Imiomics: Bringing –omics to whole body imaging: Examples in cross sectional interaction between whole-body MRI and non-imaging data

Joel Kullberg[1], Lars Johansson[1], Lars Lind[2], Håkan Ahlström[1], and Robin Strand[1]
[1]Radiology, Uppsala University, Uppsala, Sweden, [2]Medical Sciences, Uppsala University, Uppsala, Sweden

Target audience: Researchers interested in whole body MR or PET-MR imaging and image processing.

Purpose: To present the whole-body imaging concept *Imiomics* and initial examples of cross sectional interaction between MRI and non-imaging data where there is information on expected associations.

Introduction: Whole body MR and PET-MR imaging is of importance both for research and for clinical work in oncology and diabetes. Due to the lack of ionizing radiation in MR and to the widespread availability of MR scanners, large amounts of whole body image data can be collected today. The availability of this image data admits both new image analysis challenges and opportunities. Visual or manual analysis of the large amount of data collected is very time-consuming and subject to both inter- and intra-operator variability. Available tools for automated analysis do not use the full potential of the collected image data. Typically a few measurements like volumes, diameters, or SUV_{max} values are extracted from these information rich datasets. Also, integration of non-imaging biomarkers in the analysis of these datasets is not possible with traditional approaches.

We have developed an image processing concept, *Imiomics* (imaging –omics), a set of methods, including image registration, that allow statistical and holistic analysis of whole-body image data and non-imaging data. Imiomics enables creation of a *Human Imaging Atlas*, a statistical representation of intra-group distributions of image features. Imiomics analyses are holistic for three reasons: 1) the whole body is analyzed, 2) all collected image data is used in the analysis, and 3) it allows integration of all other collected non-imaging patient information in the analysis. The image registration method used utilizes quantitative whole-body water-fat MRI data, a pre-segmentation of bone from these images, and tissue specific constraints in the registration process.[1] Imiomics supports inclusion of other image data, such as DWI or PET, in the analysis. Potential applications of Imiomics include 1) to compare whole-body image feature between groups of for example sick and healthy subjects, 2) to follow changes in whole-body images in a subject over time, e.g. after intervention, 3) to assist attenuation correction in PET-MR where separation of bone and air is challenging, 4) to allow calculation of whole body images of point-by-point or tissue-by-tissue statistical interaction between imaging and non-imaging features, e.g. a correlation map between insulin levels and morphology like regional adipose tissue or muscle tissue volumes.

Methods: Subjects were recruited from an ongoing prospective study on obesity and metabolism (n=128, females=68, all subjects were aged 50 years, BMI 26.5±4.4 kg/m^2). All subjects were imaged on a 1.5T clinical MR system (Philips Achieva, Philips Healthcare, Best, Netherlands) in supine position using the body coils and a whole body water-fat imaging protocol that used a spoiled 3D multi gradient echo sequence. Scan parameters were: TR/TE1/ΔTE = 5.9/1.36/1.87 ms, 3 unipolar echoes, flip angle 3. Imaged field of view (FOV) 530×377×2000 mm^3, reconstructed voxel size 2.07×2.07×8.0 mm^3 in sagittal×coronal×axial directions, respectively. The imaging protocol and the water-fat image reconstruction have previously been described in detail.[2,3] All subjects also underwent non-imaging measurements of total fat mass (TFM), using a bioimpedance scale (Tanita, Japan), and abdominal fat using sagittal abdominal diameter (SAD), assessed using a level and a ruler, when lying in supine position.

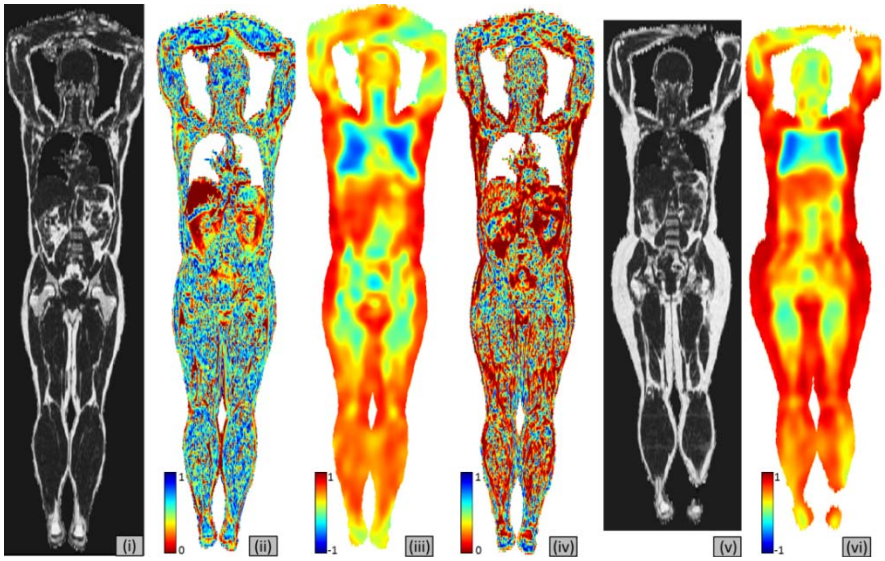

Figure 1: (i,v): Coronal slices of absolute fat content images from the male and female 'mean' subjects, respectively. (ii, *Anomaly detection*): p-map (point-wise p-values) of difference in fat content between a group with normal liver fat content (n=50) and a subject with high liver fat content (verified by explicit measurements). (iii, *Correlation*): R-map (point-wise correlation, R-values, n=60) showing correlation between local expansion and SAD. (iv, *Group-wise comparison*): p-map showing p-values of absolute fat content between groups with low vs. high SAD. (vi, *Correlation*): R-map (R-values, n=68) showing correlation between local expansion and TFM. Two-tailed t-tests without compensation for multiple tests were used for the p-maps.

One male (BMI 25.9 kg/m^2) and one female (BMI 25.5 kg/m^2) 'mean' subject was selected based on BMI and other non-imaging parameters, see Fig 1(i,v). All whole body images from the male and female subjects were registered to the 'mean' subject of same gender. The registration method has been presented and evaluated elsewhere.[1] The deformations given by the image registration method give point-to-point correspondences between all whole-body images. This allows whole-body comparisons of image intensity values and morphology (local volume or expansion assessed by the Jacobian determinant of the deformation fields).

Results: The initial examples in Fig 1 show expected associations, see figure caption for details. Fig 1(ii) shows high significance in the liver and in visceral adipose tissue, both Fig 1(iii) and (vi) show positive correlations in visceral and subcutaneous adipose tissue and in the liver and negative correlations in the lungs. Fig 1(iv) show high significance in visceral adipose tissue. The correlations in Fig 1(vi) agree well with explicitly measured volumes from the MRI data (Adipose tissue: r=0.95, p<0.001, Lean tissue: r=-0.11, p=0.158, Leg muscle: r=-0.03, p=0.668, Lung: r=-0.38, p<0.001).

Discussion: A reliable image registration method is crucial to allow accurate Imiomics analysis. The image registration method used here has been found to be robust in previous more detailed evaluations.[1] The image registration of the arms failed for some of the images due to non-standardized arm positioning. We however show in this work that Imiomics analysis gives expected results in cross-sectional whole-body studies of anomaly detection, associations, and group-wise comparisons. The negative correlation in the lungs was a finding that we had not foreseen that was also confirmed by explicit measurements. This exemplifies the potential usefulness of Imiomics in future research. Further possibilities of the Imiomics approach include completely new types of research studies applied in studies of systemic diseases like cancer and diabetes. We can for example (i) generate a human imaging atlas of normality which can be used for automated anomaly detection and quantification, (ii) perform group-wise whole body comparisons of sick vs. healthy subjects, (iii) do automated change detection, (iv) do characterization and quantification in cancer/diabetes interventions, (v) calculate whole-body imaging prediction scores of longitudinal hard endpoints, (vi) use the proposed registration technique to perform segmentations and thereby tissue and organ quantification or characterization studies and (vii) improve attenuation correction for PET-MR via separation of bone-air by use of an anatomical whole-body atlas.

Conclusion: From the example studies performed in this work, where information on expected associations were available, we conclude that Imiomics can be used for cross-sectional anomaly detection, associations and group comparisons.

References: **[1]** Strand et al, Submitted **[2]** Kullberg et al. J Magn Reson Imaging. 2009 30(1):185-93. **[3]** Berglund et al. Magn Reson Med. 2010 63(6):1659-68.

Acknowledgments: Peter Koken, Philips Research, Hamburg, Germany, for enabling data collection using moving bed MRI.