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Original article

Precision of Lunar Dual-energy X-ray Absorptiometry (iDXA) in measuring body composition among colorectal cancer patients and healthy subjects

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SUMMARY

Background & aims: High quality and precise methods are needed when monitoring changes in body composition among colorectal cancer (CRC) patients and healthy subjects. The aim of this study was to estimate precision of the Dual-energy X-ray absorptiometry (Lunar iDXA, GE Healthcare software enCORE version 16) in measuring body composition in CRC patients and healthy subjects.
Methods: Precision error of iDXA in measuring body composition was investigated in the current study. Thirty CRC patients and 30 healthy subjects, including both men and women underwent two consecutive whole-body DXA scan with repositioning. Precision estimates of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) in the abdominal region, and total fat mass (FM), fat-free mass (FFM), lean mass (LM), bone mineral density (BMD) and bone mineral content (BMC) were calculated.
Results: Precision error expressed as coefficient of variation (% CV) of VAT and SAT were estimated to be 3.56% and 3.28% among CRC patients, and 5.30% and 3.46% among healthy subjects. Estimated precision errors for body masses in the total region ranged between 0.49-1.01% and 0.40–0.88% in CRC patients and healthy subjects, respectively. Least significant change (LSC) in VAT mass, SAT mass, FM and LM were 140.9 g, 121.4 g, 637.0 g and 701.0 g, respectively, among CRC patients. Among healthy subjects the LSC in VAT, SAT, FM and LM were 80.93 g, 98.90 g, 484.0 g and 618.0 g, respectively. Only minor and non-significant differences between the two consecutive measurements for each body compartment were observed within both populations, and we found no systematic bias in the distribution of the differences.
Conclusion: The Lunar iDXA demonstrated high precision in body composition measurements among both CRC patients and healthy subjects. Hence, iDXA is a useful tool in clinical following-up and interventions targeted towards changes in body composition.

1. Introduction

Precision errors refers to the closeness of agreement between multiple and independent results of measurements under standardized conditions [1]. It is independent of trueness and the difference is due to instrumental and technical factors [2]. Progress in our knowledge on the role of body composition for several health outcomes relies on precise and noninvasive technologies able to detect clinically significant changes. Precision error in body composition technologies has been shown to vary depending on the body compartment as well as the region of interest; lean mass demonstrates lower error than fat mass, and regional body masses show higher precision errors than total body masses [1,3–5]. Moreover, different population, such as different groups of age, BMI, physical performance, hydration status, patients undergoing medication and different treatment regimens, may also affect precision error [1,3,5–16].

Due to technological advancements the last decades, Dual-energy X-ray absorptiometry (DXA) is a valid tool in measuring body compartments, and DXA's availability is increasing worldwide

Abbreviations: VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; FM, total fat mass; FFM, fat-free mass; LM, lean mass; BMD, bone mineral density; BMC, bone mineral content; CRC, colorectal cancer; % CV, percent coefficient of variation; DXA, Dual-energy X-ray absorptiometry; BMI, Body mass index; ISCD, The International Society for Clinical Densitometry; RMS SD, root mean squares of standard deviation; LSC, least significant changes.

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[1,6,17–20]. The newest instrument, GE Lunar iDXA, provides measurements of fat mass, lean mass and bone mass [1,2,4]. Recent improvements in the DXA software, enCORE™ and the application CoreScan, allows in addition determination of abdominal adipose tissue, including estimations of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) [21,22].

The International Society of Clinical Densitometry recommend to estimate precision error in samples of the population representative of the DXA facility [2]. In the present study, we investigated the precision error in sample of subjects representing two populations frequently using our DXA facility at the Department of Nutrition, University of Oslo, in Norway, i.e. colorectal cancer (CRC) patients and healthy subjects participating in lifestyle interventions. Body composition among healthy subjects is a key risk factor for developing chronic diseases [4,10,12,14–16]. Moreover, the results from the healthy subjects may be used as reference values for other populations with chronic diseases.

Most of the CRC patients experience changes in body composition mainly as a response to the disease itself but also due to different treatment modalities, such as surgical resection, stoma, chemo- or radiation therapy [23–33]. Moreover, CRC patients have increased risk of developing additional concomitant diseases related to body composition, such as cardiovascular diseases, diabetes, other malignancies and osteoporosis, as compared to healthy subjects [34–39].

Several precision studies have been conducted with DXA instruments; however none is conducted in CRC patients. Moreover, healthy subjects are a common population in many clinics undergoing lifestyle interventions or health care programs. Therefore, it is important to estimate the precision of the GE Lunar iDXA in a CRC population as well as in healthy subjects. The aim of the current study was to estimate the precision of the GE iLunar DXA (enCORE version 16) in measuring VAT, SAT, total fat mass (FM), total lean mass (LM), fat-free mass (FFM), bone mineral density (BMD) and bone mineral content (BMC) in CRC patients and healthy subjects.

2. Materials and methods

2.1. Participants

The International Society for Clinical Densitometry (ISCD) recommend to include either 30 participants with two consecutive scans or 15 participants with three consecutive scans in order to have sufficient statistical power when calculating precision error. In the present study, we performed two consecutive scans on 30 participants from two different populations. The first population was randomly enrolled CRC patient participating at the follow-ups visit in the ongoing randomized controlled dietary intervention study, CRC-NORDIET study [40], and they were all over-night fastened according to the protocol of the CRC-NORDIET study. In addition, the study included healthy adult subjects living in the Oslo area in Norway. and the healthy subjects were invited by announcement through e-mail sent to all employees and students at the Institute of Basic Medical Sciences, University of Oslo. They were encouraged to also invite their friends and family living close to the Oslo area. Since most of the studies in our DXA facility includes healthy subjects which are not over-night fastened, we chose in the present study to follow the same protocol.

2.2. Data collection

All participants underwent two consecutive whole-body scans with repositioning. A certified DXA operator (certified by the International Society for Clinical Densitometry, Middletown, USA) conducted all DXA scans and the position of the participants was according to the manufactures procedures [17]. Standard procedure for all measurements included the use of lightweight clothing and removal of all jewelry and other metal artifacts.

Height and weight of the participants were measured to the nearest 0.1 cm by a digital stadiometer and scale (Seca 285, Birmingham, UK). The scans were conducted on a GE iLunar DXA enCORE software version 16, GE Healthcare, Madison, WI, USA). The participants were positioned in a supine position on the scanning table with the arms parallel to the body, without touching the body. Tightening of legs below the knees and over the feet with straps avoided any movements during the scanning. The straps were removed between the two consecutive scans while dismounting the scanning table. Similar procedure for positioning was followed prior to the second DXA scan. All automatically calculated lines of region of interest in the enCORE software were manually quality checked and corrected when needed after each DXA scan by the DXA operator. Fat mass distributed in the android region, such as VAT and SAT, were measured. The enCORE software automatically defined the android region as the distance from the top of the iliac crest and 20% of the distance towards the lowest point of the mandible (gnathion). All other tissues were measured from the whole-body region. The GE Lunar calibration hydroxyapatite and epoxy resin phantom was daily used in order to check the DXA machine's calibration, which was found within acceptable limits of variation.

2.3. Ethics

All participants provided signed informed consent prior to the DXA scans approved by the regional Ethical committees and in accordance with the Helsinki declaration. The study was approved by the Norwegian Centre for Research Data (NSD, https://nsd.no) (Ref.no. 965801).

2.4. Statistical analyses

Data analysis was computed using Microsoft Excel 2016 and IBM SPSS Statistics software (Version 26, IBM, Armonk, NY, USA). All p-values were two-sided independent-sample t-test with a significance level of 5%. Participant descriptive data are presented as the mean and standard deviation (SD). The precision parameters, such as precision error expressed as the root mean squares of standard deviation (RMS SD), coefficient of variation (% CV) and the resulting least significant change (LSC) at the 95% confidence interval were calculated as recommended by the International Society for Clinical Densitometry (ISCD) and by using the ISCD online precision calculating tool [41]. Paired consecutive measurements from 30 subjects were needed in the precision analyses according to the ISCD protocol. This is based on the formula of degrees of freedom which defines the number of measurements that independently contribute to the mean squared standard deviation of the replicate scans: “Number measurements of each subject-1 x Number subjects in the study = df). For example: 2 scans per subject-1 x 30 subject = 30 df [2].

The percent coefficient of variation (% CV) was calculated by dividing RMS SD by the mean and multiplied by 100. Least significant change (LSC) is the least amount of change in body mass that can be considered statistically significant and values above this may be considered as clinical relevant value of change. The ISCD recommends calculating this for a 95% confidence level, conducted by multiplying the precision error by 2.77. If the difference is the same or greater than the LSC, then the change is considered to be statistically significant (LSC % CV = % CV* 2.77 (95% C.I.)). The LSC for RMS SD was calculated by multiplying the factor 2.77 by the value of RMS SD. The use of Bland–Altman plots and the calculation of mean

differences and limits of agreements at the 95% level explored agreement between the paired measurements within each population. One Sample t-test against the test value of zero was used to investigate if there was statistical difference between the two measurements.

3. Results

A total of 30 participants were included in each population, andboth populations showed equal distribution in gender (i.e. 14 men and 16 women) (Table 1). The mean BMI of the CRC patients and the healthy subjects was 26.2 kg/m^2 and 24.3 kg/m^2, respectively. The colorectal cancer patients were significant older than the healthy subjects, with a mean age of 65.7 years (+/− 6.6 years) and 35.3 (+/− 11.6) respectively. Significant higher amounts of VAT, SAT (borderline significant), total FM and lower amounts of FFM, BMC and BMD were found among the colorectal cancer patients compared to the healthy subjects (Table 1). All the CRC patients were Caucasians and the distribution of the tumor-node-metastasis (TNM) stages of the disease were 10 patients (16.7%) with TNM I, 12 patients (20%) with TNM II and 8 patients with TNM III (13.3%) (data not shown).

3.1. Precision estimates in CRC patients

Estimates of precisions in CRC patients are presented in Table 2. Average VAT mass was estimated to be 1428.2 ± 1039.1 g (Table 1). The precision estimate RMS SD for VAT mass was 50.84 g, corresponding to a 3.56% CV. Average SAT was 1335.9 g (±588.2), with a precision estimate RMS SD of 43.80 g, corresponding to 3.28% CV (Tables 1 and 2). For total body masses such as FFM, FM, LM, BMD and BMC, the precision estimates ranged from 0.49 to 1.01% CV (Table 2). . In particular, lean masses (i.e. LM and FFM) showed better precision than FM, with 0.49–0.54% CV and 0.88% CV, respectively.

Changes in VAT mass above 140.9 g and in SAT mass above 121.4 g was considered as significant biological changes (LSC), whereas for total FM and LM it was 637.0 g and 701.0 g, respectively (Table 2).

The Bland Altman plot revealed small and non-significant (One Sample t-test, p = 0.344–0.888) mean differences between the paired measurements for all body compartments. The mean difference in VAT mass was 4.4 g, whereas for SAT mass it was 1.6 g. Total lean masses (i.e. LM and FFM) and FM also showed small mean differences between the two measurements, with 23.5–41.9 g and 57.1 g respectively. Moreover, the differences for all body compartments were evenly distributed above and below the mean difference, indicating no systematic bias (Table 3, Figs. 1 and 2).

3.2. Precision estimates in healthy subjects

Estimates of precision values among the healthy subjects are presented in Table 2. The RMS SD for VAT mass was 29.2 g (average 551.7 g ± 758.5), corresponding to a 5.3% CV. For SAT mass, the precision estimate RMS SD was 35.68 g on average 1030.9 g (±617.3), corresponding to 3.46% CV (Tables 1 and 2). For total body compartments, such as FFM, LM, BMC, BMD and FM, the precision errors it ranged from 0.40 to 0.88% for (Table 2). The LSC for VAT mass and SAT mass were 80.93 g and 98.90 g, respectively, and considered as significant biological changes. Significant biological changes in total FM and LM were 484.0 g and 618.0 g, respectively (Table 2).

The Bland Altman plot among the healthy subjects revealed small and non-significant (One Sample t-test, p = 0.300–0.962) mean differences between the paired measurements for all body compartments. No systematic bias was observed due to the evenly distribution of differences above and below the mean difference for all body compartments (Table 3, Figs. 1 and 2).

4. Discussion

In the current study, we investigated the precision error of Lunar iDXA in estimating regional fat masses (i.e. VAT and SAT), as well as total body compartments, such as total FM, LM, FFM, BMD and BMC in CRC patients and healthy subjects. Most other studies investigating the precision of body composition by DXA focuses on a narrow spectre of body compartments, in contrast to this study [4,6,7,12–16,42].

In general, the precision errors by DXA in measuring different body compartments in CRC patients and the healthy subjects were in line with other studies [4,6,14–16]. Rothney et al. measured a precision error for VAT mass around 5% (i.e. 50 g on a 1 kg VAT) in

Table 1
Demographics, body composition and characteristics of the participants by population.

	CRC patients (n = 30) (men = 14, women = 16)				Healthy subjects (n = 30) (men = 14, women 16)				
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	p-value*
Age (y)	65.7	6.6	52.0	77.0	35.3	11.6	24.0	64.0	0.000
Weight (kg)	76.0	14.5	45.9	106.3	74.4	17.7	48.9	116.8	0.696
Height (cm)	170.1	7.8	155.4	188.4	174.1	10.0	159.2	198.9	0.093
BMI (kg/m^2)	26.2	4.2	16.1	34.7	24.3	3.9	17.7	33.1	0.074
VAT (g)	1428.2	1039.1	216.6	4773.8	551.7	758.5	2.2	3504.9	0.000
VAT-volume (cm^3)	1513.9	1101.4	229.6	5060.2	584.8	804.0	2.3	3712.9	0.000
SAT (g)	1335.9	588.2	78.8	2415.8	1030.9	617.3	140.5	2660.8	0.055
SAT-volume (cm^3)	1416.0	623.5	83.5	2560.7	1092.8	654.4	148.9	2820.4	0.055
FM (g)	25977.8	7540.1	11298.0	40146.5	19759.8	7411.8	8207.5	37069.5	0.002
LM (g)	46914.2	9745.0	32122.5	64969.5	51498.8	12038.7	33492.0	75682.5	0.110
FFM (g)	49486.1	10214.0	33911.6	67935.0	54399.9	12517.4	35879.0	79565.8	0.101
BMD (g/cm^2)	1.155	0.149	0.930	1.460	1.272	0.121	0.990	1.480	0.002
BMC (g)	2571.9	563.7	1789.0	3665.6	2901.1	534.3	2136.2	3915.8	0.024

CRC, colorectal cancer; BMI, Body mass index; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.
FM, total fat mass; LM, total lean mass; FFM, total fat-free mass; BMD, bone mineral density.
BMC, bone mineral content. The value of all body compartments is a mean of the two consecutive measurements.
Performed with DXA, Dual-energy X-ray Absorptiometry.
* p-value: two-sided, independent-sample t-test.

Table 2
Precision estimates and least significant change by population.

	CRC patients (n = 30)				Healthy subjects (n = 30)			
	Precision		LSC (95% CI)		Precision		LSC (95% CI)	
ROI	RMS SD	%CV	LSC-RMS SD	LSC %CV	RMS SD	%CV	LSC-RMS SD	LSC %CV
VAT mass (g)	50.84	3.56	140.91	9.87	29.20	5.30	80.93	14.67
VAT-volume (cm^3)	53.80	3.56	149.30	9.87	30.95	5.30	85.79	14.67
SAT mass (g)	43.80	3.28	121.41	9.09	35.68	3.46	98.90	9.59
SAT-volume (cm^3)	46.43	3.28	128.69	9.09	37.82	3.46	104.84	9.59
FM (g)	230.00	0.88	637.00	2.45	175.00	0.88	484.00	2.45
LM (g)	253.00	0.54	701.00	1.49	223.00	0.43	618.00	1.20
FFM (g)	243.15	0.49	673.97	1.36	220.13	0.40	610.16	1.12
BMD (g/cm^2)	0.01	0.66	0.02	1.82	0.01	0.69	0.02	1.92
BMC (g)	25.89	1.01	71.76	2.79	13.20	0.45	36.58	1.26

CRC, colorectal cancer; ROI, region of interest; RMS SD, root-mean-square error standard deviation; LSC, least significant change.
LSC-RMS SD, least significant change for the root-mean-square error standard deviation.
LSC % CV, least significant change for the root-mean-square percent coefficient of variation.
VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; FM, total fat mass.
LM, total lean mass; FFM, total fat-free mass; BMD, bone mineral density; BMC, bone mineral content.

Table 3
Bland Altman plot values, mean difference and limits of agreement of paired measurements by population.

	CRC patients (n = 30)				Healthy subjects (n = 30)			
ROI	Mean difference	SD	Upper LoA	Lower LoA	Mean difference	SD	Upper LoA	Lower LoA
VAT mass (g)	4.2	73.0	147.3	−138.9	6.2	41.5	87.6	−75.2
VAT volume (cm^3)	4.4	77.4	156.1	−147.2	6.6	44.0	92.8	−79.7
SAT mass (g)	−1.6	63.0	121.8	−125.1	−2.3	51.3	98.1	−102.8
SAT volume (cm^3)	−1.7	66.8	129.1	−132.6	−2.5	54.3	104.0	−109.0
FM (g)	57.1	325.5	695.1	−580.9	−2.2	251.3	490.2	−494.7
LM (g)	−23.5	363.0	688.0	−735.0	−27.5	319.3	598.4	−653.4
FFM (g)	−41.9	347.1	638.5	−722.3	−23.7	315.7	595.1	−642.5
BMD (g/cm^2)	0.0018	0.0108	0.0229	−0.0193	−0.0024	0.0126	0.0222	−0.0270
BMC (g)	1.3	37.2	74.3	−71.6	3.6	18.6	40.1	−32.9

CRC, colorectal cancer; ROI, region of interest; SD, standard deviation; LoA, limits of agreement.
VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; BMD, bone mineral density.
BMC, bone mineral content; FM, total fat mass; LM, total lean mass; FFM, total fat-free mass.

both obese women and in a phantom experiment, which is comparable with the results of the present study [4].

Regional fat masses showed higher precision errors than total body fat masses in both populations, also confirmed by other studies [6,7,10,12,15,16]. The observed difference in precision errors (i.e. expressed as lower % CV and the higher RMS SD and LSC RMS SD) for VAT and SAT in the CRC population compared to the healthy population may be due to the higher mean values of VAT and SAT in the CRC population. These results are supported in other studies investigating precision errors in groups with different BMI categories [6,14,15,42]. In particular, Meredith–Jones et al. reported lower % CV with increasing BMI for all body compartments, and in particular a very high % CV (44.8) for VAT mass among normal weighted subjects [15].

The small mean differences between the two measurements for all body compartments in both populations indicates high precision of iDXA. Lean masses showed lower precision error compared to fat masses in both populations, which also have been confirmed by other studies [1,3–5].

The wide limits of agreements among the CRC patients in our study reflects heterogeneity in body composition, which was expected due to the disease itself and treatment effects. It is of great importance for each clinic or research centre to know the least significant change for the different populations monitored in order to reveal biological changes and thereby deliver the optimal treatment. For instance, the LSC for VAT mass in CRC patients found in the present study indicate that changes below 140.9 g may be explained by the variation in the DXA machine, while changes above this value is seen as clinical relevant change. Likewise, changes in VAT mass below 80.93 g among healthy subjects may be due to technical aspects, whereas changes above might be a true biological change.

4.1. Limitations and strengths

Limitations of this study is the mixture of both men and women, different ages and BMI groups in both populations, shown to impact the precision errors of different body compartments [1,4,6,10–16,43]. However, this combination of subjects are representative for the DXA facility included in the current study, and contributes with valuable knowledge about the precision error and least significant change among these populations.

Strengths of this study is the exploration of the variability in precision errors of the most commonly used body compartments generated from the iDXA. Monitoring regional and total FM, LM and bone mass is of great importance during following-up of patients and estimating effects of interventions.

Another strength of this study is the use of one single operator performing the DXA scans, excluding the effect of inter-operative variability in the measurements. The results from this precision study is of great relevance for other comparable populations, such as subjects with other cancers or chronic diseases as well as other healthy populations, in which monitoring changes in body composition are in focus. As far as we know, this is the first study to explore DXA's precision in a CRC population.

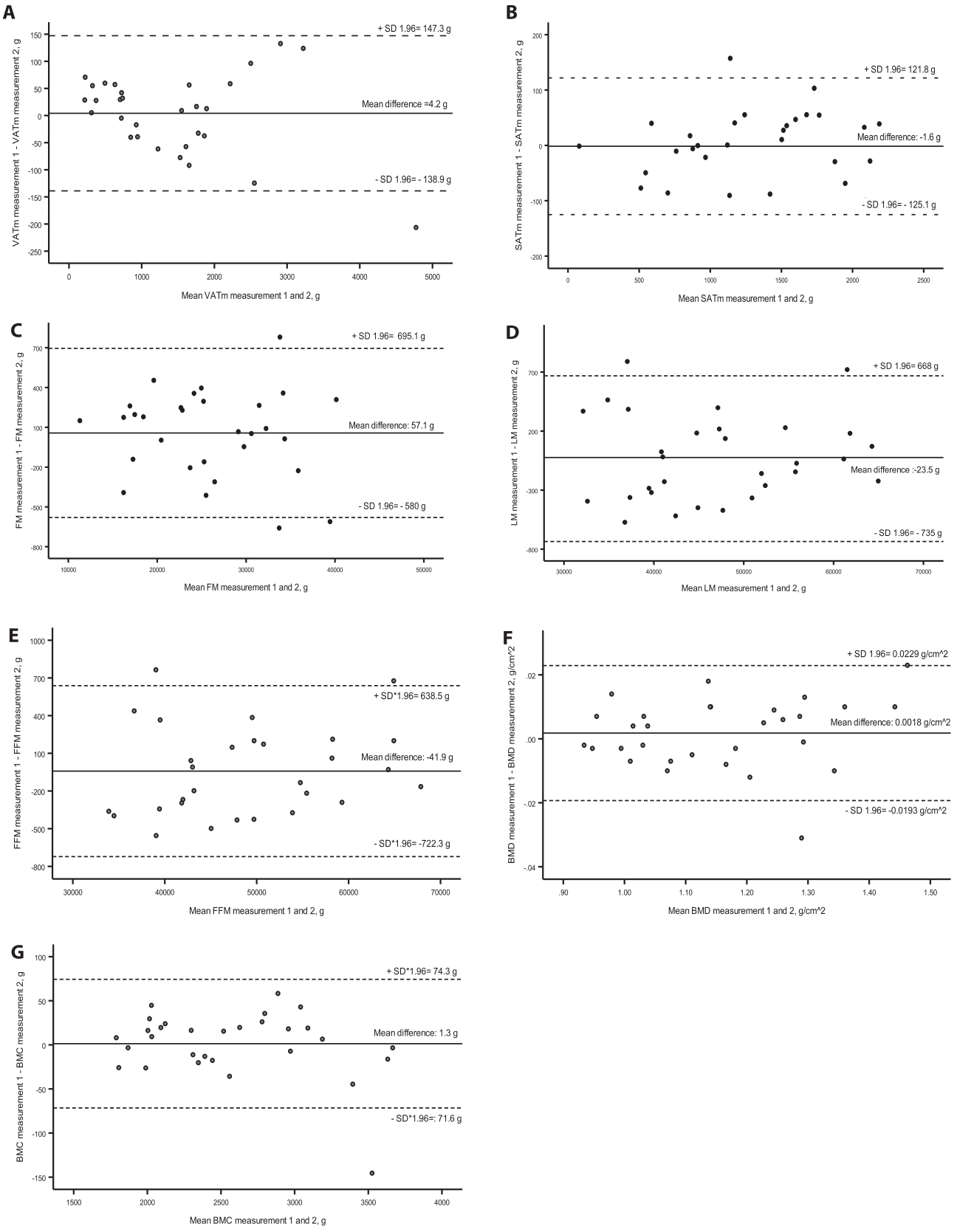

Fig. 1. Bland–Altman plot between two measurements of (A) VAT mass, (B) SAT mass, (C) FM, (D) LM, (E) FFM, (F) BMD and (G) BMC in CRC patients.

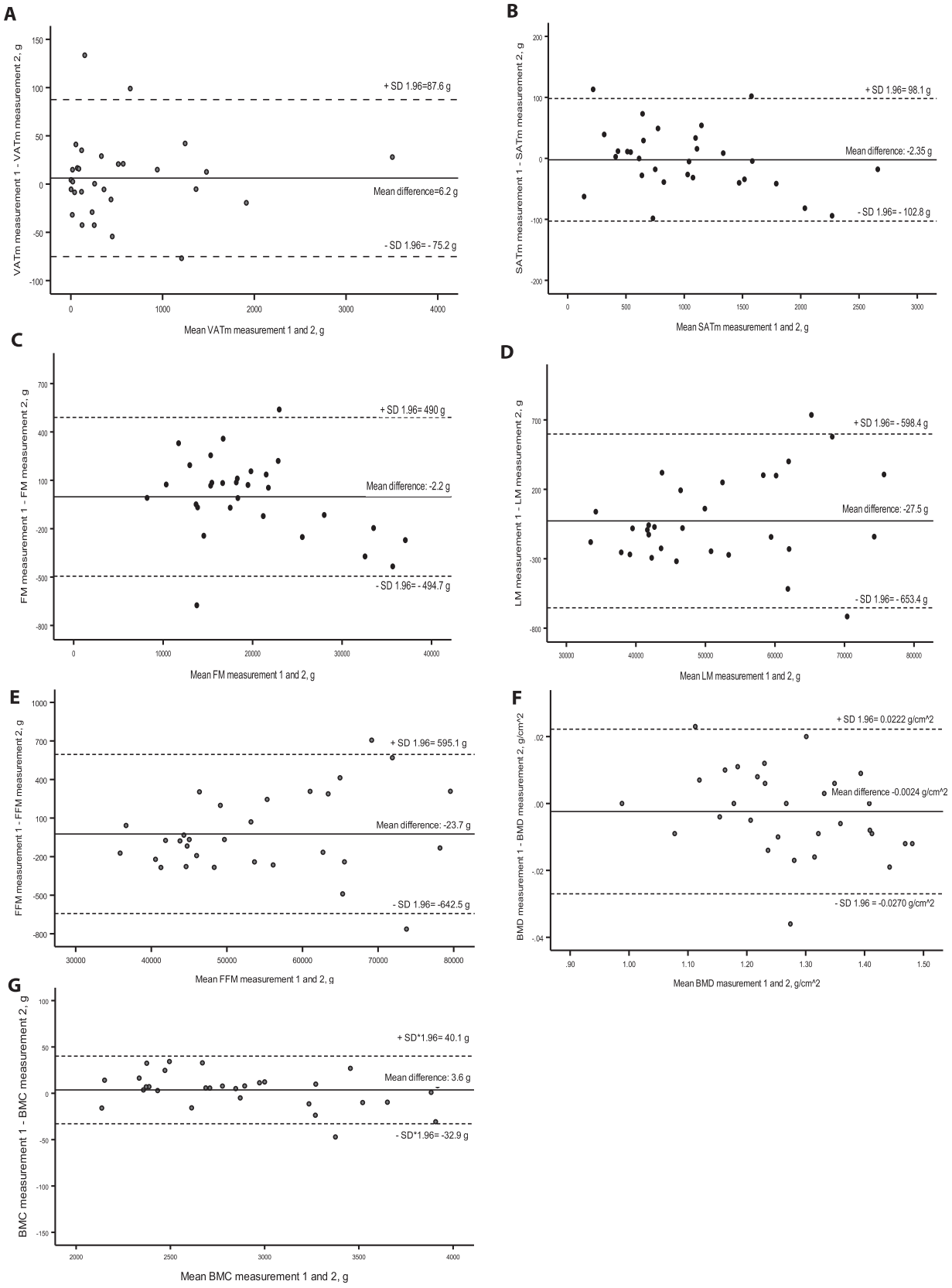

Fig. 2. Bland–Altman plot between two measurements of (A) VAT mass, (B) SAT mass, (C) FM, (D) LM, (E) FFM, (F) BMD and (G) BMC in healthy subjects.

5. Conclusion

The present study revealed high precision of Lunar iDXA for all body compartments in both CRC patients and healthy subjects. The precision estimates are comparable with other studies. Generally, higher % CV was found in regional compared to total body compartments in both populations. It is recommended for all clinics to know the precision error and least significant change of the DXA machine when interpreting body composition measurements in different populations.

Statement of authorship

Hege Berg Henriksen, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Roles/Writing - original draft, Writing – review & editing, Dena Helene Alavi, Conceptualization, Data curation, Investigation, Methodology, Resources, Project administration, Supervision, Writing – review & editing. Rune Blomhoff, Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing.

Conflict of interest and funding sources

Rune Blomhoff is a shareholder of Vitas, Oslo, Norway. The remaining authors declare that there are no conflicts of interest. This work was supported by the Throne Holst Foundation of Nutrition Research, University of Oslo, Norway.

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