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Original article

# Evaluation of the accuracy and precision of a new generation indirect calorimeter in canopy dilution mode

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SUMMARY

*Background & aims:* Indirect calorimetry (IC) is the only way to measure in real time energy expenditure (EE) and to optimize nutrition support in acutely and chronically ill patients. Unfortunately, most of the commercially available indirect calorimeters are rather complex to use, expensive and poorly accurate and precise. Therefore, an innovative device (Q-NRG®, COSMED, Rome, Italy) that matches clinicians' needs has been developed as part of the multicenter ICALIC study supported by the two academic societies ESPEN and ESICM. The aim of this study was to evaluate the accuracy and intra- and inter-unit precision of this new device in canopy dilution mode *in vitro* and in spontaneously breathing adults.
*Methods:* Accuracy and precision of oxygen consumption ($VO_2$) and carbon dioxide production ($VCO_2$) measurements were evaluated *in vitro* and in 15 spontaneously breathing healthy adults by interchanging three Q-NRG® units in a random order. *In vitro* validation was performed by gas exchange simulation using high-precision gas mixture and mass flow controller. Accuracy was calculated as error of measured values against expected ones based on volume of gas infused. Respiratory coefficient (RQ) accuracy was furthermore assessed using the ethanol-burning test. To evaluate the intra- and inter-unit precisions, the coefficient of variation (CV% = SD/Mean*100) was calculated, respectively, from the mean ± SD or the mean ± SD of the three mean values of $VO_2$, $VCO_2$, RQ and EE measured by each Q-NRG® units. *In vivo* accuracy measurement of the Q-NRG® was assessed by simultaneous comparison with mass spectrometry (MS) gas analysis, using Bland-Altman plot, Pearson correlation and paired *t*-test (significance level of $p = 0.05$).
*Results:* *In vitro* evaluation of the Q-NRG® accuracy showed measurement errors <1% for $VO_2$, $VCO_2$ and EE and <1.5% for RQ. Evaluation of the intra- and inter-unit precision showed CV% ≤1% for $VO_2$ and EE and CV% ≤1.5% for $VCO_2$ and RQ measurements, except for one Q-NRG® unit where CV% was 2.3% for $VO_2$ and 3% for RQ. Very good inter-unit precision was confirmed *in vivo* with CV% equal to 2.4%, 3%, 2.8% and 2.3% for $VO_2$, $VCCO_2$, RQ and EE, respectively. Comparison with MS showed correlation of 0.997, 0.987, 0.913 and 0.997 for $VO_2$, $VCO_2$, RQ and EE respectively ($p \leq 0.05$). Mean deviation of paired differences was 1.6 ± 1.4% for $VO_2$, -1.5 ± 2.5% for $VCO_2$, -3.1 ± 2.6% for RQ and 0.9 ± 1.4% for EE.
*Conclusion:* Both *in vitro* and *in vivo* measurements of $VO_2$, $VCO_2$, RQ and EE on three Q-NRG® units showed minimal differences compared to expected values and MS and very low intra- and inter-unit variability. These results confirm the very good accuracy and precision of the Q-NRG® indirect calorimeter in canopy dilution mode in spontaneously breathing adults.


## 1. Introduction

Both under- and over-feeding can negatively impact the clinical outcome of hospitalized patients [1–3].

Therefore, accurate and precise assessment of energy expenditure (EE) is essential to optimize nutritional prescription and

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support in acutely and chronically ill patients [1]. Although widely used, predictive formula based on anthropometric parameters (e.g. Harris & Benedict) are poorly reliable in clinical conditions because they are not capable of fully accounting for confounding factors that affect EE, such as body temperature, inflammatory or infectious status, endocrine profile, brain activity, drug administration and the evolution of metabolic conditions [4–6].

Indirect calorimetry (IC) is the only non-invasive technique to measure EE in real time from oxygen consumption ($VO_2$), carbon dioxide production ($VCO_2$) and respiratory quotient (RQ). Several indirect calorimeters are commercially available nowadays, but unfortunately most of them are rather complex to use, expensive and poorly accurate and precise [1,7–9]. The most reliable device, the Deltatrac II (Datex, Finland), is no longer on the market as its production has been discontinued 10 years ago and very few working units and spare parts still remain [9].

Consequently, an international initiative supported by two academic societies (the European Society of Clinical Nutrition and Metabolism (ESPEN) and the European Society of Intensive Care Medicine (ESICM) was launched and has led to the development and the evaluation of an innovative device in partnership with a company producing metabolic monitors (Q-NRG®,COSMED, Rome, Italy).

The Q-NRG® indirect calorimeter combines new gas analysis technologies with ergonomic design and intuitive software interface, which greatly facilitates its use compared to existing devices. In addition, gas calibration before each measurement is no longer required, which shortens the time to measurement. This new device can be used in mechanically ventilated patients as well as in spontaneously breathing subjects using a canopy hood or a face mask. In canopy dilution mode, the accuracy and precision of the gas exchange measurement between the canopy hood and Q-NRG® depends not only on the circuit tightness but also on the accuracy and precision of the internal blower and turbine flowmeter [10].

The aim of this study was to evaluate *in vitro* and *in vivo* the accuracy and the intra- and inter-unit precision of this new device in canopy dilution mode in spontaneously breathing adults.

## 2. Materials and methods

### 2.1. Study device

Q-NRG® is an innovative indirect calorimeter featuring touchscreen control, compact and lightweight design, battery-powered and warm-up free operation. In canopy dilution mode, a digital turbine flowmeter operates in series with the internal blower to draw air at a constant flow rate through the canopy hood (Fig. 1). The pumping rate is automatically calculated based on the weight of the subject and can be adapted during the measurement to prevent $CO_2$ concentration to become too high or too low. Inspired and expired air samples are collected in an internal micro-mixing chamber and then analyzed with a chemical fuel cell $O_2$ sensor and a non-dispersive infrared adsorption digital $CO_2$ sensor. Mean values of $VO_2$, $VCO_2$, RQ and EE are reported every 30 s. The device only requires a monthly calibration of the internal turbine flowmeter and gas analyzers, through quick and user-friendly procedures. This, in addition to automatic room air calibrations, guarantees accuracy in the measurements.

### 2.2. Study design

Measurement accuracy of the Q-NRG® was determined *in vitro*, using high precision gas analysis, and *in vivo*, using mass spectrometry (MS) gas analysis. RQ accuracy was furthermore assessed using the ethanol burning test. Intra- and inter-unit precision in measuring $VO_2$, $VCO_2$, RQ and EE was evaluated *in vitro* and *in vivo* by interchanging three Q-NRG® units (A,B,C) in a random order.


**Fig. 1.** Q-NRG® indirect calorimeter.

### 2.3. In vitro canopy dilution test

*In vitro* evaluation of the accuracy and precision of the Q-NRG® units was performed according to a previously described dilution method [11]. High precision gas mixture (16 ± 0.05% $O_2$ and 5 ± 0.05% $CO_2$, balance $N_2$, Airgas Specialty Gases, PA, USA) was injected with a high precision mass flow controller (F-201CV-10K, Bronkhorst, Germany) at a constant flow rate of 5 L/min (Rated accuracy ±(0.5%RD + 0.1%FS)) into a canopy-like dilution chamber in which a flow of ambient air was generated by the internal blower of the Q-NRG® units (Fig. 2A). In this method, simulated $VO_2$ and $VCO_2$ values are only dependent on the composition and flow rate of the dilution gas [11]. The simulation setup was optimized to ensure that room air inlet was not contaminated by operator's exhaled air and Q-NRG® diluted exhaust. The blower ventilation was set at 35 L/min, in order to verify the measurement accuracy within the acceptable $FeCO_2$ range (between 0.7 and 1.2%).

The three Q-NRG® units were aligned next to each other to avoid bias of measures due to fluctuations in ambient air, temperature, barometric pressure and humidity.

Each unit was calibrated in accordance with the manufacturer's instructions. Both simulated and measured $VO_2$ and $VCO_2$ values were reported at BTPS (body, temperature and pressure, saturated).

Ambient conditions used for the calculation of predicted $VO_2$ and $VCO_2$ values were provided by the internal sensors of the Q-NRG® being tested.

Q-NRG® ambient sensors were verified during the manufacturing process against reference certified instruments, periodically recalibrated as requested by ISO13485 standards. Six tests for each unit were performed in random order to cover all combination sequences, for a total of 18 measurements. Each simulation test lasted 7:30 min: dilution gas was injected into the canopy-like dilution chamber starting from minute 02:00. Measured values of $VO_2$, $VCO_2$, RQ and EE in each test were calculated as the mean values in the 04:30 ÷ 07:30 interval and then compared against expected values.

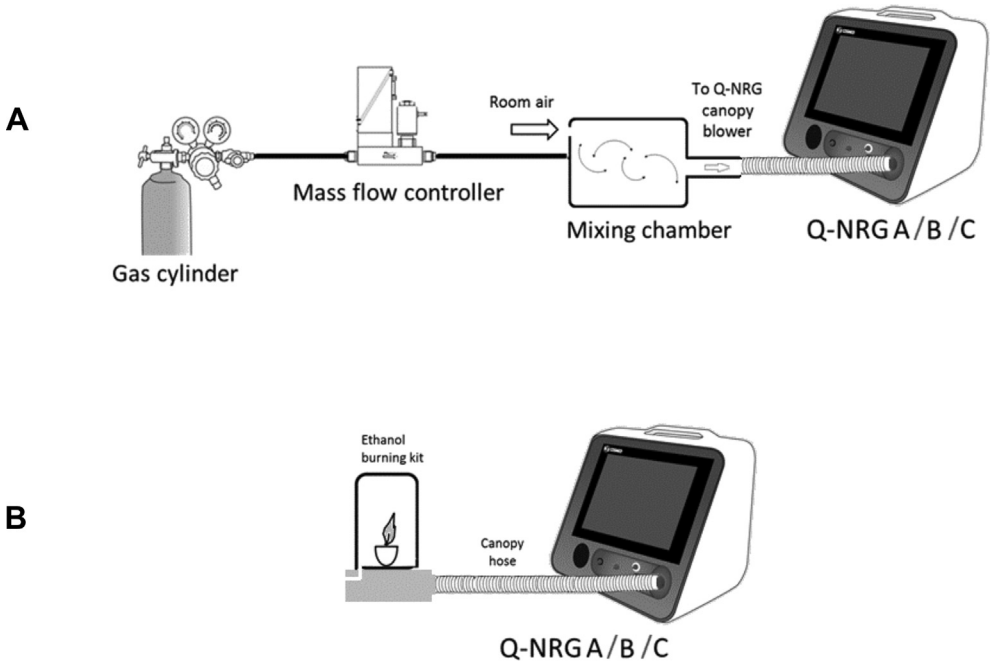



**Fig. 2.** *In vitro* setup for canopy dilution (A) and ethanol burning tests (B).

### 2.4. Ethanol burning test

The ethanol burning test is considered as a reference method to assess RQ measurement. Therefore, the accuracy of RQ measurement was assessed by connecting the canopy inlet of the three Q-NRG® units to the burning kit (burner base, alcohol burner vessel and glass cover) according to the setup shown in Fig. 2B. Each unit was calibrated in accordance with the manufacturer's instructions. Dilution flow rate was set at 35 L/min in order to obtain $FeCO_2$ within the acceptable range (between 0.7 and 1.2%). Measured RQ was calculated as the mean value over an interval of 10 min, while 96% pure ethanol was burned. According to the stoichiometric equation of ethanol, the expected RQ is equal to 0.667:

$$C_2H_5OH + 3O_2 \rightarrow 2CO_2 + 3H_2O$$

$$RQ = VCO_2/VO_2 = 2/3 = 0.667$$

The standardized acceptable range for RQ with this technique is 0.64–0.69 [12].

### 2.5. In vivo canopy dilution test

Fifteen healthy adults were enrolled after giving informed consent to perform standardized EE measurement. Measurements were conducted according to the guidelines laid down in the Declaration of Helsinki, and the protocol was approved by ethics committee (ClinicalTrials.gov Identifier: NCT03947294). Measurements were standardized according to the American Dietetic Association [13] and the Academy of Nutrition and Dietetics [14] in terms of diet, exercise and resting time. Subjects were asked to retain from food 5 h prior to the test, avoid coffee (3 h), smoking and alcohol (2 h), intense (14 h) and moderate (2 h) physical activities before the test. The tests were performed in a quiet environment, natural light and no sources of distraction. No discomfort during EE measurement was perceived by the subjects.

Both internal flowmeter and gas analysers calibration were performed for the Q-NRG® in accordance with the manufacturer's instructions. Each subject lied on the bed for 10 min before starting EE measurement.

The sequence of measurement on the three units was determined randomly for each subject. The measurement on the first unit lasted 10 min, where the first 5 min were used to establish stable baseline and the remaining 5 min were averaged for analysis. Measurements on second and third units consisted of 5 min stable EE mean values. The three consecutive measurements were done by quickly switching the hose of the same ventilated hood from one unit to another without disturbing the subject. Dilution flow was established by the unit according to its internal algorithm based on subjects' body weight to ensure $CO_2$ concentration under the canopy of around 1%. Dilution flow was identical for the three units.

### 2.6. Mass spectrometry gas analysis

Accuracy of the Q-NRG® measurements was further assessed by simultaneous measurement with a ¾ inch diameter quadrupole MS (MAX300-LG, Extrel, Pittsburgh, USA) coupled to a digital flow meter (SFM3200-AW sensor, Sensirion, Staefa ZH, Switzerland). SFM3200-AW sensor and expired air sampling line were placed in series just in front of the canopy inlet of the Q-NRG®, while the inspired air sampling line was placed near the canopy in ventilated ambient air. The MAX300-LG gas analysis system allowed measuring inspired and expired gas ions ($N_2$, $O_2$, $CO_2$ and Ar) with a precision of ± 0.0025 absolute, based on 1% Ar. Ultra high purity $N_2$ gas (99.9997%, Carbagas, Switzerland) was used for background calibration, and high precision gas mixture (16 ± 0.05% $O_2$, 5 ± 0.05% $CO_2$, balance $N_2$, Airliquid, USA) for $O_2$ and $CO_2$ measurement calibration. Mean value of three measurements of 5 min per subject were compared between the two devices for a total of 15 subjects (8 men and 7 women). Questor 5® Process Control Software (Extrel®, Pittsburgh, USA) was used to monitor and record gas exchange measurements.

### 2.7. Data acquisition and statistics

For *in vitro* dilution tests, accuracy was calculated as mean error (%) of $VO_2$, $VCO_2$, RQ and EE values measured by each Q-NRG® unit against the expected ones based on volume of gas infused.

To evaluate the intra-unit precision, the coefficient of variation (CV%) was calculated from the mean values ± SD of $VO_2$, $VCO_2$, RQ and EE measured by each Q-NRG® unit (CV % = SD/Mean*100).

To evaluate the inter-unit precision, CV% was calculated from the mean ± SD of the three mean values of $VO_2$, $VCO_2$, RQ and EE measured by each of the three Q-NRG® units.

For the ethanol burning test, the mean of RQ values was compared to the expected value of 0.667 with an acceptable range of 0.64–0.69.

For *in vivo* tests, the required sample size was estimated at 15 subjects with mean measured energy expenditure of 1′500 ± 70 Kcal to be 80% sure that the limits of a two-sided 90% confidence interval will exclude a difference in means of more than ±75 Kcal (5%), using on-line power calculator for equivalence trial (https://www.sealedenvelope.com/power/continuous-equivalence/).

All results were reported as mean ± SD. Stata/IC 13.1 software (StataCorp LP, College Station, TX, USA) was used for statistical analysis. Adjusted Bland-Altman plot and one-way ANOVA with post-hoc paired *t*-test were performed to exclude systematic errors and differences among units. The relative mean error was calculated per unit. Intra- and inter-unit variability were assessed by an intra-class correlation (ICC) and by calculating CV% respectively.

Concordance of EE values measured by Q-NRG® and MS was tested by using the Bland-Altman plot together with Pearson correlation and paired *t*-test. For statistical significance level was set at $p < 0.05$.

## 3. Results

### 3.1. In vitro dilution test

*In vitro* measurements in high precision gas mixture and flow control condition showed very good accuracy compared to the expected values with measurement errors <1% for $VO_2$, $VCO_2$ and EE and <1.5% for RQ (Table 1). Evaluation of the intra-unit precision within the Q-NRG® showed CV % <1% for $VO_2$, $VCO_2$ and EE and CV % <1.5% for RQ measurements by the units A and B, while the unit C was less accurate with CV % values < 2% for $VCO_2$ and EE and ≤3% for $VO_2$ and RQ (Table 2). Evaluation of the inter-unit precision between the three Q-NRG® units showed CV % <1% for $VO_2$ and EE and ≤1.5% for $VCO_2$ and RQ (Table 3).

### 3.2. Ethanol burning test

RQ accuracy was furthermore assessed with the Ethanol burning test. The three units measured acceptable RQ values of 0.666, 0.655 and 0.675, respectively (Table 4).

**Table 1**
Accuracy given as the mean error (%) between measured and expected values of 6 measurements per Q-NRG® unit (A, B, C).

| Q-NRG | $VO_2$ | $VCO_2$ | RQ | EE |
|---|---|---|---|---|
| A | 1.25 | −0.17 | −1.37 | −0.08 |
| B | 0.9 | −2.17 | −3.02 | −0.69 |
| C | 0.02 | −0.07 | −0.02 | −1.02 |
| Mean Error (%) | 0.72 | −0.80 | −1.47 | −0.60 |
| SD | 0.63 | 1.18 | 1.50 | 0.48 |

**Table 2**
Intra-unit precision expressed as the coefficient of variation (%) within 6 measurements per Q-NRG® unit (A, B, C).

| Q-NRG | $VO_2$ | $VCO_2$ | RQ | EE |
|---|---|---|---|---|
| A | 0.61 | 0.98 | 1.22 | 0.39 |
| B | 0.41 | 0.95 | 1.19 | 0.36 |
| C | 2.26 | 1.69 | 3.1 | 1.72 |

**Table 3**
Inter-unit precision expressed as the coefficient of variation (CV %) between the averages of 6 measurements for each of the three Q-NRG® units (A, B, C).

| Q-NRG | $VO_2$ | $VCO_2$ | RQ | EE |
|---|---|---|---|---|
| A | 243 | 241 | 0.99 | 1746 |
| B | 242 | 237 | 0.98 | 1735 |
| C | 240 | 242 | 1.01 | 1729 |
| Mean | 242 | 240 | 0.99 | 1737 |
| SD | 1.58 | 2.66 | 0.02 | 8.37 |
| % CV | 0.65 | 1.11 | 1.51 | 0.48 |

**Table 4**
RQ values obtained with the ethanol burning test for the three Q-NRG® units (A, B, C) compared to the expected value of 0.667.

| Q-NRG | RQ | % CV |
|---|---|---|
| A | 0.666 | −0.15 |
| B | 0.655 | −1.80 |
| C | 0.675 | 1.20 |
| Mean | 0.665 | −0.25 |

### 3.3. In vivo canopy test

A total of 15 healthy subjects (8 males, 7 females, Age: 38 ± 10 years, BMI 22.5 ± 2.3 kg/m$^2$) were included. Mean EE measured with the three Q-NRG® units was 90 ± 7% of predicted EE by Harris-Benedict Equation. Mean intra-subject variability for $VO_2$ and $VCO_2$ within the mean interval of 5 min was 8.4 ± 4.1 and 8.9 ± 4.8, respectively. $VO_2$, $VCO_2$, RQ and EE values obtained by each of the Q-NRG® units are described in Fig. 3. One-way ANOVA did not show any significant differences for $VO_2$ ($p = 0.993$), $VCO_2$ ($p = 0.907$), RQ ($p = 0.260$) and EE ($p = 0.999$) among the three Q-NRG® units. Bland-Altman plots showed no systematic error among Q-NRG® units (Fig. 4). Maximal average difference from the mean was 1.8% (RQ on the unit A), that was mainly due to one outlier. Inter-unit precision showed CV % < 3% for $VO_2$, $VCO_2$, RQ and EE (Table 5) and ICC of 0.976, 0.945, 0.605 and 0.977 for $VCO_2$, $VCO_2$, RQ and EE, respectively.

### 3.4. In vivo agreement between the Q-NRG® and MS

MS was used as gold standard to assess *in vivo* the accuracy of Q-NRG® measurements in canopy mode. Pearson correlation showed a highly significant correlation between the Q-NRG® and MS for $VO_2$ ($r = 0.997$), $VCO_2$ ($r = 0.987$), RQ ($r = 0.913$) and EE ($r = 0.997$) (all $p < 0.001$) (Fig. 5A). Bland-Altman analysis revealed a mean deviation of paired differences of 1.6 ± 1.4% for $VO_2$, -1.5 ± 2.5 for $VCO_2$, -3.1 ± 2.6% for RQ and 0.9 ± 1.4% for EE (Fig. 5B), which could be attributed mainly to less reliable $CO_2$ analysis (Difference: −2%) and, to a lesser extent, flow rate measurement (Difference: 1%) than $O_2$ analysis (Difference: 0.07%) (Fig. 5C). These small differences in gas analysis and flow rate measurement impacted the calculation of $VO_2$, $VCO_2$, RQ and EE values (Fig. 5D).

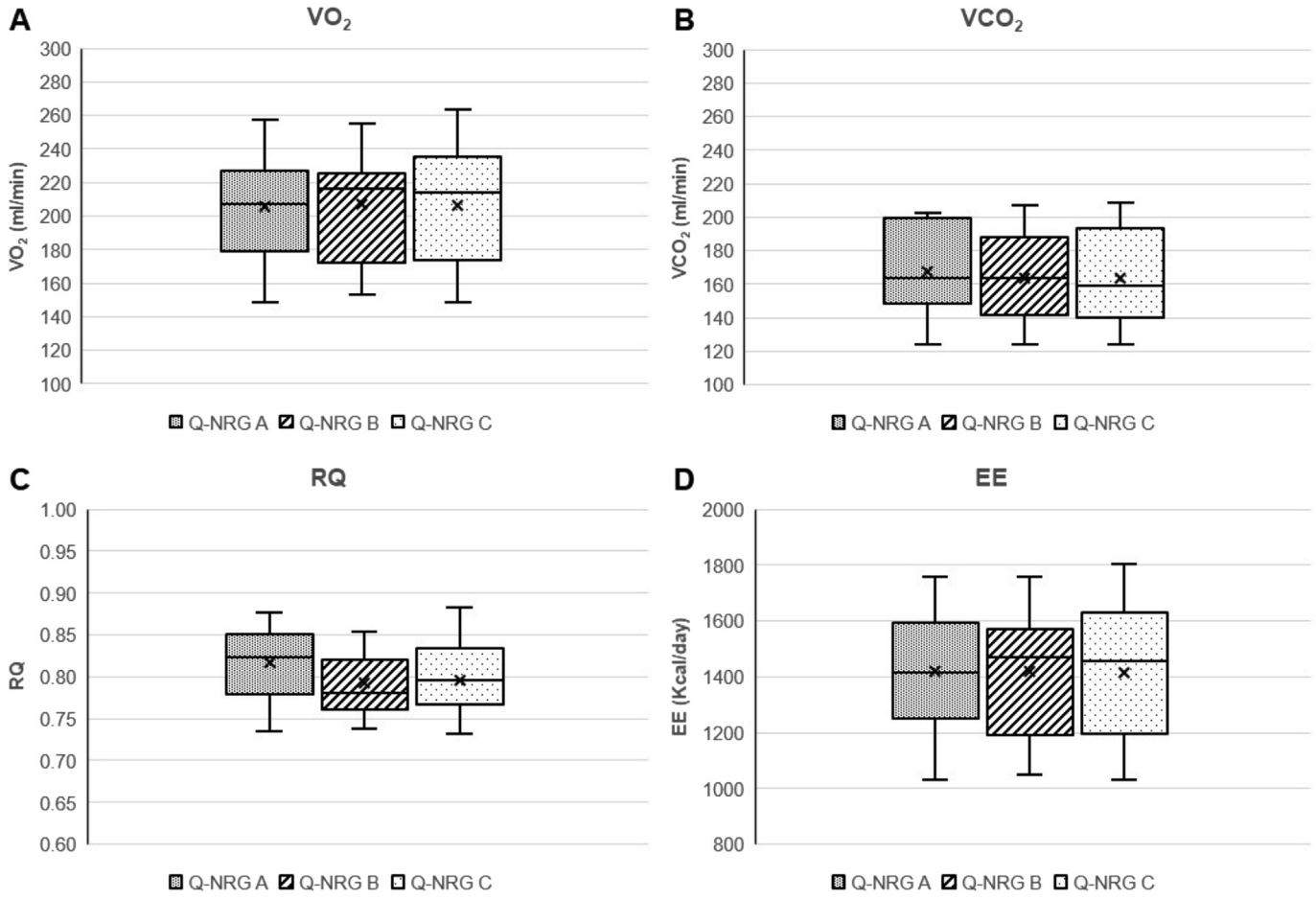



**Fig. 3.** Box plots showing $VO_2$, $VCO_2$, RQ and EE values obtained *in vivo* by each of the three Q-NRG® units (unit A = grey, unit B = stripes, unit C = points).

## 4. Discussion

This study evaluated the accuracy and intra- and inter-unit precision of $VO_2$, $VCO_2$, RQ and EE measurements of the newly developed Q-NRG® indirect calorimeter by testing *in vitro* and *in vivo* three units in canopy dilution mode.

High accuracy and intra- and inter-unit precision were found both *in vitro* and *in vivo* respectively.

The availability of accurate and precise indirect calorimeter is crucial to ensure reliable EE measurements in patients with acute or chronic diseases. Although several devices of different manufacturers are found on the market, published data regarding their validations are limited. The few available studies were performed on human subjects and used the Deltatrac II Metabolic Monitor as reference comparator, because it has been reported to exhibit the highest accuracy (measurement error <3%) and precision (error within 2%) among the previously developed devices [15].

In a previous study, Cooper et al. compared Deltatrac with five different metabolic monitors, MedGraphics CPX Ultima (Medical Graphics Corp, St Paul, MN), MedGem (Microlife USA, Golden, CO), Vmax Encore 29 System (VIASYS Healthcare Inc, Yorba Linda, CA), TrueOne 2400 (Parvo Medics, Sandy, UT) and Korr ReeVue (Korr Medical Technologies, Salt Lake City, UT). All five devices showed a larger % CV ranging from 4.8% to 10.9%, demonstrating that none of them can be considered sufficiently reliable for research purpose [16]. More recently, Graf et al. compared Deltatrac II to QuarkRMR and CCMexpress, and reported none of them would ideally replace Delatrac II due to wide limits of agreement in the measurements [9].

Schadewaldt et al. evaluated the validity and reliability of Deltatrac II and Vmax Encore both i*n vivo* and *in vitro*. *In vivo* tests showed significant differences in $VCO_2$, $VO_2$ and RQ and EE and correlation was reported acceptable for breath gas recoveries and EE, but not for RQ. *In vitro* tests reported significant variation in measurements within series relating to a rate-dependent deficiency of accuracy as well as between series relating to a variable imprecision in repeatability [11].

These few studies highlighted the urgent need to develop an indirect calorimeter that meets the clinical requirements for accurate EE assessment in patients with acute or chronic diseases.

In a previous work, we assessed *in vitro* the accuracy and precision of Q-NRG® in ventilation mode. The results showed that they differed only by ±5% even at $FiO_2$ levels as high as 70% [17], compared to the gold standard method consisting of a mass spectrometer (MAX300-LG®, Extrel CMS, USA) coupled to an external circuit including blower, flowmeter and dilution chambers [18].

The current study completes these results by demonstrating that Q-NRG® is also very accurate and precise in canopy dilution mode.

The accuracy of $VO_2$, $VCO_2$, RQ and EE measurements by the Q-NRG® was demonstrated *in vitro* by obtaining measurement differences <1.5% from the expected values in high precision gas mixture and flow control condition. This small systematic difference was confirmed *in vivo* by the comparison of simultaneous measurements between the Q-NRG® and MS. Measurement bias between the two devices seemed to be mainly due to less efficient

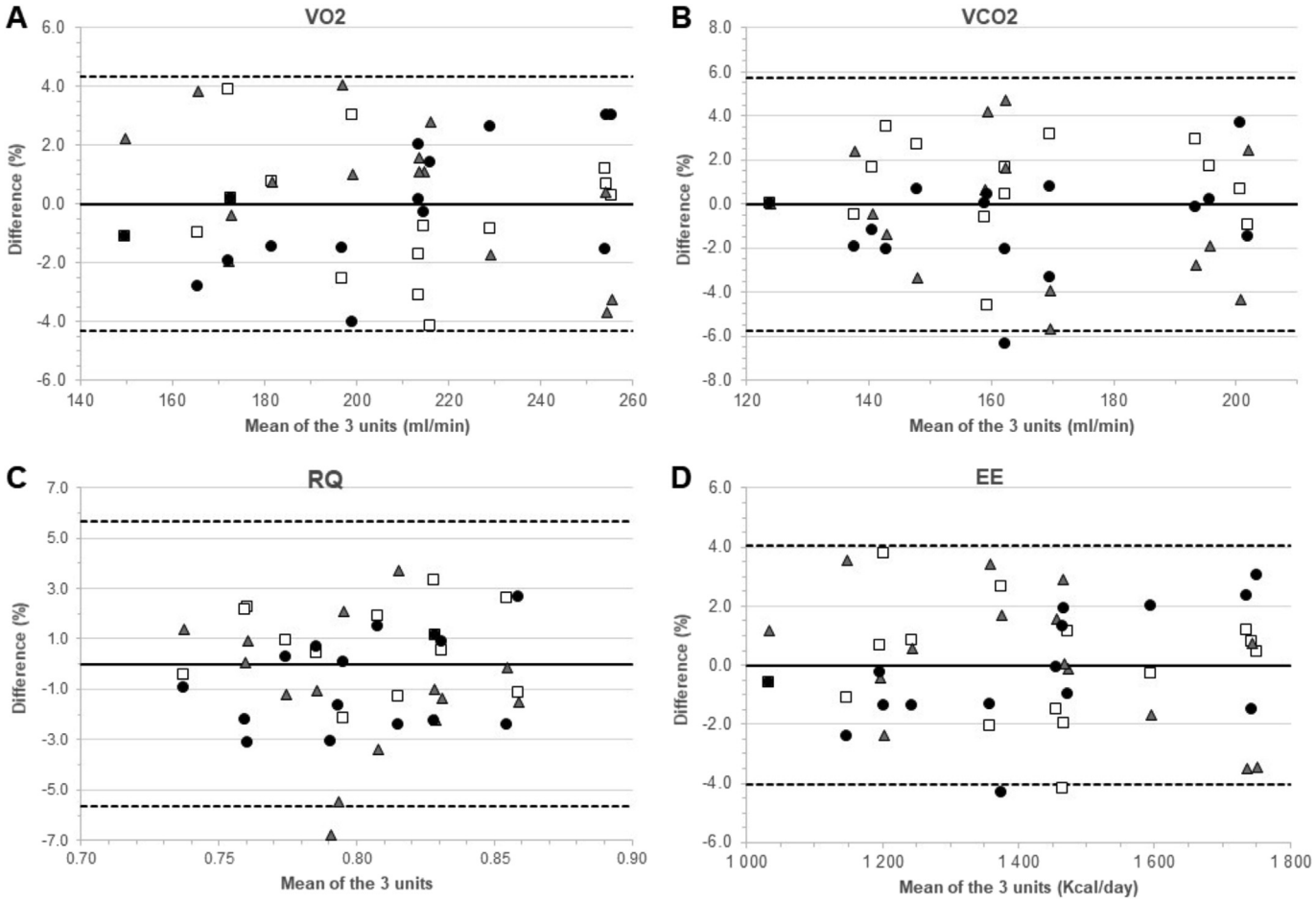



**Fig. 4.** Adjusted Bland-Altman plots for $VO_2$, $VCO_2$, RQ and EE. The three Q-NRG® units are shown in different shapes (unit A = white square, unit B = grey triangle, unit C = black circle).

**Table 5**
Inter-unit precision expressed as the coefficient of variation (CV %) between the averages of the measurements performed with the three Q-NRG® units (A, B, C) on each subject.

| | $VO_2$ | $VCO_2$ | RQ | EE |
|---|---|---|---|---|
| CV % | 2.45 | 2.99 | 2.84 | 2.26 |

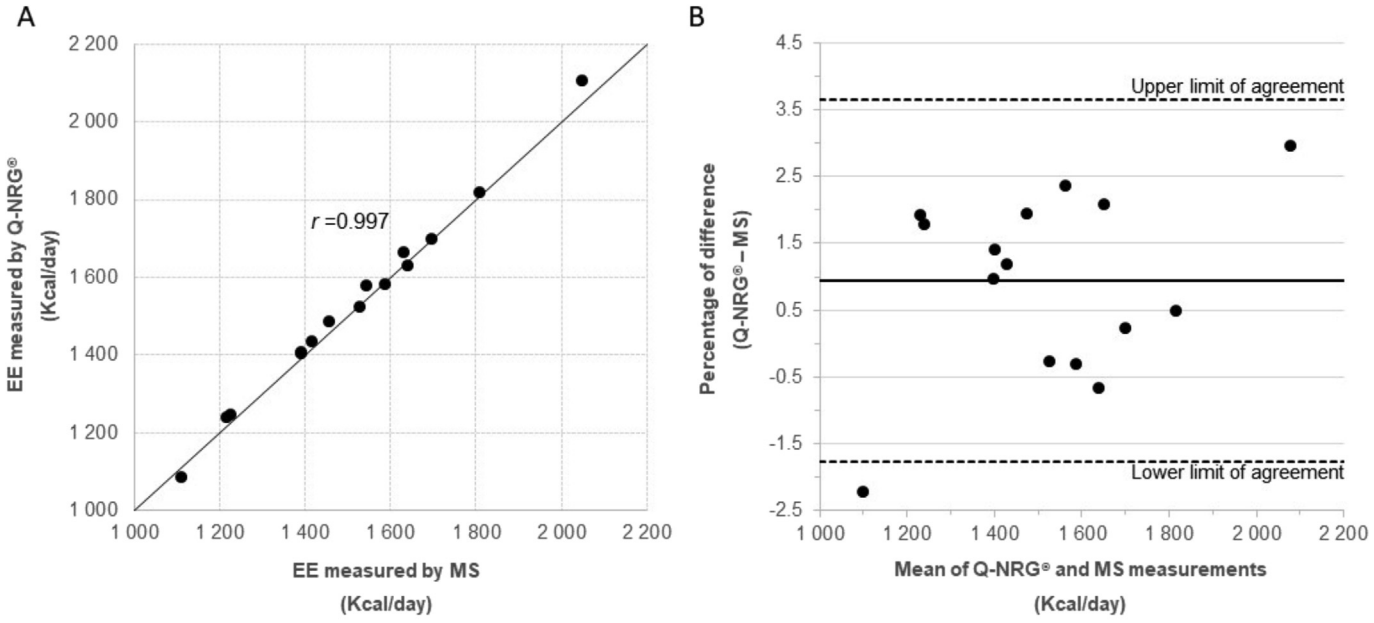
analysis of the low fraction of $CO_2$ in the air, compared to $O_2$. This bias could have been particularly enhanced in case of unstable measurement, because of different sampling times between the Q-NRG®, which provides mean values every 30 s, and the MS, which alternately measures the inspired and expired air over a 2.5-min period. Our personal experience has shown that good calibration of gases and internal turbine flowmeter by means of a periodically controlled calibration syringe is of paramount importance to maintain a measurement bias below 3%. On the other hand, the indirect calorimetry measurement should be done in a well ventilated environment to prevent $CO_2$ fraction in inspired air from changing during the measurement.

RQ value measured by Q-NRG® was found to be somewhat less accurate than the other measurements both *in vitro* and *in vivo*. However, the RQ value cumulates the measurement bias of $VO_2$ and $VCO_2$. Consequently, RQ accuracy was furthermore evaluated with the ethanol burning test, which is considered as a reference method for RQ validation. In a previous study, Kaviani et al. compared the performance of twelve metabolic monitors using the methanol burning test. Among them only five devices measured RQ within the ±2% difference from the true value 0.667 [19]. In our study, the ethanol burning test gave RQ values < 2% difference from the true value and within the acceptable range (0.64–0.69), when using Q-NRG® in canopy dilution mode.

Another objective of this study was to evaluate *in vitro* and *in vivo* the intra- and inter-unit precision of Q-NRG®. The *in vitro* results showed CV ≤ 3% and CV ≤ 1.5% for intra- and inter-unit precisions, respectively. These results are impressive, especially as part of the accuracy and variability could be due to an error in the precision mass flow controller (±0.6%). Furthermore, these results were confirmed *in vivo* by interchanging three Q-NRG® units during EE measurement in 15 healthy subjects. According to the results of this study, it is therefore possible to assume that the accuracy and precision of the new generation Q-NRG® indirect calorimeter match clinicians' requirements.

### 4.1. Study limitations

The fact that *in vitro* tests were performed on a single flow rate could be considered a study limitation. However, the *in vitro* tests have been designed to measure gas exchange in clinically relevant ranges and flow rate variation was introduced in the *in vivo* experiment. Another limitation may be the small sample size for the *in vivo* test, even though involving healthy subjects with stable metabolic condition. The measurements were




C

| Mean difference ± SD (%) | | | | |
|---|---|---|---|---|
| Flow rate | 0.95 | ± | 1.81 | % |
| $FiO_2$ | 0.07 | ± | 0.11 | % |
| $FeO_2$ | 0.07 | ± | 0.18 | % |
| $FiCO_2$ | -2.02 | ± | 6.91 | % |
| $FeCO_2$ | -2.36 | ± | 2.49 | % |

D

| Mean difference ± SD (%) | | | | |
|---|---|---|---|---|
| $VO_2$ | 1.61 | ± | 1.41 | % |
| $VCO_2$ | -1.53 | ± | 2.50 | % |
| RQ | -3.13 | ± | 2.61 | % |
| EE | 0.94 | ± | 1.38 | % |

**Fig. 5.** Scatterplot showing correlation between EE values measured by the Q-NRG® and MS in 15 subjects (A). Bland-Altman plot showing the difference (%) between the Q-NRG® and MS for EE measurement (B). Note that there are only a small systematic difference (continuous line) between the two measures, which can be attributed mainly to less reliable $CO_2$ and, to a lesser extent, flow rate measurement than $O_2$ (C). These small differences in gas and flow analysis impact the calculation of $VO_2$, $VCO_2$, RQ and EE values (D).

conducted for only 5 min per unit while, usually, clinical measurement would require 15–30 min. However, the measurements performed on healthy and relaxed subjects were sufficiently stable to be evaluated in 5-min measurements and were compared against MS gas analysis.

## 5. Conclusion

Both *in vitro* and *in vivo* measurements of $VO_2$, $VCO_2$, RQ and EE on three Q-NRG® units showed good accuracy and intra- and inter-unit precision. We concluded that the new Q-NRG® indirect calorimeter is accurate and precise. It can be applied for longitudinal studies and units can be interchanged with no influence on the results.

## Statement of authorship

Marta Delsoglio and Yves Marc Dupertuis contributed equally to the article: Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original draft, Review & Editing, Visualization.

Taku Oshima: Visualization, Writing – Review & Editing.

Mart van der Plas: Conceptualization, Methodology, Formal analysis, Investigation.

Claude Pichard: Supervision, Funding acquisition, Writing – Review & Editing.

## Conflict of interest

CP received financial support as an unrestricted academic research grant from public institutions (Geneva University Hospital) and the Foundation Nutrition 2000 Plus. CP received financial support as research grants and an unrestricted academic research grant, as well as an unrestricted research grant and consulting fees, from Abbott, Baxter, B. Braun, Cosmed, Fresenius-Kabi, Nestlè Medical Nutrition, Novartis, Nutricia-Numico, Pfizer, and Solvay, outside the submitted work. MNP reported personal fees from Cosmed during the conduct of the study. The other authors declare that they have no conflict of interest related to the current work.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2019.08.017.

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