

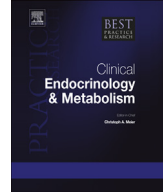


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# The role of radioiodine therapy in benign nodular goitre



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For treatment of benign nodular goitre the choice usually stands between surgery and <sup>131</sup>I therapy. <sup>131</sup>I therapy, used for 30 years for this condition, leads to a goitre volume reduction of 35–50% within 1–2 years. However, this treatment has limited efficacy if the thyroid <sup>131</sup>I uptake is low or if the goitre is large. Recombinant human TSH (rhTSH)-stimulated <sup>131</sup>I therapy significantly improves goitre reduction, as compared with conventional <sup>131</sup>I therapy without pre-stimulation, and adverse effects are few with rhTSH doses of 0.1 mg or lower. RhTSH-stimulated <sup>131</sup>I therapy reduces the need for additional therapy due to insufficient goitre reduction, but the price is a higher rate of hypothyroidism. Another approach with rhTSH-stimulation is to reduce the administered <sup>131</sup>I activity by a factor that equals the increase in the thyroid <sup>131</sup>I uptake. Using this approach, radiation exposure is considerably reduced while the goitre reduction is similar to that obtained with conventional <sup>131</sup>I therapy.

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## Introduction

<sup>131</sup>I therapy results not only in cure of hyperthyroidism but also in reduction of the thyroid volume. It has been used for treatment of Graves' disease since the 1940s, whereas its use for treatment of benign non-toxic nodular goitre (NTNG) was introduced 30 years ago [1]. In some European countries

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$^{131}\text{I}$  therapy is now a therapeutic option in line with thyroidectomy [2], and its use is supported by current guidelines [3,4]. For many years, treatment of NTNG was confined to either thyroid hormone suppressive therapy or thyroidectomy, but the former treatment is discouraged because of its poor efficacy and potential side effects, such as causing subclinical hyperthyroidism and osteoporosis [5]. In fact, many patients with goitre are ineligible for thyroid hormone suppressive therapy at the time of diagnosis due to presence of autonomously functioning thyroid nodules, reflected by suppressed or low-normal serum TSH levels [6]. The inferiority of thyroid hormone suppressive therapy is supported by a randomized trial, in which this treatment did not lead to any significant goitre shrinkage, in contrast to the effect of  $^{131}\text{I}$  therapy [7].

Here we review important clinical aspects of  $^{131}\text{I}$  therapy of patients with benign nodular goitre. The non-toxic and the toxic nodular goitre are regarded as the same disease – but at different evolutionary stages – and the two conditions will therefore be discussed in concert. We pay particular attention to recombinant human TSH (rhTSH)-stimulated  $^{131}\text{I}$  therapy, which is a relatively novel treatment modality with clear benefits compared to conventional  $^{131}\text{I}$  therapy (i.e.  $^{131}\text{I}$  therapy without rhTSH stimulation).

### Indication for goitre therapy

Many patients with goitre have no or only few symptoms [8,9]. When malignancy has been ruled out by fine needle biopsy of any suspicious thyroid nodules, many patients are better off without treatment, unless the goitre is very large [10]. There is a poor correlation between goitre size and symptoms [11], and no thyroid volume threshold can be given, above which intervention is absolutely indicated. Typical physical goitre symptoms are sensation of globulus and/or neck compression, dyspnoea, and cough. Since unspecific neck discomfort is common, also among patients without thyroid diseases, it may be difficult to settle whether neck or respiratory symptoms can be attributed to the goitre, or whether this is merely a coincidental finding. In this respect, thyroid ultrasonography, performed by the clinician, is helpful. Cosmetic complaints and fear of cancer are features of NTNG that also deserve attention. Finally, a range of other factors, such as age, comorbidity, previous neck surgery, and co-existing hyperthyroidism, must be taken into account.

Several options exist once decision to treat has been made.  $^{131}\text{I}$  therapy is often treatment of choice in patients with a solitary autonomous (and scintigraphically hot/warm) nodule. This applies also to patients with overt toxic multinodular goitre, unless the goitre is very large and compresses other neck structures. In elderly hyperthyroid individuals, without any goitre symptoms, life-long anti-thyroid drug treatment may be a legitimate choice, but such an approach will most likely not hinder continuous goitre growth.

### Surgery or $^{131}\text{I}$ therapy?

In the majority of patients referred for nodular goitre both thyroid lobes are involved and enlarged. If the diagnosis is confirmed the primary goal is to reduce the thyroid volume, with surgery and  $^{131}\text{I}$  therapy being the options. Besides the previously mentioned factors, the final decision between these two treatments may depend on the local expertise, experience, radiation regulations, and of course the preference of the patient. Patient satisfaction, risk of hypothyroidism and goitre recurrence, and the fear of overlooking a thyroid cancer are all important issues which should be taken into account. In our experience the majority of patients prefer non-surgical treatment, if offered. Thyroid surgery has the uncontested advantage of complete and rapid removal of the goitre, and it allows a thorough histological examination of the thyroid gland. There are certain situations, listed in Table 1, that favour operation. It should be emphasized that no randomized trial has compared surgery with  $^{131}\text{I}$  therapy of NTNG, and no study has evaluated the health related quality of life using a disease-specific questionnaire [12].

### Preparing the patient for $^{131}\text{I}$ therapy

$^{131}\text{I}$  therapy may be cost-effective, when compared with surgery [13].  $^{131}\text{I}$  is usually contained in a capsule which is administered orally. Most often the entire dose is given at one occasion. Differences in

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