Bone marrow patient-specific dosimetry for (177Lu)Lu-DOTA-TATE therapy in patients with and without bone metastases: methodology and absorbed dose effect correlation

Susana Veloza-Awad*[1,2,3], José A Fragoso-Negrín[1,2,4], Vignikin Aristida Adjalla[1,2], Kevin Hébert[2], Emmanuel Deshayes[1,2], Jean-Pierre Pouget[1], Pierre-Olivier Kotzki[2], Stephan G Nekolla[3,5], Manuel Bardiès*†[1,2], and Lore Santoro‡[1,2]

[1]Institut de Recherche en Cancérologie de Montpellier – CRLCC Val d'Aurelle - Paul Lamarque, Institut National de la Santé et de la Recherche Médicale, Université de Montpellier – France

[2]Institut régional de Cancérologie de Montpellier – Unicancer – France

[3]Technische Universität Munchen - Technical University Munich - Université Technique de Munich – Allemagne

[4]DOSIsoft – DOSIsoft – France

[5]Nuklearmedizinische Klinik und Poliklinik (MRI), Technische Universität Munchen - Université Technique de Munich – Allemagne

Résumé

Introduction: Peptide receptor radionuclide therapy (PRRT) with (177Lu)Lu-DOTA-TATE is used to treat patients with neuroendocrine tumors (NET) (Singh et al. 2024). Bone marrow (BM) is located in trabecular bone cavities; it is radiosensitive and can be affected by both disease and treatment, which makes it an absorbed dose-limiting organ (Wahl et al. 2021).
BM dosimetry can be performed based on different methodological approaches: blood-based, model-based with image-based activity determination, and fully patient-specific (image-based activity and absorbed dose determination). The latter is still an area of research (Hagmarker et al. 2019; Blakkisrud et al.2024; Hebert et al. 2024).

This study assesses the impact of segmentation approaches as well as the influence of bone metastases on absorbed dose (AD), and the influence of AD on clinical effect.

Material and Methods: This study included 28 patients (29 dosimetric studies) with NETs treated with (177Lu)Lu-DOTA-TATE between 2016–2023 (4 cycles × 7.4 GBq). SPECT/CT images were acquired at 4, 24, 72, and 192 h post-injection in cycles 1–2, and at 24 h in cycles 3–4, using GE Discovery NM/CT 670 (Hebert et al. 2024). The reconstruction used OSEM with attenuation, scatter, and resolution recovery corrections.

*Intervenant

†Auteur correspondant: manuel.bardies@inserm.fr

‡Auteur correspondant: Lore.Santoro@icm.unicancer.fr

(1) For all patients, each vertebra was initially classified as healthy or metastatic based on the assessment of a nuclear medicine physician. Absorbed dose (AD) was then analyzed independently for each visible vertebra in the field of view to distinguish metastatic from healthy bone marrow. Correlations were studied between (a) the number of vertebral metastases and AD to healthy bone marrow, (b) AD to healthy bone marrow, and variations in hematological parameters.

(2) Patients were grouped into: (1) no bone metastases, (2) bone metastases outside vertebral bodies, and (3) metastases in lumbar/thoracic vertebral bodies. AD was compared as follows:

cohort 1, across four VOIs : L2–L4, lumbar, thoracic, and all visible vertebrae

cohort 2, across four VOIs : L2–L4, lumbar, thoracic, and all visible vertebrae

cohort 3, across two VOIs: (unaffected) L2-L4, and all visible vertebrae.

The study was approved by the local ethics board (ICM-ART 2025/12).

Fully patient specific dosimetry was performed with OpenDose3D.

Statistical analysis considered $p \leq 0.05$ as significant, with $r \geq 0.7$ indicating strong and $r \geq 0.5$ moderate correlation.

Results: Patients without bone lesions had all individual vertebral marrow ADs below 0.6 Gy. Vertebrae with fully contained metastases showed ADs $>$ 1.6 Gy, with some exceeding 8 Gy.

A significant positive correlation ($r = 0.7$) was found between the number of vertebral metastases and the AD to healthy BM.

A moderate negative correlation ($r = -0.5$) was observed between AD to healthy BM and lymphocyte variation.

In cohort 1, mean ADs across all VOIs were similar (0.25–0.28 Gy).

In cohort 2, higher mean ADs (0.4-0.44 Gy) were found across the same VOIs.

In cohort 3, mean ADs across two VOIs were (0.54–0.55 Gy).

Within each cohort, No significant differences were found between ADs across VOIs.

A progressive increase in mean absorbed dose was observed from cohort 1 to cohort 3

Conclusions: This study supports the value of fully patient-based BM dosimetry, particularly in patients with bone metastases. Our results show that personalized dosimetry enhances understanding of treatment response and may help guide therapy planning. The observed absorbed dose-effect correlations underscore the potential of integrating BM dosimetry into clinical workflows.

References:

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Mots-Clés: Bone marrow, dosimetry, (177Lu)LuDOTATATE therapy, Peptide receptor radionuclide therapy, personalized dosimetry