의학박사 학위논문

파라미터 및 조영제 시기에 따른 CT 를 통해 측정한 근육 구성요소측정의 신뢰도 연구

Effect of parameters and contrast phase of CT acquisition on assessment of muscle quantity and quality

울산대학교 대학원

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이 논문을 의학박사 학위 논문으로 제출함

2021 년 2 월

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국문요약

연구배경

근감소증 및 지방근증을 평가하는데 있어서 전산화단층촬영 (CT)가 효과적인 비침습적 검사로 쓰이고 있다. 그러나 CT 파라미터 및 조영제 시기 및 투여 유무에 따른 측정치의 신뢰도는 잘 밝혀져 있지 않다.

연구목적

본 연구에서는 다양한 CT 파라미터를 사용하였을 때 근육의 양과 질 평가에 있어서 CT 의 신뢰도를 평가하고자 한다.

연구방법

파라미터에 따른 신뢰도를 측정하기 위하여 요추 2–4 번의 복부에 해당하는 팬텀을 이용하였다. 이 팬텀을 이용하여 CT 의 전압, 전류, 두께 및 영상 재구성 알고리듬을 변경하면서 CT 영상을 획득하였다. 근육 참조치는 팬텀의 근육 양 및 추정 근감쇄도 (45 HU)를 참조하였다. 또한 조영제 시기에 따른 CT 근육평가의 신뢰도를 측정하기 위해 4 개의 다른 시기 (조영전, 동맥기, 문맥기, 지연기)에 CT 영상을 획득한 89 명의 환자를 포함하였다. 근육 참조치는 인공지능을 통해 얻은 근육의 양 및 평균 근감쇄도를 이용하였다. 근육의 근감쇄도에 따라 골격근 영역 (SMA, -29 에서 150 HU), 정상근감쇄도근육 영역 (LAMA, 30 에서 150 HU), 저근감쇄도근육영역 (LAMA, -29

에서 29 HU)으로 나누었고, 각 파라미터 및 조영시기에서 해당하는 영역의 값 및 평균 근육감쇄도를 구하였다.

연구결과

팬텀을 통해 구한 SMA 는 CT 파라미터와 관계 없이 참조치의 91.7% 이상을 차지하였다. 그러나 정상근감쇄도 영역은 59.7–81.7%로 다양한 값을 보였다. 평균 근감쇄도는 추정 근감쇄도보다 낮게 측정되었다. 조영증강시기에 따라 SMA, NAMA, LAMA 는 유의한 차이를 보였다. 그러나 SMA 를 기반으로 한 근감소증 진단에는 영향이 크지 않았다.

결론

근육 양 평가는 CT 파라미터 및 조영증강 시기에 관계없이 신뢰도 있는 결과값을 구하였다. 그러나 근육 질 평가의 경우 CT 파라미터와 조영증강 시기에 많은 영향을 받았고 따라서 표준화된 파라미터 및 조영증강 시기에 대한 확립이 필요하겠다.

중심단어: 전산화단층촬영, 근육측정, 팬텀, 근감소증

차 례

표 목차

그림 목차

INTRODUCTION

Skeletal muscle plays a pivotal role in mobile and static functions, including body movement and maintenance of posture (1), and many studies have investigated its relationship with physical wellness, morbidity, and mortality (2, 3). As a result, sarcopenia, which is defined as loss of muscle mass and strength, is now formally recognized as a disease with an ICD Code. As the importance of muscle has been emphasized, a variety of imaging methods have been introduced for the assessment of muscle quantity.

Computed tomography (CT) is now considered to be one of the gold standards for noninvasive assessment of muscle quantity (4). The CT measurement of muscle quantity is based on the difference in the X-ray attenuation value (measured in Hounsfield units [HU]) of each pixel, given the fact that each component of the body (including skeletal muscle as well as bone, adipose tissue, and visceral organs) has a specific attenuation threshold (5, 6), which is a prerequisite for their identification in cross-sectional images. Additional CT scans with resulting additional costs and radiation dose are not needed for muscle evaluation if CT was taken as a part of patient care for any other cause, including the assessment of disease and treatment response.

Recently, the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) revised the definition of sarcopenia by adding muscle function to the former definitions based on muscle quantity, as muscle quantity by itself is limited in its ability to

predict outcomes (7). Muscle quality, which represents the micro- and macroscopic aspects of muscle architecture and composition, is also related to outcome: intra- and extramyocellular fat deposition, i.e., myosteatosis, occurs with aging or disuse of muscle and leads to decreased muscle strength and function followed by increased mortality (8). As lipid deposition lowers the density of muscle (9), a number of studies have investigated the measurement of muscle quality using CT, which can be done by measuring muscle density or stratifying the intramuscular components according to HU distributions, and its usefulness for determining prognosis has been reported, independent of muscle quantity itself (10-12).

Accordingly, CT has now emerged as an accurate measurement tool for determination of muscle quantity and quality. Nevertheless, standardized parameters for image acquisition and image phase after contrast agent administration (13) have not been determined, and it is questionable whether muscle measurement is stable if CT parameters and contrast phases are altered.

Therefore, the aim of our study was to evaluate the reliability of the measurement of muscle quantity and quality under variable CT parameters and contrast phases.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board (Asan medical Center, Republic of Korea) and the requirement to obtain informed consent was waived.

Phantom study - assessment of the effect of CT parameters

As a CT phantom, the CIRS Model 004 CT Simulator (Computerized Imaging Reference Systems, Norfolk, VA) was used: it simulated the size, shape, and CT density of abdominal muscle and subcutaneous adipose tissue at the level of the 2nd to 4th lumbar region. The target CT density of the muscle compartment was 45 HU.

Using three CT scanners (Somatom Definition AS+: Siemens Healthineers, Erlangen, Germany; Discovery CT750 HD: GE Healthcare, Milwaukee, WI; and Ingenuity Core 128: Philips Medical Systems, Best, the Netherlands), phantom images were repeatedly obtained at the level of the 3rd lumbar vertebra, with modulation of tube voltage (120 kVp and 80 kVp) and tube current (standard mAs and low mAs), leading to three different categories of radiation dose: standard dose (STD), low dose with reduced voltage (LD-kVp), and low dose with reduced current (LD-mAs). In addition, the slice thickness (thin sections [1 or 1.25 mm], medium sections [2.5 or 3 mm], and thick sections [5 mm]) and image reconstruction algorithms (filtered back projection [FBP] and iterative reconstruction [IR]) were varied. The detailed imaging parameters and their modulations are presented in **Table 1**.

Table 1. CT image acquisition parameters

	Somatom Definition AS+	Discovery CT750 HD	Ingenuity Core 128
Radiation dose†			
STD	120 kVp and 220 reference mAs	120 kVp and 100–400 mA	120 kVp and 321 reference mAs
LD-kVp	80 kVp and 220 reference mAs	80 kVp and 100–400 mA	80 kVp and 321 reference mAs
LD-mAs	120 kVp and 100 reference mAs	120 kVp and 10–300 mA	120 kVp and 168 reference mAs
Slice thickness†			
Thin section	1 mm	1.25 mm	1 mm
Medium section	3 mm	2.5 mm	3 mm
Thick section	5 mm	5 mm	5 mm
Reconstruction algorithm†	FBP IR (SAFIRE, iterative strength level 1)	FBP IR (ASIR 30%)	FBP IR (iDose4)
Field of view (mm)	380		
Kernel	standard		

Abbreviation: FBP = filtered back projection; IR = iterative reconstruction.

† A total of 18 images per device were obtained with the modulation of radiation dose (three conditions), slice thickness (three conditions), and reconstruction algorithm (two conditions).

Determination of the reference standard muscle compartment

The reference standard muscle compartment area was determined according to the segmentation of known phantom compartments, including muscle, subcutaneous fat, visceral fat, internal organs, and vertebra. Each compartment was automatically segmented according to the following processes **(Figure 1)**.

Preparation: generation of the reference map – Reference maps including the compartments of muscle, subcutaneous fat, visceral fat, internal organs, and vertebra were generated from the known phantom compartments.

Step 1: Initial segmentation of the phantom area – The area of the phantom on the CT images was separated from the background area using Otsu's thresholding method (14). Noise reduction using an anisotropic diffusion filter and mathematical morphology was simultaneously performed to generate an initial segmentation of the phantom area (15, 16).

Step 2: Rigid registration – The reference map was registered to the initial segmented area (the phantom area) using a center-of-mass match and rigid transformation (17).

Step 3: Final segmentation of the muscle compartment – The muscle compartment was segmented using the reference map.

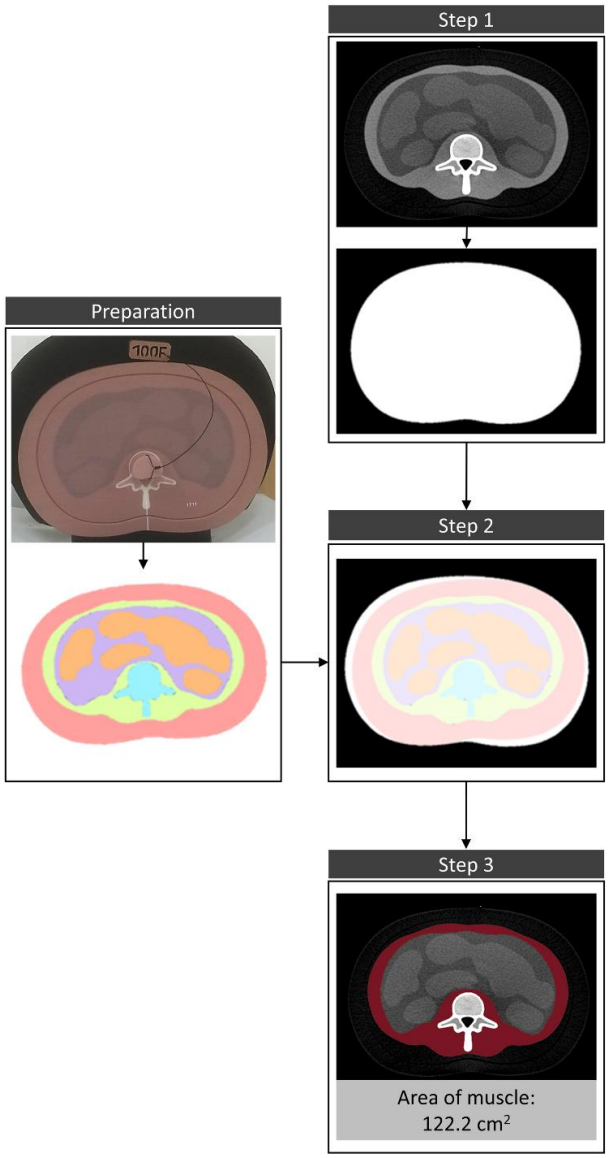

Figure 1. Determination of the reference standard muscle compartment.

The reference standard muscle compartment was determined using the following process: separation of the phantom area from the background area on the CT image (step 1), rigid registration of the reference map (preparation) onto the phantom area (step 2), and segmentation of the muscle compartment (step 3). The final area of muscle on the CT image was 122.2 cm^2.

Human study - assessment of the effect of contrast phase

Between January 2012 and December 2012, 89 consecutive subjects (mean age [range], 52.2 [28–79]; 52 men and 37 women) who underwent multiphasic abdominal CT for medical check-up at the Health Screening and Promotion Center of a single tertiary institution were retrospectively included. Multiphasic abdominal CT was performed using 16-Channel or higher CT scanners (Somatom Sensation 16, Siemens Medical Solution, Erlangen, Germany; LightSpeed 16, LightSpeed VCT, and Discovery CT 750 HD, GE healthcare, Milwaukee, WI) using the following parameters: tube voltage, 120 kVp; effective tube current, 200 reference mAs (care dose 4D; Siemens Medical Solution) or 100–400 mA (AutomA or SmartmA; GE healthcare); field of view, 30–40 cm; collimation, 0.313–0.75; and pitch, 0.98–1. Using intravenous administration of contrast agent at a rate of 3–4 mL/s, the following four different phases were obtained: pre-contrast phase, arterial phase (scan delay of 20–25 seconds from the 100 Hounsfield units [HU] threshold in the abdominal aorta), portal phase (65–72 seconds after injection of the contrast agent), and delayed phase (3 minutes after injection of the contrast agent). The images were reconstructed using the filtered back-projection technique with soft tissue reconstruction algorithm (B30f kernel; Siemens Medical Solution; Standard kernel, GE Healthcare) at a section thickness of 5 mm with no interslice gap.

Image preparation and generation of muscle quality map

Axial images at the inferior endplate level of the L3 vertebra was thoroughly selected and matched between the four phases of multiphasic abdominal CT (18) by board-certified radiologists (D.W.K. and K.W.K.) and an experienced image analyst (Y.K.) in consensus. Unless the images were matched between the four phases, they are excluded for the analysis. All muscles on the selected images (including psoas, paraspinal, paraspinal, transversus abdominis, rectus abdominis, quadratus lumborum, and internal and external oblique muscles), were segmented using a fully convolutional network-based segmentation system with mean Dice similarity coefficient of 0.96–0.97 (19).

Measurement of muscle area and density

Muscle quality map was respectively generated from CT images from phantom with the different CT parameters and those from human subjects with the four different phase images, using HU of each pixel in the segmented muscle area. They are categorized into either of the following components based on the threshold of HU (11, 18): normal attenuation muscle area (NAMA; threshold, 30 to 150 HU) and low attenuation muscle area (LAMA; threshold, -29 to 29 HU) **(Figure 2)**. The summation of pixel represented the area of each component of NAMA and LAMA. Skeletal muscle area (SMA) was defined as a total of NAMA and LAMA, after discarding pixels outside the range of -29–150 HU from segmented muscle area.

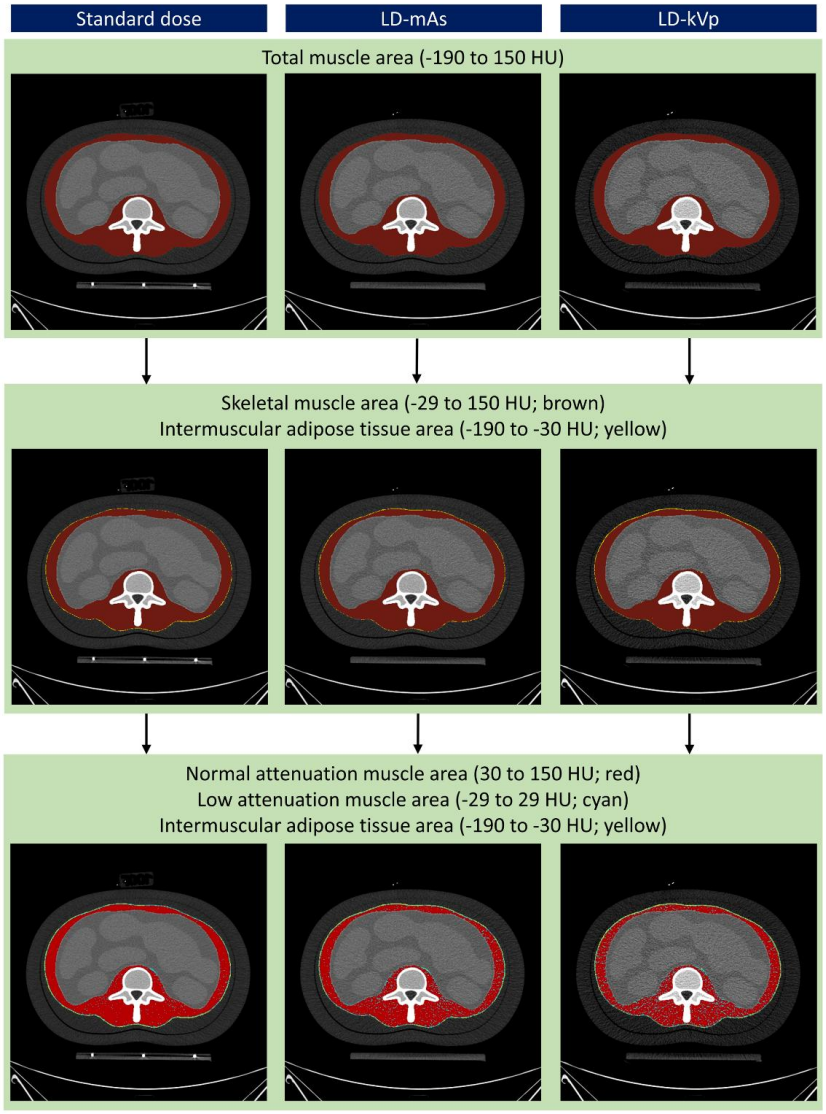

Figure 2. Segmentation of the muscle compartment and its components using HU thresholds.

The components are the areas segmented using HU thresholds to represent biological and clinical tissue components, including skeletal muscle area (SMA; composed of normal attenuation muscle area [NAMA] and low attenuation muscle area [LAMA]) and intermuscular adipose tissue area (IMA).

Statistical analysis

In the phantom study, the results obtained using different parameters were compared with those obtained with the standard protocol (i.e., STD with FBP reconstruction and thick sections [5 mm]) and with the pre-segmented area. In addition, the Dice similarity coefficient (DSC) (20) was used to evaluate the similarities of the cross-sectional areas of SMA, and NAMA with the use of CT parameters different to those in the standard protocol.

In the human subjects, comparison of the area and the mean HU of SMA and its components (i.e., NAMA and LAMA) between 4 different contrast-enhanced CT phases was evaluated using linear mixed model. Pairwise multiple comparison between two phases (precontrast vs. arterial; precontrast vs. portal; precontrast vs. delayed; arterial vs. portal; arterial vs. delayed; and portal vs. delayed) were conducted, adjusted by Scheffe's methods. The body composition indices (21, 22), including the area (SMA, NAMA, and LAMA) divided by height squared, weight, and BMI, among the 4 CT phases were compared in the same manner. To explore the clinical impact on the differences in SMA and its indices according to CT phases, the number of patients diagnosed as sarcopenia were calculated based on the cutoff of sarcopenia devised from approximately 12,000 healthy Korean subjects (23), and those on different phases were compared using McNemar's test with Bonferroni correction.

Statistical analysis was conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA), IBM SPSS Statistics for Windows, version 23.0 (IBM Corp, Armonk, NY, USA),

and MedCalc version 18.2.1 (MedCalc, Mariakerke, Belgium). P value < 0.05 was considered statistically significant.

RESULTS

Phantom study - effect of CT parameters

A total of 18 image sets were acquired, with these including various combinations of imaging parameters, including three radiation dose settings (STD, LD-mAs, and LD-kVp protocols), three different slice thicknesses (thin, medium, and thick sections), and two different reconstruction algorithms (FBP and IR). Compared with the reference standard muscle compartment, the segmented SMA values were higher with both the standard dose protocol and the LD-mAs protocol, while they were lowest with the LD-kVp protocol, regardless of the slice thickness and reconstruction algorithm **(Figure 3)**. The SMA results did not differ significantly between the thin, medium, and thick sections, or between the different reconstruction algorithms. In all the CT protocols, SMA occupied at least 91.7% of the pre-segmented area. By contrast, NAMA was not constant across the protocols, varying between 59.7% and 81.7% of the pre-segmented area, despite the fact that the target HU of muscle stated by the manufacturer (45 HU) belonged within the threshold range. Of note, the proportions of SMA and NAMA in images using IR were higher than in those using FBP in all protocols but the standard one, although the differences for SMA and NAMA were less

than 2.7% and 4.7%, respectively.

SMA showed good similarity, with the DSCs being within the range of 0.96–1.00 for muscle area and 0.94–1.00 for SMA. However, the DSCs of NAMA ranged from 0.74–0.96, showing variation that was dependent on the CT parameters **(Figure 4)**.

In all cases, the mean density of the reference standard muscle compartment was lower than the target density stated by the manufacturer (range, 39.0–44.9 HU) **(Figure 5)**. The mean density increased with thin slices (difference range, 0–1.3 HU) and low tube voltage (difference range, 3.4–3.5 HU), but decreased with low radiation dose (difference range, 1.0–1.8 HU) and IR usage (difference range, -0.1–1.2 HU).

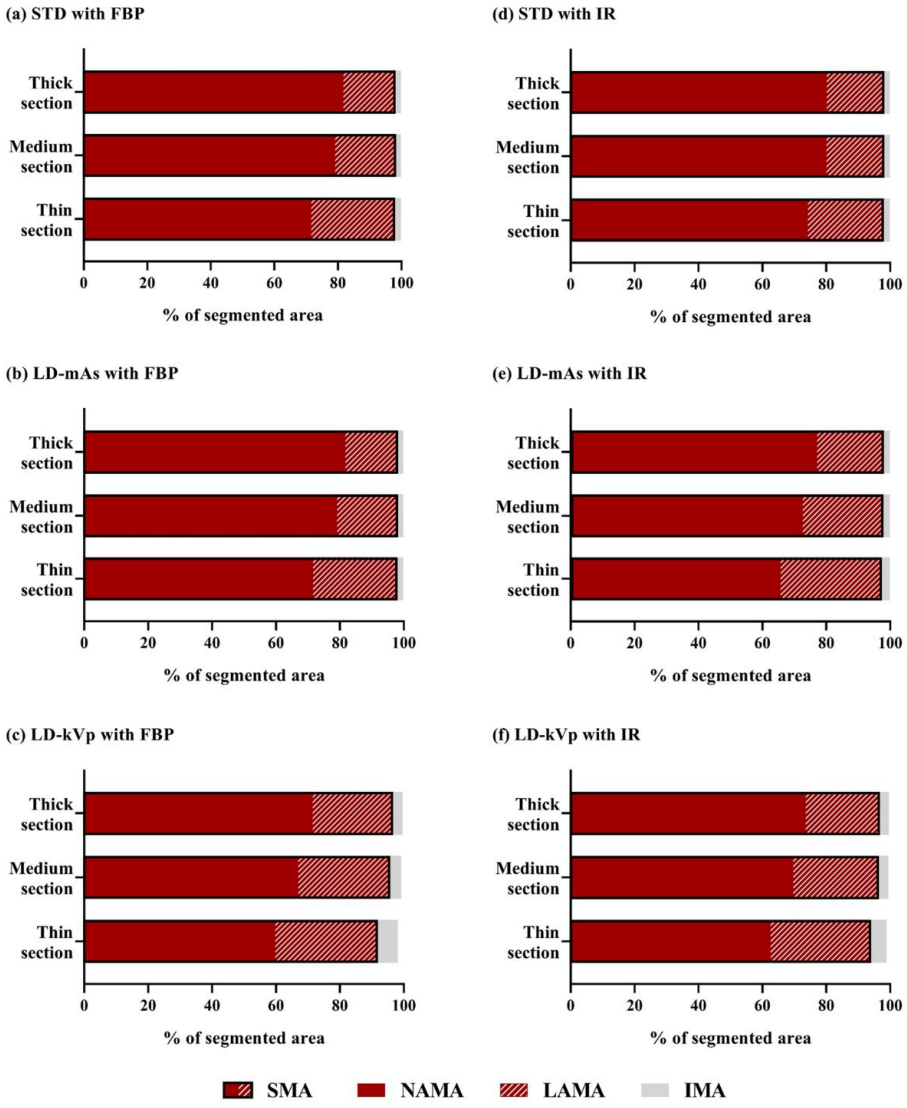

Figure 3. Proportions of the segmented areas of muscle components with different CT protocols.

The area including NAMA and LAM represents SMA.

Abbreviations: FBP = filtered back projection; IR = iterative reconstruction; IMA = intermuscular adipose tissue; LAMA = low attenuation muscle area; LD = low dose; NAMA = normal attenuation muscle; SMA = skeletal muscle area; STD = standard dose.

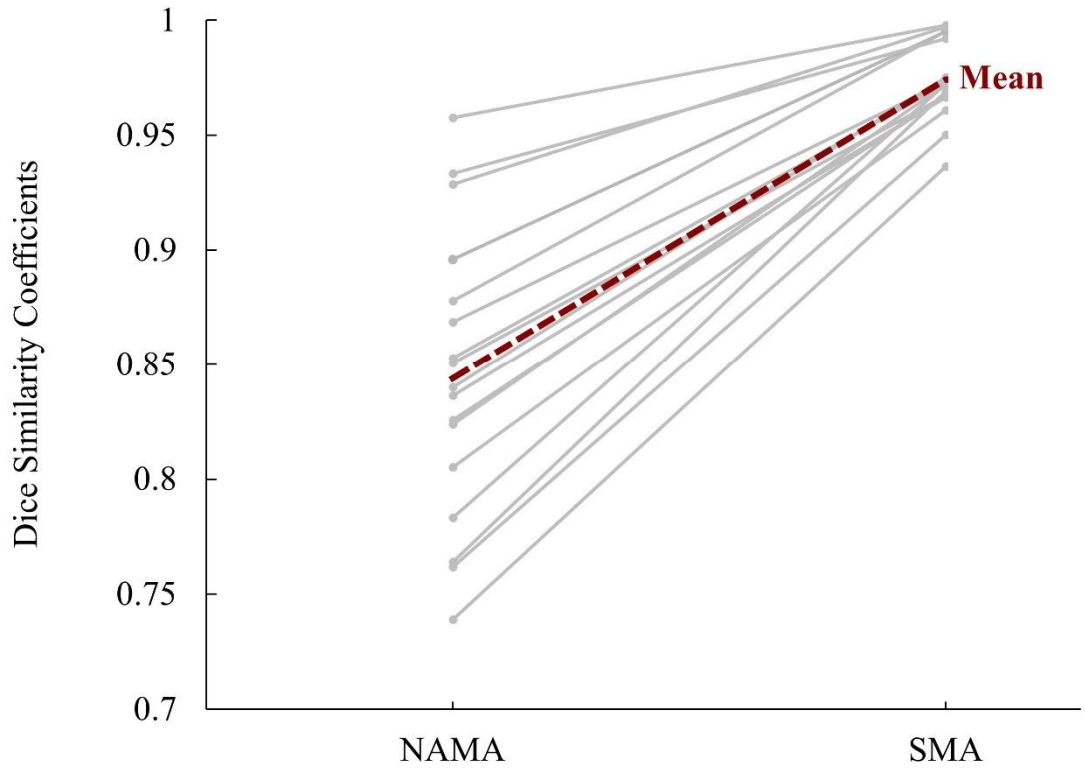

Figure 4. Dice similarity coefficients (DSC) between the variable protocols and standard protocol

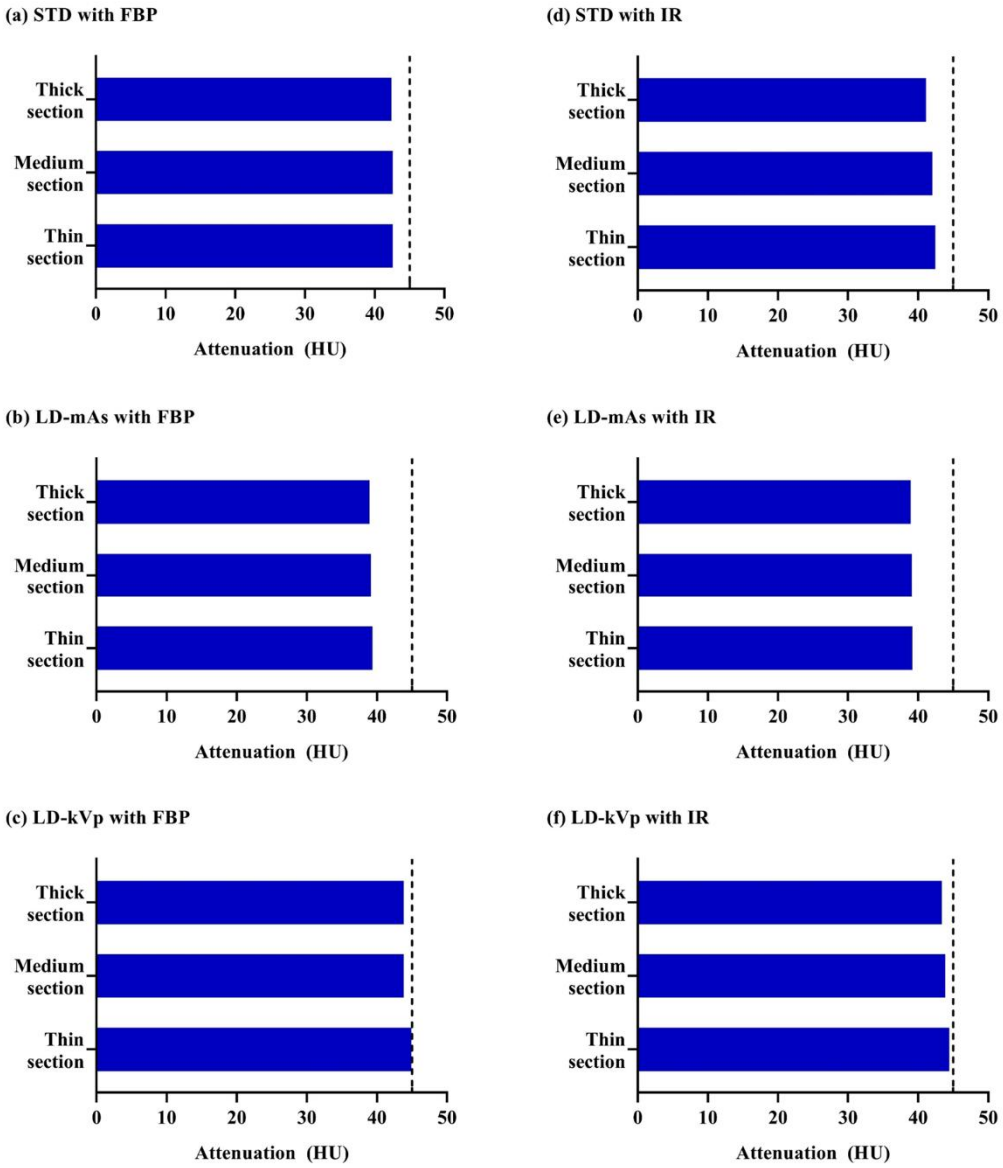

Figure 5. Mean density of the muscle compartment with different protocols.

Dashed lines indicate the target density of skeletal muscle (45 HU).

Abbreviations: FBP = filtered back projection; IR = iterative reconstruction; LD = low dose;

STD = standard dose.

Human subject study - effect of contrast phase

Mean HU of SMA increased with time delay after the contrast administration, and showed significant difference with different CT phases ($P < 0.001$; **Table 2**). Area and indices of SMA and NAMA showed higher values with later phases, whereas those of LAMA gradually decreased. Area and the indices of SMA, NAMA, and LAMA all showed significant difference among 4 CT phases ($P < 0.001$). In post-hoc pairwise comparison of two CT phases, area, area/height2, and area/BMI of SMA showed no significant difference in the comparison of pre-contrast phase vs. arterial phase ($P = 0.0682–0.0734$) and portal phase vs. delayed phase ($P = 0.3132–0.4801$) while the other measurement of SMA showed significant difference between two CT phases. By contrast, all measurement of NAMA and LAMA showed significant difference between any of the two CT phases.

Using the cutoff based on T-score < -1.0 for SMA and its indices, the number of subjects diagnosed with sarcopenia generally had tendency to be decreased with time delay after contrast administration **(Table 3)**. Nevertheless, there was no statistically significant difference in number of sarcopenia according to contrast phase. When using diagnostic cutoff of T-score < 2.0, there was no change in the number of sarcopenia according to contrast phase except for more subjects of sarcopenia on unenhanced phase compared to other phases based on the area.

Table 2. Values of SMA, NAMA, and LAMA according to CT phases

Value	Mean ± standard deviation				P value*					
	Unenhanced phase (UP)	Arterial phase (AP)	Portal phase (PP)	Delayed phase (DP)	UP vs. AP	UP vs. PP	UP vs. DP	AP vs. PP	AP vs. DP	PP vs. DP
Density (HU)	40.00 ± 5.85	46.23 ± 6.36	51.50 ± 6.84	54.17 ± 6.74	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Area (cm^2)										
SMA	136.08 ± 34.21	136.74 ± 33.72	138.15 ± 34.02	138.48 ± 33.75	0.0734	<.0001	<.0001	<.0001	<.0001	0.4801
NAMA	100.10 ± 32.08	106.49 ± 31.10	112.06 ± 31.13	114.64 ± 31.31	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
LAMA	35.98 ± 11.25	30.25 ± 11.13	26.09 ± 10.43	23.84 ± 9.30	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Area/height^2 (cm^2/m^2)										
SMA	48.40 ± 9.27	48.64 ± 9.08	49.15 ± 9.20	49.28 ± 9.09	0.0682	<.0001	<.0001	<.0001	<.0001	0.4323
NAMA	35.43 ± 9.36	37.78 ± 8.93	39.81 ± 8.84	40.73 ± 8.78	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
LAMA	12.97 ± 4.12	10.86 ± 3.94	9.35 ± 3.62	8.55 ± 3.28	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Area/weight (cm^2/kg)										
SMA	2.06 ± 0.29	2.07 ± 0.28	2.09 ± 0.28	2.10 ± 0.28	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
NAMA	1.51 ± 0.36	1.61 ± 0.34	1.70 ± 0.33	1.74 ± 0.33	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
LAMA	0.55 ± 0.15	0.46 ± 0.14	0.39 ± 0.13	0.36 ± 0.11	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Area/BMI										
SMA	5.78 ± 1.16	5.81 ± 1.13	5.86 ± 1.13	5.88 ± 1.12	0.0754	<.0001	<.0001	<.0001	<.0001	0.3132
NAMA	4.26 ± 1.24	4.53 ± 1.18	4.77 ± 1.17	4.88 ± 1.17	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
LAMA	1.52 ± 0.38	1.27 ± 0.38	1.09 ± 0.36	1.00 ± 0.31	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

* All values of SMA, NAMA, LAMA showed significant difference in global test among 4 CT phases ($P < 0.0001$) and adjusted p-value of each pairwise comparison was adjusted by Scheffe's method. P value of less than 0.05 refers to statistical significance. Abbreviations: SMA = skeletal muscle area, NAMA = normal attenuation muscle area, LAMA = low attenuation muscle area

Table 3. Prevalence of sarcopenia according to CT phases using different diagnostic criteria

Diagnostic criteria	Cutoff*	Prevalence of sarcopenia (number [%])				p values†		
		Unenhanced phase (UP)	Arterial phase (AP)	Portal phase (PP)	Delayed phase (DP)	UP vs. AP	UP vs. PP	UP vs. DP
Area								
T-score < -1.0	140.3 cm^2 (male) or 87.2 cm^2 (female)	14 (15.7)	11 (12.4)	9 (10.1)	8 (9.0)	0.250	0.063	0.031
T-score < -2.0	119.3 cm^2 (male) or 74.2 cm^2 (female)	4 (4.5)	2 (2.2)	2 (2.2)	2 (2.2)	0.500	0.500	0.500
Area/height^2								
T-score < -1.0	46.7 cm^2/m^2 (male) or 33.6 cm^2/m^2 (female)	14 (15.7)	13 (14.6)	11 (12.4)	10 (11.2)	1	0.375	0.219
T-score < -2.0	39.8 cm^2/m^2 (male) or 28.4 cm^2/m^2 (female)	3 (3.4)	3 (3.4)	3 (3.4)	3 (3.4)	1	1	1
Area/weight								
T-score < -1.0	1.90 cm^2/kg (male) or 1.59 cm^2/kg (female)	7 (7.9)	6 (6.7)	6 (6.7)	6 (6.7)	1	1	1
T-score < -2.0	1.65 cm^2/kg (male) or 1.38 cm^2/kg (female)	2 (2.2)	2 (2.2)	2 (2.2)	2 (2.2)	1	1	1
Area/BMI								
T-score < -1.0	5.71 cm^2*m^2/kg (male) or 4.07 cm^2*m^2/kg (female)	12 (13.5)	10 (11.2)	9 (10.1)	9 (10.1)	0.625	0.250	0.250
T-score < -2.0	4.97 cm^2*m^2/kg (male) or 3.46 cm^2*m^2/kg (female)	3 (3.4)	3 (3.4)	3 (3.4)	3 (3.4)	1	1	1

* Based on the cutoff devised in *Kim et al.* [23].

†Results from the pair-wise comparison between unenhanced phase and others by using McNemar's test with Bonferroni correction. P value of less than 0.05/3 = 0.017 refers to statistical significance.

DISCUSSION

To the best of our knowledge, no consensus exists over which CT parameters and contrast phase yield the most reliable muscle measurements. Indeed, although many studies have investigated the assessment of muscle quantity and quality, they have not provided the CT acquisition parameters in sufficient detail (24), which has hampered reproduction of their work. In this study, we investigated the reliability of CT measurement of muscle quantity and quality with different CT parameters and contrast phases from CT images of phantom and human subjects, using two popular methods for measuring muscle quantity and quality on CT, i.e., (a) the cross-sectional area within the defined HU thresholds, and (b) the mean density. In addition, we used the DSC to evaluate similarities in cross-sectional area over acquisitions using different parameters to the standard protocol. According to our findings, the cross-sectional SMA (-29–150 HU) with different protocols were similar to those using the standard protocol, whereas the areas of NAMA (30–150 HU) were not stable across the protocols. Regarding the contrast phase, there were significant differences in area and indices of SMA, NAMA, and LAMA; but in the clinical perspectives, difference in SMA was not substantial to diagnose sarcopenia. The mean density of the muscle compartment was inaccurate with different CT parameters and contrast phases.

The most popular attenuation threshold used to measure muscle mass (or quantity) is -29 to 150 HU. Our study revealed that the measurement of muscle quantity using these

thresholds was reliable irrespective of the CT parameters, which is consistent with a prior study involving human subjects reporting that SMA measured with thin slice thickness and low radiation dose was constant (lowered by less than 5%) (25). By contrast, the measurement of muscle quality using the mean density of the muscle compartment should be interpreted with caution. It is evident that fat deposition in muscle, which relates to poor muscle strength, mortality, and morbidity, lowers the mean density on CT (8, 9). However, our study revealed that the mean density was subject to the choice of CT parameters. Fuch et al. (25) also reported that thin slices (2 mm vs 5 mm thickness) and low radiation dose altered the mean density by 4.8 and 17.3 HU, respectively. In principle, the mean HU values should be constant irrespective of radiation dose, as the outliers of HU, caused by noise, at both ends of the range should offset each other (25). However, this was not the case for the reference standard muscle compartment in our study, probably because noise from neighboring structures such as vertebrae and adipose tissue altered the attenuation of affected pixels. As such, in situations with low SNR such as parameters using low tube current, low tube voltage, or thin slice sections, the effect could become substantial. The photoelectric effect with the low tube voltage might have altered CT density (26, 27). We also investigated the value of IR for muscle measurement on dose-reduced protocols, expecting that the reduced noise obtained would better reflect the true attenuation value of each pixel. In fact, the SMA and NAMA in images using IR occupied more pre-segmented area than they did in

images with the same protocols reconstructed using FBP. Images using the standard protocol, which implied sufficient image quality for the measurement, were the only exception to this tendency. Nevertheless, the difference between IR and FBP was trivial in all cases.

Several studies investigated the effect of the contrast phases on the muscle measurements and presented the conflicting results (25, 28-30). Indeed, three studies (25, 29, 30) found contrast phase significantly affected the area and mean HU, which results were in line with ours, whereas the other (28) showed no significant differences. The difference may be attributed to the number of population and statistical analyses and no study did not investigate the clinical aspect of muscle measurements with different contrast phases. According to our results, based on the recently suggested diagnostic cutoff of sarcopenia (23), measured area of SMA from the different contrast phases did not seem to clinically affect the diagnosis of sarcopenia.

Some authors suggested differentiating LAMA from NAMA on the basis of the HU threshold (usually using a cutoff of 30 HU) (11, 31). However, according to our results, the measurement of muscle quality based on this narrower HU threshold would not be constant across different parameters as well as contrast phases. Therefore, when the evaluation of myosteatosis or muscle quality, the CT measurement might be limited to the standardized CT parameters and contrast phases. Future studies are required to figure out which CT parameters and the contrast phase should be taken into account for the generalizability of

muscle measurements.

Our study has several limitations. First, the phantom did not fully reflect the muscle components of the human body as the HU of the muscle area was theoretically constant in the phantom. Moreover, as the phantom was primarily to measure bone density, measurement of muscle density might have been inaccurate. Thus, the measured mean HU values of the muscle compartment were all lower than the true value (i.e., 45 HU), irrespective of the CT parameters. Nevertheless, using the phantom, we were able to investigate the reliability of measurements in relation to CT parameters, as we could adjust the CT parameters free from any ethical considerations of radiation dose. A further animal or clinical study might be required to confirm our results. Second, we did not investigate the reliability of muscle measurement across the different scanners. However, we believed that it was impractical to compare them head-to-head, as each device has innate techniques in terms of dose reduction and image reconstruction. In addition, the intentions of our study were not to determine which device was superior; rather, we wanted to determine the constant effects of alterations to the parameters, irrespective of the device characteristics.

CONCLUSION

The measurement of SMA using HU threshold is a reliable method regardless of the CT parameters, and clinical acceptable methods regardless of the contrast phase. Conversely, the

measurement of muscle quality using the mean density and a narrower HU threshold was inconsistent and inaccurate, showing variations across the different CT parameters and contrast phase. Therefore, future study is warranted to determine the optimal CT protocols and contrast phase for reliable measurements.

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ABSTRACT

Objectives: To evaluate the reliability of the measurement of muscle quantity and quality under variable CT parameters and contrast phase.

Materials and Methods: In a phantom simulating the L2–4 vertebrae levels was used, CT images were repeatedly obtained with modulation of tube voltage, tube current, slice thickness, and image reconstruction algorithm. In 89 consecutive human subjects (mean age [range], 52.2 [28–79] years; 52 mean), CT images with four different phases (pre-contrast, arterial, portal, and delayed phases) were obtained after the contrast agent administration. Reference standard muscle compartments were segmented using reference maps (phantom) and deep learning algorithms (human subjects). Cross-sectional area based on the Hounsfield unit (HU) thresholds of skeletal muscle area (SMA; threshold, -29–150 HU) and its components including normal attenuation muscle area (NAMA; threshold, 30–150 HU) and low attenuation muscle area (LAMA; threshold, -29 to 30 HU), and the mean density were both used to measure the muscle quantity and quality with the different protocols and contrast phase. Signal-to-noise ratio (SNR) were calculated in the images acquired with different settings.

Results: SMA occupied at least 91.7% of the reference standard muscle compartment regardless of the CT parameters. Conversely, NAMA was not constant across the different CT parameters, varying between 59.7–81.7% of the reference standard muscle compartment. The mean density was lower than the target density stated by the manufacturer (45 HU) in all cases (range, 39.0–44.9 HU) regardless of the CT parameters. Regarding the contrast phase, there was significant difference in area and mean HU of SMA, NAMA, and LAMA. Nevertheless, difference in area and its adjusted indices of SMA did not clinically change the number of patients with sarcopenia.

Conclusions: The measurement of muscle quantity using HU threshold was reliable, regardless of the CT parameters, and clinically acceptable methods regardless of the contrast phase. Conversely, the measurement of muscle quality using the mean density and a narrower HU threshold was inconsistent and inaccurate according to the different CT parameters and contrast phases.

Keywords: Computed tomography, Muscle measurement, Phantom, Sarcopenia