Iterative Decomposition of Water and Fat with Echo Asymmetry and Least-Squares Estimation (IDEAL) Imaging of Multiple Myeloma: Discriminant Analysis for Differentiation of Tumor Staging

Miyuki Takasu[1], Chihiro Tani[1], Miho Ishikawa[1], Daisuke Komoto[1], Keizo Tanitame[1], Yuji Akiyama[1], Yoshiaki Kuroda[2], Akira Sakai[3], and Kazuo Awai[1]

[1]Department of Diagnostic Radiology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan, [2]Department of Hematology and Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan, [3]Department of Hematology, Fukushima Medical University Hospital, Fukushima, Japan

Introduction: To determine the transition from asymptomatic to multiple myeloma requiring treatment (symptomatic myeloma) can often be difficult. The International Myeloma Working Group introduced the newer Durie-Salmon PLUS staging system [1], which takes into account the number of lesions detected by MRI. However, counting focal lesions can be somewhat confusing because signal intensity often changes in the vertebral body marrow, particularly in areas adjacent to end plates. Furthermore, diffuse infiltrative disease that does not form focal abnormalities cannot be evaluated. Thus, noninvasive, quantitative measures are needed to evaluate bone marrow involvement of myeloma cells that could provide information about the extent of diffuse infiltration.

The iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) can be used to robustly separate fat and water with very high SNR efficiency [2]. Furthermore, fully separating water and fat signals allows achievement of a full dynamic range of 0-100% fat signal fraction. The present study prospectively evaluates the effectiveness of IDEAL MRI to discriminate tumor stage in patients with multiple myeloma without visible focal lesions.

Methods: Spinal MRI was performed on 26 control individuals and on 24 patients with multiple myeloma (mean age, 62.1 and 61.5 years, respectively). According to the International Myeloma Working Group classification the patients were diagnosed with MGUS (n = 5), asymptomatic (n = 7) and symptomatic (n = 12) myeloma [3]. In addition to conventional MRI sequences including sagittal T1 and T2 FSE-weighted, sagittal T2 FSE-fat-suppression, and sagittal fast STIR imaging, a sagittal IDEAL T2 fast spin-echo-weighted sequence (TR, 4000 ms; TE, 112.4 ms; averages, 6; matrix size, 448×288; FOV, 300 mm; slice thickness, 4 mm; band width, 83.3 kHz; echo train length, 16; acquisition time, 6 min 17 s) was also used in all MRI examinations. Co-registered water, fat, in-phase (water + fat), and out-of-phase (water - fat) were generated by the IDEAL software. To obtain the fat signal fraction, the volume of interest (VOI) was defined manually within the internal regions of the L1 to L3 vertebral bodies to avoid the cortex and both end plates. Patients with fractured vertebral bodies or any focal osteolytic lesions of > 0.5 cm in the long axis were excluded. The fat signal fraction was calculated for each voxel from the ratio of the signal intensity in the fat image divided by the signal intensity of the corresponding voxel in the in-phase image. The fat signal fraction was then obtained as the mean value obtained from the three vertebral bodies and compared among the control, MGUS, asymptomatic and symptomatic myeloma groups using Scheffé's post hoc test. Based on the fact that $\beta_2 m$ and albumin are essential and systematic components of the scoring system for multiple myeloma [3], the fat signal fraction and $\beta_2 m$-to-albumin ratio were entered into discriminant analysis. A linear discriminant function was formed and the discriminant scores were computed using the linear discriminant function. We compared receiver operating characteristics (ROC) curves to evaluate the diagnostic performance of the fat signal fraction, $\beta_2 m$-to-albumin ratio, and the discriminant scores of all patients obtained by the discriminant analysis.

Table 1. Comparison of fat signal fraction (FSF%) and $\beta_2 m$-to-albumin ratio (BAR).

	Control (n = 26)	MGUS (n = 5)	Asymptomatic myeloma (n = 7)	Symptomatic myeloma (n = 12)
FSF (%)	72.8 ± 5.3	68.8 ± 8.4	71.6 ± 9.7	43.9 ± 19.7*
BAR	NA	0.55 ± 0.35	0.61 ± 0.22	1.95 ± 1.44

Values are shown as means ± standard deviation.
*Significant difference between symptomatic myeloma and all other groups, p < 0.01
. NA, not applicable.

Results: The fat signal fraction was the lowest in patients with symptomatic myeloma among the four groups (Scheffé's post hoc test, p < 0.01; Table 1) and did not significantly differ among the other three groups. Two groups of patients (MGUS + asymptomatic myeloma, and symptomatic myeloma) were analyzed using discriminant analysis. The patients with MGUS and those with asymptomatic myeloma were considere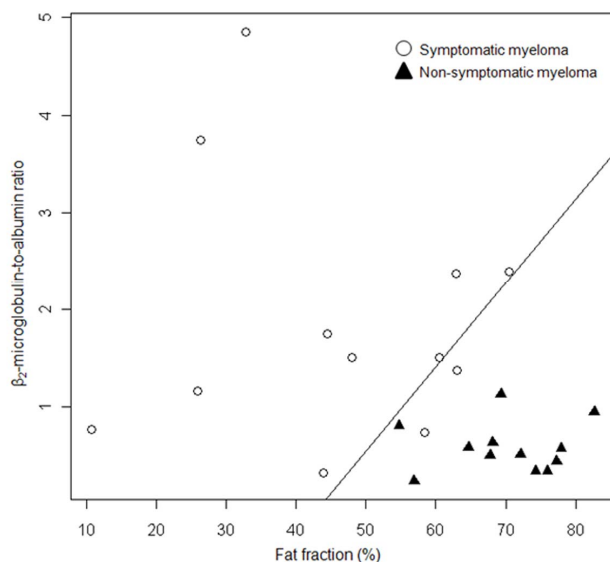d as having non-symptomatic myeloma, as the discrimination of symptomatic from non-symptomatic myeloma is essential for therapeutic decision-making. Discriminant analysis yielded a boundary for patient classification by tumor status based on the fat signal fraction and $\beta_2 m$-to-albumin ratio (Fig. 1). The AUCs of the ROC curves were 0.88, 0.10 and 0.99 for the fat signal fraction, the $\beta_2 m$-to-albumin ratio and the discriminant scores, respectively. The results for the discriminant scores were significantly better than those for the fat signal fraction or $\beta_2 m$-to-albumin ratio. The discriminant analysis correctly classified 22 (92%) of the 24 patients in each category.

Figure 1. Fat signal fraction versus $\beta_2 m$-to-albumin ratio scatter plot for non-symptomatic and symptomatic myeloma. Straight line, boundary between non-symptomatic and symptomatic myeloma.

Discussion and conclusion: The results of fat quantitation using the IDEAL sequence in MRI significantly differed between patients with symptomatic and asymptomatic myeloma. The fat signal fraction and β_2-microglobulin-to-albumin ratio facilitated the discrimination of symptomatic from non-symptomatic myeloma in patients without focal bone lesions. Asymptomatic myeloma located near the linear discriminant function on Figure 1 can be considered to have a higher risk of progression to symptomatic myeloma than when it is located far from the linear discriminant function. The discriminant model revealed that two symptomatic patients were misidentified as being non-symptomatic. These patients had relatively high fat signal fractions and low $\beta_2 m$-to-albumin ratios. One of them was diagnosed with symptomatic myeloma based on renal insufficiency within the CRAB criteria. A solitary plasmacytoma in the temporal bone of the other was diagnosed as progression to symptomatic myeloma based on a pathological fracture at the thoracic vertebrae. We attributed these misclassifications to mild infiltration of myeloma cells causing only a modest increase in $\beta_2 m$.

Fat-signal fraction maps generated using IDEAL do not directly measure or reflect fat concentrations. To do so, the fat signal fraction map must be corrected for confounding factors, namely T2* decay, complexity of fat, noise bias, and eddy current. We believe that protocol- and platform-independent quantitative techniques will be needed to truly exploit the value of quantitative fat imaging for pathologies involving bone marrow.

References: 1. Durie BG et al. (2003) Hematol J 4:379–398; 2. Reeder SB et al. (2004) MagnReson Med 51:35–45. 3. International Myeloma Working Group (2003) Br J Haematol 121:749-757.