

## The influence of biologically effective dose (BED) on the <sup>131</sup>I therapy response in patients with benign thyroid disease – nonlinear mixed effect modelling approach

January 10, 2021

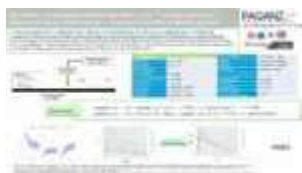
**Authors** Valentina Topić Vučenović (1,2), Zvezdana Rajkovača (3), Dijana Jelić (4), Dragi Stanimirović (3), Momir Mikov (5), Branislava Miljković (2), Katarina Vučićević (2)

**Affiliations** 1. Department of Pharmacy, Faculty of Medicine, University of Banja Luka, Bosnia and Herzegovina; 2. Department of Pharmacokinetics and Clinical Pharmacy, University of Belgrade - Faculty of Pharmacy, Republic of Serbia; 3. Institute of Nuclear Medicine and Thyroid Gland Disease, University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina; 4. Chemistry Department, Faculty of Natural Sciences and Mathematics, University of Banja Luka, Bosnia and Herzegovina; 5. Department of Pharmacology, Toxicology and Clinical Pharmacology, University of Novi Sad – Faculty of Medicine, Republic of Serbia.

**Presentation type** Poster

**Presenters** Valentina Topić Vučenović and/or Katarina Vučićević

### 📎 Attachments



**Aim.** The purpose of the study was to explore the influence of biologically effective dose (BED [Gy]), the administered radioactivity dose (Aa [MBq]), the total absorbed dose (ABD [Gy]), the maximum of absorbed dose-rate (MXR [Gy/h]) to radioactive iodine (<sup>131</sup>I) on the response in patients with benign thyroid disease.

**Materials and methods.** Data from adult patients with benign thyroid disease who had previously received a test dose of <sup>131</sup>I activity were included in the analysis. Individual thyroid exposure parameters were estimated from the population biokinetic <sup>131</sup>I model and the therapeutic activity doses (in range from 185 to 1300 MBq). Patients response was followed up at periodic intervals, starting from 4-6 weeks, up to one year after the administration of <sup>131</sup>I. A successful clinical outcome

was resolution of of hyperthyroidism. A population exposure-response analysis was performed using nonlinear mixed-effects modelling using NONMEM<sup>®</sup> (v. 7.4). The response data was modelled as ordered categorical with three levels (hyper-, eu- and hypothyroidism). The performance of the final model was evaluated using visual predictive check (VPC).

**Results.** In total 95 adult patients were analyzed, including 57 (60%) with Graves' disease, 22 (23.2%) with toxic multinodular goiter and 16 (16.8%) with toxic adenoma. The probability of the outcome was best described by a proportional-odds model, including the log-linear model of <sup>131</sup>I effect and the exponential model of the response-time relationship. Among all tested exposure measures, BED was included in the final model. Its inclusion in the base model was statistically significant ( $p < 0.001$ ). The value of 289.7 Gy was associated with 80% probability of successful treatment outcome one year after <sup>131</sup>I application in patients with median thyroid volume of 32.28 mL.

**Conclusion.** The results indicate that using BED formalism could lead to a better individualisation of the therapy. The larger thyroid volume is associated with a lower probability of a successful outcome.

## References.

1. Topic Vucenovic V, Rajkovaca Z, Jelic D, Stanimirovic D, Vuleta G, Miljkovic B, Vucicevic K. Investigation of factors influencing radioiodine ((<sup>131</sup>I)) biokinetics in patients with benign thyroid disease using nonlinear mixed effects approach. *Eur J Clin Pharmacol.* 2018;74(8):1037-1045.
2. European Commission. Council Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation, and repealing Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122 /Euratom (2014). *Official Journal of the European Union L13/2014* 57:1-73.  
doi:10.3000/19770677.L\_2014.013.eng
3. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid* 2016;26(10):1343-1421.



**Katarina Vucicevic**

Faculty of Pharmacy-University  
of Belgrade

[View all abstracts by Katarina Vucicevic →](#)

📅 2021

< External evaluation of population pharmacokinetic models of tacrolimus in adult heart transplant recipients

Determination of the pharmacodynamics of vancomycin in young infants via time-to-event analysis >

Login