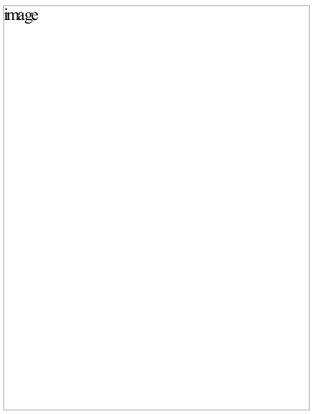

MRD in multiple myeloma: Utility of MRI

Jens Hillengass, Maximilian Merz, Stefan Delorme

PII: S0037-1963(18)30001-5
DOI: https://doi.org/10.1053/j.seminhematol.2018.02.001
Reference: YSHEM50936

To appear in: *Seminars in Hematology*

Cite this article as: Jens Hillengass, Maximilian Merz and Stefan Delorme, MRD in multiple myeloma: Utility of MRI, *Seminars in Hematology,* doi:10.1053/j.seminhematol.2018.02.001

MRD in multiple myeloma: utility of MRI

Author(s): Jens Hillengass MD[1,2], Maximilian Merz MD[2], Stefan Delorme[3]

Authors affiliation:
1) Roswell Park Cancer Institute, Buffalo NY, USA
2) University of Heidelberg, Heidelberg, Germany
3) German Cancer Research Center, Heidelberg, Germany

Corresponding Author: Jens Hillengass, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263

Abstract
The increasing percentage of patients achieving deep responses in multiple myeloma (MM) has led to the need for more sophisticated instruments to measure residual disease as a potential source of relapse. Since minimal residual disease (MRD) assessment is mostly performed on a bone marrow specimen from a certain area of the body, such samples have the limitation that they might not really represent the actual tumor burden, because focal accumulations of malignant cells might be either hit or missed. Magnetic resonance imaging (MRI) is a highly sensitive technique for the assessment of tumor burden and can be performed as whole body protocol, overcoming the problem of sampling error for MRD assessment. Despite its high sensitivity, however, MRI cannot differentiate between vital and necrotic lesions after therapy. Therefore, new fusion and functional techniques are currently under investigation, and image-guided biopsies are performed to combine the strengths of all available methods.

Manuscript
Heterogeneity of bone marrow infiltration in multiple myeloma

Other than one would expect from a systemic hematologic malignancy, multiple myeloma (MM) has been shown not always to infiltrate the bone marrow in a diffuse or homogeneous fashion, but also in a multi-nodular or mixed pattern. While at first diagnosis about 50% of patients in fact show a minimal or diffuse and somewhat homogeneous infiltration, 30% of patients have focal plasma cell accumulations, usually referred to as focal lesions (FL), inside an otherwise normal-appearing bone marrow, and another 20% have a combination of focal lesions and a diffuse infiltration(1) (Figure 1). This heterogeneity of infiltration has several implications, not only for diagnostics but also for treatment monitoring and disease biology. Comparative studies have shown that patients with focal lesions in imaging also tend to have a nodular infiltration pattern in bone marrow histology(2). When myeloma cells from fine needle aspirates from focal lesions were compared with bone marrow samples from the iliac crest, a genetic heterogeneity could be demonstrated. The degree of heterogeneity seems to depend on several factors, one being the size of the focal lesion(3).

For assessing minimal residual disease (MRD) in the bone marrow, the infiltration pattern, a focal one in particular, is important to consider, because bone marrow aspirates for MRD assessment are usually obtained in regions that can be reached with the least harm for the patient - mostly the iliac crest and the sternum. However, the percentage of monoclonal plasma cells in the aspirate can differ significantly if a focal