

**Results:**

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**Title:**

Optimizing <sup>131</sup>I Uptake After rhTSH Stimulation in Patients with Nontoxic Multinodular Goiter: Evidence from a Prospective, Randomized, Double-Blind Study

**Authors:**

Søren Fast, Viveque Egsgaard Nielsen, Peter Grupe, Steen Joop Bonnema and Laszlo Hegedüs

**Abstract:**

Prestimulation with recombinant human thyroid-stimulating hormone (rhTSH) augments radioiodine (<sup>131</sup>I) therapy for benign nontoxic multinodular goiter. The purpose of this study was to determine the optimal time interval between rhTSH and (<sup>131</sup>I) administration to enhance thyroid radioactive iodine uptake (RAIU).

**Methods:** Patients were randomized, in a 2-factorial design, to receive either a 0.1-mg dose of rhTSH (n = 60) or placebo (n = 30) and to a time interval of 24, 48, or 72 h before (<sup>131</sup>I) administration. The rhTSH- or placebo-stimulated RAIU study was performed at 4 wk after a baseline RAIU assessment in a tertiary referral center at a university hospital. A total of 90 patients (78 women; median age, 52 y; range, 22-83 y) referred to (<sup>131</sup>I) therapy for symptomatic nontoxic goiter (median goiter volume, 63 mL; range, 25-464 mL) were included in the study. Change in thyroid RAIU was determined at 24 and 96 h after (<sup>131</sup>I) tracer administration.

**Results:** In the placebo subgroups, RAIU did not change significantly from baseline. The mean (+/- SE) 24-h RAIU increased from 33.8% +/- 2.3% to 66.0% +/- 1.8% (111.2% increase) with a 24-h interval, from 36.8% +/- 2.1% to 64.6% +/- 2.7% (83.3% increase) with a 48-h interval, and from 33.0% +/- 2.7% to 49.6% +/- 2.5% (62.4% increase) with a 72-h interval. All within-group changes were highly significant (P < 0.001). The effect was negatively correlated with initial RAIU (r = -0.703, P < 0.001). The increase in 24- and 96-h RAIU was significantly higher in the rhTSH/24-h group than it was in the rhTSH/72-h group (P = 0.023 and 0.012, respectively) and insignificantly higher than in the rhTSH/48-h group (P = 0.37 and 0.26, respectively).

**Conclusion:** The effect of rhTSH on thyroid RAIU is most pronounced when administered 24 h before (<sup>131</sup>I) administration and declines with longer time intervals. Whether there is a similar time dependency for goiter reduction after rhTSH-stimulated (<sup>131</sup>I)-therapy remains to be clarified.

**Results:**

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**Title:**

Recombinant Human Thyrotropin-Stimulated Radioiodine Therapy of Nodular Goiter Allows Major Reduction of the Radiation Burden with Retained Efficacy

**Authors:**

Søren Fast, Laszlo Hegedüs, Peter Grupe, Viveque Egsgaard Nielsen, Christa Bluhme, Lars Bastholt, Steen Joop Bonnema

**Abstract:**

**Context and objective:** Stimulation with recombinant human TSH (rhTSH) before radioiodine (<sup>131</sup>I) therapy augments goiter volume reduction (GVR). Observations indicate that rhTSH has a preconditioning effect beyond increasing thyroid (<sup>131</sup>I) uptake. We test the hypothesis that an equivalent GVR might be obtained by an absorbed thyroid dose well below what has been used previously.

**Patients and design:** In a double-blinded setup, 90 patients (78 women; median age, 52 yr; range, 22-83) with a nontoxic nodular goiter (median size, 63 ml; range, 25-379 ml) were randomized to either 0.1 mg rhTSH (n=60) followed by a thyroid dose of 50 Gy or placebo followed by 100 Gy (n=30).

**Results:** At 12 months, the mean relative GVR in the placebo and the rhTSH group was identical (35±3%; P=0.81). The median administered <sup>131</sup>I-activity was 170 MBq (45-1269) in the rhTSH group and 559 MBq (245-3530) in the placebo group (70% reduction, P<0.0001). According to the official radiation regulation, hospitalization was required in 14 patients in the placebo group vs. one patient in the rhTSH group (P<0.0001). In both groups, goiter-related symptoms were effectively relieved in the majority of patients. The prevalence of myxedema (10%) did not differ among groups.

**Conclusions:** This is the first study to demonstrate that rhTSH not only increases the thyroid <sup>131</sup>I uptake, but per se potentiates the effect of <sup>131</sup>I-therapy, allowing a major reduction of the <sup>131</sup>I-activity without compromising efficacy. This approach is attractive in terms of minimizing posttherapeutic restrictions and in reducing the potential risk of radiation-induced malignancy.