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TITLE PAGE

Title:

Real-time measurement of Xenon concentration in a binary gas mixture using a modified ultrasonic

time-of-flight anesthesia gas flowmeter: a technical feasibility study

Short Title:

Ultrasonic measurement of xenon in a binary gas mixture

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STRUCTURED ABSTRACT

Background:

Xenon (Xe) is an anesthetic gas licensed for use in some countries. Fractional concentrations (%) of gases in a xenon/oxygen mixture are typically measured using a thermal conductivity meter and fuel cell respectively. Speed of sound in such a binary gas mixture is related to fractional concentration, temperature, pressure, and molar masses of the component gases. We therefore performed a study to assess the feasibility of developing a novel single sterilizable device which uses ultrasound time of flight to measure both real-time flowmetry and fractional gas concentration of Xe in O_2.

Method:

For the purposes of the feasibility study we adapted an ultrasonic time-of-flight flow meter from a conventional anesthetic machine to additionally measure real time fractional concentration of Xe in O_2. A total of 5 085 readings of Xe % were taken in the range 5% to 95%, and compared with simultaneous measurements from the gold standard of a commercially available thermal conductivity xenon analyser.

Results:

Ultrasonic measurements of Xe (%) correlated with thermal conductivity meter measurements but there was wide variability and a marked discontinuity in the middle of the measurement range.

Conclusions:

The adapted ultrasonic flow meter estimated Xe (%) but the level of accuracy is insufficient for

clinical use. With further work it may be possible to develop a device to perform both flowmetry and binary gas concentration measurement to a clinically acceptable degree of accuracy.

Word Count: Structured Abstract: 248 words; Introduction: 446 words; Discussion: 1138 words

TEXT

Introduction

Xenon (Xe) is a noble gas licensed for general anesthesia in many countries. It has a high minimum alveolar concentration (MAC) of 72% at sea level; and is therefore usually administered as a binary gas mixture with oxygen (O_2) as the balance gas.[1]

Fractional concentrations (%) of gases in common anesthetic use (O_2, N_2, CO_2, volatile agents) are typically measured using electrochemical techniques or infra-red spectroscopy. These techniques cannot be used with Xe, which is chemically inert, does not absorb infra-red light, and is not paramagnetic. However, compared to O_2 or N_2, Xe has a low thermal conductivity and slow velocity of propagation of sound (Table 1).[2,3] Therefore measurement of Xe (%): O_2 (%) mixtures usually requires two different devices: a thermal conductivity meter (TCM) and a fuel cell respectively. [4, 5]

Anesthetic gas flow is typically measured using the pneumotachograph principle; however the high density of Xe renders these devices inaccurate. Ultrasonic Flow Meters (UFM) are unaffected by gas density and provide a low cost, robust, sterilizable alternative. The Spirocell UFM (Spirocell[TM], Gill Ltd, UK) is one example, developed for use in anesthesia workstations. [a] It employs a measurement cell containing a reflex arrangement of angled sound reflectors mounted at 45 degrees to the long axis of the measurement cell, and paired transducers which alternately transmit and receive 200 kHz ultrasound pulses of 92 ns duration first against the direction of gas flow (`upstream') and then with the gas flow (`downstream') (Figure 1, inset). Downstream pulses traverse the distance between the transmitter and receiver faster than upstream pulses. By counting the number of received upstream (N_{up}) and downstream (N_{down}) pulses within a fixed time interval it is possible to calculate the time of

flight (ToF) and hence gas velocity in each direction independently of the gas mixture composition. Gas flow rate (L.min^{-1}) may then be derived by combining this information with the known internal volume of the measurement cell.

Speed of sound (c) in a binary gas mixture is related to concentration, temperature, pressure, and molar masses of the component gases based on a complex non-linear relationship [2, 6, 7] (Figure 2) given by the equation:

$$c = \sqrt{\frac{\frac{\Sigma_i w_i C_{pi}}{\Sigma_i w_i C_{vi}} RT}{\Sigma_i w_i M_i}}$$

Where c is speed of sound (ms^{-1}); w is molar fraction of each component gas i; Cp and Cv are molar specific heat at constant pressure and volume (Jmol^{-1}K^{-1}); R is the molar gas constant (8.3144598 m^2 kg s^{-2} K^{-1} mol^{-1}); T is absolute temperature (K); M is molar mass (kg mol^{-1})

Therefore, as well as measuring flowmetry of Xe: O_2 mixtures, ToF data from a UFM could potentially also provide a means of continuous real-time monitoring of Xe (%) and O_2 (%).

Through addition of a data processing module, we adapted a commercially available ultrasound ToF flow meter to derive real-time measurement of fractional concentration of xenon in a balance gas of oxygen (Xe$_{UFM}$, %), and performed a pilot study to compare the results with simultaneous measurements from the gold standard of a thermal conductivity xenon analyser (Xe$_{TCM}$, %).

Methods

Opinion was sought from our Joint Scientific Review Committee and also the Regional Ethics

Committee, and we received confirmation that formal review was not required.

Apparatus:

A UFM (Spirocell^{TM}, Gill Ltd, UK), TCM (GKM-03, INSOVT, St. Petersburg, Russia), and precision

temperature sensor (LM35Z, Texas Instruments Inc., Dallas) were connected in series, with a 3 liter

reservoir bag at either end. Standard 22 mm to 25 mm anesthetic adapters were used to make

connections between the different pieces of equipment, and all joints were sealed with hot melt glue to

ensure a gas-tight fit. The temperature sensor was mounted in a short length of corrugated anesthetic

tubing with epoxy resin. (Figure 2)

A device designed and programmed by one of the authors (DW) used a microcontroller (Arduino

Mega 2560; Sparkfun Electronics, Colorado) and associated hardware to coordinate 10-bit Analogue-

to-Digital conversion (ADC) and rolling-mean smoothing of the output from the temperature sensor;

two-way communication with the UFM and TCM via RS232 serial data interfaces; and calculation of

$Xe_{UFM}\%$ from these data streams.

The relationship between temperature-corrected speed of sound (SoS, ms^{-1}) and binary gas

concentration based on existing data for ideal gases [2] (Figure 1) was modeled to an accuracy of 0.001

% using a quintic polynomial function using a spreadsheet (Excel, Microsoft , WA). The coefficients

for the formulae used to calculate both SoS, and Xe concentration based on SoS were stored in the

microcontroller memory in the form of databases (look up tables) of pre-calculated discrete values and

covered the temperature range 10° Celsius to 40° Celsius in 0.5° Celsius increments. The microcontroller used linear interpolation to estimate the coefficients for temperatures falling between these reference values.

The microcontroller received 100 upstream (N_{up}) and 100 downstream (N_{down}) ToF pulse counts from the UFM every second. It combined this raw data with readings from the temperature sensor and coefficients from the look-up tables to derive the speed of sound in the gas mixture; and thus Xe fraction, Xe_{UFM} (%). Simultaneously, a commercial TCM designed for measurement of Xe (%) independently measured the Xe fraction, Xe_{TCM} (%), and sent values to the microcontroller at a frequency of 2 Hz.

Gas temperature (° Celsius), Xe_{UFM} (%) and Xe_{TMM} (%) were displayed in real time to two decimal places of accuracy with current time (hh:mm:ss), on a back lit liquid crystal display. These measurements, as well as N_{up} and N_{down}, were saved as uniquely labelled .csv (comma-separated value) spreadsheet files on a micro SD card, and simultaneously transmitted via a Bluetooth link to a laptop computer for analysis.

Procedure:

With the apparatus at sea level (ambient pressure 101.3 kPa), two point calibration of the TCM sensor was performed for both Xe and O_2, using calibration gas mixtures of 100% O_2: 0% Xe and 0% O_2 : 100% Xe. Both reservoir bags were completely evacuated and the apparatus was purged with 100% Xe via the stopcock to wash out any residual O_2 or room air. The reservoir bags were alternately and

repeatedly inflated and deflated to mix gas throughout the system until the indicated value of Xe_{TMM} was constant and $> 98\%$.

When movement of gas had ceased and Xe_{TCM} was stable, the reservoir bags were clamped in order to make readings under conditions of no gas flow. Twenty consecutive paired measurements of Xe_{UFM} and Xe_{TCM} were taken at 4 s intervals using the microcontroller and hardware. The clamps were removed. 20 mL aliquots of gas were aspirated and replaced with aliquots of 100% O_2 via the three-way stopcock to reduce Xe_{TCM} in approximately 0.5% increments.

The gas was mixed and a further set of 20 readings were taken as above. This procedure was repeated until the measured Xe_{TCM} was approximately 5%. When all data had been collected, a calibration check of the TCM was performed using calibration gas mixtures of 100 % O_2: 0% Xe and 0 % O_2: 100% Xe to identify any possible calibration drift.

Paired readings for Xe_{UFM} and Xe_{TCM} were presented graphically as a scatter plot and as a modified Bland-Altman (BA) plot[8] . The scatter plot incorporated a "Line of Equality" (blue) at 45 degrees to the axes as a visual reference to aid interpretation of non-linearity. The modified BA plot is a scatter plot of the difference between the paired readings (Xe_{UFM} and Xe_{TCM}) on the y- axis against the "gold standard" (Xe_{TCM}) on the x-axis. Reference lines of zero difference (black) and mean difference (blue) were added. Linear regression analysis was used to derive a line of best fit (red) to demonstrate trends in bias over the range of measured values, along with the algebraic formula for this relationship. The standard deviation (SD) of the differences between data pairs was calculated, and 95% Limits of

Agreement were defined: 95% of data points would be expected to lie in the range: Mean Difference (Bias) ±1.96 SD.

The precision of the values for Mean Difference (Bias) and Limits of Agreement were reported as 95% Confidence Interval limits: Using methods detailed previously the Standard Error (SE) was calculated from the SD of the differences. The SE was then used in conjunction with the sample size and a table of t-statistic values to calculate upper and lower 95% Confidence Interval Limits for the Mean Difference (Bias) and Limits of Agreement, which were also displayed graphically as shaded regions on the BA plot.

Analysis and plotting were performed using statistical software (MedCalc v 9.3.0: MedCalc Software, Ostend, Belgium) and routines written by an author (DW) in the scientific programming language Python (*www.python.org*).

This study was a technical feasibility study employing a novel method of measurement of Xe concentration. We decided *a priori* that for the device to be of suitable accuracy for clinical use, the readings of Xe_{UFM} should not deviate from the corresponding gold standard values, Xe_{TCM}, by more than ± 1 %. In the absence of previous experience, pilot studies, or published data for guidance, we made a conservative estimate of the minimum required sample size with the assistance of a commercially available software tool (GPower 3.0.1.0, Dusseldorf, Germany): a two-tail t-test for matched pairs of data with $\alpha = 0.05$, Power $(1 - \beta) = 0.95$, and small effect size $|r| = 0.1$ resulted in a recommended sample size of 1 302 pairs of readings.

Results

2 040 data pairs of Xe_{UFM} and Xe_{TCM} were collected. No calibration drift occurred. 11 data pairs were incomplete due to electrical interference and were excluded, leaving 2029 data pairs for analysis in the range Xe_{TCM} 5.1 % to 93.0 % (SD 5.8 %).

The scatter plot and BA analysis showed wide variability; and both individual values and variability of Xe_{UFM} increased as Xe_{TCM} increased. Linear regression analysis confirmed the trend for Xe_{UFM} to increasingly over-read as Xe_{TCM} increased, with the algebraic relationship: Xe_{UFM} (%) = 1.1 × Xe_{TCM} (%) - 3.5. There was also an unusual effect of non-linearity which was particularly prominent around the clinically relevant range of Xe_{TCM} 50 % to 80 % (Figure 3).

SE for Mean Difference (Bias) 0.13 %; SE for 95% Limits of Agreement 0.22 % ; t-statistic 1.96 (two-tail test; significance level p = 0.05; 2028 degrees of freedom) yielding the following values (95% Confidence Limits in parentheses): Mean Difference (Bias) 1.1 % (0.9 % to 1.4 %); lower 95% Limit of Agreement -10.3 % (-10.7 % to -9.8 %); upper 95% Limit of Agreement 12.5 % (12.0 % to 12.9 %).

The variability in the Xe_{UFM} readings and wide Limits of Agreement (approximately ± 10%) with respect to the gold standard of the Xe_{TCM} were clearly too great for the existing embodiment of the UFM to be used for clinical measurement of Xe.

Subsequent bench studies using an oscilloscope and high frequency data capture with a gas mixture at constant concentration of O_2 50% : Xe 50% showed that the variability in readings for Xe_{UFM} was

caused by the hardware and firmware of the UFM. This commercial UFM appeared to apply differential values for amplification to sequential raw N_{up} and N_{down} measurements over a `short' cycle of 14 successive readings, and over a `long' cycle of 8 short cycles, resulting in a bimodal saw tooth pattern which repeated every $14 \times 8 = 112$ measurements over a 1.12 s period (Figure 4).

We were unable to modify the UFM firmware to disable this unwanted effect, and therefore modified our datalogger software to compensate for this effect by applying time-averaging so that each value of Xe_{UFM} was calculated from the mean of 112 successive pairs of raw N_{up} and N_{down} readings. We then repeated the process of data acquisition as above.

3 072 values for Xe_{UFM} (each value calculated from 112 time-averaged pairs of successive N_{up} and N_{down} ToF values) and simultaneous measurements of Xe_{TCM} were collected. No calibration drift occurred. Six datasets were incomplete and were excluded, leaving 3 066 datasets for analysis in the range Xe_{TCM} 4.9 % to 94.7 % (SD 3.9).

The scatter plot and BA analysis showed reduced variability compared to the previous dataset. There was a trend for Xe_{UFM} to under-read as Xe_{TCM} increased, with the algebraic relationship: Xe_{UFM} (%) = $0.9 \times Xe_{TCM}$ (%) - 0.1. The region of non-linearity around the clinically relevant range of Xe_{TCM} 50 % to 80 % persisted (Figure 3).

SE for Mean Difference (Bias) and 95% Limits of Agreement was 0.1 %; t-statistic 1.96 (two-tail test; significance level p = 0.05; 3065 degrees of freedom) yielding the following values (95% Confidence

Limits in parentheses): Mean Difference (Bias) -3.1 (-3.2 % to -2.9 %); lower 95% Limit of

Agreement -10.8 % (-11.0 % to -10.5 %); upper 95% Limit of Agreement 4.6 % (4.4 % to 4.9 %).

Bland-Altman analysis: mean difference (bias): -3.0606 %, SD: 3.9306 %, Limits of Agreement (95%

CI): - 10.7646 % to 4.6433 % (Figure 5).

We used the collected raw N_{up} and N_{down} data and software written in *Python* to perform *post hoc*

analysis which allowed us to explore the effects of varying temperature, pressure, acoustic path

length, and pulse width on the calculated value of Xe_{UFM}. This showed that within normal ranges

encountered in clinical practice, changes in ambient temperature and pressure had no clinically

significant effect on accuracy of Xe_{UFM} (%) measurements; however any small errors in acoustic path

length and pulse width measurements made a large difference to calculated values of Xe_{UFM} (%).

Discussion

The speed of sound in a binary gas mixture is related to the ratio of the molar masses of the component gases, and also to the temperature and pressure of the gases. In conjunction with the acoustic path length, the difference in pulse counts ($N_{up} - N_{down}$) is related to the velocity of gas flow, whilst the mean ($N_{up} + N_{down} / 2$) is inversely related to the speed of sound in the gas mixture.

Ultrasound ToF measurement has been successfully applied to industrial processes as a method of real-time continuous gas composition monitoring and leak detection for gas mixtures of octofluoropropane (C_3F_8) in N_2 .[6] The sensitivity of the method is dependent on the difference in molar mass between the component gases. The difference in molar mass between O_2 and Xe (32.00 g.mol^{-1} vs 131.29 g.mol^{-1}) is less than the difference in molar mass between N_2 and C_3F_8 (28.02 g.mol^{-1} vs 188.02 g.mol^{-1}) therefore less accuracy can be expected in our application (Table 1).

The use of look up tables containing pre-calculated discrete reference values allowed the necessary complex calculations to be performed very rapidly by the microcontroller, but required large amounts of memory to store the tables. The alternative approach - performing each calculation in full - would require less memory, but greater computational resources. Both methods introduce small rounding errors to the value of Xe$_{UFM}$ %; , however these were not clinically significant. Accuracy of calculation of Xe$_{UFM}$ % could potentially be improved by using a larger look up table with smaller increments, populated with calibrated measurements from real gases rather than ideal gas data.

The analogue temperature sensor had a resolution of 0.1 °C, which was further downgraded (quantization error) by the microcontroller's 10 bit Analogue to Digital Converter (ADC). A higher

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resolution ADC or digital temperature sensor (e.g. DS18B20; Maxim Integrated, San Jose, CA); could potentially improve resolution at the expense of data acquisition time.

All measurements were performed at sea-level (ambient pressure 101.3 kPa). Future embodiments of this device could use pressure sensors and 3-dimensional look-up tables to correct the calculated values of Xe_{UFM} (%) for changes in ambient pressure. However increasing ambient pressure will also compress the transducer diaphragms, which will tend to cancel out the effect of increased pressure on the calculated value of Xe_{UFM} (%). [7]

Despite the above concerns, *post hoc* analysis showed that within normal ranges encountered in clinical practice, changes in ambient temperature and pressure had no clinically significant effect on accuracy of Xe_{UFM} (%) measurement.

It was noted that the piezoelectric transducers in the UFM used in our study were encapsulated to avoid direct contact with the gas mixture and facilitate autoclave sterilization. This could potentially result in reduced pulse amplitude and decreased ToF; and hence affect measurement accuracy.

Geometric arrangements of the transducers typically used in a ToF device include: axial, `angled crossing', and `pinched reflex' in which the transducers are mounted parallel to each other and sound is reflected through the gas by two 45 degree acoustic mirrors. The commercial UFM used in our study device uses a short acoustic path length and a pinched reflex design, probably as a compromise to allow the device to be compact and fit to an existing anesthetic machine. However measurement of a very fast event (transit of sound waves) over a relatively short acoustic path length is likely to result

in random noise and wide variation in ToF measurements. The method also requires that the acoustic path length is known to a high degree of accuracy: an error of 0.1 mm in path length measurement will have significant effect. These errors combine and are amplified by subsequent calculations to produce a significant effect on the calculated values for gas flow and concentration. Despite using time-averaged data, we were only able to achieve $\pm$ 10% accuracy in our readings, and it is interesting to note that the manufacturers of the UFM used in our study quote a similar figure of $\pm$ 10% accuracy for its intended application of gas flow and volume measurement.

We therefore believe that the short acoustic path length is the main source of variability observed in our data, however this does not explain the non-linearity observed near the middle of our measurement range which was independent of all of these factors. We suspect that the non-linearity occurs due to reverberation artifacts caused by stray reflection and diffraction of ultrasound from the acoustic mirrors and/or at the 'shoulders' of the region of constriction in the center of the measurement cell.

For the purposes of this technical feasibility study, we have adapted a commercially available anesthetic machine ultrasonic flow meter to perform additional functions for which it was not intended. We therefore are currently designing a purpose-built UFM which uses software and hardware to eliminate the sawtooth gain effect; a measurement cell with a long path length to improve accuracy; and a geometry which has no constriction in the measurement cell, and transducers orientated in an axial rather than reflex orientation to eliminate reverberation artifacts. We anticipate that with these changes, we will be able to build a device of practical dimensions which will measure Xe_{UFM} to an accuracy sufficient for clinical use ($\pm\ < 0.5$ %).

This technical feasibility study has been conducted under conditions of no gas flow. For a real-world embodiment of this device, we need to do further studies to explore the effects of varying gas flow on accuracy of Xe_{UFM} (%) measurements. In theory this should have no effect since gas flow will affect the difference ($N_{up} - N_{down}$), but not the mean ($N_{up} + N_{down} / 2$) pulse counts used to calculate the speed of sound and hence fractional concentration of the gas mixture. It should therefore be possible to derive both Xe_{UFM} (%) and volumetric measurements from the same raw ToF data as described above.

This study only considers measurement of Xe in a binary mixture of gases (Xe in O_2). For increased relevance to clinical practice, we need to do further studies to explore the effects of other gases and vapours (e.g. N_2, CO_2, water vapor) on measurement accuracy. In a clinical setting, strategies for overcoming these effects could include siting the transducers in the inspiratory limb downstream of the CO_2 absorber in a circle breathing system; and monitoring these other gases and vapors via conventional means (e.g. infrared spectroscopy), and using these readings to apply correction factors to the calculated value of Xe_{UFM}.

A commercially available anesthetic ultrasonic flow meter (UFM) can be used to estimate real-time Xe % in a binary mix with O_2. With further work, it may be possible to design a purpose-built UFM to non-invasively perform simultaneous non-invasive real-time volumetry and binary gas concentration measurement to a clinically acceptable degree of accuracy and precision.

REFERENCES

1. Franks, N.P., et al., How does xenon produce anaesthesia? *Nature.* 1998;396(6709):324.

2. Lemmon, E Huber H, McLinden M. *NIST Standard Reference Database 23, Reference Fluid Thermodynamic and Transport Properties – REFPROP, version 9.1.* National Institute of Standards and Technology, Standard Reference Data Program. Gaithersburg: Boulder MD, 2013.

3. Young, HD. Freedman RA, *University Physics*, *14th Ed.* Pearson; London, 2015.

4. King R, Bretland M, Wilkes A, Dingley J. Xenon measurement in breathing systems: a comparison of ultrasonic and thermal conductivity methods. *Anaesthesia.* 2005;60:1226-1230.

5. Lynch C 3rd, Baum J, Tenbrinck R. Xenon anesthesia. *Anesthesiology.* 2000;92(3):865-868.

6 . Hallewell G, Crawford G, McShurley D, Oxoby G, Reif R. A Sonar-based instrument for the ratiometric determination of binary gas mixtures. *Nucl. Instr. Meth. A.* 1998;A264: 219.

7. Bates R, Battistin M, Berry S, Bitadze A, Bonneau P, Bousson N, Boyd G, Bozza G, Crespo-Lopez O, Da Riva E, Degeorge C, Deterre C, DiGirolamo B, Doubek M, Favre G, Godlewski J, Hallewell G, Hasib A, Katunin S, Langevin N, Lombard D, Mathieu M, McMahon S, Nagai K, Pearson B, Robinson D, Rossi C, Rozanov A, Strauss M, Vitek M, Vacek V, Zwalinski L. Implementation of Ultrasonic Sensing for High Resolution Measurement of Binary Gas Mix Fractions. *Sensors.* 2014;14:11260-11276.

8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of

clinical measurement. *Lancet.* 1986;i:307-310.

9. Krouwer JS. Why Bland-Altman plots should use X, not (Y+X)/2 when X is a reference method.

Stat Med 2008. 27(5): 778-780.

FOOTNOTES

a) http://gillsc.com/applications/anaesthetic-gas-flow-meter/ Accessed 3 Feb 2018.

LEGENDS FOR FIGURES

Figure 1.

Apparatus showing Ultrasonic Flow Meter (UFM) and Thermal Conductivity Meter (TCM).

Arrows indicate data cables and direction of data flow.

Inset: Detail of measurement cell. A transducer acting as a transmitter (T) emits a series of ultrasound

pulses which are reflected by an acoustic mirror (M), travel along the gas pathway, and are reflected

by a second acoustic mirror to a second transducer acting as a receiver (R). The number of ultrasound

pulses received in a given time period is used to calculate the speed of sound along the gas path. The

roles of the transducers are then reversed, and ultrasound pulses are sent and received in the opposite

direction.

Figure 2.

Speed of sound (m.s^{-1}) against fractional concentration (w) for binary O_2 : Xe mixtures at ambient

pressure of 101.3 kPa and temperature of 10 (-), 20 (-), 30 (-), and 40 (-) ° Celsius.

Figure 3.

Scatter plot (a) and modified Bland-Altman plot (b) of initial data comparing Xenon concentration measurements derived from the Ultrasonic Flow Meter (Xe_{UFM}) with Thermal Conductivity Meter readings (Xe_{TCM}). N = 2 029.

Figure 4.

Plot of the mean of 513 sequential N_{up} and N_{down} time-of-flight pulse counts from the Spirocell ^{TM}

Ultrasonic Flow Meter (UFM) for a gas mix at constant concentration of O_2 50% : Xe 50%. showing

the effect of biphasic sawtooth gain applied cyclically over each group of 112 consecutive

measurements by the UFM firmware.

Figure 5.

Scatter plot (a) and modified Bland-Altman plot (b) of additional data (with time-average correction for cyclical gain), comparing Xenon concentration measurements derived from the Ultrasonic Flow Meter (Xe_{UFM}) with Thermal Conductivity Meter readings (Xe_{TCM}). N = 3 066.

TABLES

Table 1.

Comparison of physical properties of Xenon, Oxygen and Nitrogen at 20 ºC, 101.3 kPa

Gas	Molar mass $\times 10^3$ (kg.mol^{-1})	Speed of sound (ms^{-1})	Thermal conductivity (W.m^{-1}.K)
Xe	131.29	175.51	5.45×10^3
O$_2$	32.00	326.00	25.94×10^3
N$_2$	28.02	349.11	25.47×10^3