

# Multiple Myeloma and Monoclonal Gammopathy of Undetermined Significance: Importance of Whole-Body versus Spinal MR Imaging<sup>1</sup>

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## Purpose:

To examine if standard magnetic resonance (MR) imaging of the axial skeleton is sufficient for evaluation of patients with multiple myeloma (MM) or monoclonal gammopathy of undetermined significance (MGUS) or if whole-body MR is necessary.

## Materials and Methods:

A total of 100 untreated patients with MGUS ( $n = 27$ ) or any stages of MM ( $n = 73$ ) were examined with whole-body MR imaging and MR imaging of the axial skeleton. The study was approved by the institutional ethics committee, and written informed consent was given. Spinal pattern ("no diffuse involvement" or "diffuse involvement" as assessed from the signal intensity of the spinal bone marrow), serum parameters, and stage of disease were correlated with the probability of detecting extra-axial lesions with and without destruction of cortical bone by using a multiple logistic regression model.

## Results:

Of 100 patients, 39 had lesions in the axial skeleton and 37 had lesions in the extra-axial skeleton. Of the latter group, nine patients had no axial lesions and 13 patients had lesions that violated cortical bone, which implied an increased fracture risk. Because of the extraaxial location, lesions in these patients could be diagnosed with whole-body MR only. In addition, no single or combination of clinical factors observed (stage of disease, serum parameters, and spinal pattern) allowed investigators to identify patients with a significantly increased probability of having extra-axial lesions or lesions violating cortical bone.

## Conclusion:

Whole-body MR imaging has potential for use in the initial work-up of patients with MGUS or MM, since almost one-half of all observed lesions would have been missed by using spinal MR imaging only and clinical parameters could not exclude the presence of extra-axial lesions.

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**M**ultiple myeloma (MM) is a malignancy of monoclonal B-cells. Monoclonal gammopathy of undetermined significance (MGUS) is a potential precursor of MM without any signs of the malignant disease (1). While MGUS is the most common disorder of plasma cells and occurs in 2% of persons older than 50 years and in 3% of persons older than 70 years (2), MM has an incidence of 4–5 per 100 000 persons per year. In adults, hematopoietic bone marrow is located mainly in the axial skeleton, and it is hypothesized that this is the reason for the detection of most myeloma manifestations in this region (3).

Magnetic resonance (MR) imaging allows for the investigation of different tissues with excellent contrast and high spatial resolution. It is established as a tool for the diagnosis of solitary plasmacytoma of bone (4) and for staging and response assessment of nonsecretory MM (5). Different distinguishable patterns of bone marrow infiltration have been described, such as diffuse marrow involvement (6,7) and circumscribed focal lesions, which are relevant for patient prognosis (8,9). However, a nearly normal marrow pattern has also been observed in a group of patients with MM (6).

While most investigations on the use of MR imaging in MM have concerned spinal imaging, there has been one prior study, to our knowledge, that analyzed the importance of whole-body

MR imaging (10). This study group confirmed that MR imaging has a higher sensitivity for the detection of focal lesions in the skeleton than does conventional radiography in patients with MM.

The prognostic value of the number of focal lesions and the degree of diffuse infiltration of spinal lesions as seen at MR has been demonstrated in several studies for patients with symptomatic (8,9,11) and asymptomatic disease (12,13). A recent publication of the British Committee for Standards in Hematology recommended the use of whole-body MR imaging as a screening tool for patients with MM (14). However, to our knowledge, no study has examined the effect of whole-body MR imaging in patients with MGUS or MM.

This study was performed to examine whether standard MR imaging of the axial skeleton is sufficient for initial work-up of patients with MGUS and MM or if it is necessary to perform whole-body MR imaging in each of these types of patients. Furthermore, it was performed to investigate if a single factor or a combination of serum parameters or bone marrow pattern at spinal MR imaging might help predict the presence of extra-axial lesions or plasma cell tumors penetrating cortical bone.

formed consent was given. MGUS was defined according to the criteria proposed by the International Myeloma Working Group (1). Criteria used for the diagnosis and staging of MM were taken from the classification of Durie and Salmon (15). With this classification system, stage I (low mass of malignant plasma cells, no treatment required), stage II (intermediate cell mass, treatment required if in progression), and stage III (high cell mass, treatment required) can be distinguished in MM patients. To explore whether the number of lesions detected with either spinal or whole-body MR imaging would possibly lead to differences in staging, we chose the Durie-Salmon PLUS classification as one among several staging systems that have recently been suggested (11).

Criteria to include individuals into this study were as follows: MGUS or MM (stages I–III, according to the Durie-Salmon classification), no previous chemotherapy, age older than 18 years, and a World Health Organization status of at least 2. Contraindication to MR imaging was an exclusion criterion. From November 2004 to September 2007, 27 individuals with MGUS (median age, 56 years; range, 22–79 years; 17 women and 10 men) and 73 un-

### Advances in Knowledge

- In this study, nearly 50% of patients with monoclonal plasma cell disease had lesions outside the axial skeleton that would have been missed by using spinal MR imaging alone.
- MR imaging of the axial skeleton is the current standard of care for these patients, but we have shown a false-negative rate of about 10% of patients who manifest have exclusively extra-axial lesions.
- None of the usual clinical or serologic parameters could be used to exclude the presence of lesions in the extra-axial skeleton.

### Materials and Methods

#### Patients

This study was approved by the institutional ethics committee and written in-

#### Implications for Patient Care

- Staging systems of multiple myeloma including results from whole-body MR imaging might be used to supplement the clinical classification of Durie and Salmon.
- With the Durie-Salmon PLUS classification system, the inclusion of the appendicular skeleton as part of an MR survey in patients with untreated MM or MGUS causes 21% of patients to be upstaged, potentially affecting their treatment and prognosis.

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#### Abbreviations:

LDH = lactate dehydrogenase

MGUS = monoclonal gammopathy of undetermined significance

MM = multiple myeloma

STIR = short inversion time inversion-recovery

#### Author contributions:

Guarantors of integrity of entire study, T.B., L.G., B.W., S.D.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, T.B., J.H., K.F., L.G., T.M.M., B.W., K.N.; clinical studies, T.B., J.H., K.F., C.M.Z., L.G., T.M.M., B.W., H.U.K., H.G.; statistical analysis, T.B., K.F., L.G., C.H., B.W., S.D.; and manuscript editing, T.B., J.H., K.F., C.M.Z., L.G., T.M.M., C.H., B.W., K.N., H.U.K., S.D.

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treated patients with MM (35 patients with stage I [median age, 54 years; range, 31–74 years; 15 women and 20 men] and 38 patients with stages II–III [median age, 60 years; range, 27–80

years; 16 women and 22 men]) underwent standard contrast material-enhanced MR imaging of the axial skeleton (spine and sacral bone) and whole-body MR imaging. There were no significant

differences for age ( $P = .16$ , approximate Kruskal-Wallis test) and sex ( $P = .19$ , Fisher exact test) between the groups. These examinations were performed within 30 days for each patient.

**Table 1**

**MR Imaging Parameters**

| Parameter                     | MR of Axial Skeleton  |                  |                                            | Whole-Body MR   |                  |                       |
|-------------------------------|-----------------------|------------------|--------------------------------------------|-----------------|------------------|-----------------------|
|                               | T1-weighted Spin-Echo | T2-weighted STIR | Postcontrast T1-weighted Fat-saturated TSE | T1-weighted TSE | T2-weighted STIR | T2*-weighted 2D FLASH |
| Orientation                   | Sagittal              | Sagittal         | Sagittal                                   | Coronal         | Coronal          | Sagittal              |
| Section thickness (mm)        | 4                     | 4                | 4                                          | 5               | 5                | 5                     |
| Voxel size (mm <sup>2</sup> ) | 1.1 × 1.1             | 1.1 × 1.1        | 1.1 × 1.1                                  | 1.25 × 1.25     | 1.25 × 1.25      | 1.25 × 1.25           |
| Matrix                        | 256 × 256             | 256 × 256        | 256 × 256                                  | 307 × 384       | 211 × 384        | 192 × 256             |
| Field of view                 | 280                   | 340              | 280                                        | 500             | 500              | 360                   |
| Repetition time (msec)        | 500                   | 3500             | 600                                        | 627             | 3680             | 402                   |
| Echo time (msec)              | 14                    | 30               | 11                                         | 11              | 109              | 12                    |
| Turbo factor                  | ...                   | 8                | 4                                          | 5               | 33               | ...                   |
| Acquisition time*             | 10 min 42 sec         | 13 min 35 sec    | 18 min 51 sec                              | 13 min 45 sec   | 5 min 52 sec     | 5 min 51 sec          |

Note.—STIR = short inversion time inversion-recovery, TSE = turbo spin echo, 2D FLASH = two-dimensional fast low-angle shot.

\* The total acquisition time was 43 minutes 2 seconds for MR of the axial skeleton and 25 minutes 28 seconds for whole-body MR.

**Figure 1**



**Figure 1:** Spinal patterns at MR imaging. (a, c) T1- and (b, d) T2-weighted sagittal images of the lumbar spine in two patients with MM. (a, b) "No diffuse involvement" of spinal bone marrow is diagnosed from hyperintense bone marrow on T1-weighted image (a) and hypointense bone marrow on T2-weighted image (b). (c, d) "Diffuse involvement" is characterized by hypointense bone marrow on T1-weighted image (c) and hyperintense bone marrow on T2-weighted image (d).

While whole-body MR imaging was performed as part of the standard clinical work-up, MR imaging of the axial skeleton was performed as accompanying morphologic imaging within a study of dynamic contrast-enhanced MR imaging in patients with plasma cell disorders. For this retrospective study, no power analysis was performed and the sample size was determined by the inclusion and exclusion criteria as well as the period of time given above.

### MR Protocol and Evaluation

Whole-body MR was performed with a 1.5-T imager (Avanto; Siemens Medical Solutions, Erlangen, Germany) by using imaging parameters as given in Table 1 and the following coils: head coil, neck

coil, spine coil, body matrix (two), and extremity coil. The patients were positioned with their arms beside their bodies, and the series covered the region between the skull vertex and the midcalf. The distal calves and the feet were not included.

The term “whole-body MR imaging” in this context denotes an acquisition that includes the axial and appendicular skeleton in our image analysis, but not the distal parts of the arms and calves or the feet, depending on the body height of the patient. For MR imaging of the axial skeleton alone (including cervical, thoracic, and lumbar spine, and sacral bone), a 1.5-T imager (Symphony; Siemens Medical Solutions) with the parameters given in Table 1 was used with neck and spine coils. The contrast-enhanced

images were obtained at least 10 minutes after the start of contrast material infusion, during which a dynamic T1-weighted series was acquired (contrast media application: 0.1 mmol/kg, duration of infusion 30 seconds; not subject of this study). For covering the entire spine, all series were obtained in three table positions.

For all patients, the spinal MR pattern was defined as “no diffuse involvement” (bone marrow hyperintense on T1-weighted images and hypointense on T2-weighted STIR images) or “diffuse involvement” (bone marrow hypointense on T1-weighted images and hyperintense on T2-weighted STIR images) (Fig 1) as described previously (7,16). However, the spinal pattern “no diffuse involvement” does not exclude the presence of malignant plasma cells or focal lesions in the bone marrow. In addition, all focal lesions were counted separately for the axial skeleton (spine and sacral bone) and the extra-axial skeleton (all other bones). Furthermore, each lesion was defined as “in bone” (lesions confined to cancellous or cortical bone) or “violating bone” (soft-tissue mass of the lesion violating the cortical bone with infiltration of adjacent tissue). MR data were evaluated retrospectively by two radiologists (T.B. and K.F., 5 and 4 years of experience, respectively), blinded to diagnosis, at the same time in consensus reading. Between October 2007 and February 2008, images were presented randomly to the readers to avoid learning and memory bias.

**Table 2**

#### Distribution of Lesions in All Patients with MGUS or MM

##### A: Axial and Extraaxial Location

| Parameter       | Axial<br>Skeleton Only | Extraaxial<br>Skeleton Only | Axial and<br>Extraaxial | No<br>Lesion | Total     |
|-----------------|------------------------|-----------------------------|-------------------------|--------------|-----------|
| No. of patients | 11 (11)                | 9 (9)                       | 28 (28)                 | 52 (52)      | 100 (100) |
| No. of lesions  | 27 (6)                 | 25 (5)                      | 404 (89)                | ...          | 456 (100) |

##### B: Bone Involvement

| Parameter       | Axial Skeleton |                |          | Extraaxial Skeleton |                |          | Total     |
|-----------------|----------------|----------------|----------|---------------------|----------------|----------|-----------|
|                 | In Bone        | Violating Bone | Total    | In Bone             | Violating Bone | Total    |           |
| No. of patients | 37             | 15             | 39       | 37                  | 13             | 37       | 48        |
| No. of lesions  | 221 (49)       | 24 (5)         | 245 (54) | 193 (42)            | 18 (4)         | 211 (46) | 456 (100) |

Note.—Data in parentheses are percentages.

**Table 3**

#### Distribution of Lesions in Patients with MGUS

##### A: Axial and Extraaxial Location

| Parameter       | Axial<br>Skeleton Only | Extraaxial<br>Skeleton Only | Axial and<br>Extraaxial | No Lesion | Total    |
|-----------------|------------------------|-----------------------------|-------------------------|-----------|----------|
| No. of patients | 2 (7)                  | 2 (7)                       | 2 (7)                   | 21 (78)   | 27 (100) |
| No. of lesions  | 2 (13)                 | 4 (27)                      | 9 (60)                  | ...       | 15 (100) |

##### B: Bone Involvement

| Parameter       | Axial Skeleton |                |        | Extraaxial Skeleton |                |        | Total    |
|-----------------|----------------|----------------|--------|---------------------|----------------|--------|----------|
|                 | In Bone        | Violating Bone | Total  | In Bone             | Violating Bone | Total  |          |
| No. of patients | 4              | 0              | 4      | 4                   | 0              | 4      | 5        |
| No. of lesions  | 7 (47)         | 0 (0)          | 7 (47) | 8 (53)              | 0 (0)          | 8 (53) | 15 (100) |

Note.—Data in parentheses are percentages.

### Statistical Analysis: Prediction of Incidence of Extraaxial Lesions and Lesions Penetrating Cortical Bone

To investigate the association between the incidence of extra-axial lesions and several clinical parameters of patients with MM ( $n = 73$ ), a multiple logistic regression model was used for patients with MM stages I–III. The following parameters were included: creatinine, lactate dehydrogenase (LDH), calcium, platelets,  $\beta_2$  microglobulin, albumin, stage according to Durie-Salmon classification and according to the international staging system. We chose these clinical variables because they have been described as parameters for disease activity, prognostic factors (especially  $\beta_2$  mi-

croglobulin and albumin), or as markers of cell turnover (LDH). Because of missing values, data in 66 (90%) of 73 patients with MM were analyzed by using a logistic regression model. The same analysis was performed to investigate if these factors allow a prediction of cortical breakthrough.

To analyze the increasing total number and the presence of lesions in the axial or extra-axial skeleton depending on the bone marrow infiltration ("no diffuse involvement" and "diffuse involvement"), the linear-by-linear association test and the Cochran Armitage trend test were used, respectively. Statistical analysis was performed by using the statistical software package R (version 2.5.1, R Development Core Team 2007; available at [www.r-project.org](http://www.r-project.org)) and StatXact (version 7.0; Cytel Studio, Cambridge, Mass).

## Results

MR imaging of the whole body was performed by using a protocol covering the central and peripheral skeleton with sections in coronal (T1-weighted turbo spin-echo and T2-weighted STIR sequences) and sagittal (T2\*-weighted two-dimensional fast low-angle shot sequence) orientation excluding the distal arms and calves as well as the feet. In a separate examination of the axial skeleton, sagittal MR images of the spine and pelvis (T1-weighted spin-echo, T2-weighted STIR and contrast-enhanced T1-weighted turbo spin-echo fat-saturated sequences) were acquired.

Of 100 patients with MGUS or MM, 52 had no focal bone lesions. In 11 patients the lesions were confined to the axial skeleton, in nine patients the lesions were only outside the axial skeleton, and in 28 patients the lesions were found both axially and extra-axially (Table 2, Fig 2). In 15 of 39 patients with axial lesions, at least one of these lesions (24 in total) violated the cortical bone. Likewise, 13 patients with extra-axial lesions had a total of 18 solid myeloma lesions in these locations, which were growing beyond the confines of the bone (Table 2).

Of 27 patients with MGUS, only six had focal lesions at all, but these lesions were found in axial, extra-axial, or both

Figure 2



**Figure 2:** Focal lesions in the axial and extraaxial skeleton. (a) T1- and (b) T2-weighted coronal images from whole-body MR imaging in a patient with MM, with a focal lesion in the thoracic spine (arrow) and several lesions in the proximal femurs.

locations with equal frequency (Table 3). All of these were still confined to the marrow.

Only five of 27 patients (11 of whom had MGUS) without diffuse bone marrow abnormalities had focal lesions, whereas lesions were found in 43 of 73 patients with diffusely abnormal bone marrow signal intensity. Of the five former patients, three had at least one extra-axial lesion; of the latter 43 patients, nine had only axial lesions, eight had only extra-axial lesions, and 26 had lesions both axially and extra-axially (Table 4). Among the

five patients who had focal lesions but otherwise had the bone marrow pattern "no diffuse involvement, one patient had a single lesion that violated cortical bone (Table 4). Examples of focal lesions in the axial and extra-axial skeleton are shown in Figures 3 and 4.

None of the examined clinical parameters such as levels of creatinine, LDH, calcium, platelets,  $\beta 2$  microglobulin, and albumin, and international staging system showed a significant correlation with the presence of extra-axial lesions or those penetrat-

ing cortical bone. As an example, 49 patients had a  $\beta 2$  microglobulin level below 2.5 mg/L (upper limit of normal) in serum. Twenty of these patients had focal lesions: in five, only axial; in five, only extra-axial; and in 10, both axial and extra-axial. Among 15 patients with a  $\beta 2$  microglobulin level below 2.5 mg/L who had axial lesions, seven had at least one myeloma lesion (12 in total) in this location that violated the cortical bone. Of 15 patients with a  $\beta 2$  micro-

globulin level below 2.5 mg/L and extra-axial lesions, five had lesions in this location, which were no more confined to the bone (Table 5).

With multiple logistic regression analysis, a statistically significant association of the presence of axial and extra-axial lesions was observed for the stage of MM according to the staging system of Durie and Salmon. For example, patients with MM stage I were compared with patients with MM stage II (axial,  $P = .21$ ; extra-

axial,  $P = .07$ ) and III (axial,  $P = .03$ ; extra-axial,  $P = .003$ ). Neither an increasing total number nor the presence of axial or extra-axial lesions depending on the degree of bone marrow infiltration (normal or diffuse) detected at MR imaging showed a statistically significant association or trend.

In all individuals in the study, disease was additionally staged according to the Durie-Salmon PLUS classification system, comparing the stages from MR imaging of the axial skeleton with the results from whole-body MR imaging (Fig 5, Table 6). Thereby, a total of 21 patients with MGUS and all MM stages from the results of the spinal MR imaging were upstaged when the results from the extra-axial skeleton were included.

Table 4

## Distribution of Lesions according to Spinal Pattern

## A: Axial and Extraaxial Location

| Parameter              | Axial Skeleton Only | Extraaxial Skeleton Only | Axial and Extraaxial | No Lesion | Total     |
|------------------------|---------------------|--------------------------|----------------------|-----------|-----------|
| No diffuse involvement |                     |                          |                      |           |           |
| No. of patients        | 2 (7)               | 1 (4)                    | 2 (7)                | 22 (82)   | 27 (100)  |
| No. of lesions         | 4 (27)              | 2 (13)                   | 9 (60)               | ...       | 15 (100)  |
| Diffuse involvement    |                     |                          |                      |           |           |
| No. of patients        | 9 (12)              | 8 (11)                   | 26 (36)              | 30 (41)   | 73 (100)  |
| No. of lesions         | 23 (5)              | 23 (5)                   | 395 (90)             | ...       | 441 (100) |

## B: Bone Involvement

| Parameter              | Axial Skeleton |                |          | Extraaxial Skeleton |                |          | Total     |
|------------------------|----------------|----------------|----------|---------------------|----------------|----------|-----------|
|                        | In Bone        | Violating Bone | Total    | In Bone             | Violating Bone | Total    |           |
| No diffuse involvement |                |                |          |                     |                |          |           |
| No. of patients        | 4              | 1              | 4        | 3                   | 0              | 3        | 5         |
| No. of lesions         | 7 (47)         | 1 (7)          | 8 (53)   | 7 (47)              | 0 (0)          | 7 (47)   | 15 (100)  |
| Diffuse involvement    |                |                |          |                     |                |          |           |
| No. of patients        | 33             | 14             | 35       | 34                  | 13             | 34       | 43        |
| No. of lesions         | 214 (49)       | 23 (5)         | 237 (54) | 186 (42)            | 18 (4)         | 204 (46) | 441 (100) |

Note.—Data in parentheses are percentages.

## Discussion

Our study was performed to investigate if MR imaging of the axial skeleton, as used in most previous studies of patients with monoclonal plasma cell disorders, is sufficient to evaluate bone involvement in patients with MGUS and MM. Furthermore, we analyzed whether clinical markers for disease activity or the infiltration pattern at spinal MR can be used to predict extra-axial lesions not detectable at spinal MR or if a lesion will penetrate cortical bone.

MR imaging has been shown to help prognosticate asymptomatic and symptomatic myeloma in patients (8,13). In addition, this technique is more sensitive for the detection of bone marrow involvement than is a skeletal survey (10,17), which has been the standard technique according to the staging system of Durie and Salmon (15). Several authors have proposed the use of MR imaging in staging MM (9,11). Furthermore, whole-body MR imaging proved to be superior to whole-body computed tomography (CT) in a recent comparison of these modalities for detection of bone manifestations of MM (18). However, the fact that bone structure cannot be assessed by using MR imaging might lead to understaging in some patients, in whom osteolysis was diagnosed with CT but no infiltration was visible at MR imaging (19).

Table 5

Distribution of Lesions according to Serum Parameter  $\beta 2$ -Microglobulin

## A: Axial and Extraaxial Location

| Parameter       | Axial Skeleton Only | Extraaxial Skeleton Only | Axial and Extraaxial | No Lesion | Total     |
|-----------------|---------------------|--------------------------|----------------------|-----------|-----------|
| No. of patients | 5 (10)              | 5 (10)                   | 10 (20)              | 29 (60)   | 49 (100)  |
| No. of lesions  | 17 (11)             | 9 (6)                    | 123 (83)             | ...       | 149 (100) |

## B: Bone Involvement

| Parameter       | Axial Skeleton |                |         | Extraaxial Skeleton |                |         | Total     |
|-----------------|----------------|----------------|---------|---------------------|----------------|---------|-----------|
|                 | In Bone        | Violating Bone | Total   | In Bone             | Violating Bone | Total   |           |
| No. of patients | 15             | 7              | 15      | 15                  | 5              | 15      | 30        |
| No. of lesions  | 80 (54)        | 12 (8)         | 92 (62) | 49 (33)             | 8 (5)          | 57 (38) | 149 (100) |

Note.—Data in parentheses are percentages.

With the advent of faster MR sequences and large whole-body coils, one can image the whole body without the need for radioactive tracers such as with positron emission tomography-CT. Therefore, a recent publication of the British Committee for Standards in Hematology recommended the use of whole-body MR imaging as a screening tool for patients with MM (14). However, in that publication, no comparison was made between the presence of focal lesions diagnosed with spinal and whole-body MR in patients with MGUS or MM to demonstrate the actual benefit of whole-body MR.

For the group of patients in our study, 37 patients were diagnosed with extra-axial lesions, and in nine of these patients, lesions were located extra-axially without the presence of axial focal lesions. In 13 patients with extra-axial lesions, tumors violated cortical bone, and as a consequence, these patients might have an increased risk of fracture. All the above mentioned extra-axial lesions were diagnosed with whole-body MR imaging and would have been missed by using spinal MR imaging only.

Bone marrow abnormalities were found by Vande Berg et al (20) in seven of 37 individuals with MGUS who did not have clinical signs of MM. In our study, focal lesions were demonstrated in six of 27 patients with MGUS. Although focal lesions in patients with MGUS did not violate cortical bone and are relatively rare compared with in MM patients, a total of eight lesions in four patients would have been missed in our study by using spinal MR imaging only. Consequently, for a complete work-up of patients with MGUS, whole-body MR imaging might be recommended.

A normal appearance of bone marrow on spinal MR images is present at diagnosis in 50%–75% of cases untreated Durie-Salmon stage I MM and in 20% of cases of untreated Durie-Salmon stage III disease (7,21). As expected in our study, in the majority of patients with focal lesions the diagnosis was diffuse infiltration of the spinal bone marrow (43 of 48 patients), but in five patients with the spinal pattern “no

**Figure 3**

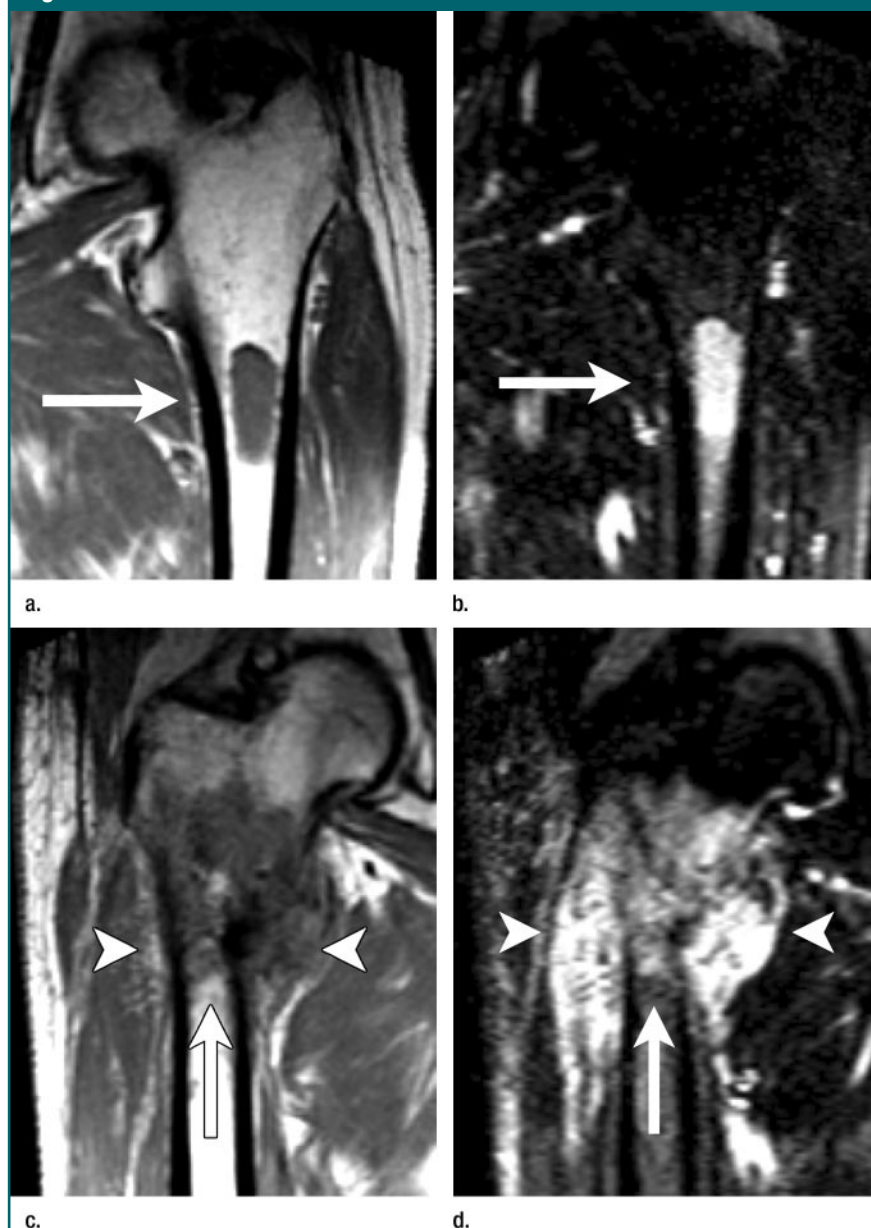


**Figure 3:** Extraaxial focal lesions at whole-body MR imaging. (a, c) T1- and (b, d) T2-weighted images of a focal lesion of the left femur within bone (arrows, a and b) and of the right femur (arrows, c and d) violating cortical bone with infiltration of the adjacent muscles (arrowheads) in a patient with MM.

diffuse involvement,” focal lesions were also demonstrated. Of these five patients, three had lesions in an extra-axial location that would not have been diagnosed with spinal MR imaging only.

Unfortunately, it does not seem possible based on our data to stratify patients for spinal or whole-body protocols by using established parameters of

disease activity, including spinal pattern at MR imaging (normal vs diffuse), serum parameters (creatinine, LDH, calcium, platelets,  $\beta 2$  microglobulin, and albumin), and the diagnosis of MGUS versus all stages of MM. Additional clinical parameters were not considered because of the limited number of patients available.

When staged according to the Durie-Salmon PLUS system, which we used as one among several examples of how MR could be used to supplement the current staging system, we found that performing whole-body MR instead of MR of the axial skeleton would put a maximum of 21 of 100 patients into a higher stage (11,22). However, the precaution has to be made that it had not been the aim of our study to examine the influence of the chosen MR imaging

method on formal staging. Furthermore, there is no MR imaging-based staging system that is generally accepted today, nor is there any proof of its significance for initiation of treatment. Classification of all individuals according to the Durie-Salmon PLUS system on the basis of the results of whole-body MR imaging caused 21 patients in our study to be upstaged compared with the results of MR imaging of the axial skeleton only.

One limitation of our study is the short follow-up of our patients, which allows no conclusions about prognostic implications of our findings. Furthermore, whole-body protocols, if they are performed within reasonable time, may have limitations regarding resolution compared with dedicated whole-spine protocols. However substantial focal myeloma lesions are clearly detectable and the clinical importance of very small lesions is questionable.

In conclusion, as extra-axial focal lesions cannot be excluded in either MGUS or MM by using spinal MR imag-

Figure 4



**Figure 4:** Focal lesions at axial MR imaging. (a) T1- and (b) T2-weighted images of focal lesions in a spinous process of the thoracic spine (arrows) in a patient with MGUS. (c) T1- and (d) T2-weighted images of a focal lesion of the vertebral body in the lumbar spine (arrow) in a patient with MM, with a normal appearance of the spinal pattern (arrowheads).

Figure 5

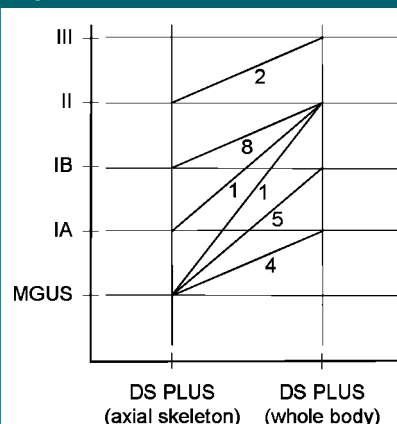


**Figure 5:** Graph shows number of patients in whom a different stage was observed after staging was performed based on Durie-Salmon PLUS (DS PLUS) classification at MR imaging of the axial skeleton and at whole-body MR imaging.

Table 6

**Durie-Salmon PLUS Classification**

| Parameter | MR of Axial Skeleton | Whole-Body MR |
|-----------|----------------------|---------------|
| MGUS      | 31                   | 27            |
| Stage IA  | 37                   | 40            |
| Stage IB  | 17                   | 14            |
| Stage II  | 11                   | 19            |
| Stage III | 4                    | 6             |
| Total     | 100                  | 100           |

Note.—Number of patients with MGUS and all stages of MM, as classified according to the Durie-Salmon PLUS classification at MR of the axial skeleton and whole-body MR.

ing and serologic parameters, we recommend the possible use of whole-body MR imaging for initial work-up in these patients.

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