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Prediction equations for plethysmographic lung volumes

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Due to the lack of information on reference values for plethysmographic lung volumes, standardized measurements were carried out on a selected sample of 482 healthy non-smoking volunteers (300 men and 182 women), aged 20–70 years, living in the Barcelona area (Spain).

Prediction equations using age, height and body surface area (BSA) as covariates were calculated for the subdivisions of lung volumes [TLC, IC, EVC, FRC, RV and RV/TLC (%)], separately for both sexes.

Simple linear equations predicted lung volumes as well as more complex equational models. BSA correction was useful for FRC but not for the other parameters. Our predicted FRC was up to 10% higher (mean 256 ml) than the FRC estimated by other studies using gas dilution techniques, but showed an acceptable agreement with the plethysmographic measurements carried out in an independent sample of 94 healthy non-smokers (42 men and 52 women) from Barcelona using different equipment.

The present study provides an internally consistent set of prediction equations for static lung volumes. Differences in predicted FRC between the present study and other reference values obtained using gas dilution measurements should be attributed to the method of measurement.

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Introduction

Measurement of total lung capacity (TLC) is recommended as the compulsory criterion to define a restrictive ventilatory defect (1–3). Likewise, it is generally agreed that the thoracic gas volume measured at the level of functional residual capacity (FRC) accompanied by information from other indices of static lung volumes is useful for the assessment of combined restrictive and obstructive ventilatory defects not identifiable by forced spirometry alone. Moreover, the evaluation of the residual volume (RV) by itself substantiates the occurrence of air trapping which may occur in the absence of reduced maximal expiratory flows by forced spirometry.

There is general agreement, however, that the medical literature lacks adequate studies on reference values for the indices of lung volume in adults measured by plethysmography (4), a situation which may hinder the clinical interpretation of these tests and ultimately their usefulness in the assessment of ventilatory capacity. Discrepancies among sets of prediction equations for static lung volumes in Caucasians probably reflect differences in the techniques applied, in the quality control of the measurements and/or in the selection of the reference subjects.

The present study provides reference equations for static lung volumes, as part of a larger collaborative project to obtain reference values for clinical pulmonary function testing from Caucasian residents in an industrial region of Spain (5,6). Moreover, the set of equations proposed has been compared with other reference values (2,3,7–10) available in the literature using an independent sample of 94 reference subjects (42 men and 52 women) from the Barcelona reference population studied with different plethysmographic equipment and technicians approximately 10 years after the initial survey.

Materials and Methods

Subjects were selected among volunteers, 15–75 years of age, living in the Barcelona metropolitan area at sea level.

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All participants had to be non-smokers. Caucasians, in good health and without evidence of cardiopulmonary or systemic disorders as ascertained by a questionnaire (5,6). We defined non-smokers as those who had never smoked or those who smoked less than 1 cigarette per day for less than 6 months and had not smoked cigarettes for more than 5 years before the onset of the study because of reasons other than symptoms potentially related to tobacco.

Of the 1560 subjects who volunteered in the study, 1044 (533 males and 511 females, 15–75 years of age) met the inclusion criteria in the protocol. The reasons for excluding the remaining 516 volunteers included questionnaire criteria (81%), physical exam (8%), chest radiography (5%), inability to perform acceptable manoeuvres (6%) and none (0%) by ECG. Because of the relationship between lung function and age, the initial cut-off age to calculate prediction equations for forced spirometry (5) and TL_{CO} (6) was established at 20 years. In addition, the analysis (5,6) excluded subjects older than 70 years of age because of the small number of subjects in the sample. The reference values for static lung volumes were obtained from a smaller sample of 482 subjects (300 men and 182 women) out of the 870 reference volunteers from 20 to 70 years because body plethysmography was performed in only two (Hospital Clínic, HC; Institut Territorial de Barcelona, ITB) of the three laboratories participating in the overall study. Data collection was carried out during 1981 and 1982. Lung function measurements were performed between 9 a.m. and 3 p.m.

One technician from each laboratory performed the tests throughout the study. Measurements of thoracic gas volume at the level of functional residual capacity (FRC) were carried out in two different types of volume-constant variable-pressure body plethysmographic equipment: Bodytest (E. Jaeger, Würzburg, Germany) and Siregnost FD 91 (Siemens, Erlangen, Germany). The subject wearing nose-clips was seated in the box and a demonstration of the shutter mechanism and proper breathing technique was carried out. He or she was asked to support the cheeks and the floor of the mouth with the hands while breathing through the mouthpiece–flowmeter assembly. Then, the door was closed and a few minutes were allowed for a relative thermal equilibrium to be reached. During this period, the box was vented to the outside to avoid overloading of the transducer. Measurements of thoracic gas volume were initiated when the box pressure was stable and the subject was relaxed and adapted to the mouthpiece and volume recordings showed a regular end-expiratory baseline during at least four to five tidal breaths. Then, at the end of expiration the shutter was closed for 2–3 s while the subject maintained the breathing pace without occluding the glottis. Using the Jaeger equipment (HC), the measurements were performed with the subject breathing gently at a rate of approximately 1 cycle s^{-1}. By contrast, in the Siemens plethysmography (ITB) the subject was required to perform regular panting at a rate of approximately 1·5 cycles s^{-1} (11–13). The tracings (shutter-closed loops) obtained in the X–Y recording during mouth occlusion (mouth pressure, Y-axis, was plotted against box pressure, X-axis) (14) were accepted if two or more breathing cycles overlapped and showed a straight line. The angle was drawn from endpoint to endpoint. Additionally, angles were excluded if the peak-to-peak pressure change in each tracing exceeded 20 kPa. A minimum of five acceptable occlusion manoeuvres was carried out in each subject and the average of the three closest measurements was reported. Calculations were made based on the following equation:

$$\mathrm{FRC} = (1/\tan a)[(Pb - P\mathrm{H_2O})/0{\cdot}133]\ \mathrm{SVC}\ [P\mathrm{box(c)}/P\mathrm{box(d)}][P\mathrm{mo(d)}/P\mathrm{mo(c)}] - V_{\mathrm{D}}\mathrm{i}$$

where $\tan a$ is the slope of the shutter-closed loop, Pb is barometric pressure in kPa, $P\mathrm{H_2O}$ is the water vapour partial pressure at 37°C in kPa, SVC is the subject's volume correction factor, SVC = 1 − (subject's body weight in kg divided by box volume in l), Pbox(c) is the calibration volume in ml, Pbox(d) is the calibration signal deflection in mm, Pmo(c) is the calibration pressure in kPa, Pmo(d) is the calibration signal deflection in mm and V_{D}i is the instrumental dead space expressed in ml.

The expired slow vital capacity manoeuvre was measured separately using a pneumotachograph (Hewlett-Packard 47804A System, Waltham, MA) and a water-sealed spirometer (model Spirotest III, E. Jaeger, Würzburg, Germany) in the HC and in the ITB, respectively. The tests were performed with the patient in the sitting position and using nose-clips. After the subjects had adapted to the mouthpiece, at least four to five tidal volumes were recorded to determine a regular end-expiratory baseline. The subject inspired to total lung capacity and slowly expired to residual volume. A minimum of three acceptable recordings with continuous expiration from TLC to RV was required, at least two of which had vital capacity differences of less than 100 ml. The largest EVC observed of the acceptable manoeuvres was taken for calculation of the subdivisions of lung volumes. Total lung capacity (TLC) was obtained as FRC plus IC; the residual volume (RV) was calculated as TLC minus expired vital capacity (EVC).

In all subjects, the standing height measured without shoes, weight and age were recorded together with the date, room temperature, humidity and barometric pressure in the testing area. Lung function results are expressed in BTPS conditions.

On a daily basis, the following steps for quality control of the equipment were undertaken: (1) the relationship between pressure–volume changes in the empty box was calibrated with a sinusoidal signal generated by a 50 ml reciprocating pump; (2) the mouth pressure transducer was calibrated with a ± 5 kPa pressure signal; (3) a 3 l calibrated syringe (W. E. Collins, Baintree, MA) was used to calibrate (at ATPS conditions) the pneumotachograph of the body box as well as the equipment used for measuring slow vital capacity. On a monthly basis, the linearity and leaks of the three pressure transducers (box, mouth and pneumotachograph) were checked. Additional quality control procedures (15,16) which involved the pneumotachograph of the two plethysmographs and the two spirometric systems used in the study were reported in detail in (5).

In one of the laboratories participating in the study (HC), intrasubject variability of FRC was examined in ten staff members of the Lung Unit: (1) on four occasions during the same day (at 9 a.m., 11 a.m., 1 p.m. and 5 p.m.); (2) daily (at 9 a.m.) during 5 days; and (3) weekly (at 9 a.m.) throughout a period of 10 weeks.

Differences in FRC between the two laboratories participating in the study (HC and ITB) were analysed in 21 healthy subjects in whom plethysmographic measurements were carried out in each centre in random order on two different days.

In 1992, during a follow-up study of the Barcelona reference population, we examined a sample of 94 reference subjects (42 men and 52 women) in whom plethysmographic measurements were not taken in the initial survey. The inclusion criteria for reference subjects (5) were confirmed again in all of these 94 individuals. The tests were carried out in one of the two laboratories (HC) participating in the initial study. An identical procedure was followed in the measurements, but different plethysmographic (MedGraphics System 1085, St. Paul, MN) and spirometric (Stead-Wells spirometer, WE Collins, Baintree, MA) equipment was used and different technicians performed the tests. Three technicians experienced in lung function testing participated in this study. In addition to the quality control procedures described above, the following controls were done: (1) checking of the time constant of the box (17); (2) checking of the software; (3) evaluation of the entire system using an isothermal lung model similar to that described in (18). The FRC data of these 94 healthy non-smoker individuals were considered sufficiently adequate to assess the results of using the prediction equations proposed in this study as well as to evaluate the differences found using the reference equations (2,3,7–10) selected in (1).

DATA ANALYSIS

Results are expressed as mean values ± SD. Prediction equations were calculated using stepwise multiple regression analysis (19). Simple linear equations with and without body surface area (BSA = weight/height^2) as an independent variable were calculated. Furthermore, regression analyses using more complex equations (with transformations and/or interactions of variables) were tested. Logarithmic, quadratic and square-root transformation of predictor variables were examined. A study of residuals (observed minus predicted value for each subject) was performed in order to check critical assumptions of the statistical analysis: (1) independence, (2) homoscedasticity and (3) normal distribution of residuals. The analysis of the prediction equations for FRC from different authors (2,3,7–10 and present study) against the observed FRC values in the 94 reference subjects mentioned above was carried out using Student's paired t test. P values lower than 0·05 were considered statistically significant.

Results

The intraindividual coefficients of variation (CV) for FRC in the hourly, daily and weekly protocols were 6%, a value similar to that reported in the literature (2,3,20–22). The 21 subjects examined in the two laboratories participating in the study did not show differences in the FRC (HC, 3158 ± 741 ml, and ITB, 3228 ± 827 ml; mean difference, 71 ± 316 ml). Likewise, no differences between laboratories were shown in the indices calculated from the slow vital capacity manoeuvre (EVC, 4234 ± 699 ml *vs.* 4277 ± 752 ml; IC, 2757 ± 601 ml *vs.* 2825 ± 60 ml; HC and ITB, respectively). Accordingly, the TLC and the RV also displayed similar results in both centres. Hence, pooled data of the two laboratories participating in the study were used to derive the reference equations.

TABLE 1. Anthropometric and lung function variables in the reference sample

	Men (n=300)	Women (n=182)
Height (cm)	170 ± 6·6	158 ± 6·6
Age (years)	36 ± 11·9	43 ± 14·6
Weight (kg)	72 ± 8·3	60 ± 8·3
BSA	25 ± 2·6	24 ± 3·0
Forced spirometry		
FVC (ml)	4837 ± 778	3404 ± 628
FEV_1 (ml)	3821 ± 666	2702 ± 555
FEV_1/FVC (%)	79 ± 5·8	79 ± 6·5
Static lung volumes		
EVC (ml)	4993 ± 781	3553 ± 647
IC (ml)	3469 ± 592	2437 ± 423
FRC (ml)	3420 ± 765	2841 ± 555
RV (ml)	1898 ± 554	1725 ± 445
TLC (ml)	6890 ± 996	5278 ± 717
RV/TLC (%)	27 ± 6·4	33 ± 7·5

BSA, body surface area (weight/height^2); FVC, forced vital capacity; FEV_1, forced expiratory volume during the first second; EVC, expired slow vital capacity; IC, inspiratory capacity; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity. Results expressed as mean ± standard deviation.

REFERENCE EQUATIONS

Anthropometric and lung function data of the reference sample and the distribution of age, height and weight for each sex are shown in Table 1 and Fig. 1, respectively. Prediction equations for FRC, EVC, IC, TLC, RV, and RV/TLC (%) ratio were calculated separately for each sex. Complex models of regression equations did not demonstrate a better prediction capability than that obtained from the simple linear equations, as assessed by the adjusted multiple correlation coefficient. Moreover, each of the simple linear equations displayed in Tables 2 and 3 (men and women, respectively) fulfilled the assumptions of the statistical analysis (independence, homoscedasticity and normal distribution of residuals) for all intervals of the predictor variables. As shown in Table 2, in men the inclusion of BSA as a predictor variable significantly

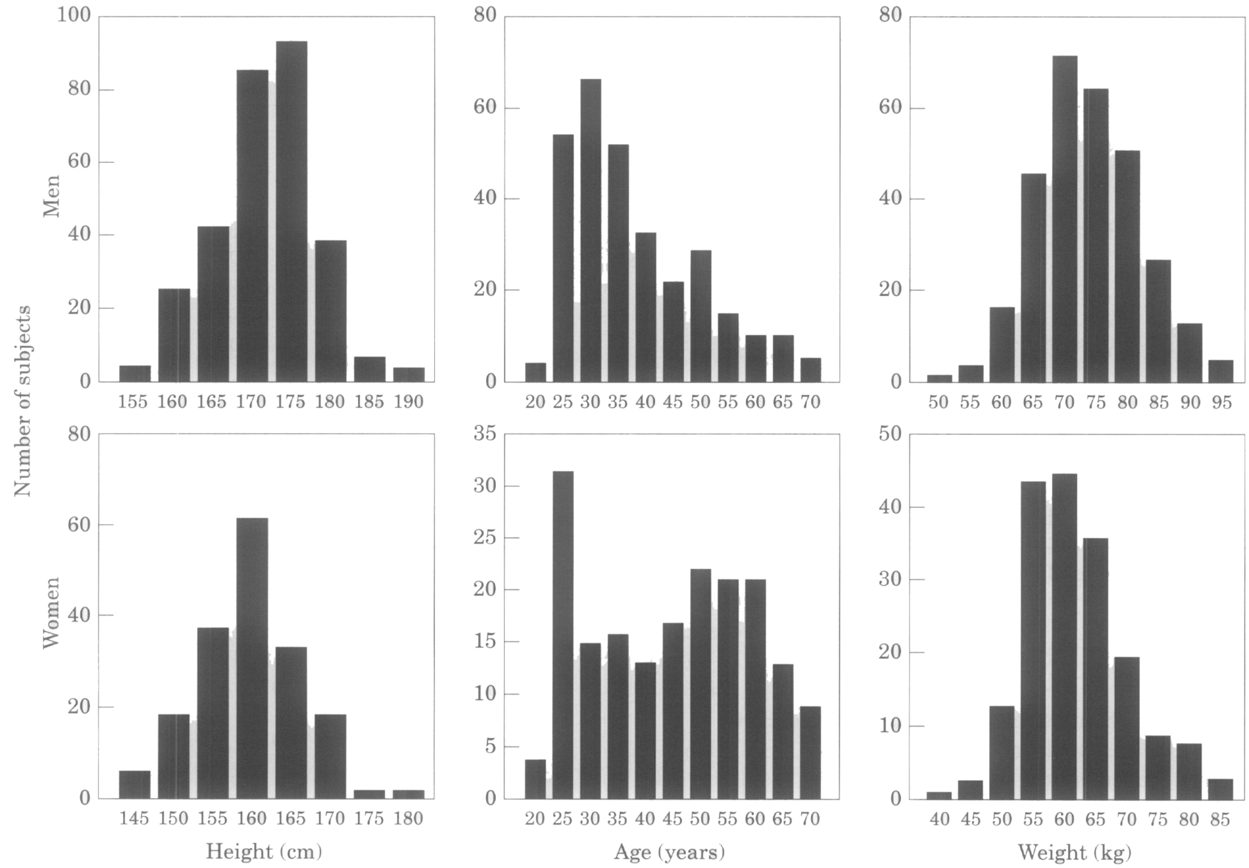

FIG. 1. Frequency distribution of age and anthropometric variables in the reference population. The range for age was 20–70 years, for height 152–189 cm in men and 142–179 cm in women and for weight 50–97 kg in men and 40–82 in women.

TABLE 2. Reference values for men: with and without body weight in the regression analysis

	Equations				R	RSD
EVC=	69·980H		−12·363A	−6427	0·67	585
	69·760H	−39·021 BSA	−10·271A	−5152	0·68	578
IC=	35·978H			−2633	0·40	545
	41·245H	+65·005 BSA		−5073	0·48	522
FRC=	57·878H		+10·148A	−6766	0·48	675
	50·244H	−137·195 BSA	+17·649A	−2318	0·65	585
TLC=	92·687H		+8·301A	−9129	0·58	808
	88·610H	−71·664 BSA	+12·144 A	−6789	0·61	790
RV=	22·618H		+20·664A	−2688	0·45	497
	20·889H	−32·596 BSA	+22·412A	−1644	0·47	492
RV/TLC (%)=			+0·277A	+17·35	0·52	5·44

H, height in cm; A, age in years; BSA, body surface area (body weight/height^2, kg cm^{-2}); EVC, IC, FRC, TLC and RV in ml; R, multiple correlation coefficient; RSD, residual standard deviation. All regression coefficients were statistically significant (P<0·05).

increased the percentage of interindividual variance (by 19%, from r^2=0·23 to 0·42) explained by the equation for FRC. Similarly, the residual standard deviation (RSD) decreased approximately by 90 ml. In women (Table 3), the inclusion of BSA only produced a modest improvement of the fitting of the equational models to the data in the equations for both FRC and IC. Negligible changes were detected in the remaining subdivisions of lung volumes.

TABLE 3. Reference values for women: with and without body weight in the regression analysis

	Equations				R	RSD
EVC=	50·283H		− 16·360A	− 3688	0·69	473
IC=	27·637H			− 1927	0·43	383
	29·061H	+52·737 BSA	− 8·271A	− 3088	0·56	354
FRC=	36·024H			− 2847	0·43	504
	30·780H	− 56·134 BSA		− 673	0·52	477
TLC=	63·661H			− 4775	0·58	584
RV=	11·331H		+11·651A	− 562	0·39	412
RV/TLC (%)=	− 0·157H		+0·257A	+47·60	0·54	6·35

H, height in cm; A, age in years; BSA, body surface area (body weight/height^2, kg cm^{-2}); EVC, IC, FRC, TLC and RV in ml; R, multiple correlation coefficient; RSD, residual standard deviation. All regression coefficients were statistically significant (P<0·05).

TABLE 4. Comparison among prediction equations for functional residual capacity

Men (n=42) Age, 45 ± 13·0 years Height, 171 ± 6·6 cm Weight, 75 ± 9·6 kg					
FRC observed (ml)	Present study (ml)	Goldman and Becklake (7) (ml)	Crapo *et al.* (8) (ml)	Grimby and Sölderholm (9) (ml)	ECSC (2,3) (ml)
3772 ± 731	3607 ± 341	3426 ± 391	3198 ± 277	3397 ± 404	3321 ± 144
Relationships between observed and predicted FRC					
Observed − predicted (ml)	169 ± 574	346 ± 582	574 ± 599	375 ± 663	452 ± 660
t, paired Student's $t$test	1·88	3·85	6·20	3·66	4·43
P	0·07	<0·001	<0·001	0·001	0·0001
Women (n=52) Age, 51 ± 13·6 years Height, 160 ± 6·9 cm Weight, 63 ± 9·4 kg					
FRC observed (ml)	Present study (ml)	Goldman and Becklake (7) (ml)	Crapo *et al.* (8) (ml)	Grimby and Sölderholm (9) (ml)	ECSC (2,3) (ml)
2984 ± 560	2900 ± 248	2648 ± 365	2718 ± 234	2618 ± 441	2624 ± 150
Relationships between observed and predicted FRC					
Observed − predicted (ml)	84 ± 433	336 ± 373	266 ± 447	366 ± 381	360 ± 475
t, paired Student's t test	1·40	6·50	4·29	6·92	5·46
P	0·169	<0·001	<0·001	<0·001	0·0001

The difference between observed minus predicted FRC corresponds to the mean of signed numbers.

COMPARISON OF REFERENCE EQUATIONS FOR FRC AMONG DIFFERENT AUTHORS

The observed FRC (Table 4, first column) corresponds to the results obtained in the 94 healthy subjects (42 men and 52 women) from the reference population reported in (5,6) but not included in the sample used to derive the prediction equations for static lung volumes. As described in Methods, static lung volumes in these 94 reference subjects were measured 10 yr after the initial survey using different equipment. In men, the differences between observed FRC minus predicted values found by Goldman and Becklake (7) (by 10%), Crapo *et al.* (8) (by 18%), Grimby and Sölderholm (9) (by 12%) and by the ECSC equations (2,3) (by 13%) were lower but also statistically significant. The present study showed the lowest mean difference between observed and predicted values for FRC (169 ± 574 ml) (P=0·07).

In women, the lowest difference (84 ± 433 ml) (P=0·17) between observed and predicted values was also obtained in the present study. The remaining authors analysed in Table 4 displayed predicted values approximately 15% below the measured FRC.

The FRC values predicted by Viljanen *et al.* (10) using body plethysmography from 512 Finnish non-smokers (268 men and 244 women) were 3·7% higher (125 ml) than that predicted by our study and only 10 ml higher than the FRC measured in the 94 healthy subjects (3339 ± 549 ml) reported in Table 4.

Discussion

Th present study provides an internally consistent set of predicted values for static lung volumes measured by body plethysmography which was lacking in the literature. The investigation followed the basic requirements of this type of survey in the following aspects: (1) number of individuals of each sex included in the protocol; (2) definition of the reference subjects (highly selected population of healthy non-smokers living in an urban area at sea level; (3) standardization of the measurements; (4) quality control procedures. As indicated, simple linear equations for TLC, EVC, IC, FRC, RV and RV/TLC (%) provided similar fits to the data when compared with more complex models with transformation of the variables. We demonstrate (Table 2) that BSA should be used as a covariate for FRC, especially for men, but is not necessary for the prediction equations of the other variables. This is consistent with the clinical observation that obesity has its greatest effect on FRC and also with the results of classical (7,9) studies on prediction equations for static lung volumes. However, it must be noted that correction for BSA in the clinical evaluation of obese subjects may lead to misinterpretation of the results. We recommend either to limit the BSA correction for FRC to a body weight equivalent to the upper 2·5 percentile of the subjects studied (i.e. 90 kg for men and 79 kg for women) or to switch to the equation which does not use BSA for patients whose body weight exceeds the 97·5 percentile.

The proposed reference equations for FRC were compared with other studies using gas dilution methods (Table 4), but similar to other studies using plethysmography (10). The ECSC equations were derived from data from a number of different studies using different methods and from differing populations as described in detail (3). The prediction equations for FRC (men and women) obtained using gas dilution techniques (7–9) showed lower predicted FRC (by 10%) than the present study. The magnitude of this difference, which is known to be larger in patients, can be explained because gas dilution techniques underevaluate lung volume of units with slow time constants.

Reported predicted values for static lung volumes generated with body plethysmography, using either volume-constant (10,23,24) or volume-displacement (25–27) plethysmography, vary markedly. Unfortunately, comparisons among studies are hindered because of concurrence of some of the following factors: (a) equations for all the subdivisions of static lung volumes measured in the same group of reference subjects were not provided (25–27); (b) subjects with different smoking categories were not analysed separately (10,24,26); (c) the size of the reference population was small (10,24,25); (d) a bias in the selection of the sample was present (25,27); (e) either the regression model was complex (10) or age was not considered as covariate (10,24).

The present study provides original prediction equations for subdivisions of static lung volumes developed from measurements using body plethysmography in 482 healthy non-smoking Caucasian adults (from ages 20—70 years) residents of Barcelona, near sea level. Reference values for FRC are approximately 10% higher than those estimated using gas dilution techniques (7–9), a difference that can be reasonably attributed to the method of measurement.

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