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RESEARCH NOTE

REVISED Wash-in and wash-out of sevoflurane in a test-lung model: A comparison between Aisys and FLOW-i [version 2; referees: 2 approved, 1 approved with reservations]

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Abstract

Background: Modern anaesthesia workstations are reassuringly tight and are equipped with effective gas monitoring, thus providing good opportunities for low/minimal flow anaesthesia. A prerequisite for effective low flow anaesthesia is the possibility to rapidly increase and decrease gas concentrations in the circle system, thereby controlling the depth of anaesthesia. **Methods:** We studied the wash-in and wash-out of sevoflurane in the circle system with fixed fresh gas flow and vaporizer setting. We compared two modern anaesthesia work stations, the Aisys (GE, Madison, WI, USA) and FLOW-i (Maquet, Solna, Sweden) in a test lung model. **Results**: We found fresh-gas flow to have, as expected, a major influence on wash-in, as well as wash-out of sevoflurane. The wash-in time to reach a stable circle 1 MAC (2.1%) decreased from an average of 547 ± 83 seconds with a constant fresh gas flow of 300 ml/min and vaporizer setting of 8%, to a mean of 38 ± 6 seconds at a fresh gas flow of 4 L/min. There were only minor differences between the two works-stations tested; the Aisys was slightly faster at both 300 and 4 L/min flow. Time to further increase circle end-tidal concentration from 1-1.5 MAC showed likewise significant associations to fresh gas and decreased from 330 ± 24 seconds at 300 ml/min. to less than a minute at constant 4 L/min (17 ± 11 seconds), without anaesthetic machine difference. Wash-out was also fresh gas flow dependent and plateaued at 7.5 L/min. **Conclusions**: Circle system wash-in and wash-out show clear fresh gas dependency and varies somewhat between the Aisys and Flow-i. The circle saturation, reaching 1 MAC end-tidal or increasing from 1-1.5 MAC can be achieved with both work-stations within 1.5 minutes at a constant fresh gas flow of 2 and 4 L/min. Wash-out plateaued at 7.5 L/min.

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Referee Status: ✓ ✓ ?

	Invited Referees		
	1	**2**	**3**
REVISED version 2 published 26 Apr 2017	✓ report	✓ report	? report
	↑	↑	
version 1 published 29 Mar 2017	? report	? report	

1 **Göran Hedenstierna**, Uppsala University Sweden

2 **Ian Smith**, University Hospitals of North Midlands NHS Trust UK

3 **Thomas Schilling**, Uppsala University Sweden, **Moritz A. Kretzschmar**, Otto-von-Guericke-University Magdeburg Germany

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Comments (0)

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Introduction

A rapid change in inspired anaesthetic agent is a requisite for the control of the depth of anaesthesia. Low flow anaesthesia has been increasingly adopted, as it is associated with several benefits, including conserving humidity and temperature, which improves the quality of anaesthesia[i]. Reducing the amount of anaesthetic agent consumed is of interest not only for reducing cost, but also for reducing environmental burden. The merits of reducing flow must not overrule safety, by maintaining adequate oxygen content in the circle, and avoiding hypoxic gas mixture, inadequate anaesthesia control and too light anaesthesia with risk for awareness[ii,iii]. Increasing and decreasing the circle system anaesthetic concentration during low and minimal flow anaesthesia calls for knowledge around the technique and kinetics of the anaesthetic gas used. We studied wash-in, increase and decrease of the end-tidal gas concentration, within the circle system with two anaesthetic machines, GE Aisys and Maquet FLOW-i, at different fixed fresh gas flow and fixed vaporizer settings in a test model. Our hypothesis was that the wash-in and wash-out should be fresh gas flow dependent, and that the time for reaching target end tidal concentrations would be faster for the FLOW-i device, which does not have a classical reservoir.

Methods

The two anaesthetic workstations, Aisys (GE Healthcare, Madison, WI, USA) and FLOW-i (Maquet, Solna, Sweden), including a standard CO_2 absorber and a standard circle system (patient circuit, adult, disposable 1.8 m; GE Healthcare) and a Humid-Vent Filter (Teleflex, Wayne, PA, USA), were connected to a 2 L elastic test reservoir (Intersugical Ltd., East Syracuse, NY, USA).

Wash-in: time to reach a stable circle concentration; end-tidal concentration of 1 and 1.5 MAC age adjusted (40 year old male) sevoflurane (2.1 and 3.1%) was studied with the circle connected to the test reservoir. Ventilation was set at tidal volume 500 ml, respiratory rate 10 and PEEP 5 cmH2O, for both devices. The oxygen fraction was set at 0.4. Ventilation settings and FiO2 was kept constant during thire test, wash-in and wash-out- Fresh gas flow was fixed at 300, 500, 1000, 2000 and 4000 ml/minute. The vaporizer setting was fixed at 8% for both devices during the wash-in and 0 at wash-out.

The time to reach 1 MAC and the time to increase from 1-1.5 MAC circle concentration was recorded for each value, based on mean of 3 repeated tests.

Wash-out: time to decrease from 1.5 MAC to 0 gas concentration with a fixed fresh gas setting of 2500, 5000, 7500 and 10000 ml/minute.

Workstations at the department of anaesthesia at Danderyds University hospital was used for the study. Gas monitoring was done with each workstations side-stream multi-gas infra-red monitor. These analysers are 0-calibrated automatically at start of the machine. The workstations are further controlled and calibrated in accordance to the service routine of the department.

Statistics

All data are presented as mean and standard deviation based on 3 repeats. The effects on time events (wash-in: increase from 0 – 1 MAC and further increase up to 1.5 MAC; wash-out: decrease from 1.5 MAC to 0 gas) between fresh gas flows and anaesthetic workstations were calculated by ANOVA. $P<0.05$ was considered to be statistically significant. Data was analysed with StatView (v1.04) for MAC.

Results

Fixed fresh gas flows had a significant impact on the speed of wash-in - time to achieve a stable circle end-tidal sevoflurane concentration of 1 MAC age adjusted (2.1%). The mean time of both machines decreased from 547 ± 83 seconds, at a fixed fresh gas flow of 300 ml/min and fixed vaporizer setting of 8%, to 38 ± 6 seconds at a fresh gas flow of 4000 ml/min. The time to further increase the circle system end-tidal sevoflurane from 1 to 1.5 MAC also showed a significant dependency on fresh gas flow: 330 ± 24 seconds, at a fixed fresh gas flow of 300 ml/min and fixed vaporizer setting of 8%, to 17 ± 11 seconds at a fresh gas flow of 4000 ml/min.

Both anaesthetic work-stations showed the same fresh-gas flow dependent for wash-in and wash-out pattern, but the Aisys showed overall a slightly faster wash-in time (Table 1 and Figure 1).

Wash-in (time to reach a stable 1 MAC circle sevoflurane concentration) was achieved within 1.5 minute at a fixed fresh gas flow of 2000 ml/min for both machines tested, 48 ± 2 and 75 ± 2 seconds for the Aisys and Flow-I, respectively (p<0.001), and within 1 minute, mean 33 ± 3 and 42 ± 3 seconds, for Aisys and Flow-i at 4000 ml/min, respectively (p<0.05). A further increase from 1 to

Table 1. Wash-in time (seconds) to reach 1 and 1.5 MAC circle concentration during constant fresh gas flow and vaporizer setting. Vaporizer set at 8%, tidal volume 500 ml, respiratory rate 10, PEEP 5 and volume controlled ventilation.

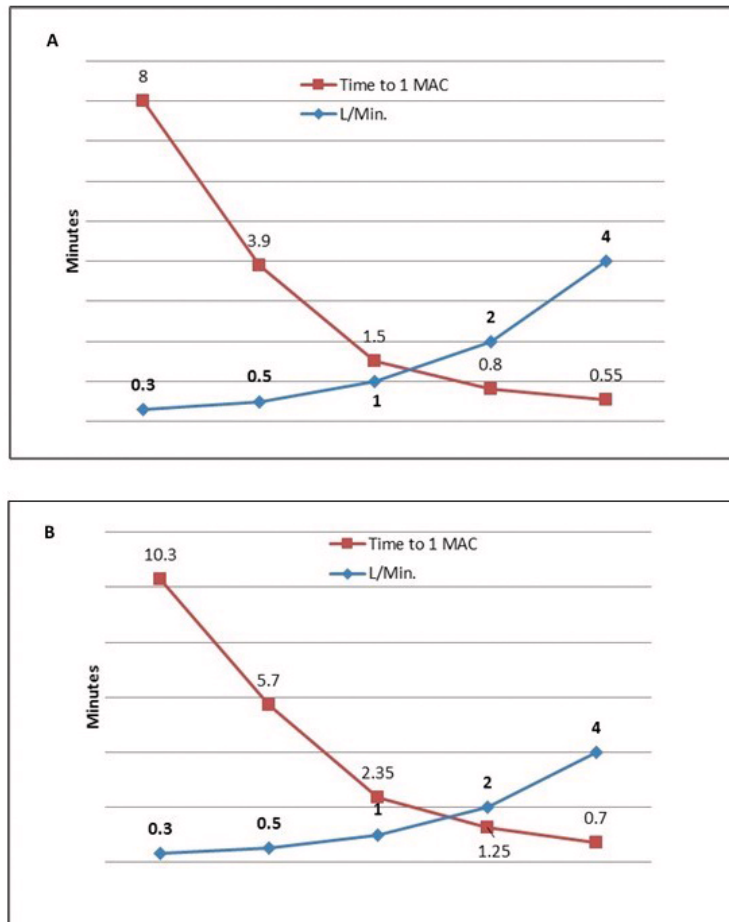|		L/min				
	MAC	0.3	0.5	1	2	4
FLOW-i	0–1	618	342	141	75	42
	1–1.5	317	191	88	46	25
Asysis	0–1	477	232	99	48	33
	1–1.5	344	165	96	22	10

Figure 1. Wash-in time (minutes) to increase to 1 MAC (sevoflurane 2.1%) for (**A**) Aysis and (**B**) FLOW-i anaesthetic work stations.

1.5 MAC was achieved within 1 minute for both machines (22 ± 3 and 46 ± 3 seconds for Asysis and Flow-i, respectively) at a fixed fresh gas flow of 2000 ml/min. When a 4000 ml/min was used, the monitoring system was not fast enough to catch the increase for the Aisys, but recorded the increases as 25 ± 10 seconds for Flow-i.

Wash-out was likewise flow dependent, and plateaued at 7.5 L/min (Table 2 and Figure 2).

Table 2. Wash-out time (seconds) to decrease from 1.5 MAC circle concentration with a constant fresh gas flow and closed vaporizer. Tidal volume 500 ml, respiratory rate 10, PEEP 5 and volume controlled ventilation.

	L/min			
	2.5	**5**	**7.5**	**10**
Aysis	15.41	4.25	2.14	2.15
FLOW-i	10.73	4.45	2.49	2.48

Dataset 1. Raw data from the wash-in increase of Et-sevoflurane at fixed fresh gas flow and vaporiser setting

http://dx.doi.org/10.5256/f1000research.11255.d156064

Dataset 2. Raw data from the wash-out of Et-sevoflurane at zero vaporiser setting and increasing fresh gas flows

http://dx.doi.org/10.5256/f1000research.11255.d156065

Discussion

The present study was set-up to evaluate the impact of fresh gas flow on saturation of and wash-out from the circle system/test-lung set up and whether the modern anaesthesia machines performed differently. We found a clear fresh-gas flow dependency for the time to saturate and wash-out of the circle and test-lung system, as expected. Wash-in to 1 MAC and further increasing the circle concentration to 1.5 MAC decreased with the fresh gas flow, and a 1 and further increase to 1.5 MAC was achieved within 1 minute at a fresh gas flow of 4 L/min. The wash-out was not further improved between 7.5 and 10 L/min fresh gas flow.
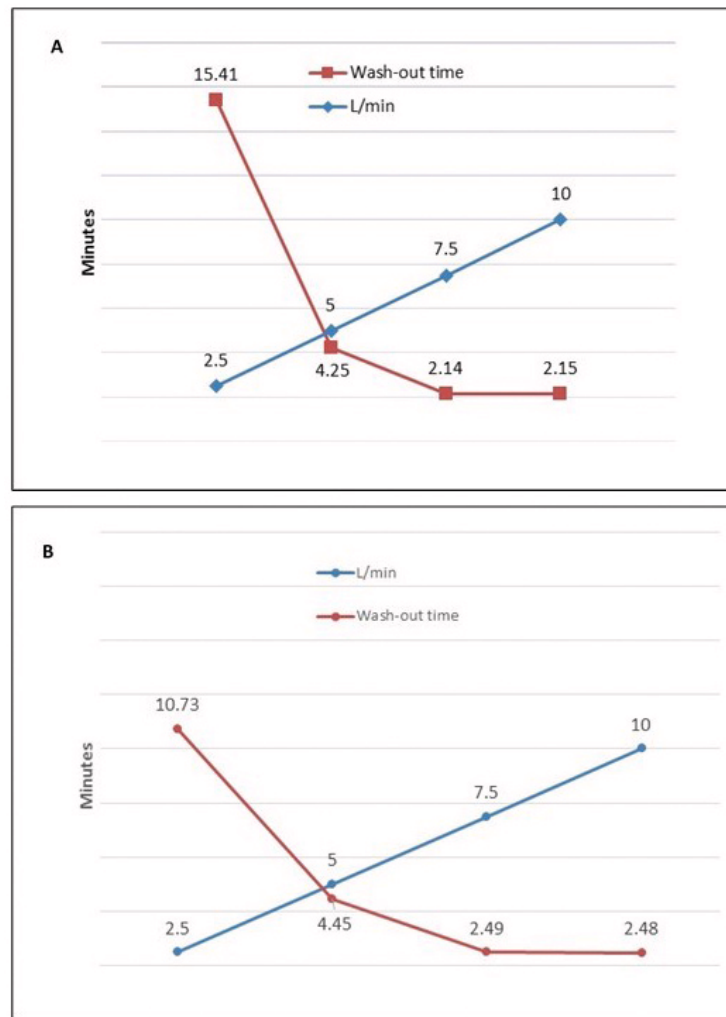
Figure 2. Wash-out time (minutes) for decrease from 1.5 to 0 MAC with sevoflurane at 3.1-0% in (**A**) Aysis and (**B**) FLOW-i anaesthetic work stations.

We found somewhat surprisingly that the Aisys was slightly faster than the FLOW-i, although the FLOW-i should have a small internal gas reservoir. Lucangelo *et al.* studied the FLOW-i performance regarding tidal volume in case of minor leakage[iv]. They found the system to be highly accurate. They also described the gas flow control in detail addressing the technical features of the flow regulators. Thus, our hypothesis was a faster saturation of the circle gas with the FLOW-i technology. We cannot give any explicit reason why the wash-in unexpectedly was slower for the FLOW-i. One contributing mechanism may be differences in the vaporizer technology. According to the Maquet user's manual, during controlled ventilation "a larger proportion of the fresh gas is added during the inspiration phase, also contributing to minimizing agent consumption". The Flow-i vaporiser only injects anaesthetic agent during inspiration and is inactive during the expiratory phase of the cycle which may contribute to the difference in wash-in. The Aisys delivers vapour continuously, like a conventional vaporizer, which might explain why wash-in to a test lung is faster. One should also acknowledge that the gas measurements were done by the built in multi-gas analysers. To what extent that could have impacted the results cannot be stated.

Dosch *et al.*[v] studied the change in circle gas composition in three anaesthetic machines and found that fresh gas flow and breathing system volume have the biggest effect on time to equilibrium. In a previous study, we analysed the wash-in of desflurane and sevoflurane during fixed fresh gas flow and vaporizer setting with the Aisys anaesthesia workstation[vi]. We found, as expected, desflurane to be associated to a significantly faster wash-in compared to sevoflurane with a significant impact from the fresh gas flow: The increase from 0.5 L/min to 1.0 L/min in fresh gas flow reduced the time to reach 1 MAC age adjusted end-tidal concentration from 15.2 ± 2.4 minutes to 6.2 ± 1.3 minutes. We found in that study a rather large variability for sevoflurane, which we considered was related to a combination of circle system gas saturation and uptake.

Kern *et al.* studied the saturation of neonatal anaesthesia systems[vii]. They found huge differences in the time to reach the end tidal

concentration above 95% of inspired. They also found wash-in times to decrease with higher fresh gas flows and higher minute ventilation rates; however, they saw that the effect of doubling fresh gas flow was variable and less than expected. Struys *et al.* made a study much like ours comparing the Zeus apparatus with direct injection of inhaled anaesthetics and the Primus apparatus using a classical out-of-circle vaporizer[viii]. They found the Zeus to have a faster time course, but their study set-up was different from ours; they used fresh gas and auto control modes, providing a high initial fresh gas bolus. We compared the novel FLOW-i with a similar injection technique and without classical reservoir, and the Aysis with a more classic design. Carette *et al.* studied the performance of the automatic control mode of the FLOW-i[ix]. The possibility to use an automatic algorithm to reach desired circle, end-tidal concentration is an interesting option and we plan to do further studies assessing the automatic technique. One limitation of the study was that it is an entirely experimental study.

There are several limitations with our study. We studied only wash-in and wash-out in a test lung and indeed there was no uptake of anaesthetic vapour from the breathing circuit and likewise no anaesthetic agent elimination from the blood during wash-out. We used the built in gas monitors. It would have been of value to have had a free-standing well calibrated multi gas sensor. One may also argue that statistical differences seen may not translate into clinical important differences. Further studies assessing the benefits and limitations with the new and costly anaesthetic works stations are warranted.

In conclusion, wash-in, saturation of and wash-out of the circle system is fresh gas flow dependent. A 1 MAC can be reached within 1 minute at a fixed vaporizer setting of 8 at a fresh gas flow of 4 L/min and further increase from 1-1.5 MAC can be reached within 1 minute at a fresh gas flow of 2 L/min. Wash-out was found likewise flow dependent, but the time to reach a zero end-tidal concentration plateaued at 7.5 L/min.

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.

Data availability
Dataset 1: Raw data from the wash-in increase of Et-sevoflurane at fixed fresh gas flow and vaporiser setting. doi, 10.5256/f1000research.11255.d156064[x]

Dataset 2: Raw data from the wash-out of Et-sevoflurane at zero vaporiser setting and increasing fresh gas flow. doi, 10.5256/f1000research.11255.d156065[xi]

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      Data Source

xi.   Jakobsson P, Lindgren M, Jakobsson JG: **Dataset 2 in: Wash-in and wash-out of sevoflurane in a test-lung model: A comparison between Aisys and FLOW-i.** *F1000Research.* 2017.
      Data Source

Open Peer Review

Current Referee Status: ✓ ✓ ?

Version 2

Referee Report 05 May 2017

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

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

In the present small but nice study the authors compared two modern anaesthesia machines (Aisys, GE, Madison, WI, USA, and FLOW-i, Maquet, Solna, Sweden) concerning the time periods of wash-in and wash-out of sevoflurane with different fresh gas flows and constant vaporizer settings in a test lung model. Jakobsson *et al.* can demonstrate that the time to reach 1 MAC (and later on to 1,5 MAC) in the circle systems depends mainly on fresh gas flow.

In addition, the authors found no major but slight differences between both anaesthetic work-stations. The fact that the Aisys seems to be a little faster than the Flow-i is surprising and cannot be related to the construction type of the respective machine.

In our opinion, the present experimental study is of importance since optimal flow rates need to be determined and confirmed for both machines.

We have some comments and questions to the authors:
1. The authors should consider to measure gas concentrations and ventilation mechanics with external, calibrated, standardized devices. The different integrated equipment may be responsible for a major part of the differences.

2. We presume that in both workstations internal test routines to determine leakage had been performed in advance and passed. However, the tolerated leakage of each system should be reported. It should be for the AISYS less than 150ml/min; however, a number for the Flow-i is not defined in its manual. Thus, leakage has to considered different in both machines.

3. In our opinion, the behavior of the gas flow through the gas analyzer may impact the significance of the results. Both machines use about 200ml/min but in the Flow-i the sample gas is returned to the circle system, whereas the AISYS leads the sample obviously to the waste gas.

4. In addition, there are different precision ranges for the vaporizers that are used in both workstations. The precision for the Flow-i ranges from +/- 0,15 ABS% to 0,4 ABS%; The Aladin vaporizer in the AISYS has a precision of +/- 10% between 18-25 °C. At fresh gas flows exceeding

5 L/min and concentrations >5 vol% the manual states that the delivered concentrations fall after a few minutes. The Flow-i is reported to have +/-15% but a temperature range is not given. The question is, were the experiments conducted in these temperature ranges? Here might be a possible explanation for the variability.

5. The manuscript would benefit from a comprehensive revision of typing errors (e.g. "competing interests" paragraph on p. 2.: has received, Pfizer; "Revised" box: "vaporization"; Introduction: "A rapid change in inspired anaesthetic agent..." – "fraction" or "concentration" is missed.)

6. We would like to ask the authors to improve the figures: Please name the X axis for better understanding, please include scatter measurements (SD, SEM).

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.

Referee Report 02 May 2017

doi:10.5256/f1000research.12427.r22257

Göran Hedenstierna
Hedenstierna Laboratory, Department of Medical Sciences, Clinical Physiology, Uppsala University, Uppsala, Sweden

The authors have made a reasonable revision of their manuscript. I have no further comments.

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 28 April 2017

doi:10.5256/f1000research.12427.r22256

✔ **Ian Smith**
University Hospitals of North Midlands NHS Trust, Stoke-on-Trent, UK

The authors have revised their manuscript to better discuss their observations and speculate on possible causes for these. Some minor typographical errors have also been corrected. While this remains a lab-type study with all of the associated limitations, these have been adequately acknowledged and the paper nevertheless provides a useful starting point for further clinical research and may also prove useful to clinicians who have recently acquired one or other of these workstations

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.

Version 1

Referee Report 24 April 2017

doi:10.5256/f1000research.12142.r21842

? **Ian Smith**
University Hospitals of North Midlands NHS Trust, Stoke-on-Trent, UK

The authors have examined the effect of fresh gas flow rates on the wash-in and wash-out of a single volatile anaesthetic agent in two modern anaesthetic workstations under experimental conditions.The investigation is essentially in two parts. The first shows that wash-in and wash-out and flow dependent for both anaesthesia machines. As these are exponential processes, this finding is entirely predictable and rapid wash-in (or wash-out) will only be achieved at fairly high fresh gas flow rates, whatever the internal design of the anaesthetic machine. While it is still important to define optimal flow rates for new equipment, this part of the paper does not really provide any very new information.

The second part of the study is potentially far more interesting and this is the comparison between the two systems. The authors speculated, quite appropriately in my opinion, that wash-in and wash-out would be faster with the Flow-i system due to its lower internal volume. However, they did not find this to be the case, especially with regard to wash-in where, in fact, the Flow-i was actually the slower of the two systems. What I find very disappointing is that the authors do not really address why they did not obtain the results they anticipated. Although their discussion mentions a few related points, there is almost nothing concerning the differences between the two systems studied or what the implications of these findings might be. The authors also seem not to have commented on the fact that differences between the two machines were not consistent between wash-in and wash-out and whether this provides any insight

into the observed results. For me, this would be a far more interesting paper if these differences were explored in a bit more detail. I would also be interested to know if I needed to change the way I altered vapouriser settings and flow rates in practice were I to switch from one of these systems to the other.

One possible explanation for the apparent differences has already been mentioned in a previous review, namely that there was not really a difference at all, but that using the in-built gas analysers of the machines resulted in apparent differences due to differences in sampling times/mechanisms/algorithms. I also wonder if differences in the vapouriser technology might explain the findings, at least in part. According to the Maquet user's manual, during controlled ventilation "a larger proportion of the fresh gas is added during the inspiration phase, also contributing to minimising agent consumption". Our technical staff tell me that the Flow-i vapouriser only injects anaesthetic agent during inspiration and is inactive during the expiratory phase of the cycle. If this is correct, and if the Aisys delivers vapour continuously, like a conventional vapouriser, that might explain why wash-in to a test lung is slower than expected. It is also likely under those circumstances that the difference between the machines would be reduced if higher respiratory rates were used and might also be completely different during spontaneous ventilation. Do the authors have detailed knowledge of how the two vapouriser systems function?

Although the Flow-i, unexpectedly, was slower than the Aisys, this was not consistently observed and again I think this deserves some discussion. For wash-in from 0–1 MAC, the Aisys was consistently faster, with times ranging from 64–79% those of the Flow-i. However, for wash-in from 1–1.5 MAC, the times were much less consistent, ranging from 109% to 40% those of the Flow-i. Neither was any pattern evident for the second stage wash-in, with the Aisys actually being slower at 0.3 and 1 l/min, but faster at 0.5, 2 & 4 l/min. Can the authors explain this at all? Could sampling error be enough to explain the differences?

The wash-out results are even more confusing. The Flow-i was slower from 5 to 10 litres/minute, but the wash-out times were so fast that the differences are small and probably within the limits of sampling error. However, at 2.5 l/min the Flow-i was 70% faster. This faster wash-out is entirely consistent with the lower internal volume of the Flow-i (as hypothesised by the authors) and, to me, lends support to the concept that the unexpected observations during wash-in are probably related to differences in the function of the vapourisers.

As the authors state, this was a test model study. However, the results are likely to be used to inform clinical practice. The problem is that the results are unlikely to be reproduced in clinical practice. As the authors used a test lung, there was no uptake of anaesthetic vapour from the breathing circuit. Adding a patient compartment is likely to delay the wash-in of the anaesthetic machine compartment due to uptake of anaesthetic. This should affect both machines to a similar degree, although if the Flow-i preferentially injects vapour during inspiration while the Aisys does not, it is possible that the addition of a patient may affect the systems differently. Wash-out will also be delayed by the addition of anaesthetic vapour to the breathing system from the patient's lungs. This should affect both systems equally, but in this case will differ with the duration of anaesthesia delivery and hence the amount of agent taken up by the patient. Do the authors have any clinical data to indicate by how much their findings are actually altered in clinical practice?

A few other comments:
What determined the number of repeat measurements? In the methods it is stated wash-in times were determined "based on [the] mean of 3 repeated tests", but in the statistics section it is said data are means "based on 3–5 repeats".

It is stated that data are shown as means and standard deviation. However, all of the tables and figures show only mean data. Standard deviations are only given for the data specifically highlighted in the main text. Without standard deviations, the degree of imprecision of the data cannot be assessed.

Although a statistically significant p value is defined, the authors do not state the minimum size of differences which they considered to be clinically important. In a few cases, the differences are only a few seconds and of little consequences, but in quite a few cases, the differences are 100 seconds or more and represent quite large percentage differences between the systems. An indication of a minimal clinically-important difference, in association with an indication of the degree of variability, would greatly aid interpretation of the results.

Statistical tests have been applied to the differences in wash-in and wash-out for both systems (combined) at high versus low gas flows, even though these differences are large in magnitude and highly predictable. However, statistical tests do not appear to have been reported for the far more interesting differences between the anaesthesia machines at each flow rate.

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

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?
Partly

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.

Referee Report 13 April 2017

doi:10.5256/f1000research.12142.r21357

Göran Hedenstierna
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This is a straightforward and simple, in a good sense, model study on the wash-in and wash-out of an anesthetic gas in a test lung model. Comparison has been made between two commercially available anesthesia machines, Aisys and Flow-i. A major finding was that with increasing gas flow, wash-in and wash-out times were reduced, as might be anticipated. The difference was small between the two anesthesia machines but there was a slight difference that in itself was unexpected, i.e. the Aisys being a little faster than the Flow-i. The Aisys uses conventional reservoir bag whereas the Flow-i uses an internal reflector that, at least in theory, should reduce any dead space effect and thus shorten time constants in gas dynamics.

I have some comments.

Firstly, the wash-in and wash-out times have been measured in a lung model, the same for both anesthesia machines but the gas concentration has been measured with built in equipment in the Aisys and Flow-i and thus different for the two anesthesia machines. At least I interpret of the results this way. This means that there might be a difference in results that are not caused by the different techniques of internal gas reservoir. With different gas analyzers the results may be related to how the analyzers have been calibrated and what algorithms have been used. Ideally, one should use the same gas analyzer for both machines if the intention has been to test the effect of the design of the gas reservoir. This is my major comment and I suggest that the gas analyzers should be compared to an independent reference. Other comments follow below.

Abstract line 14: 300 *ml/min*.
Methods, wash in: You might have used additional settings of the ventilator such as tidal volume, respiratory rate and PEEP. At least you might discuss this.
Results, page 4 line 3 under figure 1: was *not* fast enough.
Discussion, page 5, third last line in the right column: Why as expected?
Page 6, left column, second paragraph: Zeus

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?
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.

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*) 13 Apr 2017
Jan Jakobsson, Department of Physiology and Pharmacology, Karolinska Institutet, Sweden

Dear Referee

Thank you for comments;
We acknowledge the limitation using the machine gas monitor. Both machines are equipped with "standard" side-stream multi-gas monitors. These instruments have an internal calibration at start up. We did perform a startup prior to each test. It should also be noticed that we performed the study with standard anaesthetic machines used at our department, machines used for ordinary patient care. We performed the test during late afternoons and evenings. Thus we do expect the IR-multi-gas readings to be adequate.

Abstract line 14: 300 *ml/min*.
There is indeed a text error in the abstract line 14 please excuse, should read 300 ml/min., no doubt

The ventilator settings are presented in the methods section; *The ventilation was set at tidal volume 500 ml, respiratory rate 10 and PEEP 5 cmH2O, for both devices.*

Results, page 4 line 3 under figure 1: much agree, the **was** is indeed missing, please excuse

Discussion, page 5, third last line in the right column: Why as expected?
This is simply because all authors are clinically active and we are so used to see the lower solubility benefit and subsequently faster "blood compartment wash-in" associated to desflurane as compared to sevoflurane. This can indeed be argued when looking merely at circle system equilibration/wash-in. Thank you for most adequat comment.

Page 6, left column, second paragraph: Zeus,
This referes to the Zeus anaesthesia apparatus (Dräger, Lubeck, Germany)

I hope our comments/responses are acceptable and your adequate and effective review.

Best regards
Jan Jakobsson, on behalf of all authors

Competing Interests: None