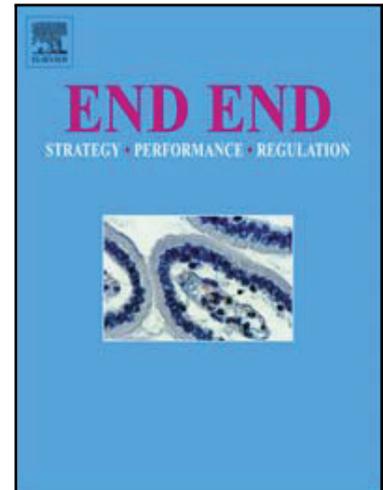


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A comparison of two different software packages for the analysis of body composition using computed tomography images

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1 Highlights

- 2
- We clarify the equivalence of body composition analysis from computed
- 3 tomography (CT) images using two different software packages.
- Analysis was performed using SliceOmatic and OsiriX packages on 50 patients
- 4 who had undergone tri-phasic scans.
- Body composition measures were significantly different between the two
- 5 software packages, but the clinical significance of these is doubtful.
- However, we recommend that for serial body composition analysis and for
- 6 comparative purposes, the software package employed should be consistent.
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12 **A comparison of two different software packages for the analysis of body**
13 **composition using computed tomography images**

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43

44 **Running Head:** Software Packages for Body Composition Analysis

45

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

50

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52

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56

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; myosteatorsis; OsiriX;
82 SliceOMatic

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84 Introduction

85 Computed tomography (CT) analysis of body composition to measure fat mass (FM) and fat
86 free mass (FFM), calculate skeletal muscle index (SMI), and diagnose sarcopenia and
87 myosteatorsis has become increasingly common, with literature now linking sarcopenia and
88 myosteatorsis with reduced overall survival [1, 2], decreased tolerance to chemotherapy [3,
89 4] and increased complications [5, 6] following surgery in patients presenting with various
90 types of malignancy.

91 However, the methodology for calculating body composition from CT images is variable
92 between studies, from the nature of the CT scan used including the vertebral level, to the
93 use of contrast medium, to the software used to perform the analysis. The impact of the use
94 of contrast medium in CT scanning in body composition analysis has previously been
95 recognised to have a significant effect upon results, especially the diagnosis of myosteatorsis
96 [7, 8]. Despite these inconsistencies in analysis, the results of these studies are used
97 interchangeably, with the definition of neither sarcopenia or myosteatorsis stipulating any
98 conditions about how these derived values are calculated.

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

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

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110 **Methods**

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

126 Scan Acquisition

127 During the study period there were two CT scanners in use at Nottingham University
128 Hospitals NHS Trust where the study was conducted; (1) Ingenuity 128; Phillips Healthcare,
129 Best, The Netherlands and (2) Optima CT660, GE Healthcare, WI, USA and these were
130 calibrated once per week to ensure that quality assurance testing was met for the
131 Hounsfield Unit (HU) density of air (HU=-1000) and water (HU=zero). Arterial and
132 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]:

$$149 \text{ Total body fat mass (FM) (kg) = } 0.042 \times [\text{total adipose tissue area at L3 (cm}^2\text{)}] + 11.2$$

$$150 \text{ Total body fat free mass (kg) = } 0.3 \times [\text{total skeletal muscle area at L3 (cm}^2\text{)}] + 6.06$$

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

154 Statistical Analysis

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

164 **Results**

165 Of the 50 patients included during the study period of April 2014 to September 2015 there
166 were 33 males and 17 females, with a mean body mass index (BMI) of 30.4 (SD 4.0) kg/m².

167 Skeletal Muscle Index (SMI)

168 Analysis of body composition by OsiriX gave a significantly greater value for SMI than scans
169 analysed using SliceOmatic (53.8 cm²/m² vs. 51.3 cm²/m², p<0.0001) on Wilcoxon matched-
170 pairs signed rank test, performed due the D'Agostino-Pearson test demonstrating a lack of
171 normality in the data from OsiriX analysis (K2=7.831, p=0.012). This difference remained
172 between scans analysed in non-contrast and arterial phase, however there was no
173 difference in scans analysed in the portovenous phase (Table 1).

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

177 Fat Mass (FM)

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

182 The correlation between FM analysis using OsiriX and SliceOmatic was significant (r=0.997,
183 p<0.0001) and Bland Altman testing revealed no evidence of a systematic bias (average bias
184 = -0.680) (Figure 2).

185 Fat Free Mass (FFM)

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

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

194 Mean Skeletal Muscle Hounsfield Units (SMHU)

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

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

203 Discussion

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

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

226 less than the difference in SMHU between different phases of CT scan (in OsiriX analysis a
227 difference of 5.1 HU was seen between non-contrast and portovenous scans and 5.3 HU in
228 SliceOmatic analysis). This discrepancy in radiodensity of skeletal muscle has been
229 documented previously [7] and its clinical relevance questioned. Therefore, with such a
230 small difference this is very unlikely to impact significantly upon the diagnosis of
231 myosteatorsis. Similarly, the difference between software packages was minimal in FM
232 analysis, with an overall difference of 0.7 kg, which represents just 1.8% of the overall mass
233 from OsiriX analysis. The difference was more pronounced in SMI and FFM analysis, with a
234 difference of 2.5 cm²/m² (4.6%) and 2.1 kg (3.9%) respectively, which are more likely to
235 represent a clinically relevant difference. This difference in body composition variables has
236 not been demonstrated previously, and the results of body composition analysis using OsiriX
237 and SliceOmatic software packages are used interchangeably within the literature.

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

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

248

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

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265 Conflict of Interest:

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

271

272 Author Contributions:

273 All authors contributed to the

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

278

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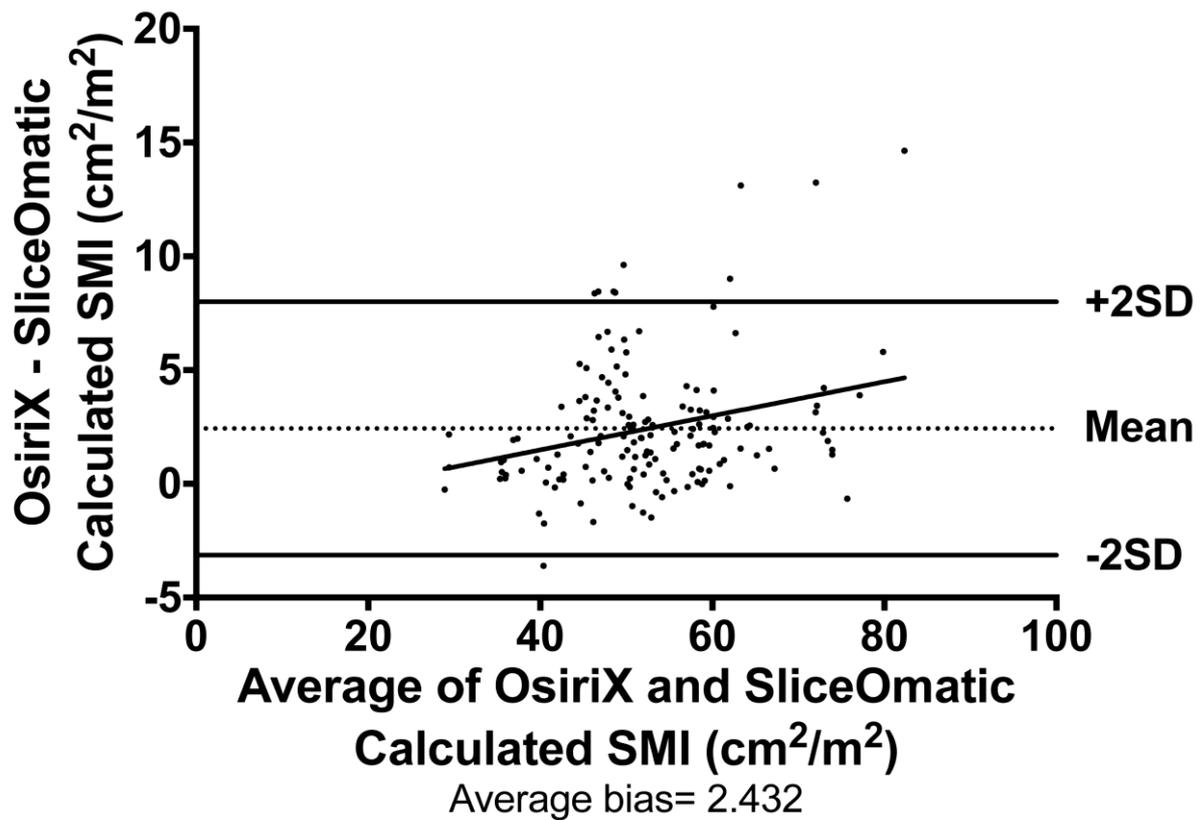
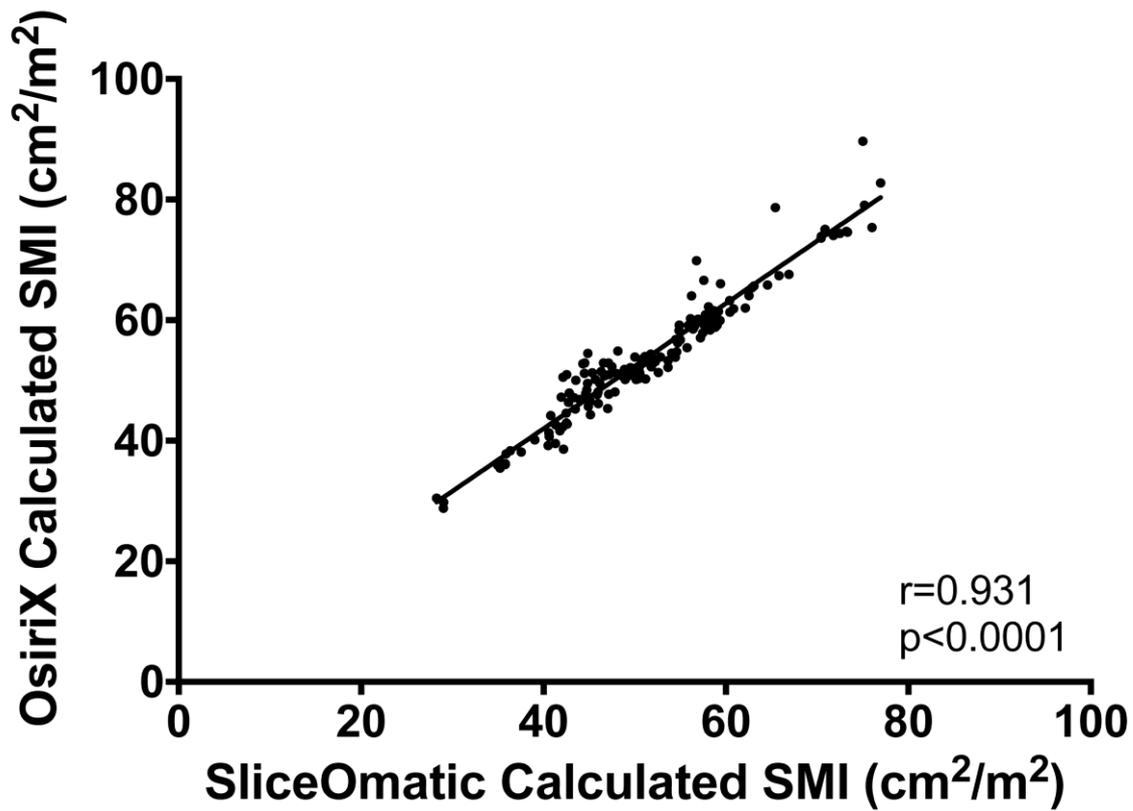
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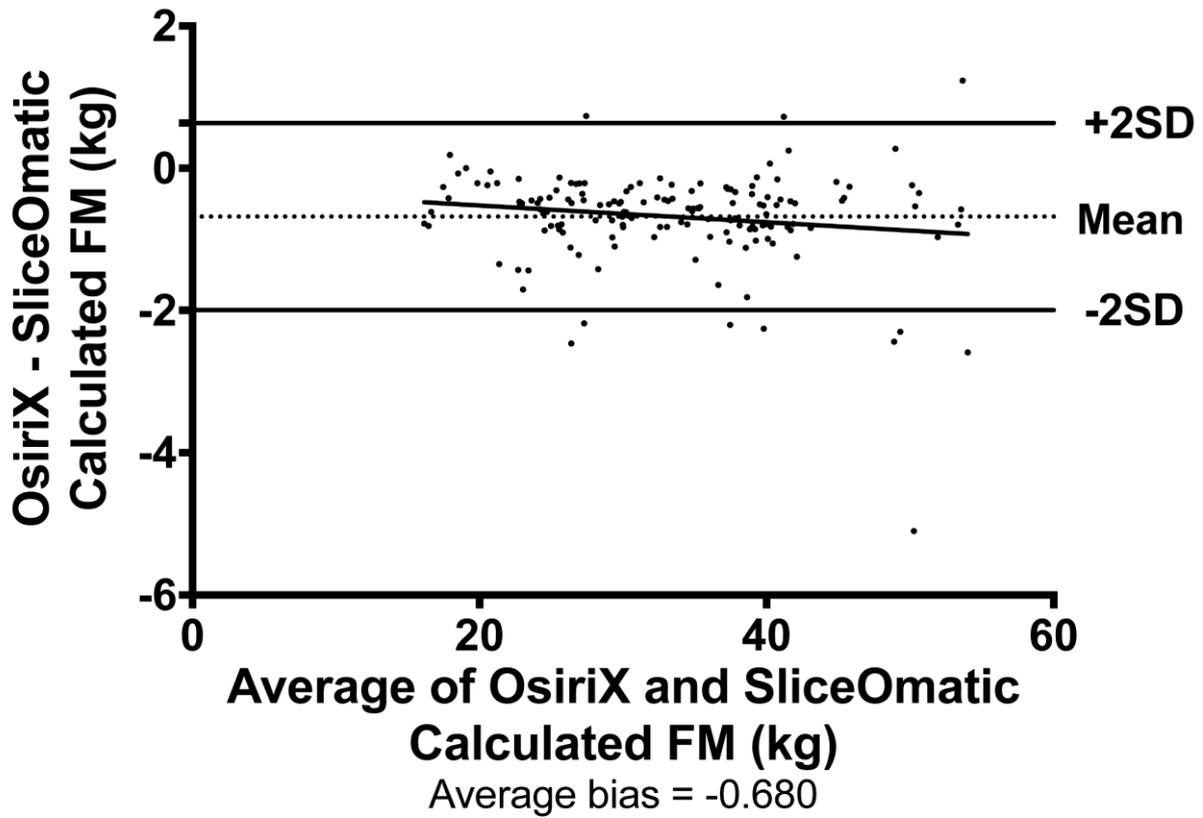
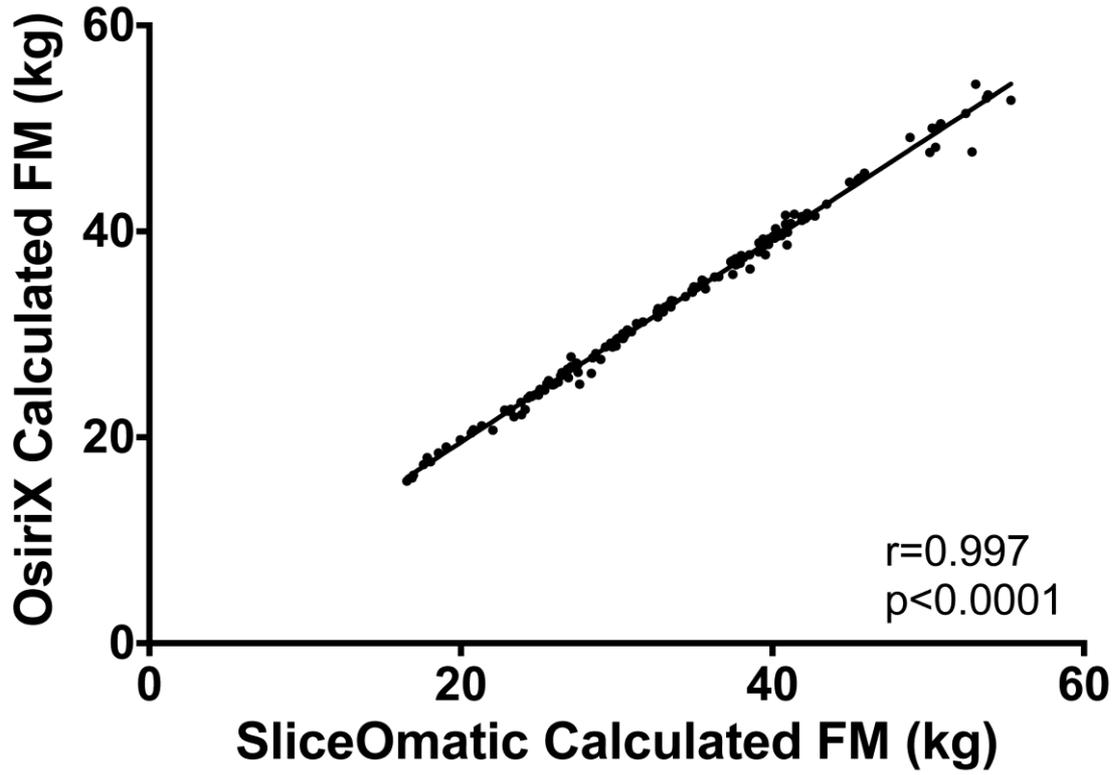
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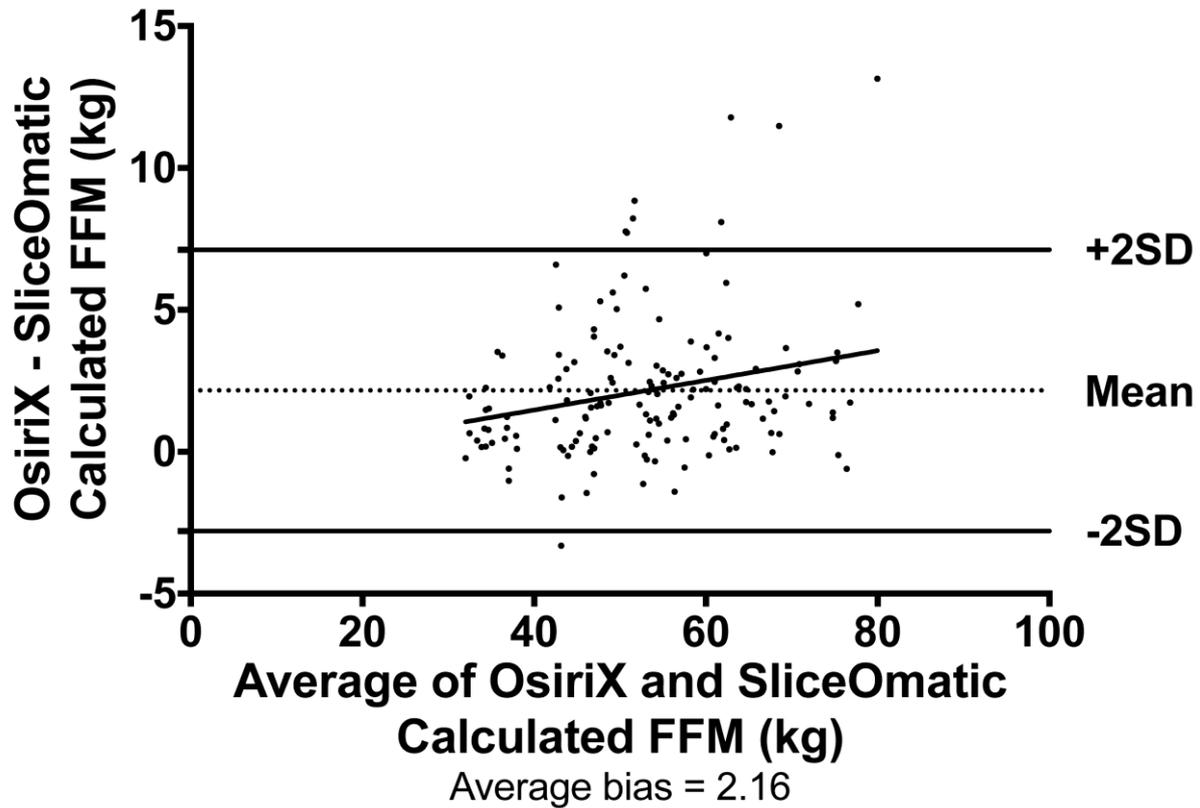
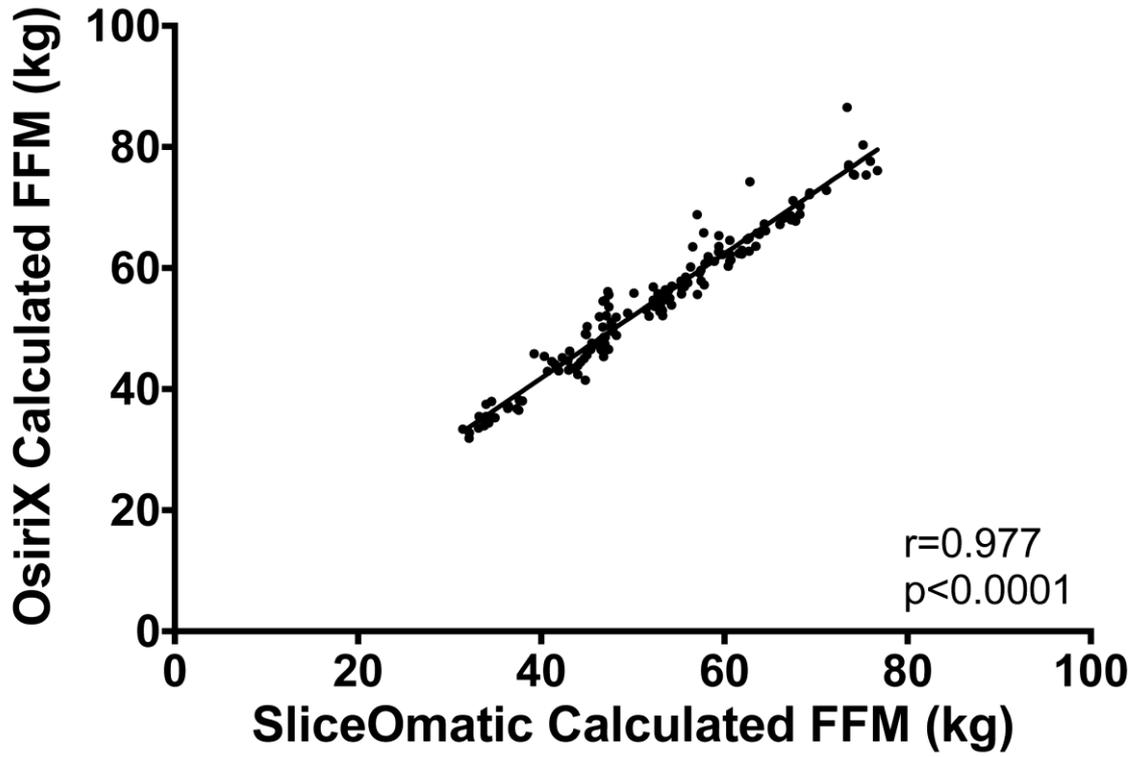
- 322 Figure 1 – Correlation between mean skeletal muscle index (SMI) calculated using OsiriX and
323 SliceOmatic software packages and Bland Altman plots to assess for systematic bias.

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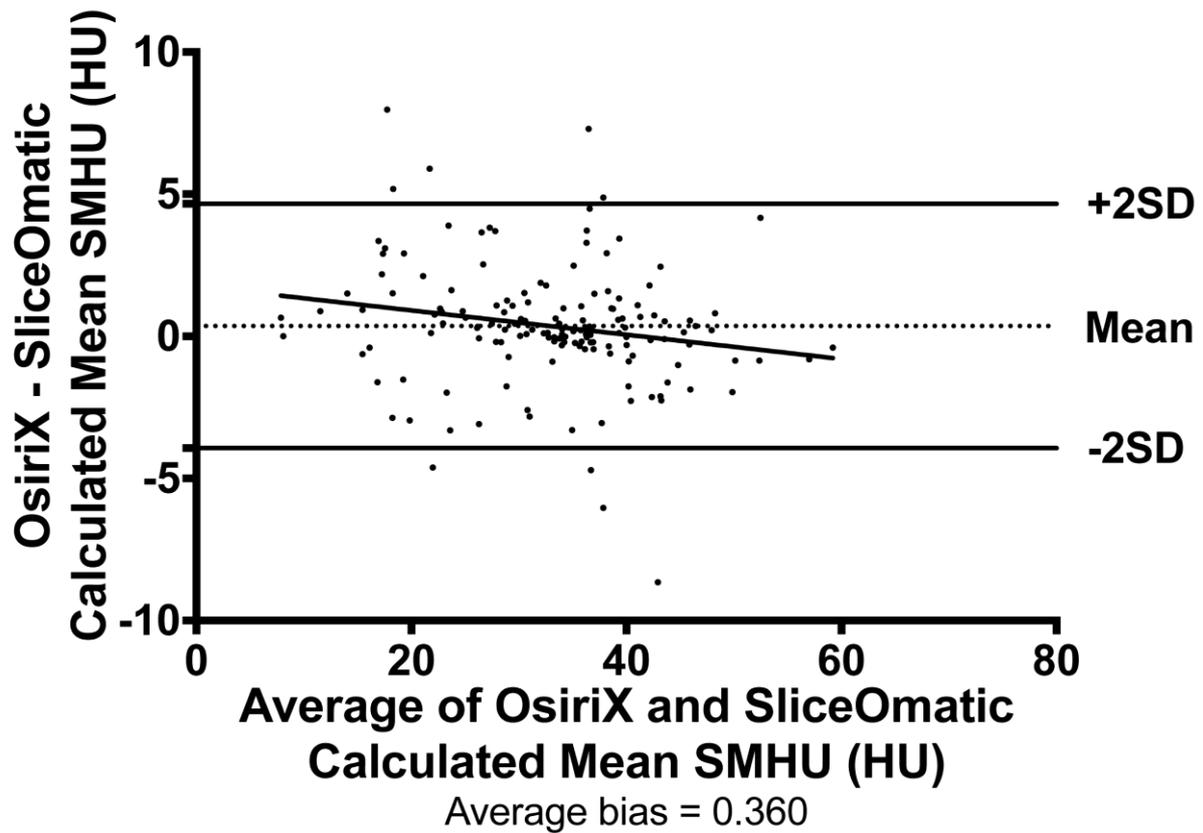
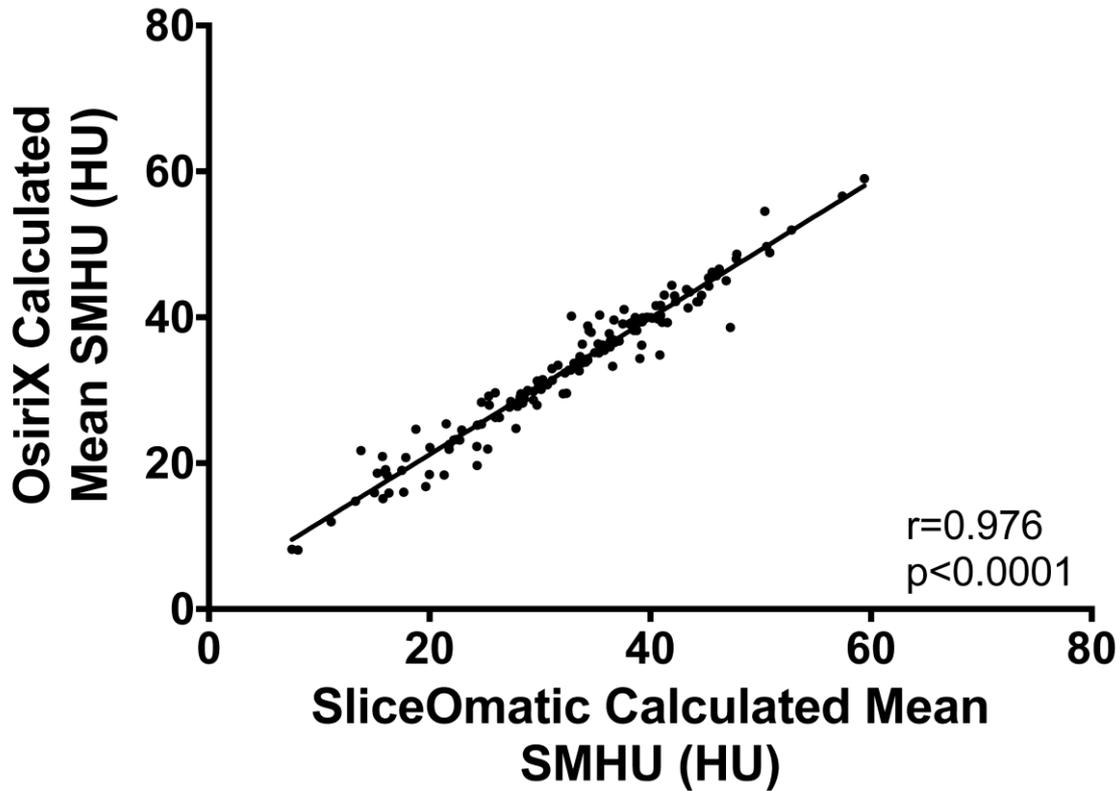
325 Figure 2 – Correlation between fat mass (FM) calculated using OsiriX and SliceOmatic
326 software packages and Bland Altman plots to assess for systematic bias.

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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.

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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.

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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 (cm²/m²) ± 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

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