# Voxel-Based Transient Alterations in Brain Glucose Metabolism After High-Dose Melphalan Conditioning in Multiple Myeloma: A Longitudinal FDG-PET Study

**Ahmed Msherghi1,** Franklin Wong1, Guofan Xu1, Osama Mawliawi1, Max Wintermark1

**Presenting Author Affiliation : MD Anderson Cancer Center, Houston, TX, USA. Email: AAMsherghi@mdanderson.org**

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

## Background

High dose melphalan conditioning chemotherapy used in multiple myeloma is commonly associated with cognitive and neuropsychiatric symptoms (1, 2). However, the underlying brain changes remain poorly understood. Previous reports published in the Journal of Nuclear Medicine and the Journal of Clinical Oncology have demonstrated spatial and temporal associations between chemotherapy-related cognitive impairment and post-chemotherapy hematologic malignancy patients, including those with leukemia; however, these studies provided only cross-sectional snapshots, did not include longitudinal follow-up of the same patients, lacked correlation with detailed clinical data, and did not stratify findings by chemotherapy type or dose (3, 4). In contrast, the present study investigates longitudinal changes in cerebral glucose metabolism following high-dose melphalan and examines their association with patient-reported symptoms.

## Methods

We conducted a retrospective longitudinal analysis of paired pre- and post-treatment [$^{18}$F]FDG-PET/CT scans from 37 patients with multiple myeloma treated with high-dose melphalan. Voxel-based analyses were performed to assess metabolic changes across three post-treatment time points: within 6 months, between 6 and 15 months, and beyond 15 months after chemotherapy. In a subset of nine patients, metabolic findings were correlated with symptom severity using the Edmonton Symptom Assessment System (ESAS) (5).

## Results

Within the first 6 months after treatment, patients demonstrated a reproducible pattern of increased glucose metabolism predominantly involving frontoparietal regions, including the angular gyrus, anterior orbital gyrus, and several right frontal cortical areas ($p < 0.05$).

## Results

These metabolic increases were associated with worsening fatigue, anxiety, sleep disturbance, and pain scores on ESAS, whereas patients without detectable metabolic changes showed stable symptom profiles. At intermediate follow-up (6–15 months), no persistent metabolic abnormalities were observed in the melphalan cohort. By late follow-up (>15 months), cerebral metabolism had fully normalized in all evaluated regions.

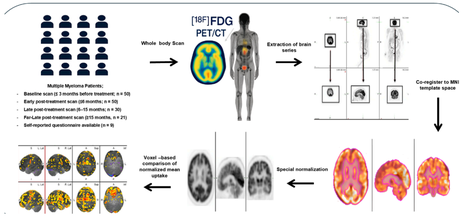
## Conclusion

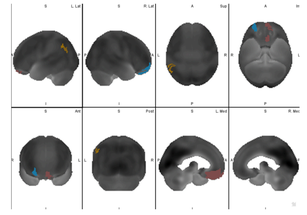
Conclusion: High dose melphalan induces transient, region-specific increases in frontoparietal brain metabolism that parallel the early neuropsychiatric symptom burden experienced by multiple myeloma patients. These metabolic changes resolve over time, suggesting a reversible process rather than permanent neurotoxicity. FDG-PET/CT may serve as a valuable imaging biomarker for detecting and monitoring melphalan-related neuropsychiatric effects.'

## References

1. Moreau P, Attal M, Facon T. Frontline therapy of multiple myeloma. Blood. 2015;125(20):3076-84.
2. Giralt S, Garderet L, Durie B, Cook G, Gahrton G, Bruno B, et al. American Society of Blood and Marrow Transplantation, European Society of Blood and Marrow Transplantation, Blood and Marrow Transplant Clinical Trials Network, and International Myeloma Working Group Consensus Conference on Salvage Hematopoietic Cell Transplantation in Patients with Relapsed Multiple Myeloma. Biol Blood Marrow Transplant. 2015;21(12):2039-51.
3. Msherghi A, Salim HA, Wong FC, Xu G, Mawlawi OF, Elhadi M, et al. Chemotherapy-induced modulation of brain glucose metabolism in leukemia patients: A retrospective comparative study. Journal of Clinical Oncology. 2025;43(16_suppl):e18572-e.
4. Msherghi A, Wong F, Xu G, Mawlawi O, Elhadi M, Alsharedi M, et al. (18)F-FDG PET Reveals Voxel-Based Decreases in Brain Glucose Uptake After Chemotherapy in Leukemia Patients: A Retrospective Matched-Control Study. J Nucl Med. 2025.
5. Hui D, Bruera E. The Edmonton Symptom Assessment System 25 Years Later: Past, Present, and Future Developments. J Pain Symptom Manage. 2017;53(3):630-43.

No conflict of interest to declare.



***Caption:*** Comparison of patients less than six months post-chemotherapy in the melphalan group with decreased metabolism in the right anterior orbital gyrus in blue, increased metabolism in the left inferomedial orbital gyrus in brown, and in the orbital gyrus in sandy brown.