, rapid wash-in and wash-out. It would indeed be interesting to study also lower fresh-gas flows to assess whether there is differences in performance.

Conclusions
Wash-in times, time to saturate internal and external gas reservoir including circle system, CO2 absorber and a test-lung volume of 4 litre, with fixed 3 MAC vaporizer settings decreased as the FGF increased, but plateaued at around flow rates of 4–4.8 l/min (optimal flow) on both AM. It is more effective, in terms of consumption of AA, to use optimal flow than lower or higher flow rates. Wash-out times plateaued at around flow rates of 4–6 l/min, higher FGF than that does not produce faster wash-out times. Further studies are required to confirm our findings in clinical practice, but also to study the end tidal target algorithms available on the AMs.

Data availability
Dataset 1: Raw data for the measurements: Flow-I sevoflurane, Flow-I desflurane, Aisys sevoflurane and Aisys desflurane. DOI, 10.5256/f1000research.13064.d183806[11]

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    Data Source

Open Peer Review

Current Referee Status: ✓ ✓ ✓

Version 2

Referee Report 26 February 2018

✓ **Moritz A. Kretzschmar** [iD] [1,2], **Thomas Schilling** [3]

[1] Department of Anaesthesiology and Intensive Care Medicine, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany
[2] Hedenstierna Laboratory, Uppsala University, Uppsala, Sweden
[3] Department of Surgical Sciences, Hedenstierna Laboratory, Uppsala University, Uppsala, Sweden

Our questions and comments are addressed appropriately in the revised version. Attributing the differences in wash-in time to the different agent delivery technique is very plausible, and presents a further interesting field to study, although we do take notice that the differences are small and the clinical impact will probably be minute.

Competing Interests: No competing interests were disclosed.

Referee Expertise: Kinetics of volatile anesthetics, ventilation/perfusion relationship of the lung, thoracic anesthesia

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Referee Report 10 January 2018

✓ **Katarina Hallen**
Department of Anaesthesiology and Intensive Care Medicine, Institute of Clinical Sciences, The Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden

The most interesting is
1. Sevo is much faster at FGF 2 in Aisys.
2. Des is much faster at FGF> 4 in Aisys

However, the results report is confused, as Table 1 indicates that it contains both times to fastest deployment and time to plateau, while the table only contains one time per machine and gas.

Figure 1. Is it exactly the same principle of the circles in the two respirator machines? There should be 1

Figure for each machine, as the design of the circle may affect gas consumption.

Fig.2. Put labels on all shoulders in the Figure instead of caption. Put headlines in the Figure to facilitate reading. In 2a, there should be Flow-I SEV, 2b Flow-I DES, in 2c Aisys SEV and 2d Aisys DES.

Both Sevoflurane and Desflurane interfere chemically with the absorber, especially when dry, as in these experiments. This might give a certain difference in the consumption of gas. How does the authors comment on this? Is it exactly the same principle of the circles in the two respirator machines? There should be 1 Figure for each machine, as the design of the circle may affect gas consumption.

Fig.2. Put labels on all shoulders in the Figure instead of caption. Put headlines in the Figure to facilitate reading. In 2a, there should be Flow-I SEV, 2b Flow-I DES, in 2c Aisys SEV and 2d Aisys DES.

Both Sevoflurane and Desflurane interfere chemically with the absorber, especially when dry, as in these experiments. This might give a certain difference in the consumption of gas. How does the authors comment on this?

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Referee Report 04 January 2018

Sirirat Tribuddharat (iD) , **Thepakorn Sathitkarnmanee**

Department of Anesthesiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

The authors have addressed my concerns appropriately in the revised version. However, there are some issues that need additional revision. The authors should insert a reference for "1 MAC adjusted of a 40 year-old (2% for sevoflurane and 6% for desflurane)" in the Methods. The sentence "There are slightly lower values suggested." in the Limitations should be changed into "There are slightly different values suggested." since, according to the study of Nickalls RWD. BJA 2003; 91: 170-4, 1 MAC adjusted of a 40 year-old for sevoflurane and desflurane are both lower and higher, ie. 1.8% for sevoflurane and 6.6% for desflurane. Please also insert a reference for this sentence.

Competing Interests: No competing interests were disclosed.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Referee Report 15 December 2017

Moritz A. Kretzschmar (iD) [1,2], **Thomas Schilling** [3]

[1] Department of Anaesthesiology and Intensive Care Medicine, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany

[2] Hedenstierna Laboratory, Uppsala University, Uppsala, Sweden

[3] Department of Surgical Sciences, Hedenstierna Laboratory, Uppsala University, Uppsala, Sweden

Thank you for the opportunity to review this interesting article. It is wonderful to see research on basic science addressing questions which are often taken for granted in clinical practice.

We do have a few questions:

1. What is the clinical value of comparing sevoflurane and desflurane at the same MAC, if just the machines are of interest (and the solubility and clinical effects are negligible), would it not have been better to use the same vol%?

2. There are only two factors influencing wash-in to the circuit, and those are circuit volume and fresh gas flow. Setting aside the patient at the end of the anesthesia machine, this study evaluates the wash-in/-out of the total apparatus dead space. To better compare the measurements from the Aisys and the Flow-I, it would be necessary to reference the volumes (bag/volume reflector, internal tubing, respective soda lime canister etc.) of both machines up to the y-piece. We presume they were not identical, but by how much do they differ?

3. The wash-in time plateaued at around minute ventilation, which was to be expected, as both systems could be considered almost closed, with only minimal leakage. For the wash-out, the lowest FGF that eliminates rebreathing should indicate the plateau. Whereas with sevoflurane there is no apparent difference between the machines, reflecting the relationship between circle volume and FGF, the difference with desflurane is quite interesting. Could some materials used in the Flow-i have absorbed desflurane – We are thinking of the volume reflector or valves?

4. We cannot completely follow the data files: if the main stream sensor was placed after the y-piece, the high data points reflect Fi of the agent. Why was this position chosen and not the proximal (to the y-piece) end of the expiratory tube. This could have eliminated inspiratory/expiratory mixing in the acquisition, as the values were not recorded synchronized to the breath cycle.

5. An illustration of the experimental setup could enhance understanding for the reader.

6. The information of Figures 1 and 2 are redundant – they are repeated in Fig 3.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Referee Expertise: Kinetics of volatile anesthetics, ventilation/perfusion relationship of the lung, thoracic anesthesia

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response (*Member of the F1000 Faculty* and *F1000Research Advisory Board Member*) 16 Dec 2017
Jan Jakobsson, Department of Physiology and Pharmacology, Karolinska Institutet, Sweden

We do have a few questions:

- What is the clinical value of comparing sevoflurane and desflurane at the same MAC, if just the machines are of interest (and the solubility and clinical effects are negligible), would it not have been better to use the same vol%?

The aim of the study was to compare the anaesthetic works-station and the two third generation in haled anaesthetics, aiming for an similar end-tidal 1 MAC gas concentration and subsequently time to wash-out has from these gas volumes.

- There are only two factors influencing wash-in to the circuit, and those are circuit volume and fresh gas flow. Setting aside the patient at the end of the anesthesia machine, this study evaluates the wash-in/-out of the total apparatus dead space. To better compare the measurements from the Aisys and the Flow-I, it would be necessary to reference the volumes (bag/volume reflector, internal tubing, respective soda lime canister etc.) of both machines up to the y-piece. We presume they were not identical, but by how much do they differ?

The present study was set up to gain insight to whether the machine different in time need to saturate internal and externa has reservoirs, including an anticipated normal adult lung volume.

- The wash-in time plateaued at around minute ventilation, which was to be expected, as both systems could be considered almost closed, with only minimal leakage. For the wash-out, the lowest FGF that eliminates rebreathing should indicate the plateau. Whereas with sevoflurane there is no apparent difference between the machines, reflecting the relationship between circle volume and FGF, the difference with desflurane is quite interesting. Could some materials used in the Flow-i have absorbed desflurane – We are thinking of the volume reflector or valves?

We are not able to assess potential losses. Both machines are "tested" and approved for use with both sevoflurane and desflurane.

- We cannot completely follow the data files: if the main stream sensor was placed after the y-piece, the high data points reflect Fi of the agent. Why was this position chosen and not the proximal (to the y-piece) end of the expiratory tube. This could have eliminated inspiratory/expiratory mixing in the acquisition, as the values were not recorded synchronized to the breath cycle.

The main-stream gas monitor was attached in parallel with in side-stream nipple. The readings, the recorded and presented values were the highest and stable values at each time-point.

- An illustration of the experimental setup could enhance understanding for the reader.

A graph of the set-up is added

- The information of Figures 1 and 2 are redundant – they are repeated in Fig 3.

Deleted as suggested

Competing Interests: See main manuscript

Referee Report 12 December 2017

doi:10.5256/f1000research.14163.r27918

? **Sirirat Tribuddharat** iD , **Thepakorn Sathitkarnmanee**

Department of Anesthesiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

This report is interesting and may have clinical relevant in routine practice. However, the authors should address to the following points:

1. A figure showing the diagram of the circuit assembly including the test lung should be included. It's quite confusing about the number of 'Y-piece'. Normally, the test lung should be attached to the humidifier-filtered connected to a Y-piece. Why using 2 reservoir bags when normally only 1 is used in routine practice? Where is the location of the main stream sensor?

2. Please quote a reference for '1 MAC adjusted of a 40 year-old (2% for sevoflurane and 6% for desflurane). It's quite different from "Nickalls RWD. BJA 2003; 91: 170-4".

3. We have both anesthetic machines. The flowmeters on both Flow-i and AISYS are digitally controlled. They can be adjusted with accuracy of only 1 decimal place of litre, i.e., 0.1 L/min. Although the display on AISYS shows 2 decimal placed, i.e., 2.00 L/min, we can adjust flow of 0.1 L/min at a time only. How can the authors set FGF at 4.75 L/min?

4. The caption of Figures 3 and 4 does not match the figure, e.g., (a) in figure but (A) in caption.

5. The wash-in time derived from a test lung may not be inferred to human lung. The major confounding factor of wash-in time is anesthetic agent uptake from lung into human body 'three compartments' which affected by blood gas partition coefficient, cardiac output, organ tissue flow, organ tissue volume, and blood-tissue partition coefficient. That makes sevoflurane having longer wash-in time at same MAC and FGF. The test lung model did not take into account these factors. The authors should address to this point.

6. The wash-out time has the same problem. The test lung did not consider amount of anesthetic agent uptake into the body which has to be eliminated out of the body into account. Normally, at the same MAC, sevoflurane has longer wash-out time compared with desflurane because of higher blood-gas, blood-tissue and blood-fat solubility. The authors should address to this point.

References

1. Nickalls RW, Mapleson WW: Age-related iso-MAC charts for isoflurane, sevoflurane and desflurane in man.*Br J Anaesth*. 2003; **91** (2): 170-4 PubMed Abstract

2. Kapoor MC, Vakamudi M: Desflurane - revisited.*J Anaesthesiol Clin Pharmacol*. 2012; **28** (1): 92-100 PubMed Abstract | Publisher Full Text

3. Cowles AL, Borgstedt HH, Gillies AJ: Uptake and distribution of inhalation anesthetics agents in clinical practice.*Anesth Analg*. **47** (4): 404-14 PubMed Abstract

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response (*Member of the F1000 Faculty* and *F1000Research Advisory Board Member*) 16 Dec 2017

Jan Jakobsson, Department of Physiology and Pharmacology, Karolinska Institutet, Sweden

This report is interesting and may have clinical relevant in routine practice. However, the authors should address to the following points:

- A figure showing the diagram of the circuit assembly including the test lung should be included. It's quite confusing about the number of 'Y-piece'. Normally, the test lung should be attached to the humidifier-filtered connected to a Y-piece. Why using 2 reservoir bags when normally only 1 is used in routine practice? Where is the location of the main stream sensor?

A graph of the set-up is added
- Please quote a reference for '1 MAC adjusted of a 40 year-old (2% for sevoflurane and 6% for desflurane). It's quite different from "Nickalls RWD. BJA 2003; 91: 170-4".

We used the FDA approved USP desflurane information sheet and Baxter Summary of Product characteristics; the 1 MAC for 40-45 years adult is set at 6 % (www.baxter.com.pr/healthcare_professionals/.../suprane.html*). Likewise for sevoflurane we used the FDA and Baxter product documentations, stating 1 MAC at aye of 40 being 2.1 % but we used for this study the MAC 2 and 6 %.*

- We have both anesthetic machines. The flowmeters on both Flow-i and AISYS are digitally controlled. They can be adjusted with accuracy of only 1 decimal place of litre, i.e., 0.1 L/min. Although the display on AISYS shows 2 decimal placed, i.e., 2.00 L/min, we can adjust flow of 0.1 L/min at a time only. How can the authors set FGF at 4.75 L/min?

The flow setting should be with 1 decimal, the 4.75 is incorrect for the Flow-I corrected

- The caption of Figures 3 and 4 does not match the figure, e.g., (a) in figure but (A) in caption.

Corrected excuse the edit mistake

- The wash-in time derived from a test lung may not be inferred to human lung. The major confounding factor of wash-in time is anesthetic agent uptake from lung into human body 'three compartments' which affected by blood gas partition coefficient, cardiac output, organ tissue flow, organ tissue volume, and blood-tissue partition coefficient. That makes sevoflurane having longer wash-in time at same MAC and FGF. The test lung model did not take into account these factors. The authors should address to this point.

This is indeed merely an experimental test-lung set-up and we cannot comment on the human uptake and elimination, e.g. the impact of the different blood gas solubility for the agents tested.

- The wash-out time has the same problem. The test lung did not consider amount of anesthetic agent uptake into the body which has to be eliminated out of the body into account. Normally, at the same MAC, sevoflurane has longer wash-out time compared with desflurane because of higher blood-gas, blood-tissue and blood-fat solubility. The authors should address to this point.

These, comments 6 & 7, are indeed one of limitations with our study, it is merely a test lung study. We have addressed the limitation in the discussion section, and we also clearly state that further studies are warranted confirming our results in the clinical setting. We still believe that our study provide information around the machines, how the workstations performs during wash-in and wash-out of the gaseous phases. The uptake, blood solubility and likewise elimination must of course be taken into account.

Competing Interests: See main manuscript

Referee Report 20 November 2017

? **Katarina Hallen**
Department of Anaesthesiology and Intensive Care Medicine, Institute of Clinical Sciences, The Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden

Thank you for asking me for a peer review.

I have some questions to the authors regarding the study: The impact of fresh gas flow on wash-in, wash-out time and gas consumption for sevoflurane and desflurane, comparing two anaesthesia machines, a test-lung study. by J. Jakobsson.

1. Is there a difference between the two vaporizer used in the experiment?
2. Comment on the difference in a direct-injection and a bypass affect how respirators works.
3. Why the maximum inflow of the two gases? This is not clinically relevant. Would not it be better for another group with half the inflow, 4% and 8%?
4. Why non-parametric tests? Is this normal distribution of data?
5. The figures are not sufficient quality, high solution pictures please.
6. Explain in an educational way how you calculate gas consumption.
7. Do you have any theory why Aisys is faster at low flow with desflurane? Do you have any theories?
8. Why does it take longer to wash-out desflurane than sevoflurane in a mechanical lung model? This does not correspond to the clinical picture.
9. Does desflurane have lower density than sevoflurane? Is that why it takes longer to wash-out the desfluran? Can you come up with some theories about the most remarkable result in the study?
10. I can not find sevoflurane wash-out in Figure 4.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response (*Member of the F1000 Faculty* and *F1000Research Advisory Board Member*) 26 Nov 2017
Jan Jakobsson, Department of Physiology and Pharmacology, Karolinska Institutet, Sweden

Thank you for valid comments. Please find below responses to your queries.
- Is there a difference between the two vaporizer used in the experiment?

Yes indeed both the technique to create the gaseous phase, the internal reservoir and the respiratory phase when gas is introduced into fresh gas. The Flow-i "injects gas" during inspiration while the Aysis has a more traditional vaporizer technique. The internal gas volume, reservoir is smaller in the Flow-i. This is the reason for our interest in comparing the machine, to assess how these different solution create difference during a rapid wash-in, gas bolus.

- Comment on the difference in a direct-injection and a bypass affect how respirators works.

The aim of the study was indeed to study how these different techniques act in a test-lung set up at different flow rates. It would also be interesting to study lower vaporizer settings at that study may be worth carrying out.

- Why the maximum inflow of the two gases? This is not clinically relevant. Would not it be better for another group with half the inflow, 4% and 8%?

The aim of this study was to study the bolus, high concentration performance. It would indeed be of interest to study lower setting.

- Why non-parametric tests? Is this normal distribution of data?

Traditional paremetric test was used, ANOVA test.

- The figures are not sufficient quality, high solution pictures please.

We will improve image

- Explain in an educational way how you calculate gas consumption.

The formula is derived from the reference.

- Do you have any theory why Aisys is faster at low flow with desflurane? Do you have any theories?

This may be an effect of the different vaporizer techniques and the phase during inspiration/expiration gas is delivered to the fresh gas.

- Why does it take longer to wash-out desflurane than sevoflurane in a mechanical lung model? This does not correspond to the clinical picture.

The finding is also to us somewhat surprising. One must acknowledge that this is merely the lung volume and circle wash-out. The low blodd gas solubility impacts the biological wash-out from the human body. It does not describe the elimination from volumes per see.

- Does desflurane have lower density than sevoflurane? Is that why it takes longer to wash-out the desfluran? Can you come up with some theories about the most remarkable result in the study?

The longer wash-out may be related merely to the huger amount of gas, the 6 % gas volume.

- I can not find sevoflurane wash-out in Figure 4.

The Figure 4 A. presents sevoflurane wash-out.

Competing Interests: Author of paper, see previous competetive interest statemnet

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