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Making the most of the imaging we have: using head MRI to estimate body composition

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Abstract

Aim—To investigate the use of clinical head magnetic resonance imaging (MRI) in determining body composition and to evaluate how well it correlates with established measures based on abdominal computed tomography (CT).

Materials and Methods—Ninety-nine consecutive patients were identified who had undergone both brain MRI and abdominal CT within a 2-week span. Volumes of fat and muscle in the extracranial head were measured utilising several techniques by both abdominal CT and head MRI.

Results—MRI-based total fat volumes in the head correlated with CT-based measurements of fat in the abdomen using both single-section ($r=0.64$, $p<0.01$) and multisection ($r=0.60$, $p<0.01$) techniques. No significant correlation was found between muscle volumes in the abdomen and head.

Conclusion—Based on the present results, head MRI-based measures may provide a useful surrogate for CT measurements of abdominal fat, particularly in patients with neurological cancers, as head MRI (and not abdominal CT) is routinely and repeatedly obtained for the purpose of clinical care for these patients.

Introduction

During the last decade there has been an increased focus on the importance of body composition and its impact on cancer patients, with effects on quality of life,¹ treatment response, treatment-related toxicity,² and survival.^{3,4} Weight gain with cancer treatment has been shown to be associated with an increased risk of recurrence.^{5,6} Substantial weight loss has been associated with decreased survival in some cancer patients^{7,8}; however, weight and body mass index (BMI) do not provide reliable estimates of the distribution of body fat or lean body mass and can be confounded by metabolic issues in cancer patients, such as ascites, lymphoedema, and dehydration.⁹ Increasing evidence suggests that weight, BMI, and body surface area (BSA) are poor overall indicators of nutritional status^{1,10–12} and that weight and BMI do not predict treatment-related toxicity.^{1,13–15} Therefore more precise phenotypic measurements of body composition have been increasingly sought and used.¹⁶

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Based on these newer phenotypic body composition measures, increased visceral adiposity has been associated with increased risk of cancer^{17,18} and decreased survival.^{19,20} The pattern of decreased lean body/muscle mass along with increased adipose tissue mass has been identified as a deleterious type of body composition change in some cancer patients.⁹ Low muscle mass is common among patients with malignancies,^{1,10,21,22} with low muscle mass having been shown to predict toxicity among diverse cancer treatments.^{1,2,15,23,24}

Tools that can be used to more precisely estimate body composition phenotype are therefore of increasing interest and importance in caring for cancer patients, particularly with regard to determining whether patients are able to tolerate specific therapeutic regimens and identifying those at higher risk of complications of specific treatments. Body composition phenotype can be estimated by many different methods such as bioelectric impedance analysis, air displacement plethysmography, and dual-energy X-ray absorptiometry with varying sensitivity and specificity, but all require additional equipment over what is traditionally found in an oncology practice.⁹ Magnetic resonance imaging (MRI) has been shown to be very accurate in distinguishing different fat-containing body compartments, but is not often used in clinical practice because of high costs.¹⁶ Thus, in current clinical research, body composition estimates often involve the use of abdominal computed tomography (CT), with this technique allowing for accurate volume estimation of different tissue compartments such as fat and muscle.^{15,25,26} As abdominal CT is routinely obtained in clinical practice for patients with numerous malignancies to help establish diagnoses, plan treatment, estimate treatment response, and facilitate tumour surveillance, CT is a very convenient choice for determining body composition phenotype in many cancer patients; however, there are some cancer patients, especially those with neurological cancers, who do not routinely undergo abdominal CT imaging for clinical purposes. In the authors' experience, patients with brain tumours often have dramatic changes in weight, body fat, and lean body mass, which are often related to long-term glucocorticoid use. These changes affect functional status, quality of life, and perhaps even survival (e.g., diabetes, steroid myopathy). The addition of abdominal CT for the purpose of estimating body composition in this population, although potentially useful, would add radiation exposure and increase cost for these patients. For many of these patients, brain (head) MRI is the typical routine imaging obtained for diagnostic and treatment purposes. Therefore, the rationale for the present study was to determine whether head MRI could be used to estimate body composition phenotype and thus avoid the need for additional imaging studies with their associated additional costs and radiation exposure. Prior research has shown high correlations between CT and MRI based measures not only in cadaveric studies²⁷ but also between body MRI and abdominal CT measurements in healthy subjects.²⁸ To the authors' knowledge head MRI has not been used to date to assess body composition. Therefore, the aim of the present study was to determine whether a head MRI-based phenotypic body composition measure, based on extracranial fat and muscle in the head, would correlate with established body composition measures based on abdominal CT.

Materials and methods

Design and patient selection

This protocol was approved and patient consent was waived by the institutional review board. The radiology information system was searched for patients who had undergone both CT of the abdomen and MRI of the head within a 2-week time span between January 2007 and December 2008. To be included in the study, patients had to be at least 18 years of age, and the images had to be available for review in the electronic imaging archive. Exclusion criteria included any repeat examinations of the same patient (only one scan per patient was included in the study) and images judged to be of such poor quality (e.g., patient motion or artefacts) so that quantitative measures could not be obtained. A total of 99 patient records and imaging results met the inclusion criteria and were reviewed. Age, gender, race, BMI, height, weight, and clinical indication for the examinations were collected. All data were collected under the supervision of the institutional review board and in compliance with the Health Insurance Portability and Accountability Act of 1996.

CT measurements

Two-dimensional (2D) multisection muscle and adipose tissue measures were obtained from two 5 mm contiguous axial sections at the level of the lumbar disk between the fourth and fifth vertebrae using 5 mm reconstructions of abdominal CT scans. Tissues with attenuation between -190 to -30 HU were defined as adipose tissue. The Medical Image Processing, Analysis, and Visualization (MIPAV- <http://mipav.cit.nih.gov/>) application was used to segment the images based on anatomical boundaries. Using tissue-specific thresholds, total abdominal adipose volume (ABf-CT), total abdominal muscle volume (ABm-CT), and intramuscular fat (i.e., fat not within the subcutaneous or visceral compartment; ABimf-CT) were quantified within the sections.

MRI measurements

For the new head MRI-based measures, multiple parameters and techniques were tested. First, 2D multisection measures were developed to include large subsections of the patient's head. Subsequently, 2D single-section measures were developed at a predefined level.

Muscle and adipose composition within the extracranial head was measured using Mimics segmentation software (v.14.0.0.90, Materialise, Leuven, Belgium, 2010). T1 axial images of the brain (5 mm thickness) were imported into the software. Threshold levels were first chosen to sub-select the muscles (temporalis, masseter, lateral and medial pterygoids, and muscles of the posterior neck). Threshold values were manually adjusted for each patient to maximise selection of muscle tissue while excluding other tissues of differing T1 signal (e.g., brain, fat, bone, tendons). Sections were selected from the inferior-most aspect of the posterior fossa to the superior-most aspect of the orbit. Using selection tools available in the program, tissues outside of the selected muscles were eliminated manually, section by section, for all patients. These 2D multisection muscle measures of the head were then recorded as Hm-MRms. As an alternative multi-section muscle measure, this technique was used with a larger subsection of the patient's head, with the sections selected from the

inferior-most aspect of the posterior fossa to the vertex, with these 2D multisection muscle measures of the whole head to the vertex recorded as WHm-MRms.

In order to maximise reproducibility and minimise between-subject variability, a single-section measure was also selected. The location for this single section measure was defined as the level one section caudal to the temporomandibular joint (e.g., chosen because this is the level at which the musculature generally has maximum volume). Because of differing orientation of the medial and lateral pterygoid muscles, the bulk of muscle measured tended to be the lateral pterygoid.²⁹ Using thresholding described above and available tools in Mimics, only the muscles in the masticator space were selected (masseter, temporalis, and lateral and medial pterygoids) and 2D single-section measures of muscles of the head were recorded as Hm-MRss (Fig 1a).

Similar processes were subsequently repeated for fat measures with thresholds for the selection of adipose tissues. For these measures, only fat signal within the soft tissues was included and the bone marrow was manually deleted. 2D multisection fat measures of the head extending from the inferior most posterior fossa to the superior-most orbit were recorded as Hf-MRms. As an alternative adipose measure, the subcutaneous fat was manually subtracted, section by section, and the deep fat measure of the head was recorded as Hdf-MRms. The single-section fat measure was obtained at the same section location as was used for the single section muscle measure; 2D single-section fat measure of the head was recorded as Hf-MRss (Fig 1b).

Interobserver variability was evaluated by having two readers independently measure fat and muscle areas using the single-section technique for 30 randomly selected patients.

Statistical analysis

As described above, three abdominal CT volume measurements (ABf-CT, ABimf-CT, and ABm-CT), three fat (Hf-MRms, Hdf-MRms, Hf-MRss), and three muscle MRI volume measurements (Hm-MRms, WHm-MRms, Hm-MRss) were obtained in 99 patients. These volumes are summarised using means, standard deviations (SDs), medians, minimums, and maximums. The single-section MRI fat and muscle measurements were assessed by two readers independently for 30 of the 99 participants. Lin's concordance correlation coefficient was used to assess the agreement between the two readers.^{30,31} Differences in the two reader's measurements were plotted against the mean of the two measurements, and a linear regression model was used to see if the differences depended on the actual area. A paired t-test was used to see if the means differed between the two readers. Pearson's correlation coefficients were used to quantify the strength of the linear association between the abdominal CT-based measures and the head MRI-based measures, overall and within the subgroups defined by sex, age (<60, ≥60), BMI (categorised as overweight or not), and cancer status (patients were not required to have a cancer diagnosis to be included in the study). Wald tests were used to compare the Fisher *r*-to-*z* transformed correlations between the different subgroups. Multiple linear regression was then used to see which demographic and MRI measurements were jointly associated with the CT measurements and to see whether the slopes depended on the patient characteristics. R^2 values are presented to denote the proportion of variance in a CT measurement that is determined by MRI measurements

and other variables. Results with $p < 0.05$ were considered statistically significant. SAS version 9.3 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

Results

Patients

Patient characteristics are summarised in Table 1. Of the 99 patients who met inclusion criteria, 79 (80%) were White, 16 (16%) Black, two (2%) Hispanic, and two (2%) Asian. Patients ranged in age from 22 to 91 years with a median of 64 years. Fifty-nine patients (60%) were female. The BMI was either included in the clinic notes (in the electronic medical records) or was calculable based on documented height and weight for 79 (80%) of the patients. BMI measurements ranged between 16.9 and 39.9 kg/m² with a median of 24.8 kg/m²; 49% of the patients were overweight or obese. Sixty-eight of the patients had an imaging indication of cancer or documented personal history of cancer.

Reader agreement

A scatterplot of the reader differences in fat measurements versus the mean of the two fat measurements is shown in Fig 2a. The differences in the fat measurements fall around the zero (no difference) line, indicating that the fat measurements are not significantly different between the two readers ($p = 0.33$). Also, it is seen that the differences do not depend on the actual fat measurement ($p = 0.67$). Lin's concordance correlation between the two readers was 0.79 with a 95% confidence interval (CI): 0.61, 0.89; 87% of the differences were within $\pm 25\%$ of the mean of the reader's measurements. A scatterplot of the reader differences in muscle measurements versus the mean of the two muscle measurements is shown in Fig 2b. Lin's concordance correlation between the two readers was 0.72 with a 95% CI: 0.51, 0.85. The majority of the differences in the muscle measurements fall below the zero (no difference) line, indicating that the muscle measurements differ between the two readers ($p = 0.01$). Also, there is some indication that the agreement is worse for bigger muscle areas, but the slope is not statistically significant ($p = 0.18$).

CT and MRI measurements

Total abdominal fat and muscle volumes (cm³) obtained by CT and fat and muscle volumes (cm³) obtained using brain MRI are shown in Table 2. Coefficients of variation ranged from 42.4% to 65% for the CT measurements and 20.6% to 35.3% for the MRI measurements.

CT versus MRI comparisons

Fat-fat measurements—Pearson correlations of the abdominal CT-based and head MRI-based fat measurements are summarised in Table 3. The strongest correlations with total abdominal CT fat measures were seen with the single-section and multiple-section MRI measures of total fat ($r = 0.64$ and 0.60 , respectively). The correlation between total abdominal CT fat measurements and head deep-fat MRI measurements was weaker ($r = 0.37$). Correlations between the abdominal CT measurements of intramuscular fat and the MRI fat measurements were lower ($r = 0.42$, 0.35 , and 0.27 for Hf-MRss, Hf-MRms, and Hdf-MRms, respectively) although still significant ($p < 0.01$ for each correlation). Differences in correlations by sex, age (< 60 , ≥ 60), overweight status, and cancer status were

then assessed. In general, the CT and MRI fat measurements did not differ considerably between these subgroups of patients. The only significant differences were the correlation between ABf-CT and Hf-MRms, which differed between those with no cancer ($r=0.78$) and those with cancer ($r=0.52$; $p=0.04$), and the correlation between ABimf-CT and Hdf-MRms, which differed between males ($r=0.56$) and females ($r=0.07$; $p=0.01$).

Multiple regression models were used to assess the association between the CT and MRI fat measurements, after adjustment for sex, age, BMI, and cancer status. The only clinical patient characteristic significantly associated with ABf-CT was BMI ($p<0.0001$), with higher BMI predicting greater abdominal fat. All MRI fat measurements were still significantly associated with ABf-CT, after adjusting for BMI and the other patient characteristics. The R^2 values for models predicting ABf-CT without and with BMI increased from 0.38 to 0.64, 0.14 to 0.60, and 0.37 to 0.66 for Hf-MRms, Hdf-MRms, and Hf-MRss, respectively, using the observations with non-missing BMI data. Both age ($p=0.002$) and BMI ($p=0.001$) were significantly associated with ABimf-CT, with older age and greater BMI predicting greater intramuscular fat. Only Hf-MRss was significantly associated with ABimf-CT, after adjusting for age, BMI, and the other patient characteristics ($p=0.02$). The R^2 increased from 0.16 to 0.30 in the models excluding and including the clinical characteristics.

Muscle–muscle measurements—Pearson's correlation between the abdominal CT-based and head MRI-based muscle measurements are summarised in Table 3. None of the MRI-based muscle measurements were significantly correlated with the abdominal CT-based muscle measurements. Additionally, no significant correlations were seen when data were sub-grouped based on sex, age, overweight status, or cancer status.

Multiple regression models were used to assess the association between the CT and MRI muscle measurements, after adjustment for sex, age, BMI, and cancer status. The only patient characteristic significantly associated with ABm-CT was BMI ($p<0.0001$), with larger BMI predicting greater abdominal muscle volume. None of the MRI muscle measurements were significantly associated with ABm-CT, after adjusting for BMI and the other patient characteristics.

Discussion

To the authors' knowledge, this is the first time head MRI has been used in an attempt to provide a quantitative phenotypic measure of body composition based on extracranial fat and muscle. Most prior studies investigating treatment effects and body composition in cancer patients have used abdominal CT.^{15,25,26} Therefore, head MRI would be a novel avenue for obtaining imaging-based body composition measures, which may be especially useful in patient populations that do not routinely undergo abdominal CT.

The aim of the present study was to determine whether a head MRI-based phenotypic body composition measure would correlate with established body composition measures based on abdominal CT. To this end, 99 consecutive adults were examined, who had essentially concurrent abdominal CT and head MRI examinations, using fat and muscle volumes

measured by an established method (abdominal CT) as the reference standard to which the head measures were compared. The fat and muscle composition measures of the extracranial head (i.e., excluding brain and skull) were easily obtained from clinically performed T1-weighted head MRI images using available commercial software. Several 2D measurements were obtained in order to find the most suitable measurement. Significant correlations were found between head MRI fat volumes (Hf-MRms, Hdf-MRms, Hf-MRss) and abdominal CT fat volumes (ABf-CT, ABimf-CT). Correlations between MRI fat measurements and total abdominal fat measures were significant after adjusting for BMI and other patient characteristics. Significant correlations between the fat measurements are not unexpected as patients with prominent abdominal adipose tissue would also be expected to often have prominent upper neck/face/skull base adipose tissue. Comparing different methods of measurement, correlations were stronger using single-section measurements than with multisection measurements, possibly due to decreased variability with the single-section measurement.

No significant correlation was found between any head muscle measure and abdominal muscle measures. The lack of correlation was somewhat unexpected but could be related to multiple technical factors. First, the use of multiple head MRI sections to determine the muscle volume may be prone to error in measurements. Head MRIs obtained for clinical purposes can have varying positioning of the head with section angling during acquisition being more variable than section angling for abdominal CT. This variability can result in differing amounts of musculature being included in the acquisition. Another potential technical source for error was that head size was not controlled for on the multisection measurements. Thus, the number of sections varied from patient to patient in the multiple-section measurements due to patients with larger heads having more sections included than patients with smaller heads. To minimise this error, an alternative measure was tested that was thought to be less susceptible to variability: a single section at the level of the pterygoid muscles. This technique standardised the section location and craniocaudal extent of the region of acquisition (although it did not eliminate section angle effects). Lastly, another possible technical source of error was related to jaw position. Previous reports have shown that the position of the jaw affects measurements of the volume of the muscles of mastication.^{32,33} Jaw position was not controlled in the present study and would be difficult to control in clinical practice.

The lack of correlation between abdominal CT-based and head MRI-based muscle measures could alternatively be related to physiological (rather than technical) factors. Physiological factors that influence the muscle volume in the head likely differ from those affecting muscle volume of the abdomen. For example, a bed-ridden patient would be expected to have decreased trunk muscle volumes; however, if the same patient is still taking food by mouth and talking, it is reasonable to expect that the volumes of the muscles of mastication may be relatively preserved.

For the most part, the present investigation did not find differences in correlations between image-based measures by sex, age, overweight, or cancer status; however, the correlation between abdominal intramuscular fat and head deep fat was higher in male than female patients (0.56 versus 0.07). Also, a prior study by Prado²³ and colleagues has suggested that

sex may influence clinical outcomes: these investigators found body composition to be an independent predictor of chemotherapy toxicity in female, but not male, colon cancer patients. Given these findings, future studies investigating the relationship between body composition and treatment-related toxicity should take patient sex into consideration.

Abdominal CT-based body composition phenotype has been shown to be an important factor in predicting treatment outcomes^{2,15,23} as summarised by Prado.³⁴ In the present study, a moderately strong correlation between head MRI-based fat measures and accepted abdominal CT-based fat measures was found. Therefore, it is plausible that head MRI fat measures provide a reasonable and convenient estimate of body composition phenotype regarding fatty tissue. The lack of correlation between abdominal and head muscle measures could be due to differing functionality of musculature in these compartments. Measuring body composition on head MRI may prove beneficial for populations that already have brain MRI performed for the diagnosis or treatment response-monitoring purposes, such as patients with brain cancer. To what degree these imaging phenotypes can be useful in predicting clinical outcomes, is a focus for future study. One area of particular interest would be to evaluate the extent to which head MRI-based phenotypic measures of body composition predict treatment-related side effects, morbidity, and survival in patients with primary brain malignancy.

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Figure 1. Examples of MRI images with highlighted tissue. (a) Head muscle (Hm-MRss) and (b) head fat (Hf-MRss); measurements using a single axial T1-weighted MRI image.

Figure 2.

Scatterplots showing interobserver variability between measurements ($n=30$). (a) Head fat (Hf-MRss). No difference was seen between the two observers' fat measurements ($p>0.05$) and there was no correlation between differences in measurements and area of fat. Lin's concordance correlation coefficient of 0.79. (b) Head muscle (Hm-MRss). A difference between the observers' muscle measurements was seen ($p=0.01$) with a trend towards greater differences in patients with larger areas of muscle ($p>0.05$). Lin's concordance correlation coefficient of 0.72.

Table 1Participant characteristics ($n=99$).

Characteristic	n (%)
Age, years	
Median (range)	64 (22–91)
<50	23 (23)
50–59	12 (12)
60–69	32 (32)
70–79	19 (19)
80+	13 (13)
Gender	
Female	59 (60)
Male	40 (40)
Race/ethnicity	
Non-Hispanic White	79 (80)
African American	16 (16)
Hispanic	2 (2)
Asian	2 (2)
Body mass index ($n=79$)	
Median (range)	24.8 (16.9–39.3)
<18.5	2 (3)
18.5–24.9	38 (48)
25–29.9	21 (27)
30+	18 (23)
Cancer	68 (69)

Table 2

Summary of computed tomography (CT) and magnetic resonance imaging (MRI) measurements ($n=99$).

Measurement	Variable	Mean	SD	Median	Min	Max
Abdominal CT						
Fat	ABf-CT	425.74	212.44	398.21	24.64	918.47
Intramuscular fat	ABimf-CT	14.18	9.22	12.00	1.13	40.76
Muscle	ABm-CT	514.66	218.25	489.53	127.73	982.41
MRI						
Head fat volume	Hf-MRms	349.98	110.27	343.94	151.71	669.48
Head deep-fat volume	Hdf-MRms	131.56	41.37	125.80	57.51	248.32
Head fat single-section volume	Hf-MRss	41.446	14.618	39.574	9.856	98.758
Whole head muscle volume	WHm-MRms	210.62	48.76	207.43	111.43	357.97
Head muscle volume	Hm-MRms	189.43	43.49	189.91	83.86	301.00
Head muscle single section volume	Hm-MRss	15.74	3.24	15.736	6.663	22.022

All measurements are in cm^3 .

SD, standard deviation; CT measurements: ABf-CT, total abdominal adipose volume; ABm-CT, total abdominal muscle volume; ABimf-CT, intramuscular fat (i.e., fat not within the subcutaneous or visceral compartment). MRI measurements: Hf-MRms, multisection fat measures of the head extending from the inferior most posterior fossa to the superior-most orbit; Hf-MRss, single-section fat measure of the head; Hdf-MRms, deep fat measurement of the head after subtracting the subcutaneous fat; WHm-MRms, multisection muscle measures of the whole head to the vertex; Hm-MRms, multisection muscle measures of the head; Hm-MRss, single-section measures of muscles of the head.

Table 3

Pearson's correlation coefficients between computed tomography (CT) and magnetic resonance imaging (MRI) measurements ($n=99$).

MRI measurement	Abdominal CT measurement	
	ABf-CT ^a	ABimf-CT ^a
Hf-MRms	0.598	0.350
Hdf-MRms	0.374	0.271
Hf-MRss	0.635	0.423
ABm-CT ^b		
WHm-MRms	0.106	
Hm-MRms	0.074	
Hm-MRss	0.100	

CT measurements: ABf-CT, total abdominal adipose volume; ABm-CT, total abdominal muscle volume; ABimf-CT, intramuscular fat (i.e., fat not within the subcutaneous or visceral compartment).

MRI measurements: Hf-MRms, multisection fat measures of the head extending from the inferior most posterior fossa to the superior-most orbit; Hf-MRss, single-section fat measure of the head; Hdf-MRms, subcutaneous fat was manually subtracted, section by section, and the deep fat measure of the head; WHm-MRms, multisection muscle measures of the whole head to the vertex; Hm-MRms, multisection muscle measures of the head; Hm-MRss, single-section measures of muscles of the head.

^a $p < 0.01$.

^b $p > 0.25$.