Supporting Information

S-1

Continuous real time breath gas monitoring in the clinical environment by proton-transfer-reaction-time of flight-mass spectrometry

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The supporting material contains additional figures and tables that are relevant to the manuscript. Moreover a detailed description of the data processing algorithm for the automatic recognition of alveolar and inspiratory phases is given.

Table of contents:

S-2 Description of the Data processing algorithm

The data processing algorithm worked as follows:

1. An indicator m/q had to be specified. This mass was used in the algorithm to differentiate between alveolar and inspired phases.
2. Tolerance intervals for alveolar and inspired phases had to be defined. E.g. when the tolerance interval for alveolar phases was set to 10%, all intensities within a breathing cycle, which were higher than 90% of the maximum intensity, were assigned to alveolar phases. If the tolerance interval for inspired phases was set to 2%, for instance, all intensities within a breathing cycle, which were lower than 2% of that cycle's maximum were attributed to inspired air.
3. A minimal duration of a breath in seconds could also be set. Breaths that were shorter would be marked as non reliable and were excluded from processing. Additionally, a minimally required number of data points could be defined. If it was set to 2, for instance, breaths with less than 2 alveolar data points were also regarded as non reliable.
4. Substance intensities could be normalized automatically onto primary ion counts if desired.
5. Phase resolution determined by means of the algorithm could then be applied to all m/q of interest.

Figure S-2 shows a plot using acetone as tracker substance to distinguish between alveolar and inspiratory phases.

Table S-1 Demographic data of study participants

	Male	Female	Age (Average) [years]	Age (Range) [years]	BMI (Average)	BMI (Range)	Smokers	Non Smokers
All Participants	15	17	38	22 - 53	23.92	19.92 - 36.30	6	26
Clinicians	11	4	38	26 - 50	23.69	20.23 - 36.30	4	11
Controls	3	4	29	22 - 44	22.40	19.92 - 25.71	1	6
Nurses	1	9	45	35 - 50	25.67	20.43 - 33.79	1	9

Table S-2 Response times of propofol and typical breath VOCs (e.g. ecetone, isoprene) for PTR-ToF-MS measurements using different transfer lines (PEEK, silco steel) with different lengths (1.2 m, 6 m), different additional sampling flows (20, 50, 70 mL/min) and different temperatures (26, 60, 80°C)

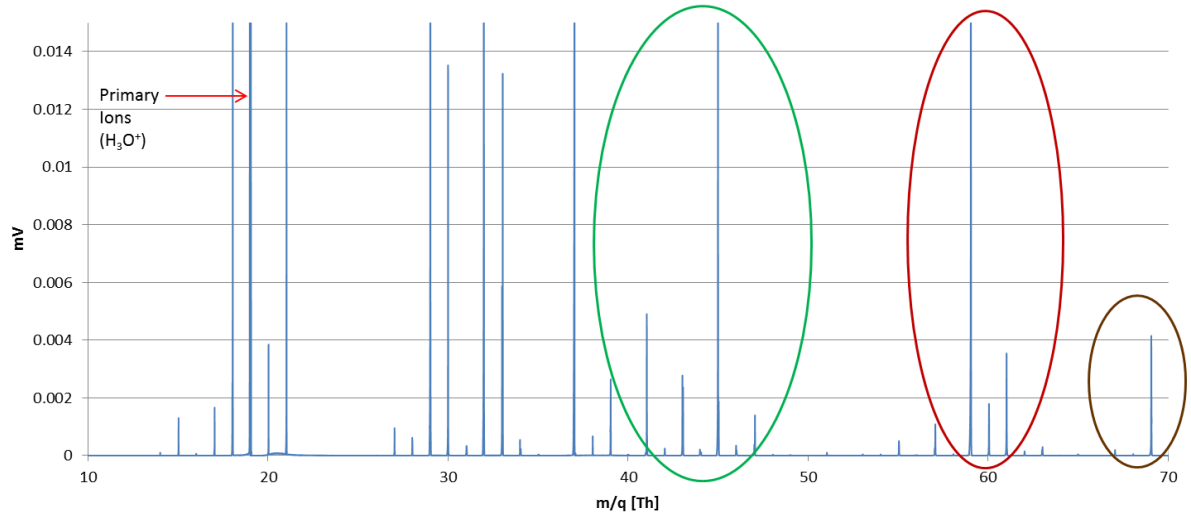
Material	Length [m]	Additional sampling flow [ml/min]	Temperature [°C]	Response time of propofol [sec]	Response time of typical breath VOCs [sec]
PEEK	1.2	20	60	10	1
	6	20	26	>120	5.5
			60	40	5
Silico Steel	1.2	20	60	2	1
			80	1.5	< 1
	6	20	26	55	5.5
			60	7	5
	6	20	80	5	5
		50		3	3
		70		2.5	2.5

Table S-3 List of tentatively identified VOCs in the breath of a mechanically ventilated patient

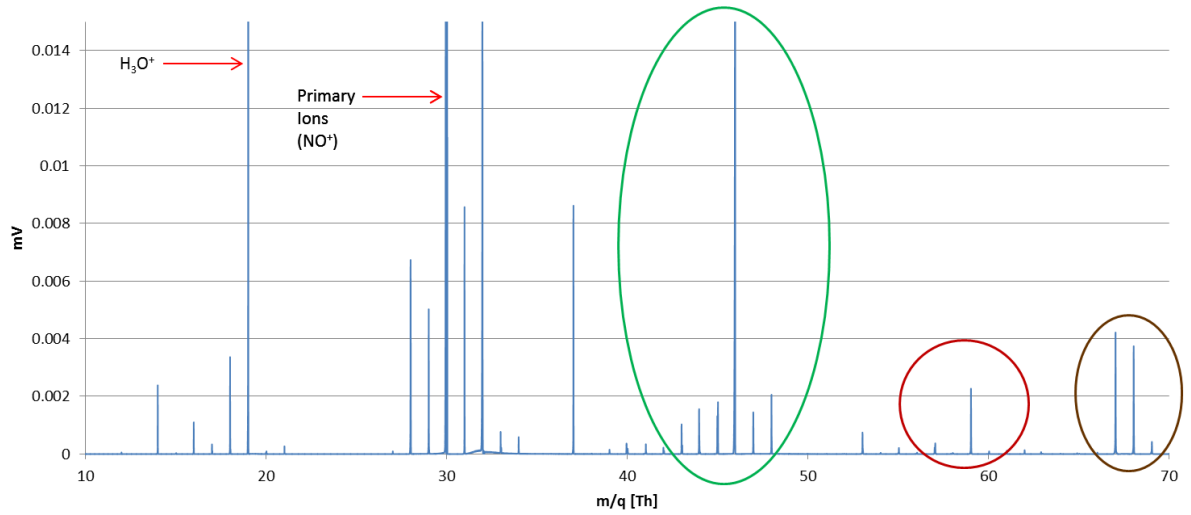
Peak Number	Measured Mass [m/q]	Exact Mass [m/q]	Error [ppm]	Sum Formula	Tentative Identification
1	18.03382	18.03394	-6.54	$(H_3N)H^+$	Ammonia
2	31.01784	31.01796	-3.71	$(CH_2O)H^+$	Formaldehyde
3	33.03349	33.03361	-3.48	$(CH_4O)H^+$	Methanol
4	44.99711	44.99722	-2.44	$(CO_2)H^+$	carbon dioxide
5	57.06988	57.06999	-1.91	$(C_4H_8)H^+$	Butene
6	59.04914	59.04926	-1.96	$(C_3H_6O)H^+$	Acetone
7	60.052609	60.05261	-0.03	$(C^{13}C_2H_6O)H^+$	Acetone isotope
8	61.06479	61.06490	-1.87	$(C_3H_8O)H^+$	Isopropanol
9	63.0263	63.02641	-1.75	$(C_2H_6S)H^+$	Dimethylsulfide
10	69.06989	69.06999	-1.43	$(C_5H_8)H^+$	Isoprene
11	73.064908	73.06480	1.48	$(C_4H_8O)H^+$	Butanal
12	77.05972	77.05982	-1.28	$(C_3H_8O_2)H^+$	Propanediol
13	79.05423	79.05434	-1.40	$(C_6H_6)H^+$	Benzene
14	85.101293	85.10118	1.33	$(C_6H_{12})H^+$	Cyclohexane
15	87.080556	87.08044	1.33	$(C_5H_{10}O)H^+$	Pentanal
16	91.075467	91.07341	22.59	$(C_4H_{10}O_2)H^+$	1,4-Butanediol
17	99.08044	99.08056	-1.17	$(C_6H_{10}O)H^+$	Cyclohexanone
18	137.13248	137.13259	-0.79	$(C_{10}H_{16})H^+$	Limonene
19	179.14316	179.14249	3.72	$(C_{12}H_{18}O)H^+$	Propofol
20	181.0112	181.00661	25.34	$(C_4H_2OF_6)^+$	Sevoflurane fragment
21	198.99884	198.99994	-5.51	$(C_4H_2OF_7)^+$	Deprotonated Sevoflurane

Figure S-1 Mass spectra (m/q 10-70, 180s average) from breath analysis in a spontaneously breathing volunteer using different ionization reagents. a) H3O+ mode b) NO+ mode c) O2+ mode. Red Circle: Acetone – protonated acetone can be found in all three ionization modes; brown circle: isoprene – in H3O+ mode protonated isoprene is detected, in NO+ and O2+ mode protonated isoprene is still detected even though deprotonated isoprene (mass 67) shows the highest abundance; green circle: hydrocarbons show high fragmentation in the O2+ mode compared to the other two modes. H3O+ is still abundant in high concentrations after switching to other ionization modes

a



b



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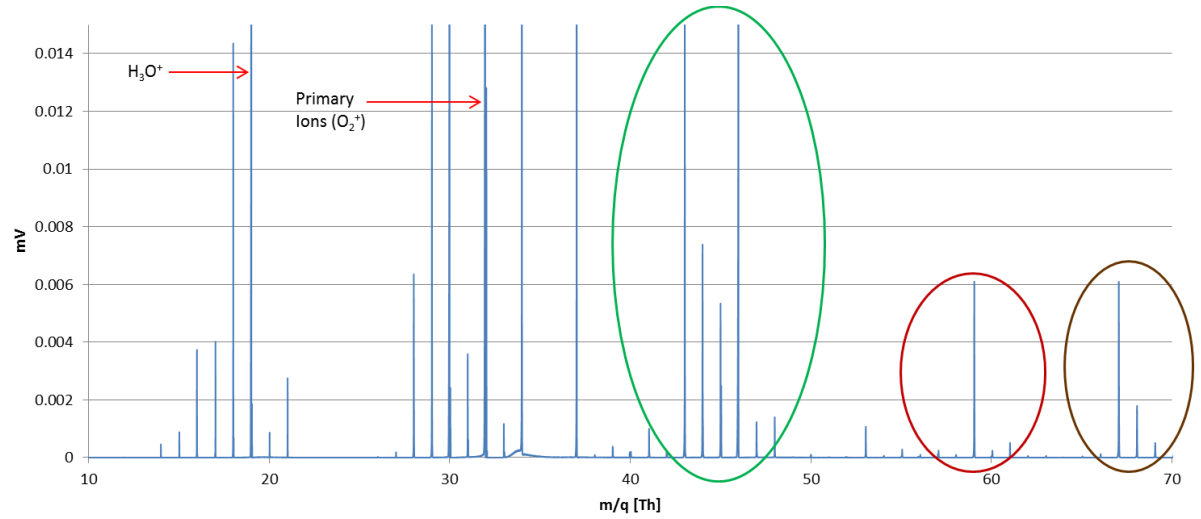


Figure S-2 Recognition of alveolar phases using isoprene as tracer substance. Blue trace: isoprene signal. Blue background: inspiration, red background: alveolar phases

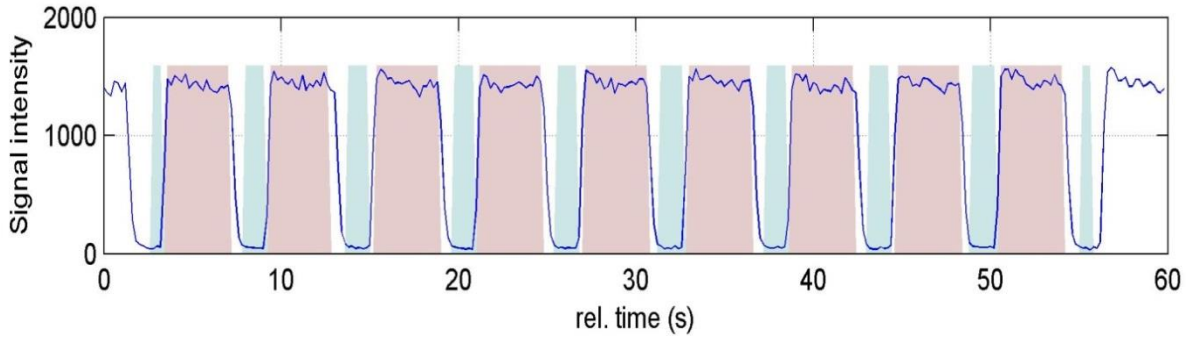


Figure S-3 Mass spectrum averaged over 10 breaths on a logarithmic scale. Breath sampled from a mechanically ventilated patient. Detailed description of peak numbers can be found in table 2

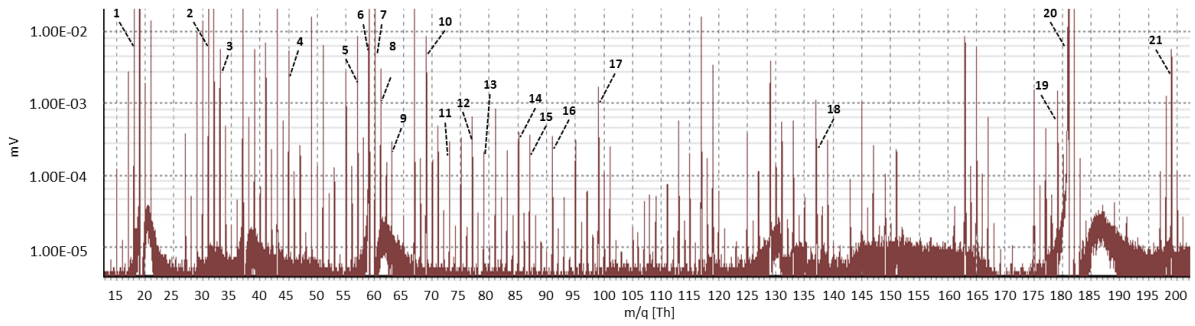
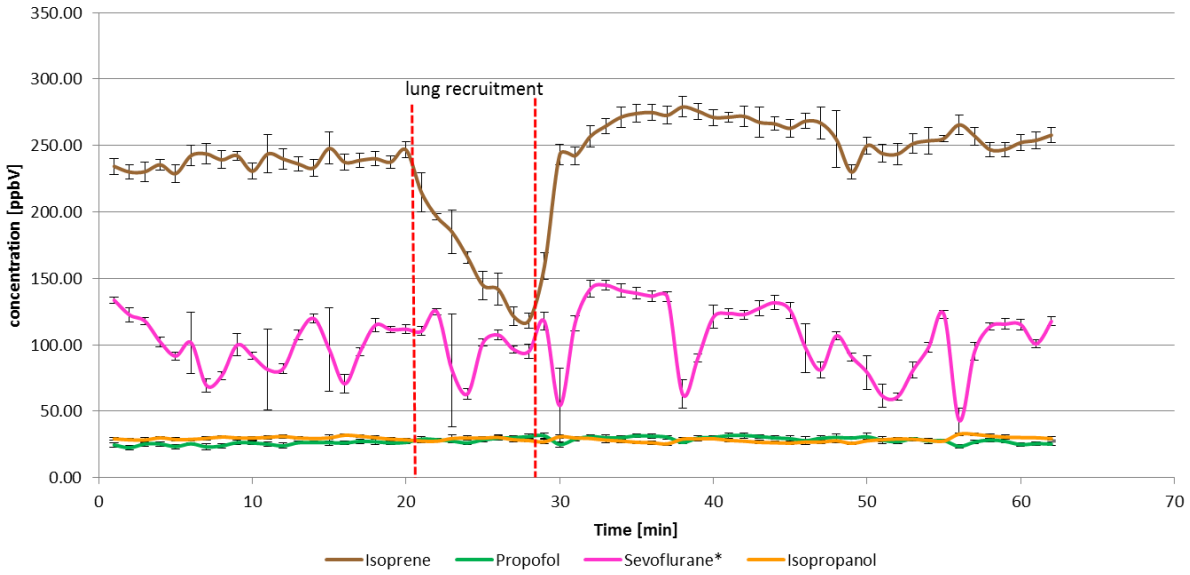


Figure S-4 Continuous breath monitoring in two additional mechanically ventilated patients on the intensive care unit. The diagrams show alveolar concentrations (in ppbV) of isoprene, propofol, sevofluorane and isopropanol over a time of 60 minutes. Sevoflurane concentration was divided by a factor of 200 in diagram (a) and by a factor of 400 in diagram (b) for better visibility. Mean alveolar concentrations and variations refer to data averaged over 1 minute.

a



b

Figure S-5 Comparison of room air concentrations (y-axis) with alveolar (red dots)) concentrations (x-axis) determined in volunteers not working in the clinical environment by means of the breath tracker data processing algorithm