# The relationship between computed tomography-derived body composition and survival in colorectal cancer: the effect of image software

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## **Abstract**

**Background** In the literature, there is considerable variation of the proportion of patients reported as having a low skeletal muscle index (SMI) (sarcopenia) or skeletal muscle radiodensity (SMD) (myosteatosis). The aim of the present study was to compare two commonly used software packages, one manual and one semi-automated to quantify body composition of patients with colorectal cancer.

Methods The study included 341 patients with colorectal cancer. ImageJ and Slice-O-Matic were used to quantify the computed tomography images for total fat index, visceral obesity (visceral fat index, VFI), high subcutaneous fat index (SFI), sarcopenia (SMI), and myosteatosis (SMD). Bland–Altman analysis was conducted to test agreement of the two software programs for these indices. Survival analysis was carried out using previously defined thresholds and Cox regression.

**Results** In Bland–Altman analysis, ImageJ gave consistently higher values for all body composition parameters (P < 0.001), resulting in more patients classified as high SFI (P < 0.001) and high VFI (P < 0.001) and fewer patients being classified as low SMI (P < 0.0001) and SMD (P < 0.001). The difference between SFI calculated using ImageJ and Slice-O-Matic was +7.9%. The difference between VFI, calculated using ImageJ and Slice-O-Matic, was +20.3%. The difference between low SMI and SMDs, estimated using ImageJ and Slice-O-Matic, was +2.9% and +1.2%, respectively. SFI, VFI, SMI (Dolan), SMD (Dolan), SMI (Martin), and SMD (Martin) were significantly associated with shorter overall survival using ImageJ (all P < 0.05).

**Conclusions** ImageJ when compared with Slice-O-Matic gave higher values of different body composition parameters, and this impacted on the number of patients classified according to defined thresholds and their relationship with survival.

Keywords Colorectal cancer; ImageJ; Slice-O-Matic; Survival; Body composition

Received: 24 October 2019; Accepted: 11 February 2020

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## Introduction

Colorectal cancer (CRC) is the fourth leading cause of cancer mortality in developed countries. Approximately 50% of those diagnosed will die from their cancer or comorbid disease. In a similar manner to other solid organ tumours, disease progression is associated with nutritional and

functional decline resulting in poor response to treatment and poor survival.  $^{3,\ 4}$ 

The relationship between weight loss and poor outcomes in these patients with cancer has long been established. Recently, computed tomography (CT)-derived body composition analysis has confirmed that the main prognostic component of this weight loss is skeletal muscle mass.<sup>3–5</sup> Skeletal muscle

is a highly physiologically active organ and accounts for about 40–45% of body weight. Skeletal muscle is highly plastic and can respond to a variety of stimuli. As a result, skeletal muscle volume has been closely related to morbidity and mortality leading to a significant increase in interest in skeletal muscle when investigating fragility, cachexia, and sarcopenia.<sup>5, 6</sup>

In addition to skeletal muscle volume, fat volume and density have been associated with outcomes in patients with cancer. Two recent studies reported that patients with elevated visceral fat had lower functional capacity, greater treatment-related toxicities, and poorer overall survival.<sup>7, 8</sup>

Currently, there are several software programs that calculate CT-derived body composition at the third lumbar vertebrae. The two most commonly used software packages are ImageJ (National Institutes of Health, Bethesda, USA) and Slice-O-Matic 5.0 (TomoVision, Montreal, Canada). ImageJ reguires the manual analysis of areas of interest including the quadratus lumborum, psoas, rectus abdominus, erector spinae muscles, internal transverse, and external oblique muscle groups, whereas Slice-O-Matic carried out the same analysis in a semi-automated manner. Irving and co-workers directly compared the values generated for adipose tissue and skeletal muscle cross-sectional areas from these software packages in 26 patients with a mean percentage difference of less than 2%.9 Teigen and co-workers directly compared the values generated from these software packages in 51 patients with a mean percentage difference of less than 1%.<sup>10</sup>

Therefore, in small cohort studies, CT-derived body composition parameters analysed by ImageJ and Slice-O-Matic give similar but not identical results. The aim of this study was, for the first time, to compare body composition analysis using both ImageJ and Slice-O-Matic and their relationship with survival in a large cohort of patients undergoing surgery for CRC.

## Materials and methods

#### Computed tomography images analysis

Computed tomography (CT) scans were conducted at a tube voltage of 120 kV, with 5 mm slice thickness, and a  $512 \times 512$  image resolution. An individual CT slice was acquired at the level of the third lumbar vertebra from 341 CRC patients. All 341 CT images were analysed by two software programs, ImageJ and Slice-O-Matic.

#### **ImageJ**

ImageJ is a Java-based image processing and analysing program developed by NIH and is free to be downloaded from their website (Version 1.52, https://imagej.nih.gov/ij/download.html). ImageJ is able to evaluate the density of each pixel, and with the latest advances in the package, density

has been calibrated to reflect true HU values. Region of interest measurements include total fat area (TFA), visceral fat area (VFA), and skeletal muscle area (SMA) with an attenuation threshold from -190 to +150 HU (i.e. -190 to -30 for adipose tissue and -29 to +150 for skeletal muscle). Generally, TFA was quantified by depicting the outer contours of the abdominal wall, while VFA was performed by outlining the inner contour of the psoas and abdominal wall muscles. Similarly, SMA was measured by manually delineating muscle areas including the quadratus lumborum, psoas, rectus abdominus, erector spinae muscles, internal transverse, and external oblique muscle groups, and SFA was calculated by subtracting VFA from TFA. Skeletal muscle radiodensity (SMD, HU) was measured from the same ROI used to calculate SMI, as its mean HU.

#### Slice-O-Matic

Slice-O-Matic Version 5.0 (TomoVision, Magog, Canada; 64 bit; available at https://www.tomovision.com/index.html) was used to perform CT image segmentation process within different body composition regions. The adipose tissue was segmented to distinguish between intramuscular adipose tissue, visceral (intra-abdominal) adipose tissue, and subcutaneous adipose tissue using predefined thresholds. SMAs included quadratus lumborum, psoas, rectus abdominus, erector spinae muscles, internal transverse, and external oblique muscle groups. Every tissue cross-sectional area was initially tagged with standard HU ranges using thresholding function, as intramuscular adipose tissue, visceral (intra-abdominal) adipose tissue, and subcutaneous adipose tissue were set -190 to -30 HU while skeletal muscle was set -29 to +150 HU. Once the appropriate threshold HU ranges were set, compartmental segmentation was computed.

#### **Body composition measurements**

All results of body composition parameters (TFA, VFA, SFA, and SMA) were later divided by the square of the patient's height in meters to generate total fat index (TFI, cm<sup>2</sup>/m<sup>2</sup>), visceral fat index (VFI, cm<sup>2</sup>/m<sup>2</sup>), subcutaneous fat index (SFI, cm<sup>2</sup>/m<sup>2</sup>), and skeletal muscle index (SMI, cm<sup>2</sup>/m<sup>2</sup>). These indices were then compared with established thresholds for body composition status (*Table* 1).

#### Statistical analysis

For each parameter comparison, normality of the data was assessed by Shapiro–Wilk normality tests. Spearman's rank correlation coefficient was used to examine the strength of the interrelationship between ImageJ and Slice-O-Matic for

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Table 1 CT-derived body composition measures and thresholds used

#### Body composition measurement

High SFI<sup>12</sup>

Males > 50.0 cm $^2/\text{m}^2$  and females > 42.0 cm $^2/\text{m}^2$  Visceral obesity $^{8,13}$ 

VFA: males  $> 160 \text{ cm}^2$  and females  $> 80 \text{ cm}^2$ 

Sarcopenia

SMI (Dolan)<sup>14</sup>

Males: BMI  $< 25 \text{ kg/m}^2$  and SMI  $< 45 \text{ cm}^2/\text{m}^2$  or BMI  $\ge 25 \text{ kg/m}^2$ and SMI  $< 53 \text{ cm}^2/\text{m}^2$ 

Females: BMI  $<25\ \text{kg/m}^2$  and SMI  $<39\ \text{cm}^2/\text{m}^2$  or BMI  $\geq25\ \text{kg/m}^2$ 

and SMI  $< 41 \text{ cm}^2/\text{m}^2$ 

SMI (Martin)

Males: BMI < 25 kg/m<sup>2</sup> and SMI < 43 cm<sup>2</sup>/m<sup>2</sup> or BMI  $\ge$  25 kg/m<sup>2</sup> and SMI  $< 53 \text{ cm}^2/\text{m}^2$ 

Females: BMI  $< 25 \text{ kg/m}^2$  and SMI  $< 41 \text{ cm}^2/\text{m}^2$  or BMI  $\ge 25 \text{ kg/m}^2$ and SMI  $< 41 \text{ cm}^2/\text{m}^2$ 

Myosteatosis SMD (Dolan)<sup>14</sup>

BMI < 25 kg/m<sup>2</sup> and SMD < 34 HU or BMI  $\geq$  25 kg/m<sup>2</sup> and  $SMD < 32 H\overline{U}$ 

SMD (Martin)8

BMI  $< 25 \text{ kg/m}^2 \text{ and SMD} < 41 \text{ HU or BMI} \ge 25 \text{ kg/m}^2 \text{ and}$ SMD < 33 HU

BMI, body mass index; CT, computed tomography; SMI, skeletal muscle index; SMD, skeletal muscle radiodensity; SFI, subcutaneous fat index; VFA, visceral fat area.

[Correction added on 30 May 2020 after first online publication: BMI  $\leq$  25 kg/m<sup>2</sup> has been corrected to BMI < 25 kg/m<sup>2</sup>, and BMI > 25 kg/m<sup>2</sup> has been corrected to BMI  $\ge$  25 kg/m<sup>2</sup> in this current version.1

each body composition parameter. Correlation coefficient was considered as a weak linear relationship with values 0 to 0.300, moderate with values 0.300 to 0.700, and strong

with values 0.700 to 1.000. In addition, the difference between ImageJ and Slice-O-Matic for each body composition parameter was tested using Wilcoxon test. The determination of proportional bias between two software programs (ImageJ and Slice-O-Matic) was carried out using Bland-Altman analysis.

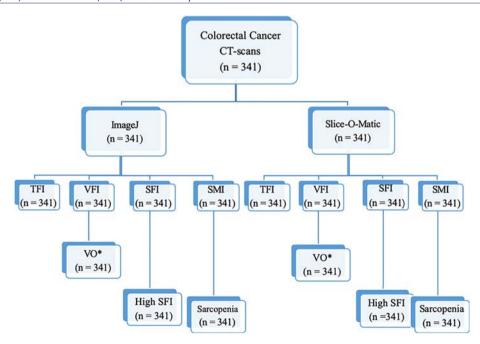
Mortality within 30 days of the index procedure or during the index admission results in exclusion from subsequent survival analysis. The time between the date of surgery and the date of death of any cause was used to define overall survival. Survival data were analysed using univariate and multivariate Cox regression. Those variables associated to a degree of P < 0.1 were entered into a backward conditional multivariate model. Kaplan-Meier curves for overall survival were constructed over a 60 month period. Missing data were excluded from analysis on a variable by variable basis. Two-tailed P values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS software (Version 21.0. SPSS Inc., Chicago, IL, USA).

## Results

#### **Patients**

A total of 341 CRC patients were selected for CT scans. A flow diagram of the patients included in each analysis is presented in Figure 1.

Figure 1 Flow diagram of body composition parameters analysed by ImageJ and Slice-O-Matic. SFI, subcutaneous fat index; SMI, skeletal muscle index; TFI, total fat index; VFI, visceral fat index; VO\*, visceral obesity.



#### Association between ImageJ and Slice-O-Matic

The overall mean TFI was significantly correlated between ImageJ and Slice-O-Matic ( $R^2=0.996,\ P<0.001$ ). The overall mean SFI was significantly correlated between ImageJ and Slice-O-Matic ( $R^2=0.969,\ P<0.001,\ Table$  2). The overall mean VFI was significantly correlated between ImageJ and Slice-O-Matic ( $R^2=0.919,\ P<0.001,\ Table$  2). The overall mean SMI was significantly correlated between ImageJ and Slice-O-Matic ( $R^2=0.927,\ P<0.001,\ Table$  2). The overall mean SMD was significantly correlated between ImageJ and Slice-O-Matic ( $R^2=0.971,\ P<0.001,\ Table$  2).

The mean percentage difference for TFI was calculated using ImageJ and Slice-O-Matic [+9.3% (0.56), P < 0.001]. The mean percentage difference for SFI was calculated using ImageJ and Slice-O-Matic [+7.9% (0.17), P < 0.001,  $Table\ 2$ ]. The mean percentage difference for VFI was calculated using ImageJ and Slice-O-Matic [+20.3% (0.21), P < 0.001,  $Table\ 2$ ]. The mean percentage difference for SMI was calculated using ImageJ and Slice-O-Matic [+2.9% (0.49), P < 0.001,  $Table\ 2$ ]. The mean percentage difference for SMD was

calculated using ImageJ and Slice-O-Matic [+1.2% (0.09), P < 0.001, *Table* 2].

## Bland—Altman analysis between ImageJ and Slice-O-Matic

The mean difference of TFI using ImageJ and Slice-O-Matic was 13.1 (-10.1% to +36.3%), respectively, and 1.17% (4/341) of patients were outside the 95% confidence interval (CI) (P < 0.001, Figure 2). The mean difference of VFI using ImageJ and Slice-O-Matic was 5.4 (-22.9% to +48.9), respectively, and 3.23% (11/341) of patients were outside the 95% CI (P < 0.001, Figure 3). The mean difference of SFI using ImageJ and Slice-O-Matic was 5.4 (-39.5% to +50.3%), respectively, and 3.23% (11/341) of patients were outside the 95% CI (P < 0.001, Figure 4). The mean difference of SMI using ImageJ and Slice-O-Matic was 2.3 (-6.5% +11.7%), respectively, and 2.64% (9/341) of patients were outside the 95% CI (P < 0.001, Figure 5). The mean difference of SMD using ImageJ and Slice-O-Matic was 0.5 (-3.8% to +4.8%),

Table 2 Mean (SD) CT body composition parameters measurements and correlation coefficient test using ImageJ and Slice-O-Matic

Body composition parameters	Software program	Ν	Mean (SD)	R <sup>2</sup> (P-value)	Mean percentage difference (SD)	<i>P</i> -value
VFI (cm <sup>2</sup> /m <sup>2</sup> )	ImageJ Slice-O-Matic	341 341	70.6 (39.6) 57.7 (36.4)	0.919 (<0.001 <sup>a</sup> )	+20.3% (0.21)	<0.001 <sup>b</sup>
SFI (cm <sup>2</sup> /m <sup>2</sup> )	ImageJ Slice-O-Matic	341 341		0.969 (<0.001 <sup>a</sup> )	+7.9% (0.17)	<0.001 <sup>b</sup>
SMI (cm <sup>2</sup> /m <sup>2</sup> )	ImageJ Slice-O-Matic	341 341	46.5 (9.7) 44.0 (9.6)	0.927 (<0.001 <sup>a</sup> )	+2.9% (0.49)	<0.001 <sup>b</sup>
SMD (cm <sup>2</sup> /m <sup>2</sup> )	ImageJ Slice-O-Matic	341 341	34.5 (8.3) 34.1 (8.3)	0.971 (<0.001 <sup>a</sup> )	+1.2% (0.09)	<0.001 <sup>b</sup>

Body composition parameters included VFI, SFI, and SMI. CT, computed tomography; SD, standard deviation; SFI, subcutaneous fat index; SMI; skeletal muscle index; VFI, visceral fat index.

Table 3 The relationship between body composition and overall survival in patients with CRC using ImageJ and Slice-O-Matic

	Software _	Threshold value (N, %)	Univariate Cox regression	Mu	Multivariate Cox regression		
Body composition	program	Yes	HR (95% CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value	
Visceral obesity	ImageJ	256 (75.1)	0.58 (0.40-0.86)	0.007	0.58 (0.40-0.86)	0.007	
_	Slice-O-Matic	210 (61.6)	0.72 (0.50-1.04)	0.084	_	0.636	
High SFI	lmageJ	271 (79.5)	0.48 (0.32-0.70)	< 0.001	0.48 (0.32-0.70)	< 0.001	
_	Slice-O-Matic	245 (71.8)	0.54 (0.37-0.79)	0.001	_	0.683	
Sarcopenia (Dolan)	lmageJ	157 (46.0)	1.92 (1.32–2.80)	0.001	_	0.154	
•	Slice-O-Matic	209 (61.3)	2.04 (1.34-3.10)	0.001	2.04 (1.34-3.10)	0.001	
Sarcopenia (Martin)	lmageJ	157 (46.0)	1.75 (1.21–2.55)	0.003	1.75 (1.21-2.55)	0.003	
·	Slice-O-Matic	203 (59.5)	1.66 (1.11–2.48)	0.012	_	0.595	
Myosteatosis (Dolan)	ImageJ	131 (38.4)	1.62 (1.12–2.34)	0.010	_	0.992	
	Slice-O-Matic	141 (41.3)	1.73 (1.20–2.50)	0.004	1.73 (1.20-2.50)	0.004	
Myosteatosis (Martin)	ImageJ	191 (56.0)	0.93 (0.64–1.34)	0.689	_	0.474	
	Slice-O-Matic	181 (53.1)	2.07 (1.40–3.06)	< 0.001	2.07 (1.40–3.06)	< 0.001	

<sup>&</sup>lt;sup>a</sup>Calculated with one sample *t*-test.

<sup>&</sup>lt;sup>b</sup>Calculated with Wilcoxon test.

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Figure 2 Bland–Altman analysis of total fat index (TFI) (cm²/m²) obtained using ImageJ and Slice-O-Matic. Bland–Altman analysis displays the mean difference (red line) and the 95% CI LoA (±1.96 SD, green lines). Mean = ((ImageJ measure of TFI + Slice-O-Matic measure of TFI)/2). Difference = (ImageJ measure of TFI – Slice-O-Matic measure of TFI).

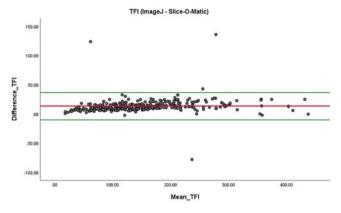


Figure 3 Bland–Altman analysis of visceral fat index (VFI) (cm<sup>2</sup>/m<sup>2</sup>) obtained using ImageJ and Slice-O-Matic. Bland–Altman analysis displays the mean difference (red line) and the 95% CI LoA (±1.96 SD, green lines). Mean = ((ImageJ measure of VFI + Slice-O-Matic measure of VFI)/2). Difference = (ImageJ measure of VFI – Slice-O-Matic measure of VFI).

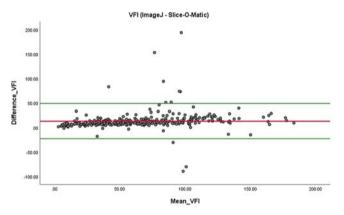


Figure 4 Bland–Altman analysis of subcutaneous fat index (SFI)  $(cm^2/m^2)$  obtained using ImageJ and Slice-O-Matic. Bland–Altman analysis displays the mean difference (red line) and the 95% CI LoA ( $\pm 1.96$  SD, green lines). Mean = ((ImageJ measure of SFI + Slice-O-Matic measure of SFI)/2). Difference = (ImageJ measure of SFI - Slice-O-Matic measure of SFI).

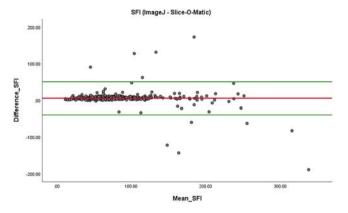


Figure 5 Bland–Altman analysis of skeletal muscle index (SMI) (cm²/m²) obtained using ImageJ and Slice-O-Matic. Bland–Altman analysis displays the mean difference (red line) and the 95% CI LoA (±1.96 SD, green lines). Mean = ((ImageJ measure of SMI + Slice-O-Matic measure of SMI)/2). Difference = (ImageJ measure of SMI – Slice-O-Matic measure of SMI).

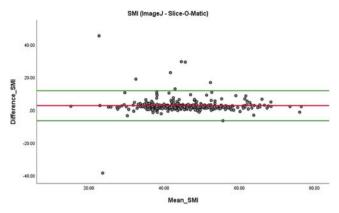
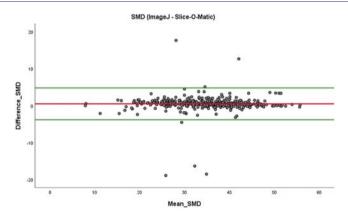


Figure 6 Bland–Altman analysis of skeletal muscle radiodensity (SMD) (HU) obtained using ImageJ and Slice-O-Matic. Bland–Altman analysis displays the mean difference (red line) and the 95% CI LoA (±1.96 SD, green lines). Mean = ((ImageJ measure of SMD + Slice-O-Matic measure of SMD)/2). Difference = (ImageJ measure of SMD – Slice-O-Matic measure of SMD).



respectively, and 1.76% (6/341) of patients were outside the 95% CI (P < 0.001, Figure 6.

## Body composition and overall survival between ImageJ and Slice-O-Matic

In total, 256 (75.1%) patients were classified as having visceral obesity using ImageJ compared with 210 (61.6%) patients using Slice-O-Matic. In total, 271 (79.5%) were classified as having an elevated SFI using ImageJ compared with 245 patients (71.8%) using Slice-O-Matic.

In total, 157 (46%) were classified as sarcopenic (Dolan) using ImageJ compared with 209 (61.3%) using Slice-O-Matic. In total, 131 (38.4%) were classified as having myosteatosis (Dolan) using ImageJ compared with 141 (41.3%) using Slice-O-Matic. In total, 157 (46%) were classified as sarcopenic (Martin) using ImageJ compared with 203

(59.5%) using Slice-O-Matic. In total, 191 (56%) were classified as having myosteatosis (Martin) using ImageJ compared with 181 (53.1%) using Slice-O-Matic.

On univariate Cox regression survival analysis, VO when analysed with ImageJ was significantly associated with overall survival (HR: 0.58, 95% CI 0.40–0.86, P = 0.007, Table 3 and Figure 7A). In contrast, on univariate Cox regression survival analysis, VO when analysed with Slice-O-Matic was not significantly associated with overall survival (P = 0.084, Table 3 and Figure 7B). On multivariate Cox regression analysis, VO when analysed with ImageJ remained independently associated with overall survival (HR: 0.58, 95% CI 0.40–0.86, P = 0.007, Table 3)

On univariate Cox regression survival analysis, SFI was significantly associated with overall survival when analysed with ImageJ (HR: 0.48, 95% CI 0.32–0.70, P < 0.001, Table 3 and Figure 8A). On univariate Cox regression survival analysis, SFI was significantly associated with overall survival when

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Figure 7 (A) The Kaplan–Meier curve for visceral obesity and overall survival using ImageJ (*P* = 0.007). (B) The Kaplan–Meier curve for visceral obesity and overall survival using Slice-O-Matic (*P* = 0.084).

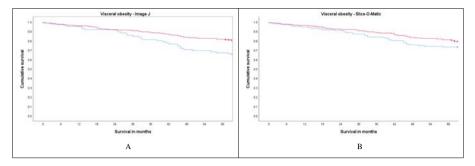
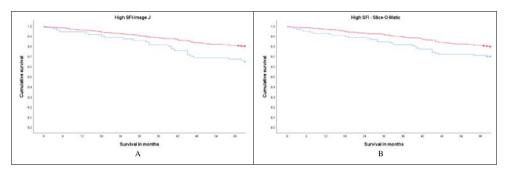


Figure 8 (A) The Kaplan–Meier curve for subcutaneous fat index (SFI) and overall survival using ImageJ (P < 0.001). (B) The Kaplan–Meier curve for SFI and overall survival using Slice-O-Matic (P = 0.001).



analysed with Slice-O-Matic (HR: 0.54, 95% CI 0.37–0.79, P<0.001, Table 3 and Figure 8B). On multivariate Cox regression analysis, SFI when analysed with ImageJ remained independently associated with overall survival (HR: 0.48, 95% CI 0.32–0.70, P<0.001, Table 3)

On univariate Cox regression analysis, sarcopenia (Dolan) was significantly associated with overall survival when analysed with ImageJ (HR: 1.92, 95% CI 1.32–2.80, P = 0.001, Table 3 and Figure 9A). On univariate Cox regression analysis, sarcopenia (Dolan) was significantly associated

with overall survival when analysed with Slice-O-Matic (HR: 2.04, 95% CI 1.34–3.10, P = 0.001, Table 3 and Figure 9B). On multivariate Cox regression analysis, sarcopenia (Dolan) when analysed with Slice-O-Matic remained independently associated with overall survival (HR: 2.04, 95% CI 1.34–3.10, P = 0.001, Table 3).

On univariate Cox regression analysis, sarcopenia (Martin) was significantly associated with overall survival when analysed with ImageJ (HR: 1.75, 95% CI 1.21–2.55, P = 0.003, Table 3 and Figure 10A). On univariate Cox

Figure 9 (A) The Kaplan–Meier curve for sarcopenia (Dolan) and overall survival using ImageJ (P = 0.001). (B) The Kaplan–Meier curve for sarcopenia (Dolan) and overall survival using Slice-O-Matic (P = 0.001).

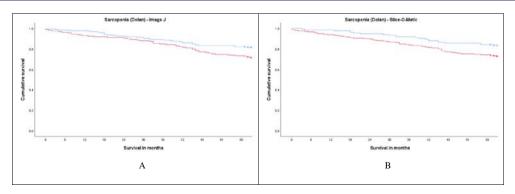
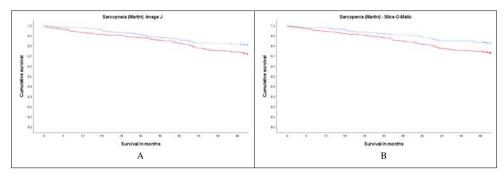


Figure 10 (A) The Kaplan–Meier curve for sarcopenia (Martin) and overall survival using ImageJ (*P* = 0.003). (B) The Kaplan–Meier curve for sarcopenia (Martin) and overall survival using Slice-O-Matic (*P* = 0.012)



regression analysis, sarcopenia (Martin) was significantly associated with overall survival when analysed with Slice-O-Matic (HR: 1.66, 95% CI 1.11–2.48, P = 0.012, Table 3 and Figure 10B). On multivariate Cox regression analysis, sarcopenia (Martin) when analysed with ImageJ remained independently associated with overall survival (HR: 1.75, 95% CI 1.21–2.55, P = 0.003, Table 3).

On univariate Cox regression analysis, myosteatosis (Dolan) was significantly associated with overall survival when

analysed with ImageJ (HR: 1.62, 95% CI 1.12–2.34, P = 0.01, Table 3 and Figure 11A). On univariate Cox regression analysis, myosteatosis (Dolan) was significantly associated with overall survival when analysed with Slice-O-Matic (HR: 1.73, 95% CI 1.20–2.50, P = 0.004, Table 3 and Figure 11B). On multivariate Cox regression analysis, myosteatosis (Martin) when analysed with Slice-O-Matic remained independently associated with overall survival (HR: 1.73, 95% CI 1.20–2.50, P = 0.004, Table 3).

Figure 11 (A) The Kaplan–Meier curve for myosteatosis (Dolan) and overall survival using ImageJ (P = 0.010). (B) The Kaplan–Meier curve for myosteatosis (Dolan) and overall survival using Slice-O-Matic (P = 0.004).

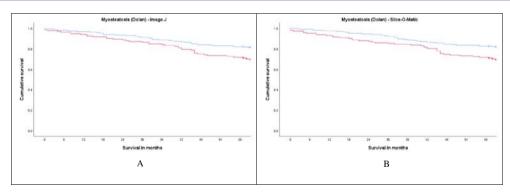
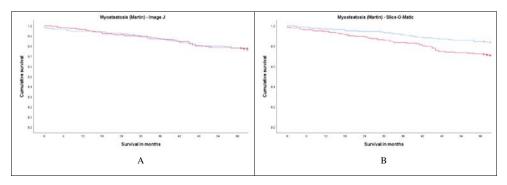


Figure 12 (A) The Kaplan–Meier curve for myosteatosis (Martin) and overall survival using ImageJ (P = 0.689). (B) The Kaplan–Meier curve for myosteatosis (Martin) and overall survival using Slice-O-Matic (P < 0.001).



On univariate Cox regression analysis, myosteatosis (Martin) was not significantly associated with overall survival when analysed with ImageJ (P=0.689, Table~3 and Figure~12A). On univariate Cox regression analysis, myosteatosis (Martin) was significantly associated with overall survival when analysed with Slice-O-Matic (HR: 2.07, 95% CI 1.40–3.06, P<0.001, Table~3 and Figure~12B). On multivariate Cox regression analysis, myosteatosis (Martin) when analysed with Slice-O-Matic remained independently associated with overall survival (HR: 2.07, 95% CI 1.40–3.06, P<0.001, Table~3).

#### **Discussion**

The present study showed that ImageJ and Slice-O-Matic derived values for TFI, SFI, VFI, and SMI were strongly associated. However, ImageJ consistently gave higher values for all body composition parameters. As a consequence, these higher values resulted in more patients being classified as viscerally obese (~14%) and fewer patients being classified as sarcopenic (~14%) using standard thresholds previously described. Finally, such differences between the software packages estimates altered the relationship of the body composition indices with overall survival. Therefore, CT-derived body composition is not only dependent on the age, sex, body mass index, and the systemic inflammatory response but it would appear to be also dependent on the software package used. <sup>15</sup>

There was a consistent proportional systematic bias in the values calculated by the two software packages for TFI, VFI, SFI, and SMI. The lower values from the Slice-O-Matic analysis may be explained by the semi-automated procedure such that there was an underestimation relative to the manual ImageJ procedure. For example, ImageJ requires the user to draw around the areas of interest on the CT scan, whereas

Slice-O-Matic automatically selects the areas of interest to calculate the total area. With reference to fat and muscle tissue, Slice-O-Matic may classify areas as part of adjacent structures. Indeed, this limitation is acknowledged for some CT scans in the Slice-O-Matic manual, and an additional image editing component to the software is included to allow for fine tuning of automated images based on expert clinical and anatomical knowledge.<sup>10</sup>

Several limitations associated with this study should be acknowledged. This study was carried out on retrospectively collected CT scans, and both ImageJ and Slice-O-Matic image analysis was carried out once for each scan. Nevertheless, the present study reflects the real world use of these software packages.

In conclusion, the present study showed that ImageJ, compared with Slice-O-Matic, gave higher values of different body composition parameters. The impact of different software programs on the appropriate classification thresholds should be taken into account when carrying out CT-derived body composition analysis in patients with CRC.

# **Acknowledgement**

The authors certify that they comply with the ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2017.<sup>16</sup>

## Conflict of interest

The authors declare no potential conflicts of interest.

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