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Investigating Imaging Techniques in Multiple Myeloma

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Investigating Imaging Techniques: What They Mean for Multiple Myeloma” is sponsored by Amgen. This program is intended for physicians. Here’s your host, Dr. Charles Turck.

Dr. Turck:
Patients with multiple myeloma frequently suffer from myeloma bone disease, or MBD, which can lead to skeletal-related events, bone pain, and hypercalcemia.[1] But several newer imaging techniques have emerged to improve the detection and monitoring of this disease.[2] On today’s program, we’ll dive into what differentiates one technique from another and take a look at how we can put these methods into practice.

This is ReachMD, and I’m Dr. Charles Turck. Joining me to discuss the role of imaging in multiple myeloma is Dr. Jens Hillengass, Professor of Oncology and Internal Medicine and Chief of Myeloma at Roswell Park Comprehensive Cancer Center in Buffalo, NY. Dr. Hillengass, welcome to the program.

Dr. Hillengass:
Thank you so much for having me!

Dr. Turck:
To start us off, can you give us a high-level overview of multiple myeloma?

Dr. Hillengass:
Sure. So, multiple myeloma is a B cell malignancy that’s characterized by the proliferation of abnormal, clonal plasma cells that infiltrate and proliferate primarily in the bone marrow.[3] The myeloma cells overactivate osteoclasts, which can lead to osteolytic lesions resulting in bone pain and fractures.[4] These patients may also develop renal dysfunction, hypercalcemia, anemia, and elevated monoclonal paraproteins.[5] Demographically, this disease accounts for a little more than 10 percent of hematologic malignancies[3] and occurs in all races, with higher rates in African Americans and lower rates in Asian populations.[3]

To understand the pathophysiology of myeloma bone disease, it’s important to start with what happens in normal bone. Normally within this tissue, there’s a coordinated activity of osteoclasts resorbing bone and osteoblasts building bone at the same time and same site, and these two cell types are in a continual balanced activity taking place in the adult skeleton.[6]

In multiple myeloma, the osteoclasts accumulate close to the myeloma cells, increasing bone resorption and suppressing bone formation. These bone lesions are lytic, with no osteoblastic response.[6]

Dr. Turck:
That’s a great overview, Dr. Hillengass, thank you. So, let’s dig a little deeper into this issue of bone resorption and skeletal destruction in untreated multiple myeloma. What can you tell us about this and the risk of skeletal-related events, or SREs, such as radiation to the bone, pathologic fractures, surgery to the bone, and spinal cord compression?[7]

Dr. Hillengass:
So, as mentioned earlier myeloma bone disease is a frequent complication in myeloma with about 80 percent of patients suffering from bone structure abnormalities in conventional x-rays at diagnosis.[3] And over the course of the disease, up to 90 percent of patients develop lytic lesions.[8]

Myeloma bone disease can lead to severe skeletal-related events, such as pathologic fractures spinal cord compression.[7] In fact, about 40 percent of patients actually present with an SRE at diagnosis.[7] And these SREs in turn are associated with disabilities such as kyphosis, bone pain,[9] walking impairment, permanent deformity, and even paralysis,[10] all of which can significantly reduce quality of life.[11,12]

Dr. Turck:
So Dr. Hillengass, let's focus on how we recognize and detect lytic lesions. Can you share some imaging modalities that are currently in use?

Dr. Hillengass:
Yeah, absolutely so there are two main categories of imaging we use in myeloma. The first are the x-ray based imaging modalities which detect lytic bone lesions in multiple myeloma.[13] These include whole-body skeletal surveys and computed tomography, or CT.[13] While in the past, conventional skeletal surveys were the standard of care, these are now obsolete and should be replaced by CT.[2,14]

X-ray scanners are obviously widely available and affordable, and they can detect the skeletal areas that are mainly involved in this disease and lesions that are at risk of fracturing, especially in the long bones. Unfortunately, they have a rather low sensitivity since lytic lesions only become evident on skeletal surveys when about 30 to 50% of the bone has been destroyed.[13,15]

With CT, we achieve a higher sensitivity, which can help in detecting small osteolytic lesions especially in the axial skeleton and to a certain degree even soft tissue masses. We can also estimate the risk of fractures or evaluate the stability of a collapsed vertebrae which makes CT the gold standard among imaging techniques in myeloma.[13] But CT does impose a slightly higher level of radiation exposure for patients than X-rays, and it also has a relatively limited role in assessing response to therapy.[13]

This leads to the other main category of imaging which allows for detection of bone marrow lesions before the actual mineralized bone has been destroyed, and these are magnetic resonance imaging, or MRI, and positron emission tomography combined with computed tomography, or PET/CT. In addition to a high sensitivity for the detection of bone marrow infiltration, functional PET and MRI techniques can evaluate the cellularity and micro-circulation within the bone marrow as well as metabolic tumor activity.[13]

Dr. Turck:
For those just joining us, this is ReachMD. I'm Dr. Charles Turck and today I'm speaking with Dr. Hillengass about current diagnostic imaging modalities available to detect myeloma-induced bone disease.

And continuing on that track, Dr. Hillengass, can you walk us through the strengths and limitations of these two techniques as well, starting with MRIs?

Dr. Hillengass:
Sure. MRI is a highly sensitive imaging method that enables early detection of bone marrow infiltration from multiple myeloma before actually lytic lesions appear on CT. Unlike CT, the visualization of large volumes of bone marrow with MRI doesn't require any radiation exposure.[13] MRI also represents the gold standard technique for detection of spinal cord compression or nerve compression and the presence of soft tissue masses.[2,13]

But MRI also carries a high cost compared to X-rays and prolonged acquisition times upward of 40 to even 60 minutes.[2,13] It's also not a reliable tool for investigating the actual mineralized bone because it relies on the water content of a tissue for image acquisition.[2]

PET/CT combines the functional bone marrow and soft tissue imaging of the PET and the bone imaging with CT to enable detection of hypermetabolic lesions and their exact anatomic location. It's highly sensitive and can distinguish between active and inactive disease. This, in turn, makes PET/CT a great tool to assess response to therapy.[2] But like MRIs, PET/CTs have higher costs than X-rays, and because both PET and CT cause radiation exposure, this needs to be taken into account as well.[13]

Dr. Turck:
Dr. Hillengass, let's return to CT imaging for a moment and consider whole-body low-dose CT, or LDCT, which I understand can identify lesions otherwise negative on whole-body X-rays just like conventional CT, but operates at a lower radiation dose.[13] Can you elaborate on that?

Dr. Hillengass:
Yes. Whole-body low-dose CT, like you said, provides a higher sensitivity for the detection of small osteolytic lesions and more accurately assessing the extent of bone destruction compared to skeletal surveys.[16] It's also faster and much more convenient for the

patient, with an acquisition time of about a minute. And importantly, as its name suggests, low-dose CT exposes patients to less radiation than conventional CT.[1,3] CT should oftentimes be the first choice when assessing patients with bone pain, especially in patients for whom MRI is contraindicated.[2,13]

Dr. Turck:
Before we close, Dr. Hillengass, I'd like to come back to the broader outlook on diagnostic imaging for multiple myeloma and get your thoughts on what we should keep top of mind going forward.

Dr. Hillengass:
So, I think the main concept to take away here is that detection of lesions to the bone and bone marrow is absolutely critical in our assessment of myeloma, especially during screening and at first diagnosis because it often dictates the decision to start treatment. Furthermore, with more patients achieving deeper remission, there is an ongoing need for sensitive imaging techniques that can actually assess patient responses to treatment.[17]

And we covered several imaging methods available today, each with their own strengths and limitations, and several that are complementary. But across them all we're placing a stronger and stronger emphasis on detection sensitivity and how essential this is for identifying painful bone lesions or sites of bone disease that are at risk of fracture.[13]

And while skeletal surveys have previously been considered the gold standard for baseline evaluations of bone disease, that standard has shifted as we adopt more sensitive techniques like CT, MRI, and PET/CT. This is where I think we need to keep pushing ahead to help improve the prognosis for our patients with multiple myeloma.[2,13]

Dr. Turck:
Well, with those forward-thinking priorities in mind, I want to thank my guest, Dr. Jens Hillengass, for helping us better understand the current landscape of diagnostic imaging modalities available to detect myeloma-induced bone disease. Dr. Hillengass, it was great speaking with you today.

Dr. Hillengass:
Thanks so much! It was my pleasure.

Announcer:
This program was sponsored by Amgen. If you missed any part of this discussion, visit reach-m-d-dot-com-slash-industry-feature. This is ReachMD. Be Part of the Knowledge.

References

1. Terpos E, Moulopoulos LA, Dimopoulos MA. Advances in Imaging and the Management of Myeloma Bone Disease. *J Clin Oncol*. 2011; 29: 1907-1915.

2. Zamagni E, Tacchetti P, Cavo M. Imaging in multiple myeloma: How? When?. *Blood*. 2019;133(7):644-651. doi:10.1182/blood-2018-08-825356

3. Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 Patients With Newly Diagnosed Multiple Myeloma. *Mayo Clin Proc*. 2003;78: 21-33.

4. Giuliani N, Colla S, Rizzoli V. New insight in the mechanism of osteoclast activation and formation in multiple myeloma: focus on the receptor activator of NF-kappaB ligand (RANKL). *Exp Hematol*. 2004;32(8):685-691. doi:10.1016/j.exphem.2004.03.015

5. Terpos E, Raje N, Croucher P, Garcia-Sanz R, Leleu X, Pasteiner W, Wang Y, Glennane A, Canon J, Pawlyn C. Denosumab compared with zoledronic acid on PFS in multiple myeloma: exploratory results of an international phase 3 study. *Blood Adv*. 2021; 5(3):725-736.

6. Roodman GD. Mechanisms of Bone Metastasis. *N Engl J Med* 2004; 350: 1655-64.

7. Terpos E, Morgan G, Dimopoulos MA, et al. International Myeloma Working Group Recimmendations for the Treatment of Multiple Myeloma-Related Bone Disease. *J Clin Oncol*. 2013; 31:2347-2357.

8. Dimopoulos M, Terpos E, Comenzo RL, et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques In the diagnosis and monitoring of multiple Myeloma. *Leukemia* 2009; 23, 1545-1556.

9. Ludwig H, Zojer N. Supportive care in multiple myeloma. *Best Practice & Research Clinical Haemotology*. 2007; 4: 817-835.

10. Tosi P. Diagnosis and Treatment of Bone Disease in Muliple Myeloma: Spotline on Spinal Involvement. *Scientifica*. 2013; 1: 104546.

11. Jordan K, Proskorovsky I, Lewis P, et al. Effect of general symptom level, specific adverse events, treatment patterns, and patient characteristics on health-related quality of life in patients with multiple myeloma: results of a European, multicenter cohort study. *Support Care Cancer* (2014) 22: 417-426.

12. Body JJ, Pereira J, Sleeboom H, Maniadakis N, Terpos E, Acklin YP, Finek J, Gunther O, Hechmati G, Mossman T, Costa L, Rogowski W, Nahi H, von Moos R. Health resource utilization associated with skeletal-related events: results from a retrospective European study. *Eur J Health Econ*. 2016;17(6):711-21.

13. Zamagni E, Cavo Michele. The role of imaging techniques in the management of multiple myeloma. *British Journal of Haemotology* 2012;159, 499-513.

14. Hillengass J, Moulopoulos LA, Delorme S, Koutoulidis V, Mosebach J, Hielscher T, Drake M, Rajkumar SV, Oestergaard B, Abildgaard N, Hinge M, Plesner T, Suehara Y, Matsue K, Withofs N, Caers J, Waage A, Goldschmidt H, Dimopoulos MA, Lentzsch S, Durie B, Terpos E. Whole-body computed tomography versus conventional skeletal survey in patients with multiple myeloma: a study of the International Myeloma Working Group. *Blood Cancer* J. 2017;7(8):e599.

15. Pianko MJ, Terpos E, Roodman GD, et al. Whole-body low-dose computed tomography and advanced imaging techniques for multiple myeloma bone disease. *Clin Cancer Res*. 2014;20(23):5888-5897. doi:10.1158/1078-0432.CCR-14-1692

16. Gleeson TG, Moriarty J, Shortt CP, et al. Accuracy of whole-body low dose multidetector CT (WBLDCT) versus skeletal survey in the detection of myelomatous lesions, and correlation of disease distribution with whole-body MRI (WBMRI). *Skeletal Radiol* (2009) 38: 225-236.

17. Hillengass J, Usmani S, Rajkumar SV, Durie BGM, Mateos MV, Lonial S, Joao C, Anderson KC, García-Sanz R, Riva E, Du J, van de Donk N, Berdeja JG, Terpos E, Zamagni E, Kyle RA, San Miguel J, Goldschmidt H, Giralt S, Kumar S, Raje N, Ludwig H, Ocio E, Schots R, Einsele H, Schjesvold F, Chen WM, Abildgaard N, Lipe BC, Dytfeld D, Wirk BM, Drake M, Cavo M, Lahuerta JJ, Lentzsch S. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders. *Lancet Oncol*. 2019;20(6):e302-e312.

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