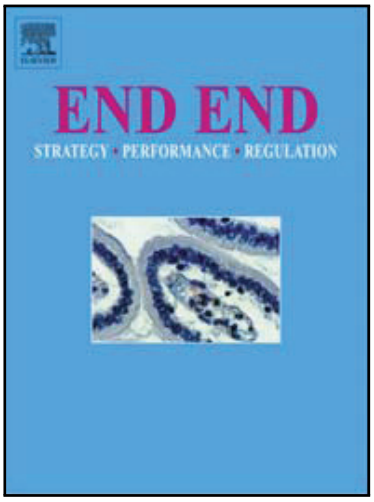
Accepted Manuscript



A comparison of two different software packages for the analysis of body composition using computed tomography images

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Highlights

- We clarify the equivalence of body composition analysis from computed tomography (CT) images using two different software packages.
- Analysis was performed using SliceOmatic and OsiriX packages on 50 patients who had undergone tri-phasic scans.
- Body composition measures were significantly different between the two software packages, but the clinical significance of these is doubtful.
- However, we recommend that for serial body composition analysis and for comparative purposes, the software package employed should be consistent.

A comparison of two different software packages for the analysis of body composition using computed tomography images

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Running Head: Software Packages for Body Composition Analysis

Abbreviations used: CT = computed tomography; DICOM = Digital Imaging and Communications in Medicine; FFM = fat free mass; FM = fat mass; HU = Hounsfield units; SAT = subcutaneous adipose tissue; SMHU = skeletal muscle Hounsfield units; SMI = skeletal muscle index; VAT = visceral adipose tissue

Word Count: 1969 (excluding abstract, references, tables and figures)

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Abstract

Objectives: Body composition analysis from computed tomography (CT) imaging has become widespread. However, the methodology used is far from established. Two main software packages are in common usage for body composition analysis, with results used interchangeably. However, the equivalence of these has not been well established. The aim of this study was to compare the results of body composition analysis performed using the two software packages to assess their equivalence.

Methods: Tri-phasic abdominal CT scans from 50 patients were analysed for a range of body composition measures at the third vertebral level using OsiriX (v7.5.1, Pixmeo, Switzerland) and SliceOmatic (v5.0, TomoVision, Montreal, Canada) software packages. Measures analysed were skeletal muscle index (SMI), fat mass (FM), fat free mass (FFM) and mean skeletal muscle Hounsfield Units (SMHU).

Results: The overall mean SMI calculated using the two software packages was significantly different (SliceOmatic 51.33 vs. OsiriX 53.77, $p<0.0001$), and this difference remained significant for non-contrast and arterial scans. When FM and FFM were considered, again the results were significantly different (SliceOmatic 33.7kg vs. OsiriX 33.1kg, $p<0.0001$; SliceOmatic 52.1kg vs. OsiriX 54.2kg, $p<0.0001$, respectively), and this difference remained for all phases of CT. Finally, when mean SMHU was analysed, this was also significantly different (SliceOmatic 32.7 HU vs. OsiriX 33.1 HU, $p=0.046$).

Conclusions: All four body composition measures were statistically significantly different by the software package used for analysis, however the clinical significance of these differences

78 is doubtful. Nevertheless, the same software package should be utilised if serial
79 measurements are being performed.

80

81 Key words: computed tomography; body composition; sarcopenia; myosteatosis; OsiriX;
82 SliceOMatic

83

Introduction

Computed tomography (CT) analysis of body composition to measure fat mass (FM) and fat free mass (FFM), calculate skeletal muscle index (SMI), and diagnose sarcopenia and myosteatosis has become increasingly common, with literature now linking sarcopenia and myosteatosis with reduced overall survival [1, 2], decreased tolerance to chemotherapy [3, 4] and increased complications [5, 6] following surgery in patients presenting with various types of malignancy.

However, the methodology for calculating body composition from CT images is variable between studies, from the nature of the CT scan used including the vertebral level, to the use of contrast medium, to the software used to perform the analysis. The impact of the use of contrast medium in CT scanning in body composition analysis has previously been recognised to have a significant effect upon results, especially the diagnosis of myosteatosis [7, 8]. Despite these inconsistencies in analysis, the results of these studies are used interchangeably, with the definition of neither sarcopenia or myosteatosis stipulating any conditions about how these derived values are calculated.

There are currently two software packages used commonly to analyse body composition from CT scans: SliceOmatic (TomoVision, Montreal, Canada) and OsiriX (Pixmeo, Switzerland), the results of which are also used interchangeably. One study in patients with rectal cancer [9] has suggested that SliceOmatic, ImageJ (National Institutes of Health, Bethesda, MD, USA), FatSeg [Biomedical Imaging Group Rotterdam of Erasmus MC, Rotterdam, The Netherlands, using MeVisLab (Mevis Medical Solutions, Bremen, Germany)] and OsiriX analysis provide excellent levels of agreement. However, this study [9] did not consider mean skeletal muscle Hounsfield Unit as a surrogate for myosteatosis. The aim of

the present study was to compare the SliceOmatic and OsiriX software packages and determine if there was a difference in calculated measures of body composition, namely SMI, FM, FFM and mean skeletal muscle Hounsfield units (SMHU), using CT scan images.

Methods

In a single centre retrospective study, CT scans from 50 patients who underwent triple phase abdominal scans (non-contrast, arterial and portovenous phases) between April 2014 and September 2015 were analysed using two different software packages; SliceOmatic v5.0 and OsiriX v7.5.1. The patients were initially identified retrospectively from the Computerised Radiology Information System (CRIS v 2.09, HSS, Healthcare Systems, Mansfield, UK). The underlying pathology necessitating the CT scan was variable, and included trauma, suspected intra-abdominal or gastrointestinal bleeding, pancreatic or hepatic pathology and renal lesions. Three axial slices were selected from each tri-phasic abdominal CT scan (total analysed slices in the study = 50 x 3 = 150 slices). Each slice was anatomically localised using coronal and sagittal multi-planar reformats (MPRs) to ensure it specifically lies at the third lumbar vertebra (L3). Slices were analysed as Digital Imaging and Communication in Medicine (DICOM) images obtained from the Picture Archiving and Communication System (PACS). Electronic patient data were collated for patient demographics, including height and weight data from within one month of the date of the CT scan.

Scan Acquisition

During the study period there were two CT scanners in use at Nottingham University Hospitals NHS Trust were the study was conducted; (1) Ingenuity 128; Phillips Healthcare, Best, The Netherlands and (2) Optima CT660, GE Healthcare, WI, USA and these were calibrated once per week to ensure that quality assurance testing was met for the Hounsfield Unit (HU) density of air (HU=-1000) and water (HU=zero). Arterial and portovenous phase scans were obtained using intravenous administration of contrast

133 medium (100 ml fixed dose of Iopamidol, Niopam 300, Bracco, Buckinghamshire, UK). The
134 timings of different phase scans were standardised, firstly with an unenhanced scan, then
135 the arterial phase performed at 10-20 seconds and finally the portovenous scan at 65
136 seconds.

137 Body Composition Analysis

138 The three phases of CT scan slice on each individual patient were analysed by a single
139 observer, our group having previously established high rates of inter-observer reliability
140 (SMI r^2=0.975, p<0.0001; mean SMHU r^2=0.965, p<0.0001) in the analysis of body
141 composition variables using the techniques adopted in this study [7]. The software
142 packages, SliceOmatic and OsiriX were each used to calculate the cross-sectional area of
143 skeletal muscle, visceral and subcutaneous/intramuscular adipose tissue. The different
144 tissue types were identified by their differing radiodensities; skeletal muscle of -29 to +150
145 HU, visceral adipose of -150 to -50 HU and subcutaneous/intramuscular adipose of -190 to -
146 30 HU. The mean SMHU density was also recorded for all scans analysed.

147 Previously described regression equations for the calculation of whole body FM and FFM
148 from a single cross-sectional CT slice were used [10]:

149 Total body fat mass (FM) (kg) = 0.042 x [total adipose tissue area at L3(cm^2)] + 11.2

150 Total body fat free mass (kg) = 0.3 x [total skeletal muscle area at L3 (cm^2)] + 6.06

151 The cross-sectional area of skeletal muscle was also transformed into the skeletal muscle
152 index (SMI) by modifying it by patient height.

153

Statistical Analysis

Statistical analysis was performed using SPSS (v22.0, IBM, SMSS Statistics, Armonk, NY, USA) and GraphPad Prism v6.0 (GraphPad, La Jolla, CA, USA). FM, FFM, SMI and mean SMHU density values, with data checked for normality using the D'Agostino-Pearson normality test. Data were compared between different software packages using the Student t-paired test when normality was confirmed, and the Wilcoxon matched-pairs signed rank test when the data were not distributed normally. Pearson's coefficient of correlation was used to compare the body composition values calculated from the two different software packages and Bland Altman plots utilised to reveal any systematic error between the analyses. All analyses were performed using two tailed testing with a significance level set at $p<0.05$.

Results

Of the 50 patients included during the study period of April 2014 to September 2015 there were 33 males and 17 females, with a mean body mass index (BMI) of 30.4 (SD 4.0) kg/m^2.

Skeletal Muscle Index (SMI)

Analysis of body composition by OsiriX gave a significantly greater value for SMI than scans analysed using SliceOmatic (53.8 cm^2/m^2 vs. 51.3 cm^2/m^2, $p<0.0001$) on Wilcoxon matched-pairs signed rank test, performed due the D'Agostino-Pearson test demonstrating a lack of normality in the data from OsiriX analysis ($K2=7.831$, $p=0.012$). This difference remained between scans analysed in non-contrast and arterial phase, however there was no difference in scans analysed in the portovenous phase (Table 1).

There was a significant positive correlation in SMI between analysis conducted using OsiriX and SliceOmatic software ($r=0.965$, $p<0.0001$) and evidence of a positive systematic bias on Bland Altman testing (average bias = 2.432) (Figure 1).

Fat Mass (FM)

FM calculated by OsiriX was significantly lower than that calculated by SliceOmatic (33.1 kg vs. 33.7 kg, $p<0.0001$) as calculated by the student t-paired test as the data were demonstrated to be normally distributed, and this difference was seen when all individual phase data were analysed (Table 1).

The correlation between FM analysis using OsiriX and SliceOmatic was significant ($r=0.997$, $p<0.0001$) and Bland Altman testing revealed no evidence of a systematic bias (average bias = -0.680) (Figure 2).

Fat Free Mass (FFM)

Analysis of FFM using the two software packages demonstrated significantly greater values with OsiriX analysis versus SliceOmatic (54.2 kg vs. 52.1 kg, $p<0.0001$) as calculated by the student t-paired test as the data were demonstrated to be normally distributed. This finding remained consistent in slices analysed in non-contrast, arterial and portovenous phases (Table 1).

There was a significant positive correlation between analysis of FFM performed using OsiriX versus SliceOmatic software packages ($r=0.977$, $p<0.0001$) and there was evidence of a systematic bias on Bland Altman testing (average bias = 2.16) (Figure 3).

Mean Skeletal Muscle Hounsfield Units (SMHU)

The mean SMHU density was overall significantly higher when analysed using OsiriX versus SliceOmatic software (33.1 vs. 32.7 HU, $p=0.046$) as calculated by the student t-paired test as the data were demonstrated to be normally distributed. However, when the individual phases of CT scan were compared, there were no significant differences between OsiriX and SliceOmatic (Table 1).

There was a significant positive correlation in the mean SMHU between the two software packages ($r=0.976$, $p<0.0001$) and no evidence of any systematic bias (average bias = 0.360) (Figure 4).

Discussion

This study provides evidence of the relative clinical equivalence of analysis of body composition measures analysed by two different software packages, namely OsiriX and SliceOmatic. However, statistically significantly greater SMI, FFM and mean SMHU values and significantly lower FFM were demonstrated when the analyses were performed with OsiriX compared with SliceOmatic. There was significant positive correlation for all measures when the two software packages were compared, although Bland Altman testing revealed evidence of a significant systematic bias when analysing SMI and FFM. The results of the present study are similar to those of the previously published comparison of OsiriX, SliceOmatic, ImageJ and FatSeg [9] which found that body composition in terms of cross-sectional muscle area, visceral adipose tissue area and subcutaneous adipose tissue area had excellent levels of agreement, suggesting that the results of analysis using the different software packages could be used interchangeably. However, this study suggested evidence of a systematic bias in the analysis of SMI and FFM which should be considered when comparing results of body composition analysis performed using different software packages. That study [9], however, did not include myosteatosis, as calculated by the mean SMHU value, which is becoming increasingly utilised in body composition analysis. In addition, the present study considered the different phases of abdominal CT (non-contrast, arterial and portovenous) which was not considered by the previous literature; indeed no statement is made regarding the phase of CT scan considered by the previous study [9].

Whilst the results of the present study demonstrate statistically significant differences in body composition variables by software package used for analysis, the clinical significance of several of these outcomes is doubtful. The mean SMHU was different by just 0.4 HU, much

less than the difference in SMHU between different phases of CT scan (in OsiriX analysis a difference of 5.1 HU was seen between non-contrast and portovenous scans and 5.3 HU in SliceOmatic analysis). This discrepancy in radiodensity of skeletal muscle has been documented previously [7] and its clinical relevance questioned. Therefore, with such a small difference this is very unlikely to impact significantly upon the diagnosis of myosteatosis. Similarly, the difference between software packages was minimal in FM analysis, with an overall difference of 0.7 kg, which represents just 1.8% of the overall mass from OsiriX analysis. The difference was more pronounced in SMI and FFM analysis, with a difference of 2.5 cm^2/m^2 (4.6%) and 2.1 kg (3.9%) respectively, which are more likely to represent a clinically relevant difference. This difference in body composition variables has not been demonstrated previously, and the results of body composition analysis using OsiriX and SliceOmatic software packages are used interchangeably within the literature.

This study was conducted retrospectively. However, all scans were performed on individual patients at the same time, so whilst the hydration status was not known, it would be consistent for all scans and, therefore, would not impact upon these results. Height and weight data were not always available from the date of the scan which may render the calculation of body composition measures less accurate.

Further work on body composition analysis is necessary in order to standardise the methodology used to calculate clinical body composition outcomes including the presence of sarcopenia and myosteatosis. This should include muscle biopsy samples of the rectus abdominis at the L3 vertebral level to correlate radiological and histological analysis of skeletal muscle.

This is the first study to investigate the analysis of body composition variables including myosteatosis by software package of analysis, and has demonstrated statistically significant differences in values in all outcomes. Although some statistically significant differences were demonstrated between the two software packages, these are unlikely to be clinically relevant. However, given the demonstrable differences in body composition measures, it is suggested that the two packages should not be used interchangeably for clinical or research purposes.

Conflict of Interest:

None of the authors has any direct conflicts of interest to declare. IAM has received research funding from Mars Inc. and serves on the advisory board of IKEA for unrelated work. DNL has received unrestricted research funding and speaker's honoraria from Fresenius Kabi, BBraun and Baxter Healthcare for unrelated work. He has also served on advisory boards for Baxter Healthcare and AbbVie in the past.

Author Contributions:

All authors contributed to the

- conception and design of the study
- collection, analysis or interpretation of data
- drafting the article or revising it critically for important intellectual content
- and final approval of the version to be published.

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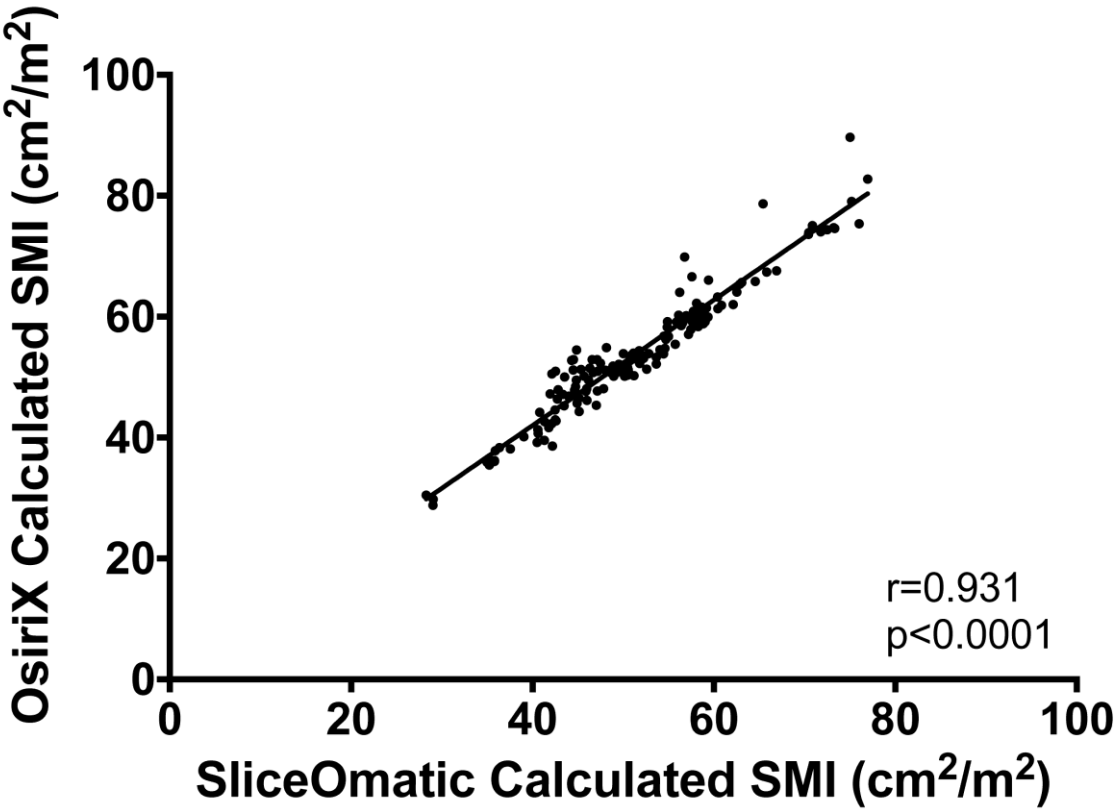
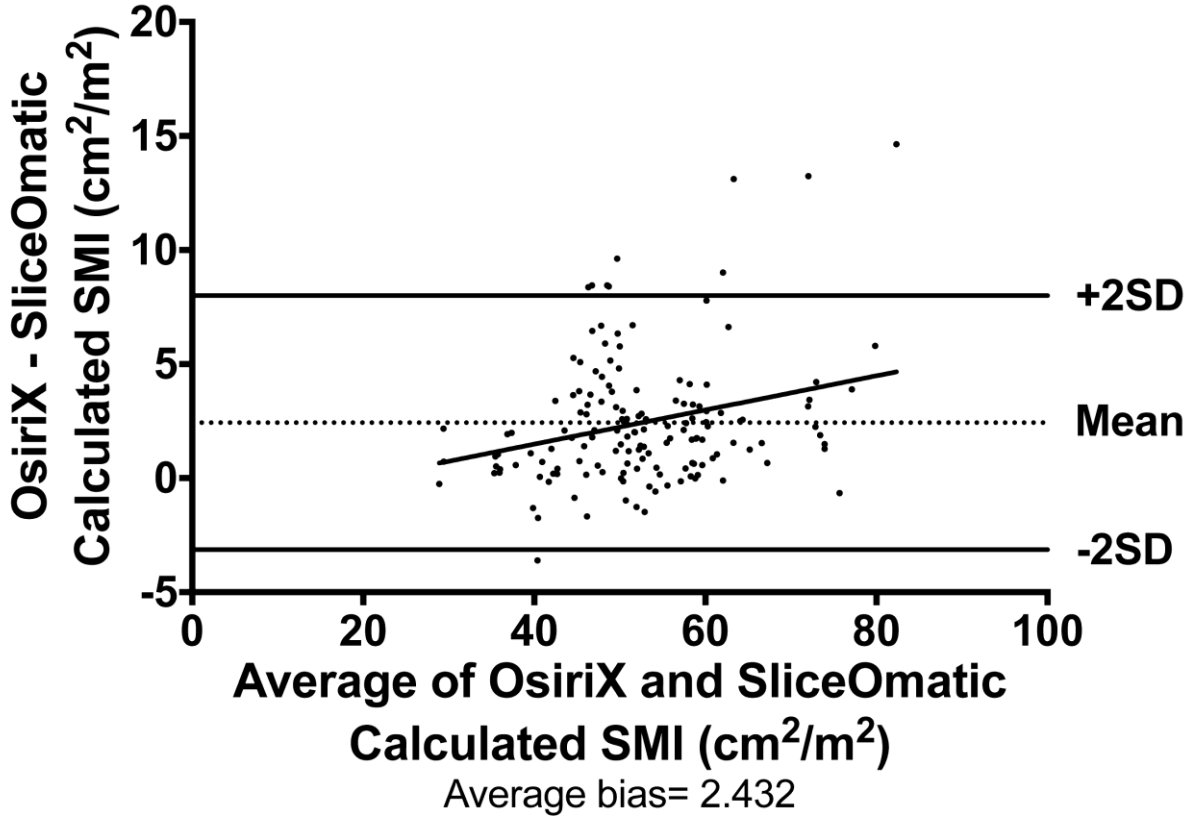
320 **Legends for figures**





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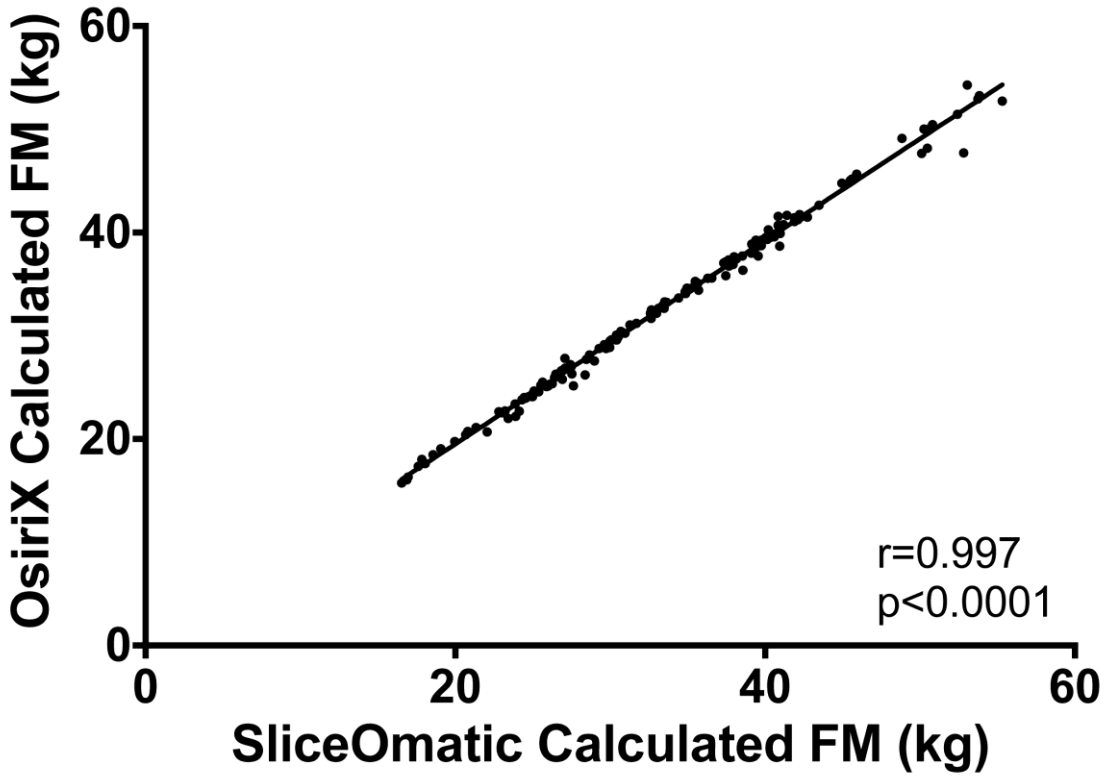
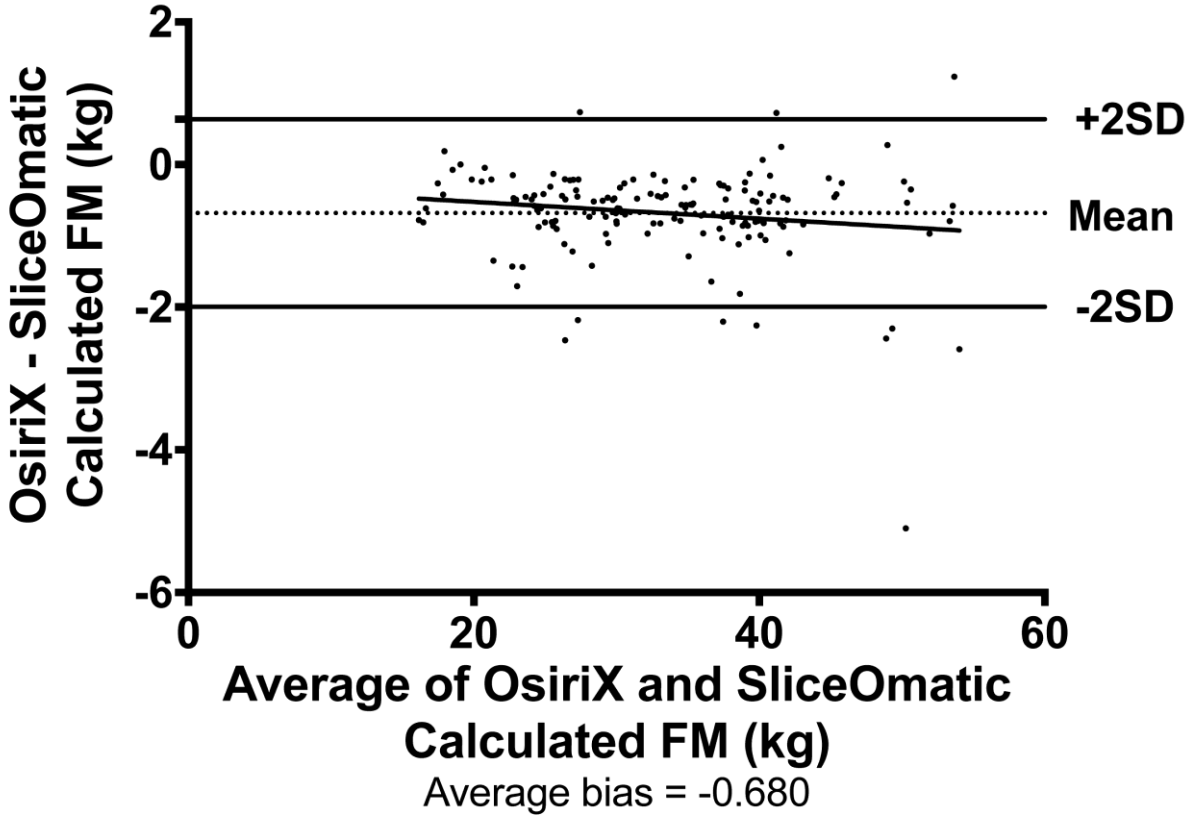
322 Figure 1 – Correlation between mean skeletal muscle index (SMI) calculated using OsiriX and

323 SliceOmatic software packages and Bland Altman plots to assess for systematic bias.

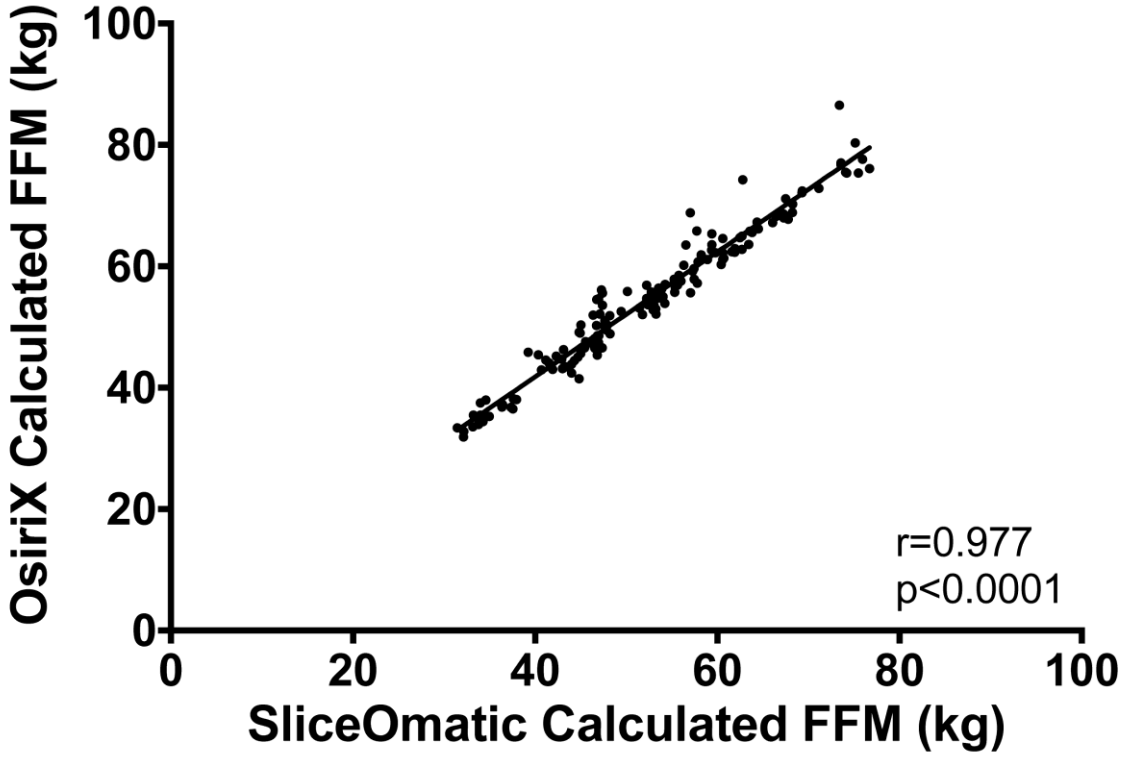

OsiriX Calculated FM (kg)
60
40
20
0
0
20
40
60
SliceOmatic Calculated FM (kg)
r=0.997
p<0.0001

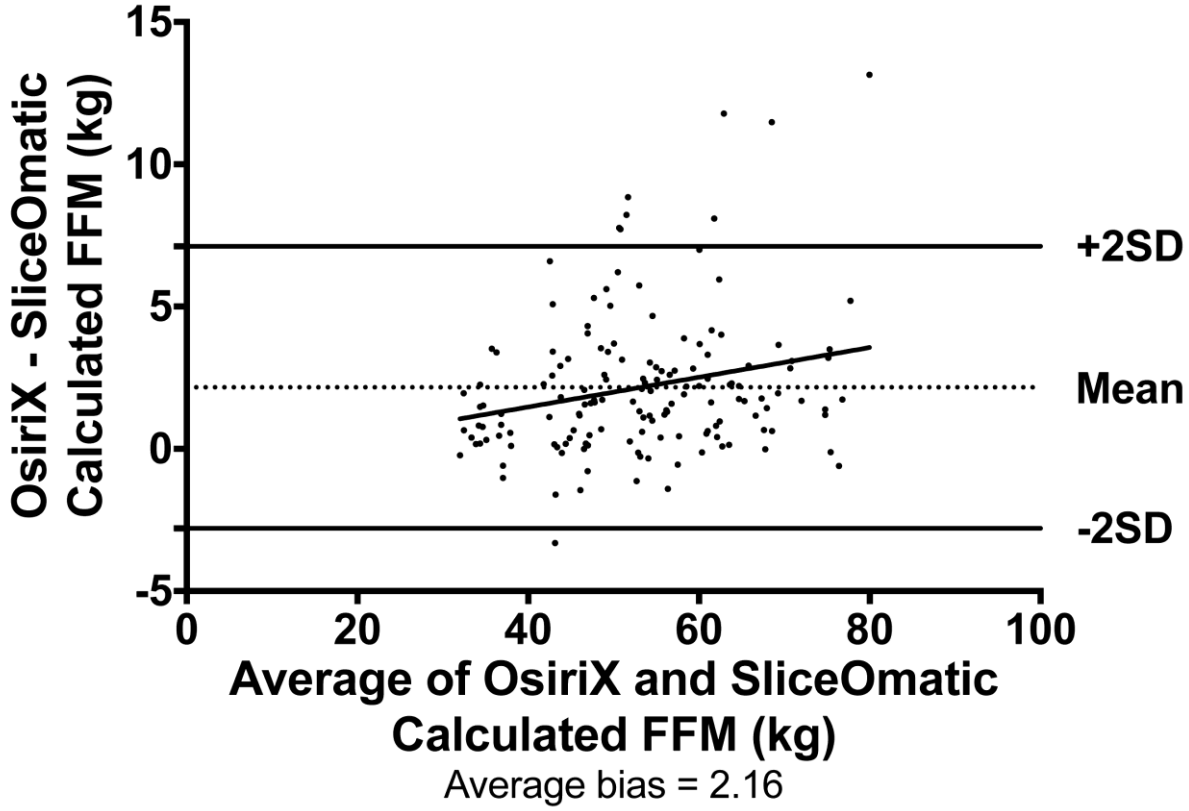

OsiriX - SliceOmatic Calculated FM (kg)
2
0
-2
-4
-6
+2SD
Mean
-2SD
0
20
40
60
Average of OsiriX and SliceOmatic Calculated FM (kg)
Average bias = -0.680

324

325 Figure 2 – Correlation between fat mass (FM) calculated using OsiriX and SliceOmatic

326 software packages and Bland Altman plots to assess for systematic bias.

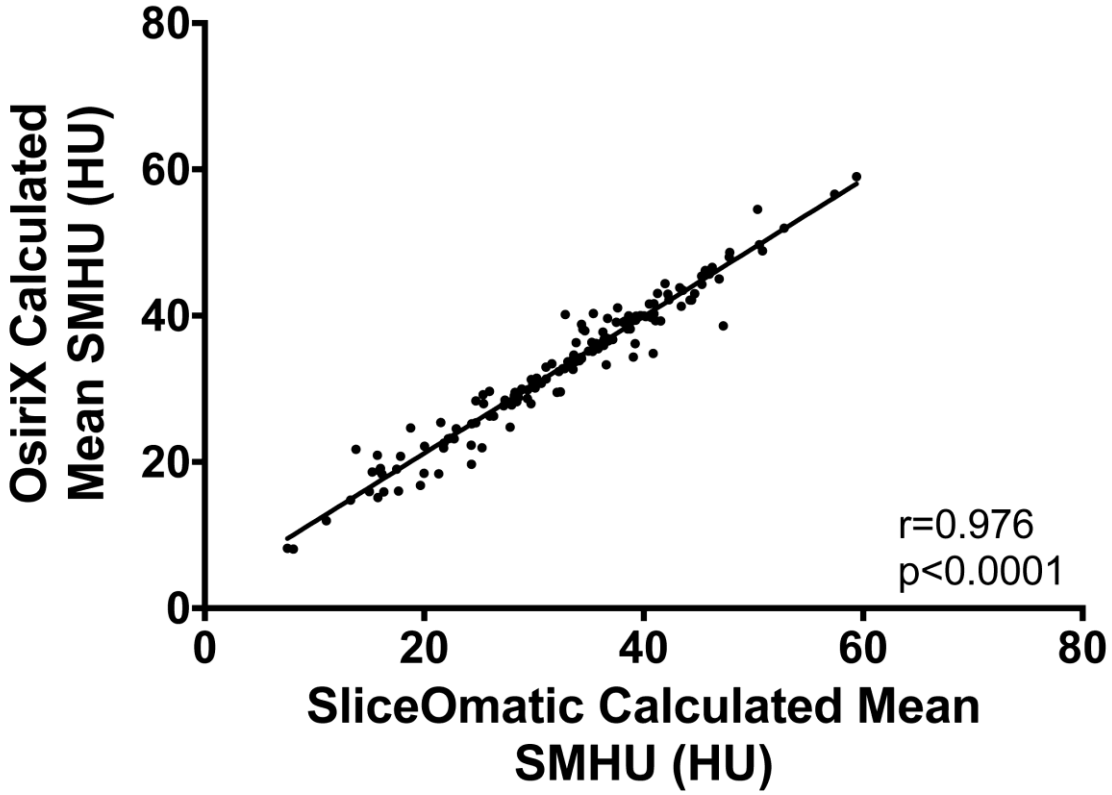

OsiriX Calculated FFM (kg)
100
80
60
40
20
0
0
20
40
60
80
100
SliceOmatic Calculated FFM (kg)
r=0.977
p<0.0001

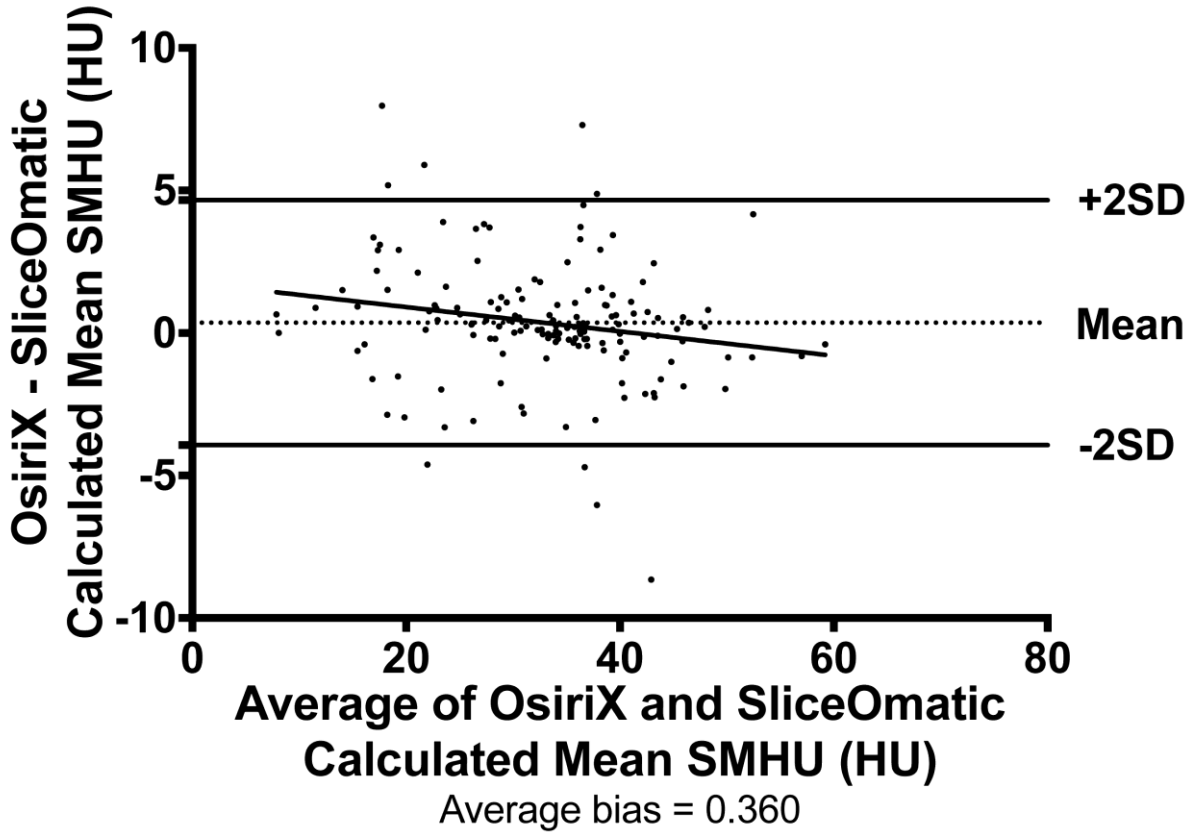

OsiriX - SliceOmatic Calculated FFM (kg)
15
10
5
0
-5
+2SD
Mean
-2SD
0
20
40
60
80
100
Average of OsiriX and SliceOmatic Calculated FFM (kg)
Average bias = 2.16

327

328 Figure 3 – Correlation between fat free mass (FFM) calculated using OsiriX and SliceOmatic

329 software packages and Bland Altman plots to assess for systematic bias.


OsiriX Calculated Mean SMHU (HU)
SliceOmatic Calculated Mean SMHU (HU)
r=0.976
p<0.0001
0
20
40
60
80


OsiriX - SliceOmatic Calculated Mean SMHU (HU)
Average of OsiriX and SliceOmatic Calculated Mean SMHU (HU)
+2SD
Mean
-2SD
Average bias = 0.360
10
5
0
-5
-10
0
20
40
60
80

330

331 Figure 4 – Correlation between mean skeletal muscle Hounsfield Units (SMHU) calculated
332 using OsiriX and SliceOmatic software packages and Bland Altman plots to assess for
333 systematic bias.

334

335

336 Table 1 – Comparison of body composition measures calculated by OsiriX versus SliceOmatic

337 software packages in non-contrast, arterial and portovenous phase scans.

338

	Non-Contrast Phase Scan	Arterial Phase Scan	Portovenous Phase Scan
Skeletal Muscle Index (cm^2/m^2) ± standard deviation			
SliceOmatic	51.0 ± 10.1	51.4 ± 10.1	51.6 ± 9.9
OsiriX	53.3 ± 10.4	53.6 ± 11.1	54.4 ± 10.7
Mean difference between modalities	-2.3 ± 2.2	-2.2 ± 3.3	-2.7 ± 3.0
P Value	<0.0001	<0.0001	0.189
Fat Mass (kg)			
SliceOmatic	34.1 ± 9.1	33.7 ± 8.9	33.5 ± 9.0
OsiriX	33.4 ± 9.0	33.0 ± 8.7	32.8 ± 9.0
Mean difference between modalities	0.7 ± 0.6	0.7 ± 0.8	0.7 ± 0.5
P value	<0.0001	<0.0001	<0.0001
Fat Free Mass (kg)			
SliceOmatic	51.8 ± 11.3	52.1 ± 11.3	52.3 ± 11.3
OsiriX	53.9 ± 11.7	54.1 ± 12.1	54.8 ± 11.9
Mean difference between modalities	-2.1 ± 2.0	-2.0 ± 2.9	-2.4 ± 2.7
P value	<0.0001	<0.0001	<0.0001
Mean Skeletal Muscle Hounsfield Units (HU)			
SliceOmatic	30.1 ± 9.3	33.0 ± 9.9	35.4 ± 10.2
OsiriX	30.6 ± 8.6	32.7 ± 9.4	35.7 ± 10.0
Mean difference between modalities	-0.5 ± 2.2	0.3 ± 2.1	-0.2 ± 2.4
P value	0.120	0.213	0.450

339

340