Further Investigation on High-intensity Focused Ultrasound (HIFU) Treatment for Thyroid Nodules: Effectiveness Related to Baseline Volumes

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Rationale and Objectives: Several minimally invasive thermal techniques have been developed for the treatment of benign thyroid nodules. A new technique for this indication is high-intensity focused ultrasound (HIFU). The aim of this study was to assess effectiveness in varying preablative nodule volumes and whether outcome patterns that were reported during studies with other thermal ablative procedures for thyroid nodule ablation would also apply to HIFU.

Materials and Methods: Over the last 2 years, 19 nodules in 15 patients (12 women) whose average age was 58.7 years (36–80) were treated with HIFU in an ambulatory setting. Patients with more than one nodule were treated in multiple sessions on the same day. The mean nodule volume was 2.56 mL (range 0.13–7.67 mL). The therapeutic ultrasound probe (Echopulse THC900888-H) used in this series functions with a frequency of 3 MHz, reaching temperatures of approximately 80°C–90°C and delivering an energy ranging from 87.6 to 320.3 J per sonication. To assess the effectiveness of thermal ablation, nodular volume was measured at baseline and at 3-month follow-up. The end point of the study was the volume reduction assessment after 3 months' follow-up. Therapeutic success was defined as volume reduction of more than 50% compared to baseline. This study was retrospectively analyzed using the Wilcoxon signed rank test and Kendall tau.

Results: The median percentage volume reduction of all 19 nodules after 3 months was 58%. An inverse correlation between preablative nodular volume and percentage volume shrinking was found (tau = −0.46, $P < .05$). Therapeutic success was achieved in 10 out of 19 patients (53%).

Conclusions: HIFU of benign thyroid nodules can be carried out as an alternative therapy for nodules ≤3 mL if patients are refusing surgery or radioiodine therapy.

Key Words: HIFU; thyroid nodule; ultrasound; thermal ablation.

INTRODUCTION

Despite its small size, the thyroid gland receives great medical attention. To our current knowledge, variability multitude of pathologies are present in the gland itself, that is, thyroid cancer, hormone balance complaints, Graves disease, Hashimoto disease, nodular goiter, iodine deficiency goiter, and thyroid nodules. The last mentioned are divided into benign, malignant, hypofunctional, and hyperfunctional nodules and can be diagnosed quite precisely with modern equipment (1). Benign thyroid nodules are showing a wide prevalence, and the standard therapy options for collateral symptoms are surgery—most frequently hemithyroidectomy and thyroidectomy—or radioiodine therapy (2–9). Both therapies have their advantages but hold several drawbacks. The most common are life-lasting hypothyreosis, infections, and other iatrogenic injuries for surgical intervention and hypothyreosis, infections, and endocrinopathy for radioiodine therapy (10–12). In addition, radioiodine therapy is in principle available only for treating hyperfunctional nodules, whereas surgical intervention is often recommended for hypofunctional nodules or cysts even though modern diagnostic methods are able to exclude malignancy and, therefore, suggesting less harmful therapy for symptomatic nodules (10).

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Considering all these facts, research investigated alternatives that do not share these disadvantages, and several minimally invasive techniques were developed for treating benign thyroid nodules. New promising alternatives are ethanol sclerotherapy (13), radiofrequency ablation (8,9), microwave ablation (7,14,15), laser ablation (16–20), and high-intensity focused ultrasound (HIFU) (21–24). Most of these therapy options were assessed intensively over the past years, leading to significant results, which converted them in routine clinical practice (8,9,15,20). However, HIFU, which is the least invasive and at the same time the most precise technique, still needs more detailed data concerning the treatment of the thyroid gland (21–27). Our workgroup assessed several ablative techniques including HIFU (21–24,28–32). To add complementary data related to this new technique, our research was focused on investigating characteristics regarding effectiveness that occurred in other minimally invasive techniques (15), and determine factors that allow a precise prognosis of therapy success. As nodule volume is the crucial assessment parameter of both treatment success and patient comfort, the main criterion of judgment was volume evaluation. The author especially aimed to search if a negative correlation between preablative nodule volume and percentage of volume reduction could be established and to determine a threshold volume value that implies a limitation related to a single HIFU session.

MATERIALS AND METHODS

Study Design

This is a retrospective analysis of data generated in a single-arm, open-label, baseline-controlled study. The study complied with institutional review board, ethics committees, informed consent regulations, International Committee on Harmonization Good Clinical Practice Guidelines, the Declaration of Helsinki, and local regulations. The treatment protocol detailed by Korkusuz et al. was used in this study (21–25).

Patients

Patients were enrolled at our outpatient clinic. Eligible patients were presenting symptomatic thyroid nodules, cosmetic concerns, and either refused surgery or proved to present contraindications for it. Patients were excluded for having asymptomatic nodules, histologic evidence for malignancy (histologic probe received by Fine Needle Aspiration Biopsy), positive Tc-99m methoxy-isobutyl-isonitrile (MIBI) uptake in cold nodules, or conspicuous calcitonin measurement. Patients with nodular volumes larger than 10 mL were excluded because of extended treatment durations with the system used in this study (21–27).

Treatment Procedure and Equipment

The system used in this study (Echopulse THC900888-H, THERACLION SA, Malakoff—France) has two separate ultrasound (US) systems embedded within a single device. The imaging system works between frequencies of 7.5 and 12 MHz, and the therapeutic system is driven at 3 MHz. Sonications lead to temperatures of approximately 80°C–90°C at focal point. Heat is produced by absorption of acoustic energy and its conversion into thermal energy (25). The operatory setting is shown in Figure 1.

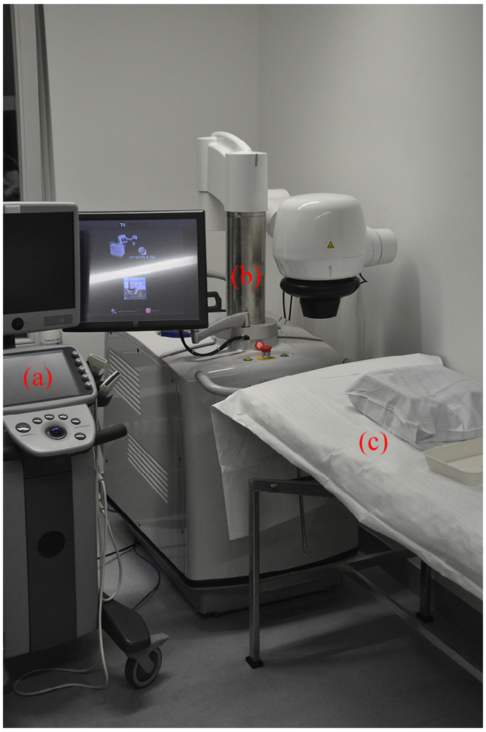

Figure 1. This figure shows the operative setting: (a) A separate ultrasound (US) system used to confidently identify the intended nodule. (b) The high-intensity focused ultrasound (HIFU) system used in this study (Echopulse THC900888-H, THERACLION SA, Malakoff—France). (c) A regular treatment couch with a head-shaped pillow to support the patients' head while hyperextending their neck.

A probe with a maximal focal point penetration depth of 2.4 cm and a disposable cooling kit were used. The system automatically selected the following safety margins: (1) 0.5 cm to the skin, (2) at least 0.3 cm to the trachea, and (3) 0.2 cm to the carotid. The mean energy per sonication varied between 87.6 and 320.3 J at focus.

Before each treatment, a cooling kit was installed, and the system underwent a general test of function. The nodular volume was measured using the Echopulse US system. Local skin and fascia infiltration with Mecain 1% and intravenous application of 500 mg Metamizole were carried out as anesthesia. This was followed by the positioning of the US probe on the hyperextended neck, with the patient in supine position. Primary marking of relevant anatomic structures was carried out. The system automatically generated a sonication map, the targeted nodule and the marked structures around it. Sonications were delivered in a screw pattern while adjusting the energy level after each single sonication. A given