European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-024-06711-z

EDITORIAL

Artificial intelligence-based application in multiple myeloma

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Multiple myeloma (MM) is a hematological disease characterized by abnormal clonal proliferation of malignant plasma cells in the bone marrow (BM). Approximately, its estimated incidence is around 600,000 new cases per year worldwide, and the median 5-year survival of MM patients is about 82% [1].

MM generally presents with anemia, osteolytic bone lesions, and, to a lesser extent, renal failure. Initial evaluation of patients with multiple myeloma should be performed with laboratory parameters such as hemoglobin, serum creatinine, serum calcium, the monoclonal component (immunoglobulin light chains), and protein electrophoresis by immunofixation [1, 2].

MM tumor burden follows the Durie-Salmon classification [3]; while the Revised International Staging System (R-ISS) [3, 4] considers serum biomarkers, such as β2-microglobulin, albumin, and lactate dehydrogenase in conjunction with malignant cell genomic features (t 4;14; t 14;16).

The treatment of this disease consists of a combination of an injectable proteasome inhibitor (i.e., bortezomib), an immunomodulatory agent (i.e., lenalidomide), and dexamethasone. The standard of care for eligible patients is represented by autologous hematopoietic stem cell transplantation, followed by lenalidomide [5, 6].

Currently, in the diagnosis, prognosis, and management of MM patients, hybrid positron emission tomography (PET) and computed tomography (CT) with 2-deoxy-2-[^{18}F]-fluoro-D-glucose ([^{18}F]-FDG PET/CT) plays an important role [7–10]. The Italian Myeloma Criteria for PET Use (IMPeTUs Criteria), based on the Deauville Criteria, has been proposed to standardize the interpretation of [^{18}F]-FDG PET/CT in patients with MM [11, 12]. The [^{18}F]-FDG PET/CT has a high sensitivity and specificity (80–100%) in detecting the lytic bone lesions in MM patients [7, 8], and its ability to discern between metabolically active and inactive lesions is considered an important tool in evaluating the treatment response, may further stratify MM patients [7, 8].

In this context, artificial intelligence (AI) and radiomics find an important field of application. The quantitative features that go beyond the human threshold, obtained according to specific software and standard features extraction processes, could provide an important diagnostic and prognostic information on the MM, better defining the therapeutic pathway of these patients [13–19].

Actually, we read with a great interest an article by Sachpekidis et al. [13]. In this study, 44 patients with previously untreated MM who underwent whole-body [^{18}F]-FDG PET/CT were analyzed. Automated [^{18}F]-FDG PET/CT segmentation and volumetric semi-quantification were performed in all patients. The bones, liver, and muscles segmentation by a convolutional neuronal network was performed, and according to the AI approach, 10 different SUV thresholds were applied to identify the BM infiltration [13]. In particular, 4 of these thresholds had already been tested in the application of the Al in MM, while the remaining 6 were obtained based on modifications and implementation of the previous existing SUV thresholds [13]. The quantification of whole-body metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were calculated for each patient. In particular, MTV (mL) represents the volume of MM lesions with SUV greater than a predefined threshold, while TLG was obtained as the product of SUV and MTV for the segmented regions (TLG = SUVmean × MTV). Imaging interpretation was made using the IMPeTUs Criteria [11, 12] by two nuclear physicians. BM biopsies were performed within 4 weeks of the [^{18}F]-FDG PET/CT and the infiltration rate of plasma cells in the BM was calculated. Therefore, fluorescence in situ hybridization was performed, and high-risk chromosomal abnormalities, as deletion 17p13 and/or translocation t(4;14) and/or translocation t(14;16) were founded.

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Published online: 08 April 2024

The main result of this article [13] was the significant and positive correlation between quantitative PET/CT parameters, such as MTV, TLG, and BM infiltration with all 10 [^{18}F]-FDG uptake AI thresholds. In terms of overall survival (OS) and progression-free survival (PFS), the univariate and multivariate analyses showed that whole-body higher MTV and TLG were significantly associated with shorter OS and PFS. According to the AI approach, these quantitative volumetric PET/CT parameters have been an important tool to predict the MM patient outcome [13, 14]. Moreover, the IMPeTUs Criteria application showed that the number of focal BM uptake lesions, extramedullary disease, and the presence of cytogenetic abnormalities had an adverse effect on PFS.

Mannam et al. [14] evaluated 40 patients with MM and lytic skeletal metastases that underwent a [^{18}F]-FDG PET/CT. The aim of this study was to evaluate the diagnostic performance of PET and CT radiomic features to differentiate bone metastases from multiple myeloma lesions. A total of 138 PET and 138 CT radiomic features by manual semi-automatic segmentation were extracted. The first- and second- order CT and PET texture radiomic features contributed to differentiating the bone metastases from multiple myeloma lesions. The machine learning models using the CT parameters were found to be better at differentiating these two bone pathological conditions compared to the models using only the PET parameters. However, the combined approach between the PET and CT machine learning models showed better overall performance than the CT and PET models used alone [14].

These interesting articles [13, 14] highlight the importance of prognostic and diagnostic information from the combined approach between automated and volumetric quantitative PET/CT parameters and AI/radiomic features extraction. AI has the potential to develop the machine learning models that predict many tumor features, such as intratumoral heterogeneity, complement and substantiate invasive tissue, and lay the foundations for personalized and robust methods that are not affected by manual or operator-dependent interventions, in order to optimize the medical resources for these oncological patients [13, 14].

Declarations

Ethical approval Institutional Review Board approval was not required because the paper is an editorial.

Informed consent Not applicable.

Conflict of interest The authors declare no competing interests.

References

1. Cowan AJ, Green DJ, Kwok M, Lee S, Coffey DG, Holmberg LA, et al. Diagnosis and management of multiple myeloma: a review. JAMA. 2022;327(5):464–77. https://doi.org/10.1001/jama.2022.0003.
2. Caers J, Garderet L, Kortüm KM, O'Dwyer ME, van de Donk NWCJ, Binder M, et al. European myeloma network recommendations on tools for the diagnosis and monitoring of multiple myeloma: what to use and when. Haematologica. 2018;103(11):1772–84. https://doi.org/10.3324/haematol.2018.189159.
3. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, Bladé J, et al. International staging system for multiple myeloma. J Clin Oncol. 2005;23(15):3412–20. https://doi.org/10.1200/JCO.2005.04.242.
4. D'Agostino M, Cairns DA, Lahuerta JJ, Wester R, Bertsch U, Waage A, et al. Second revision of the international staging system (R2-ISS) for overall survival in multiple myeloma: a European myeloma network (EMN) report within the HARMONY project. J Clin Oncol. 2022;40(29):3406–18. https://doi.org/10.1200/JCO.21.02614.
5. Pawlyn C, Davies FE. Toward personalized treatment in multiple myeloma based on molecular characteristics. Blood. 2019;133(7):660–75. https://doi.org/10.1182/blood-2018-09-825331.
6. Boussi LS, Avigan ZM, Rosenblatt J. Immunotherapy for the treatment of multiple myeloma. Front Immunol. 2022;28(13):1027385. https://doi.org/10.3389/fimmu.2022.1027385.
7. Cavo M, Terpos E, Nanni C, Moreau P, Lentzsch S, Zweegman S, et al. Role of ^{18}F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group. Lancet Oncol. 2017;18(4):e206–17. https://doi.org/10.1016/S1470-2045(17)30189-4.
8. Zanoni L, Mattana F, Calabrò D, Paccagnella A, Broccoli A, Nanni C, Fanti S. Overview and recent advances in PET/CT imaging in lymphoma and multiple myeloma. Eur J Radiol. 2021;141:109793. https://doi.org/10.1016/j.ejrad.2021.109793.
9. Klain M, Maurea S, Gaudieri V, Zampella E, Volpe F, Manganelli M, et al. The diagnostic role of total-body 18F-FDG PET/CT in patients with multiple tumors: a report of the association of thyroid cancer with lung or renal tumors. Quant Imaging Med Surg. 2021;11(9):4211–5. https://doi.org/10.21037/qims-21-36.
10. Ponsiglione A, Nappi C, Volpe F, Klain M. Expanding the long-axial field-of-view PET-CT horizons: unveiling new arrows in our quiver. Eur J Nucl Med Mol Imaging. 2024. https://doi.org/10.1007/s00259-024-06665-2.
11. Zamagni E, Nanni C, Dozza L, Carlier T, Bailly C, Tacchetti P, et al. Standardization of ^{18}F-FDG-PET/CT according to Deauville criteria for metabolic complete response definition in newly diagnosed multiple myeloma. J Clin Oncol. 2021;39(2):116–25. https://doi.org/10.1200/JCO.20.00386.
12. Nanni C, Versari A, Chauvie S, Bertone E, Bianchi A, Rensi M, et al. Interpretation criteria for FDG PET/CT in multiple myeloma (IMPeTUs): final results. IMPeTUs (Italian myeloma criteria for PET USe). Eur J Nucl Med Mol Imaging. 2018;45(5):712–719. https://doi.org/10.1007/s00259-017-3909-8.
13. Sachpekidis C, Enqvist O, Ulén J, Kopp-Schneider A, Pan L, Jauch A, et al. Application of an artificial intelligence-based tool in [^{18}F]FDG PET/CT for the assessment of bone marrow involvement in multiple myeloma. Eur J Nucl Med Mol Imaging. 2023;50(12):3697–708. https://doi.org/10.1007/s00259-023-06339-5.
14. Mannam P, Murali A, Gokulakrishnan P, Venkatachalapathy E, Venkata Sai PM. Radiomic analysis of positron-emission

tomography and computed tomography images to differentiate between multiple myeloma and skeletal metastases. Indian J Nucl Med. 2022;37(3):217–226. https://doi.org/10.4103/ijnm.ijnm_111_21.
15. Tagliafico AS, Dominietto A, Belgioia L, Campi C, Schenone D, Piana M. Quantitative imaging and radiomics in multiple myeloma: a potential opportunity? Medicina (Kaunas). 2021;57(2):94. https://doi.org/10.3390/medicina57020094.
16. Piscopo L, Zampella E, Klain M. [18F]FET PET/MR and machine learning in the evaluation of glioma. Eur J Nucl Med Mol Imaging. 2024;51(3):797–9. https://doi.org/10.1007/s00259-023-06505-9.
17. Stanzione A, Cuocolo R, Bombace C, Pesce I, Mainolfi CG, De Giorgi M, et al. Prediction of 2-[18F]FDG PET-CT SUVmax for adrenal mass characterization: a CT radiomics feasibility study. Cancers (Basel). 2023;15(13):3439. https://doi.org/10.3390/cancers15133439.
18. Fanni SC, Greco G, Rossi S, Aghakhanyan G, Masala S, Scaglione M, et al. Role of artificial intelligence in oncologic emergencies: a narrative review. Explor Target Antitumor Ther. 2023;4(2):344–54. https://doi.org/10.37349/etat.2023.00138.
19. Gabelloni M, Faggioni L, Fusco R, Simonetti I, De Muzio F, Giacobbe G, et al. Radiomics in lung metastases: a systematic review. J Pers Med. 2023;13(2):225. https://doi.org/10.3390/jpm13020225.