

## LETTER TO THE EDITOR

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# Response to letter: 'why so many doses, and why now?'

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Dear Editor,

We appreciate the thoughtful comments from Drs Bilgiç and Akovalı (1) regarding our recently published case report (2) and are grateful for the opportunity to respond to their letter.

Our primary intention of publishing this case was to raise awareness about the long-term, potentially life-threatening complications of radioactive iodine therapy in very young children with extensive pulmonary metastases. The case was identified and retrospectively enrolled in the German Malignant Endocrine Tumors (GPOH-MET) Registry to support broader efforts toward data-driven improvements in pediatric thyroid cancer care. It is important to note that our team was not involved in the treatment or clinical management of the patient described. We believe that cases such as this one, discussed in the context of current developments, can help to question and re-evaluate old and yet possibly still established treatment patterns and strengthen the visibility of contemporary approaches.

We fully agree that the cumulative number of RAI treatments and the relatively short intervals between them in this case likely contributed to the development of fatal lung fibrosis. Indeed, this tragic outcome underscores the critical importance of individualized (dosimetry-guided) RAI therapy and the necessity of allowing sufficient time between therapies for potential tissue recovery and to correctly assess the result achieved – principles, which are now better established and more widely implemented than they were at the time of this patient's treatment.

### Regarding the specific questions:

(i) On continued RAI despite biochemical response: the retrospective nature of our case review limits our ability to reconstruct the clinical decision-making in full detail. While thyroglobulin levels decreased, it remains unclear how much weight was given at the time to (interpreted persistent) imaging findings or perceived clinical progression. Current evidence, as the authors rightly mention, supports more conservative approaches, particularly in light of evolving insights into thyroglobulin kinetics and spontaneous disease regression. We learned from publications such as those by Biko et al. (3) persistent spontaneous decreases thyroglobulin and clinically stable partial remissions have been observed after repeated RAI therapy, despite the initially incomplete remission, leading to the conclusion that the administration of further courses of RAI therapy should be handled restrictively. Colleagues were able to show a decline of thyroglobulin levels of about 35% in all patients, although all last post-therapy 131 scans were positive, and follow-up CT scans showed no progression (3).

(ii) On the role of modern imaging and dosimetry: we concur wholeheartedly. The advances in diagnostic imaging, treatment planning, and dosimetric approaches over the past two decades have profoundly changed pediatric DTC management. We referenced these advancements specifically to underscore how this case would likely be managed differently today. This is also the rationale behind the establishment of our national pediatric reference center for nuclear medicine, i.e. RAI therapy, which aims to harmonize and modernize care, reduce unnecessary radiation exposure, and hopefully prevent poor or even fatal outcomes in the future.



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In conclusion, we thank Drs Bilgiç and Akovalı for their constructive remarks, which highlight critical lessons from past experience and affirm the shared goal of safer, evidence-based care for children with DTC.

#### **Declaration of interest**

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work reported.

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## References

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- 2 Kuhlen M, Kunstreich M, Eilsberger F, et al. Pediatric differentiated thyroid carcinoma leading to fatal lung fibrosis. Eur Thyroid J 2025 14 e240341. (https://doi.org/10.1530/ETJ-24-0341)
- 3 Biko J, Reiners C, Kreissl MC, et al. Favourable course of disease after incomplete remission on (131)I therapy in children with pulmonary metastases of papillary thyroid carcinoma: 10 years follow-up. Eur J Nucl Med Mol Imaging 2011 38 651–655. (https://doi.org/10.1007/s00259-010-1669-9)