

## Imaging in multiple myeloma: Computed tomography or magnetic resonance imaging?

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### Abstract

Multiple myeloma (MM) is the second most common type of hematological disease with its incidence rising in the elderly. In MM, the extent of the bone disease increases both morbidity and mortality. The detection of lytic bone lesions on imaging, especially computerized tomography (CT) and magnetic resonance imaging (MRI) is crucial to separate asymptomatic from symptomatic MM patients even when no clinical symptoms are present. Although radiology is essential in the staging and management of patients with MM there is still high variability in the choice between MRI and CT. In addition, there is still suboptimal agreement among readers. The potential of medical imaging in MM is largely under-evaluated: artificial intelligence, radiomics and new quantitative methods to report CT and MRI will improve imaging usage.

**Key Words:** Multiple myeloma; Imaging; Magnetic resonance imaging; Computed tomography; Quantitative imaging

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**Core Tip:** Introduction of new quantitative scores and biomarkers to predict multiple myeloma (MM) prognosis, possibly outperforming current staging methods to create new reliable standards for disease prediction and monitoring is an opportunity for further research in MM imaging.

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## INTRODUCTION

Multiple myeloma belongs to the so-called plasma cell dyscrasias which are pathological conditions including monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), and full-blown multiple myeloma (MM)[1]. Epidemiological studies show that, on the one hand, around 5% population over 70 is MGUS carriers and around 1% of them will turn into MM every year. On the other hand, around 10% SMM population evolves into full-blown MM[1]. Finally, the early MM mortality, *i.e.* the number of MM patients that die within the first year after diagnosis, is nowadays around 28%, with a peak of 35% among older patients[1]. The single or, more frequently, multiple bone lesions are biologically determined by the proliferation of abnormal cells from a single clone and the excessive and unbalanced activation of osteoclasts eroding the bone starting from the medulla and then reaching the cortical bone and even the extra-osseous soft-tissues. However, MM has a heterogeneous genetic architecture which is evident among different patients with the same disease. Genetic heterogeneity is evident also in the same patient where different focal bone lesions may have different genetic patterns[2-4]. MM patients are classically described and defined by the CRAB-criteria (Calcium elevation, Renal insufficiency, Anemia, Bone lesion), indeed symptoms of MM patients vary from bone pain or pathological fractures over renal failure and anemia to calcium elevation and even immune deficiency. It is not known why up to 20% of patients with SMM become symptomatic within 2 years, while one third does not progress to MM within a decade [5], therefore there are several unmet research questions that need to be addressed. In MM patients, having a single focal lesion > 5 mm in diameter identified by mean of computed tomography (CT) or magnetic resonance imaging (MRI) is currently used to identify high-risk SMM patients to upstage them to MM according to the International myeloma working group updated criteria for the diagnosis of multiple myeloma[6]. Therefore, detection of lytic bone lesions on imaging has been recognized crucial since 2003 when the international myeloma working group replaced the classical Durie-Salmon staging system with a more complex and complete revised version called Durie-Salmon plus system. This latter system replaced radiography for identifying bone involvement with the increased sensitivity of MRI, CT or Positron emission tomography (PET)[7]. Therefore, the detection of lytic bone lesions on imaging, especially CT and MRI, is becoming crucial from the clinical viewpoint to separate asymptomatic from symptomatic MM patients. According to Rajkumar *et al*[8] bone imaging in MM is relevant for diagnosis because osteolytic lesion detection justifies the beginning of a treatment. Medical imaging is required for several reasons: (1) Localization of bone pain; (2) Prevention of complications such as pathologic fractures on long bones (*i.e.* femur) and vertebral pathological fractures; (3) Identification of focal lesions with high risk of progression; (4) To identify sites of extra-medullary disease; and (5) Identification of sites at potential risk of neurologic complications (Figure 1). In spite of the pivotal role of medical imaging in MM patient care, there is still considerable heterogeneity in clinical practice regarding imaging usage in MM, essentially due to the high variability in the choice between various imaging methods and the high variability in image interpretation[9,10]. In this editorial, the unmet research questions in the usage of imaging in MM are reported and possible future directions are discussed.

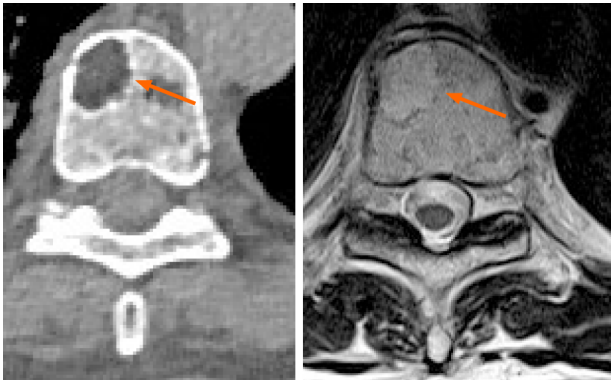
## POTENTIAL OF MEDICAL IMAGING IN MM

Firstly, it must be underlined that the detection of lytic bone lesions with a diameter > 5 mm can be done with both CT and MRI and no study directly compared the two modalities regarding patients' outcomes after CT or MRI. At least in theory, MRI could have some advantages, such as the possibility to introduce functional sequences such as diffusion weighted sequences, but, no clear advantage of one technique over another has been found, even when a systematic review approach was adopted[11, 12]. Regelink *et al*[12] found that there was only few additional lesions detected by both PET and MRI if CT was used as reference test (detection rate 1.00 and 1.00-1.25 respectively). In addition, the review by Regelink *et al*[12] review was limited by the suboptimal methodological quality of the involved studies due to lack of a technical details. It could be suggested that both MRI and CT have equal diagnostic value and there is no clear advantage to prefer one of the two techniques (Table 1). The scientific community is waiting for thorough comparative future studies, possibly focusing on prognostic value and follow-up. Furthermore, an analysis of multiple bone lesions

**Table 1 Specific advantages and disadvantages of computed tomography and magnetic resonance imaging in multiple myeloma**

	Availability	Reader expertise	Radiation dose	Repeatability among different readers	Repeatability among different scanners	Availability of reporting guidelines	Ability to detect > 5 mm focal lesions	Exam duration
CT	High	Medium	Similar to total body CT	High	Medium	Low	High	Less than 10 min
MRI	Medium	Low	None	Medium	Medium	Low	High	More than 30 min

CT: Computed tomography; MRI: Magnetic resonance imaging.



**Figure 1 Computed tomography and magnetic resonance imaging of the same lytic lesion located into the vertebral body acquired in the same week for different reasons.** No major differences in detection capabilities are evident.

detected on CT and MRI could be performed using artificial intelligence and radiomics [13]. Up-to-date, radiomics[14] is a quantitative radiological promising technique, with the ultimate goal to improve cancer treatment by improving prognostic capabilities of medical imaging. Radiomics is a complex, quantitative feature-based tool for image analysis described as the conversion of images to higher dimensional data and the subsequent mining of these data for improved decision support[14]. In MM, a recent application of radiomics improved the radiological evaluation of focal and diffuse pattern on CT by increasing the area under the curve of radiologists[15]. Accuracy of radiologists compared to the reference standard was lower (64%) than the accuracy using a radiomics approach (79%)[15]. In addition, machine learning-based classifiers resulted a satisfactory in differentiating MM lesions from those of tumor metastasis of the spine evaluated on MRI[16]. Radiomics was also on PET/CT in MM to elaborate a prognosis model predicting outcome in transplant-eligible newly diagnosed patients [17]. Finally, radiomics has been used with MRI to correlate features with the clinical and hematological response in multiple myeloma patients undergoing systemic treatment. In detail, one textural feature (GLSZM large area low gray level emphasis), in the study by Ekert *et al*[18] resulted to be correlated also with the bioptic degree of bone marrow infiltration.

## CONCLUSION

Introduction of new quantitative scores and biomarkers to refine diagnosis, to predict MM prognosis, possibly outperforming current staging methods to create new reliable standards for disease prediction and monitoring is an opportunity for further research in MM imaging.

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