

LASER-INDUCED INTERSTITIAL THERMOTHERAPY IN TREATMENT OF SOLID NODULES OF THYROID.

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Summary:

Introduction. pending on the application of laser-induced interstitial thermotherapy (LITT) in the treatment of solid thyroid nodules for today is the definition of indications and contraindications, techniques and technology performance, efficiency and improved long-term results.

The aim of the study. Studing the effect of LITT on parathyroid tissue and functional capacity of thyroid gland, determining the factors affecting the timing of replacement of host connective tissue and its capacity to develop evidence to reapply thermotherapy.

Materials and methods. using the LITT there were treated 272 patients with a nodular goiter with no signs of cystic degeneration. All patients – women from 22 to 68 years. The volume of nodules was within the range from 0.8 to 5.0 cm³. On ultrasonic characteristics, in particular echoic nodules were: 46 – hypoechoic, 189 – isochoric and 37 – hyperechoic. There was used a diode laser Lakhta Milon. LITT was performed on such parameters: the wavelength of 1060 nm, continuous operation, output power ranging from 2.5 to 3.2 watts. LITT was controlled by ultrasound. Changes in the nodule, parathyroid tissue and gland function after LITT was determined on the second day after 2 weeks, 1, 3, 6, 9 and 12 months after the procedure.

Results and discussion. on the second day after laser thermotherapy aseptic inflammation develops in nodules, but their size increases on 25–30 %. Later, in a certain period the survey, the size of nodules decreased, rates of hormonal function did not changed. 6 months after LITT with sizes of nodules up to 2 cm³ complete replacement of connective tissue occurred in all cases of hypo- and isochoric nodes and 71% - hyperechoic, and in sizes from 2 to 5 cm³ – 75% of hypoechoic structures, 18 % and isochoric there was no beneficial effect hyperechoic nodes. In cases of treatment failure called for the repeated LITT, after which all patients had complete reduction of the nodule.

Conclusions. in the developed mode LITT does not cause destructive changes in parathyroid tissue and hormonal gland function. Duration of regression and replacement of the nodule by connective tissue determines it's echogenicity and volume. Indications for re-use of thermotherapy is the residual tissue at the nodule within the more than 42 % of the initial volume in six months after treatment and the presence in it thyroid epithelium.

Key words: nodular goiter, treatment, laser-induced interstitial thermotherapy.

Introduction

Today it is generally accepted the fact that since the detection of nodular goiter before the indications for surgical treatment effective methods of conservative treatment do not exist [Grinyova 2003]. From the 80's of the last century in the treatment of this pathology it is used the technique of sclerotherapy of nodules. However, it has some significant disadvantages and complications: regression nodule volume does not exceed 50 %, available destruction of paranodular tissue, expressed pain syndrome.

Since 1998 there has been developed and implemented the technique of laser-induced interstitial thermotherapy (LITT) in the treatment of thyroid solid nodules. [Privalov et al. (2002), Grinyova (2003), Faizrakhmanov (2006), Mogutov (2009), Valcavi et al. (2010)]. Today it is widely used in the countries of America, Western Europe, Russia, Asia and Japan. According to literature data Russian endocrine surgeons have experience of treating more than 3,000 patients with different nidal pathology of thyroid gland. However, despite the widespread use of the method and acquired experience, there are issues of determining the indications and contraindications, technique and technology of its performance, efficiency rise and improvement of treatment outcomes that are need to be discussed and not unsolved to the end [Cakir B. et al. (2006), (2009), Dossing, Bennedbaek, Hegedus (2006), Papini et al. (2007), Shidlovskiy V., Shidlovskiy A., (2009)].

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Work objective

To study the impact of LITT on round nodule tissue and functional ability of thyroid gland, to identify factors that affect the terms of nodule replacement with connective tissue and its volume, to develop indications for repeated use of thermotherapy.

Materials and methods

Using LITT there were treated 358 patients with nodular goiter without the signs of cystic degeneration. All patients – women aged from 22 to 68. Before treatment they underwent the following examinations: ultrasound evaluation of the nodule and round nodular tissue, puncture biopsy of the nodule from three points with followed by cytological study, determination of the level of thyrotrophin, thyroxin, calcitonin, anti-thyroid peroxidase antibodies, general analyses of blood and urine, duration of bleeding and clotting time, blood test for infections (syphilis, hepatitis).

Nodule volume was in the range from 0,8 to 5,0 cm³. In 208 cases it did not exceed 2 cm³, and in 150 patients – from 2 to 5 cm³. According to ultrasonic characteristics, particularly in echogenicity nodules were as follows: 61 – hypoechoic, 249 – isoechoic and 48 – hyperechoic (Table 1). Blood supply of the nodule in capsular type is not reinforced in all patients. The part of unaffected with nodule tissue of thyroid (out-of-node parenchyma), was determined by the formula in cm³: $V_t = V_{tg} - V_n$; where V_t – volume of residual tissue, V_{tg} – volume of thyroid gland, and V_n – volume of the nodule. In 196 patients residual tissue of the gland was >80 %, in 115 patients – from 80 to 60 % and in 47 – was 60-55 %.

Table 1. Echogenicity and volume of nodules in examined patients

Echogenicity Volume	hypoechoic	isoechoic	hyperechoic
Up to 2 cm ³ n = 208	41	131	36
2 – 5 cm ³ n = 150	20	118	12
Total	61	249	48

We used diode laser “Lakhta-Milon”. LITT was conducted under the following parameters: wavelength 1060 nm, continuous mode, radiated power in the range from 2,5 to 3,2 watts. Run of the LITT was under sonographic control.

Changes in the nodule, round nodular tissue and function of the gland after the LITT were determined on the second day, in 2 weeks, in 1, 3, 6, 9 and 12 months after the manipulation. Changes of nodules' volume and their structure were studied using ultrasound machine “TOSHIBA” Nemio XG SSA – 580 A, levels of thyrotrophin, thyroxin and anti-thyroid peroxidase antibodies (using immunoenzyme method), morphological changes in punctates from the nodule and paranodular tissue (on the second day and in a month after treatment) and only from the area of the nodule in cases of incomplete its reduction during 9 months after the LITT and in 6 months after the repeated LITT.

LITT effectiveness was estimated by the percentage of nodule regress in comparison with the original data according to the following criteria: high efficiency – over 80 %, moderate efficiency – within 80 – 50 %, low efficiency – from 25 to 50 % and unsatisfactory result – less than 25 %.

Results and discussion

On the second day after the LITT the volume of nodules increased on 20-35 % in comparison with the original data. Percentage of their increase depended on the echogenicity. Hyperechoic nodules increased on 20-25 %, isochoic – on 25 – 30 %, and hypoechoic – on 25 – 35 %. The increase of nodules' volume is a result of aseptic inflammation and edema of tissue inside the nodule. At cytological study of the nodules' tissue there were revealed the signs of aseptic inflammation (leukocytic infiltration, edema of interstitial tissue). In punctate from the paranodular tissue the signs of inflammation were absent. Indices of anti-thyroid peroxidase antibodies, thyrotrophin and thyroxin were not significantly different from the original data ($p>0,05$).

Two weeks after the treatment, according to the ultrasound investigation, the nodules' volume decreased to initial indices (before treatment) and their echogenicity did not change. Levels of anti-thyroid peroxidase antibodies, thyrotrophin and thyroxin were within normal limits.

In one month after treatment the decrease of nodules volume was in the range from 28 to 42 % ($32 \pm 0,4$ %, $p<0,01$) and was different depending on the echogenicity. So hyperechoic nodules decreased in average on 28 – 30,0

%, and iso- and hypoechoic – on 31 – 42 %. At cytological study in the tissue of nodules was determined fibrous transformation and in some patients, mainly with the initial nodules' volume more than 2 cm³, in addition there were signs of aseptic inflammation or edema of interstitial tissue. In paranodular parenchyma pathomorphological changes were absent. Indices of antibodies to microsomal fraction, levels of thyrotropin and thyroxine were within normal limits and in comparison with the data in the second week after the LITT did not change significantly. ($p>0,05$).

Complete replacement of the nodule with connective tissue was noted in three months in 138 patients (38,6 %). Among these patients 134 patients had nodule's volume before treatment less than 2 cm³ (hypoechoic – 36, isoechoic – 80, hyperechoic – 18) and 4 – from 2 to 5 cm³, all isoechoic. In all these patients changes of the functional activity of the thyroid were within euthyroidism and, in comparison with indices in a month were not reliable ($p>0,05$). Residual tissue volume in the area of the nodule was from 0,1 to 0,2 cm³, and regression of nodule's volume was from 84 to 92 %. Connective tissue was at cytological study of the nodule area tissue. In the other 220 patients regression of nodule's volume was in the range from 37 to 68 %.

In the sixth month of observation in 138 patients, who had confirmed replacement of nodules with connective tissue – scar volume did not change. Among other 220 patients, 96 had sonographic signs of the nodules replacement with scar tissue, volume of which was from 0,2 to 0,4 cm³, and decrease of nodules' volume in comparison with the original data was from 72 to 84 %. Connective tissue was at cytological study of the nodule area. Among these patients in 63 – nodule's volume before the LITT was less than 2 cm³, and by the echogenicity – in 3 hypoechoic, in 51 – isoechoic and in 9 – hyperechoic. In 33 cases nodules' volume was within 2 – 5 cm³. Among them there were 16 hypoechoic and 13 isoechoic. In general for six months after the LITT replacement of nodules with the connective tissue was in 234 patients (65,4 %), and decrease of nodules' volume was from 72 to 92 %. In other 124 patients decrease of nodules' volume was from 41 to 58 %.

In the ninth month after the LITT there were no changes of connective tissue volume in the area of nodules. In 123 patients regression of nodules' volume in comparison with the results for six months did not exceed 5 % and in total, in comparison with the original data, decrease of nodules in these patients in the process of treatment was in the range from 46 to 61 %. Before treatment 10 of these patients had hyperechoic nodules and less than 2 cm³; 113 patients had nodules from 2 to 5 cm³ and 5 had hypoechoic nodules, 96 patients – isoechoic and 12 – hyperechoic. Connective tissue and follicular epithelium cells of thyroid gland were revealed at cytological study of the nodule area. All these patients underwent a repeated session of the LITT using the power 3,0 – 3,2 watts and procedure duration from 10 to 15 min.

In three months after the repeated LITT replacement of the nodule with connective tissue was in 72 patients. Residual nodules' volume was from 0,4 to 0,6 cm³, and regression in comparison with the initial volume was from 73 to 76 %. In other 51 patients regression of the nodule's volume was in the range from 59 to 71 %.

In the sixth month of observation after the repeated LITT in 72 patients who had confirmed replacement of nodules with connective tissue – scar volume did not change. In 51 patients was observed sonographic pattern of parenchyma nodules replacement with echodense tissue volume of which was from 0,45 to 0,6 cm³, and at cytological study present connective tissue was without thyroid epithelium. So, replacement of the nodule tissue with connective tissue was after the repeated LITT in all cases.

Absence at different terms after the LITT the pathomorphological changes in round nodule tissue, increase above normal content in blood of antibodies to thyroid peroxidase, thyreotrophin and thyroxin suggests that thermotherapy of the nodule using the laser energy in selected modes does not cause the destruction of the thyroid gland parenchyma and disorders of its functional state.

Our experience of application of the LITT in the treatment of the thyroid solid nodules testifies to the high efficiency of this technique. Positive effect of treatment was achieved in all cases among 358 treated patients. High efficiency of treatment was noted in 234 patients (65,4 %), moderate – in 124 patients (34,6 %). There were no cases of low efficiency and unsatisfactory results of the LITT.

We consider, that the factors, that determine the effectiveness of the LITT in the treatment of nodular euthyroid goiter is volume and echogenicity of the nodule. (Table 2).

Table 2. Effectiveness of the LITT, volume and echogenicity of nodules

Nodules' volume and echogenicity	up to 2 cm ³ (n = 208)			from 2 to 5 cm ³ (n = 150)		
	hypo-echoic	iso-echoic	hyper-echoic	hypo-echoic	iso-echoic	hyper-echoic
Before treatment	41	131	36	20	118	12
Cure completed	41	131	26	15	21	0
In six months after the LITT	100 %	100 %	71 %	75 %	18 %	
Repeated LITT			10 29 %	5 25 %	97 82 %	12 100 %

The nodules with initial volume up to 2 cm³ had higher rate of regression and less scar volume after the LITT. The vast majority of these nodules replaced on the connective tissue within 3-6 months after the LITT. Residual volume of the scar did not exceed 12% from the initial nodule's volume. Regression of the nodules with initial volume 2-5 cm³ was longer, and the volume of residual tissue was from 15 % to 40%. In the overwhelming majority of cases these nodules needed the repeated LIIT (Table 2, Figure 1).

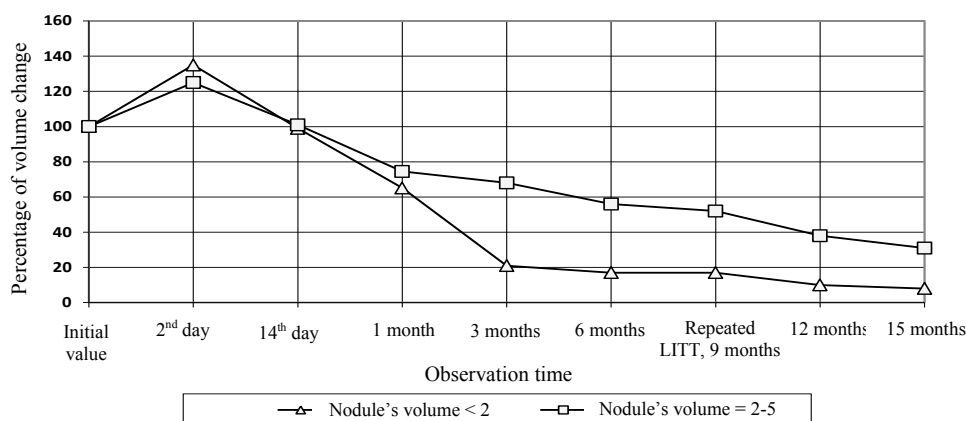


Figure 1. Changes of nodules' volume in different terms after the LITT

Echogenicity of nodules significantly affects the rate of their regression and the volume of residual scar. So hypoechoic nodules reacted intensely with volume increase on the second day after the manipulation, regressed faster and replacement for the scar was observed within 3-6 months ($p < 0,01$). Repeated LITT mostly was needed for the nodules with volume from 2 to 5 cm³ and the part of hyperechoic nodules with volume up to 2 cm³. Reactive edema of isoechoic nodules was less expressed and replacement of them with connective tissue was observed within 3-15 months after the LITT, and residual volume, that is the scar volume, was in the range from 9 to 28 % from the initial one. Hyperechoic nodules least of all reacted to the LITT with reactive edema and volume increase, and residual tissue volume on the place of the nodule was in the range from 15 to 36 % from the indices to the treatment (Figure 2).

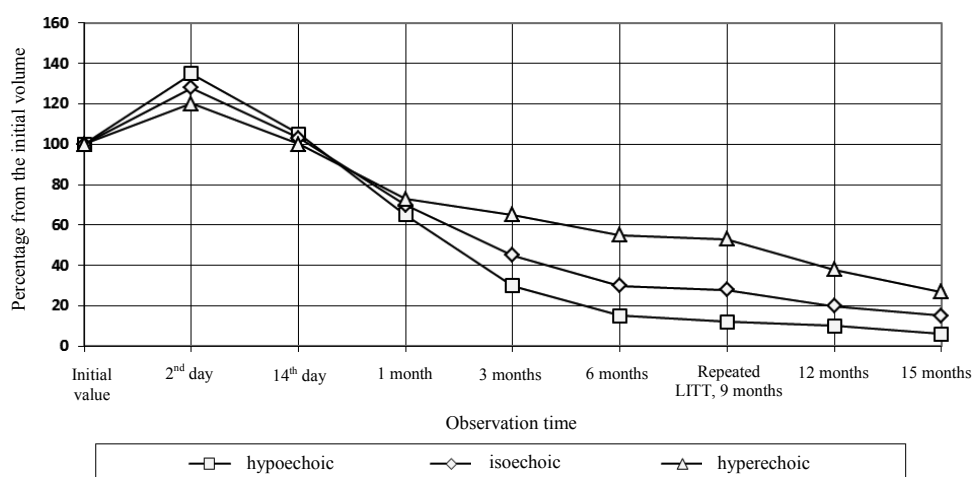


Figure 2. Intensity of regression of different echogenicity nodules.

Nodule regression and the volume of scar tissue did not depend on the age of patients and the percentage of unchanged tissue of the thyroid gland before treatment.

Indication for the repeated LITT we consider slow regression of the nodule, especially within 6 – 9 months after treatment, decrease of its volume in the range up to 58 %, in the presence of epithelium of thyroid gland in the residual tissue according to the data of fine-needle puncture aspiration.

Conclusions

Laser-induced interstitial thermotherapy does not cause destructive changes in the round nodule tissue and disorders of the function of thyroid gland in the selected modes and technique.

Result of the laser-induced interstitial thermotherapy is full replacement of nodule's tissue with connective tissue. Its effectiveness makes 100 %.

Speed and completeness of replacement of the nodule with connective tissue after laser-induced interstitial thermotherapy depend on the volume and echogenicity of the nodules. At volume up to 2 cm³ complete replacement on the connective tissue of hypo- and isoechoic nodules occurred in all patients, and hyperechoic – in 71 %. About 75 % of patients with nodules volume of which is from 2 to 5 cm³ needed the repeated thermotherapy application. This applies to all patients with hyperechoic nodules, 25 % – with hypoechoic and 82 % – isoechoic nodules.

Patients with residual tissue of nodular formation need the repeated thermotherapy. Absolute indication for its performance is slow nodule reduction, in the presence of nodular parenchyma among the connective tissue elements.

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