Laser-induced interstitial thermotherapy in treatment of recurrent nodular goiter and thyroid cancer

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ABSTRACT

Laser-induced interstitial thermotherapy was performed in 29 patients with recurrent nodular and multinodular goiter, and in 3 patients with recurrent inoperable thyroid cancer. There were used transcutaneous puncture under ultrasonic control, diode lasers with wavelength 805, 980, and 1060 nm, quartz monofibers, special computerized thermometer with microthermocouples. Disappearance or significant reduction of nodes in the most goiter cases, and regress of tumor in the cancer cases were marked during observation period (0.5 - 2.5 years).

Keywords: Laser, thermotherapy, thyroid gland, goiter, cancer

1. INTRODUCTION

The number of goiter patients continues to grow annually and so the problems of this pathology treatment do not lose their actuality and urgency. Conservative treatment methods do not always give desired effect. Traditional surgical methods of thyroid gland treatment are traumatic, often accomponied by complications and do not prevent recurrence of the disease (up to 40%). At present time the nodal formations of thyroid gland are more and more treated with active, low-invasive surgical operations under ultrasonic control. These operations allow eliminating pathological focus by direct physical or/and chemical action and at the same time keeping the main mass of hormonoproducing parenchyma of the gland. Background for working out and application of these methods were:

- extensive introduction to clinical practice of ultrasonic equipment, which allows revelation of changes in thyroid structure with high resolution;
- high informativeness of aspiration puncture and possibility of cyto-morphological verification of disease, especially if the puncture is performed under ultrasonic control;
- considerable difficulties during repeated operations on the thyroid gland in cases of recurrence.

The aim of our investigation is to ground the possibility of clinical application of high-intensive laser radiation to destruct thyroid tissue under ultrasonic control in cases of recurrent nodular and multinodular goiter and recurrent inoperable thyroid cancer. We based on the recent experimental study of laser interstitial thermal action on thyroid glands of dogs [1].

2. MATERIALS AND METHODS

The laser-induced interstitial thermotherapy (LITT) was applied to 29 patients with recurrent nodular and multinodular euthyroid goiter and to 3 patients with recurrent inoperable thyroid cancer. Apart from clarification of anamnesis and

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physical examination, the patients were subjected to ultrasonic, radioisotopic, hormonal, cytological, and morphological investigations.

All patients with recurrent goiter (women aged 40-79) had 1-3 concomitant diseases. Duration of goiter disease before the operation was 1-5 years. The recurrence of disease appeared in 6-30 years. In most cases repeated cytological investigation of preparations, extracted at previous operation, approved the diagnosis of nodular/multinodular micro/medium/macro-follicular colloidal goiter . The signs of autoimmune process in surrounding tissue were found in the third of patients, sclerotic degenerate changes in the node and paranodular tissue were found in the another third of patients. According to ultrasonic data of node sizes varied from 10 to 45 mm.

For many years most of patients were under observation of endocrinologist, they took thyroid drugs under control of the level of threeiodinthyronin, thyroxin of blood serum (T3, T4) and thyrotropic hormone of hypophysis (TTH). Despite this treatment recurrent goiter appeared in 6-10 years after operation in 6 patients, in 11-20 years in 12 patients, in 21 – 30 years in 11 patients, in more than 30 years in 3 patients. The nodes gradually grew that was the indication to their destruction. 16 patients complained of discomfort in the neck area, 9 patients of the difficulty in swallowing, 3 patients of the respiratory disorders lying on the back, 3 patients were indicated to thermotherapy because of cancerophobia.

Investigation of hormone profile was conducted with the help of immunochemical luminescent analyzer "Immulight" of firm DPC (USA). For echolocation of thyroid gland we used devices "Aloka 500" and "Aloka 650" with 7.5 MHz sensor in the real-time mode. The scanning of thyroid gland was performed with ^{99}Tc and gammatomograph "Scinticart MB-9200" of firm "Gamma" (Hungary).

Aspiration puncture of thyroid gland was performed before the laserthermy according to standard method under ultrasonic control. After fixation of the material with 96% alcohol the smears were colored by the Romanovski method and then microscopy was conducted.

Trepanobiopsy was performed with the 1mm Silverman needle under ultrasonic control. The material was fixed with 10% formalin and colored with hemotoxilin and eosin with subsequent microscopy. The procedure was performed before laserthermy, on $2^{d} – 3^{d}$ day, $5^{th} – 7^{th}$ day, and in a month after laserthermy.

Laser destruction was performed with diode lasers of wavelength 805 nm (9 patients), 980 (9) and 1060 (11). Delivery of radiation was conducted with quartz-quartz monofiber of 0.4–0.8 mm diameter.

In the process of LITT patients lied on the back with a bolster under their shoulders. In such position thyroid gland is more accessible for different manipulations. After the cleansing of the surgical area with 0.5% solution of chlorhexedine bigluconate (hybitan) in 70% ethyl alcohol there was performed local anaesthesia of a puncture point using 0.5% novocaine solution.

The puncture of a node was performed under ultrasonic control with 0.8 mm needle either on the middle line of the neck, or on the side surface in the node projection. The fiber was inserted into the node through the needle. The position of the fiber in the goiter tissue was controlled with ultrasonics. The needle was removed and the laser thermotherapy. was performed. In accordance with node size we performed 1-4 procedures of thermotherapy.

Radiation power ranged from 2 to 3 W, exposure 2-10 min. These parameters were chosen on basis of previous experiments on dogs [1], in which we studied in particular the dynamics of inflammatory and reparative processes in thyroid gland and surrounding organs irradiated by diode lasers in different modes. At determination of the parameters we also took into account the node sizes, patient's state of health, patient's esthesia, and dynamics of visual ultrasonic monitoring during laserthermy .

In the group of patients with recurrent thyroid cancer the IV^{th} stage of tumor process was determined in all 3 cases. Among patients there were 2 women and 1 man aged 51-73. Two patients with medullary and 1 patient with papillary thyroid cancer were previously subjected to palliative operations. One patient with medullary cancer had strongly pronounced compression syndrome, that is why he was put a tracheostomy. Patients with medullary cancer had post-

operating radiotherapy course (40 Gy). Because of progress of tumor process and impossibility of radical operation, the patients were subjected to the laserthermy in technique, worked out at treatment of nodular goiter.

For safety the laserthermy was combined with dynamic temperature control, performed with special computerized thermometer, allowing for difference in temperature of thermodetectors and surrounding it tissue, caused by laser radiation [2]. As thermodetectors we used thermocouple, placed in quartz capillary with outer diameter 0.5 mm. Measuring and correcting temperature are performed in real-time mode. Thermodetectors were placed with the help of a needle outside thyroid gland: by trachea and vascular-nervous bundle of the neck (fig.1).

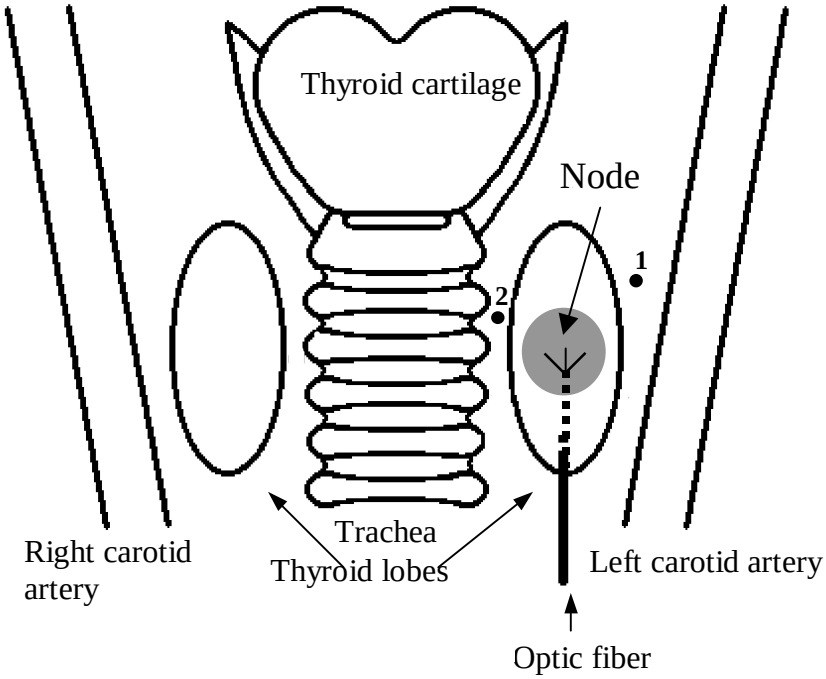

Fig. 1. Scheme of disposition of a fiber and thermodetectors at laserthermy of a thyroid node. Detector 1 is placed between a thyroid lobe and vascular-nervous bundle, detector 2 between the lobe and trachea.

3. RESULTS AND DISCUSSION

All the patients tolerated the LITT procedure well. During its performance they noticed the feeling of "foreign body" at the injection area, feeling of compression and burning in case of close fiber disposition to the thyroid gland capsule. The pain remained for 1.5 – 2 days and was easily released by non-narcotic analgesics.

During laserthermy in 0.5-1.0 min after the beginning of treatment a hyperechoic "spot" was noticed near distal end of fiber on ultrasonic scanner display (fig.2b), the "spot" was gradually increasing, and to the end of the procedure it was "covering" most of the node (fig.2c). We consider that this effect is explained by gassing caused by thermic laser action.

On the 2^{nd} – 3^{d} day little increase of the node sizes in the exposed area was noticed. Since the 2^{nd} day after the procedure in the place of the node, treated with laserthermy, hypoechoic zone without distinct borders was forming (fig.2d). Decrease of echo density of node at that time is apparently associated with the edema and the phenomena of aseptic inflammation. In 1-3 months after the laserthermy at the nodes place was noticed a zone of non-homogeneous hypoechogeniety without distinct borders and with increasing evidence of focal fibrous changes. Later on echographic picture was characterized by decrease of the node and marked fibrous changes in it (fig.2e).

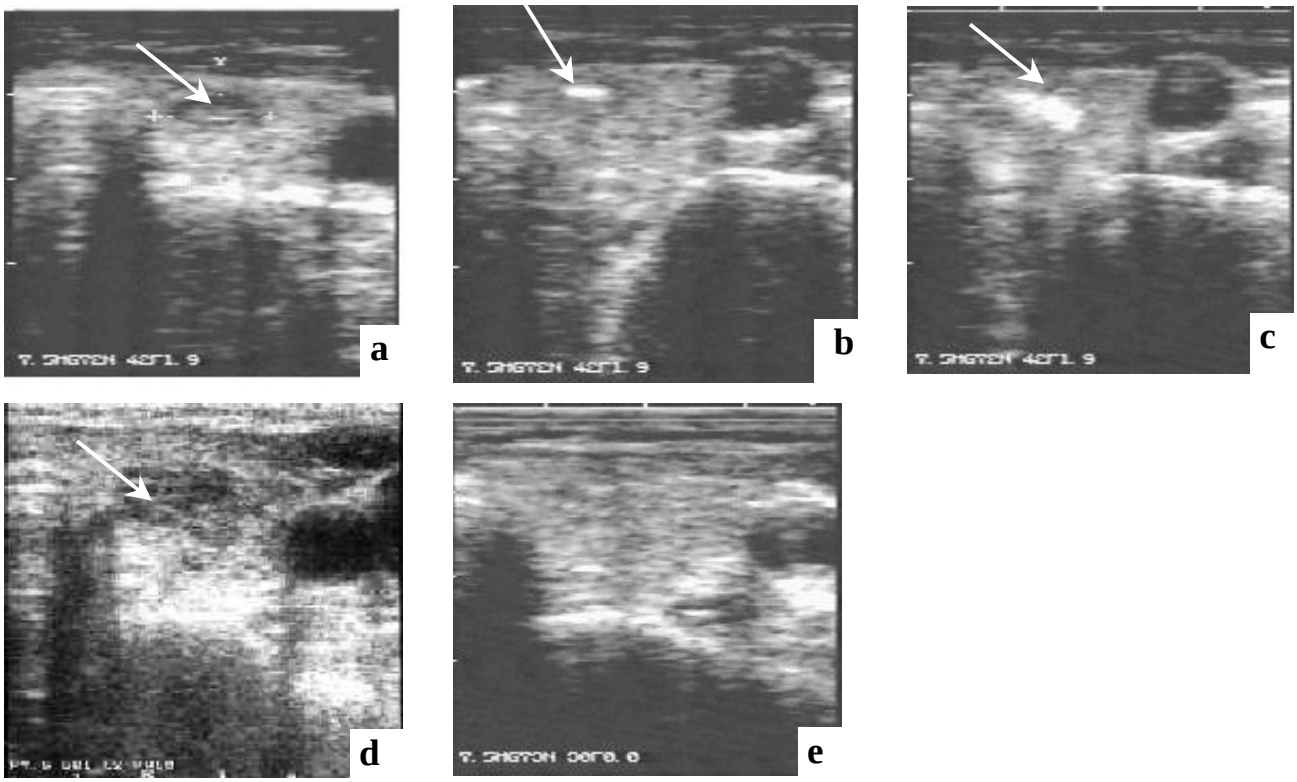

Figure 2. Echographic picture of laserthermy of thyroid gland node (left lobe);
a) befor laserthermy: a heterogeneous node with hypoechogenous thin rim;
b) the beginning of laserthermy: a hyperechogenous "spot" in the zone of laser radiation action;
c) the end of laserthermy: a hyperechogenous zone without distinct borders in the node projection;
d) 2 days after laserthermy: a hypoechogenous zone in the node projection;
e) 1,5 years after laserthermy: no node.

In case of a large node we repeated the laserthermy. There were performed 2 procedures in 10 patients, 3 procedures in 6 patients with interval 5-10 days. Duration of observation varied from 6 months to 3 years. In 2 patients nodes disappeared, in 10 patients during 1.5 year observation the volume of nodes decreased by 1/2, in 10 patients by 1/3, but there was no growth of the nodes in any of patients.

During laserthermy and subsequent dynamic observation we did not reveal any reliable differences associated with wavelength of the used in the procedures diode lasers.

After the local laser thermotherapy the functional state of thyroid gland was not disturbed, that was proved by clinical and biochemical examinations: T4 and TTH levels were not changed (table 1).

Table 1. Level of thyroid hormones before and after LITT

	T4	TTH
Before LITT	20 ± 4	1,8 ± 0,4
After LITT	18 ± 4	1,9 ± 0,4

During laserthermy patients with recurrent thyroid cancer felt discomfort in the neck area, mild pain with irradiation to the lower jaw, which lasted 1.5 – 2 days. On the 2nd day intumescense appeared in the affected area. During ultrasonic monitoring we saw that tumor node became less echogenous, the borders became less distinct. The control examination (clinical examination and analysis of ultrasonic and computer tomography data) in 6 – 12 months revealed decrease of the tumor node sizes, hardening of its structure, sclerosing and disappearance of the compression syndrome.

There were no complications during laserthermy procedures. Dynamic temperature control during LITT did not register critical temperature increase outside thyroid gland by the trachea and vascular-nervous bundle of the neck (fig.3).

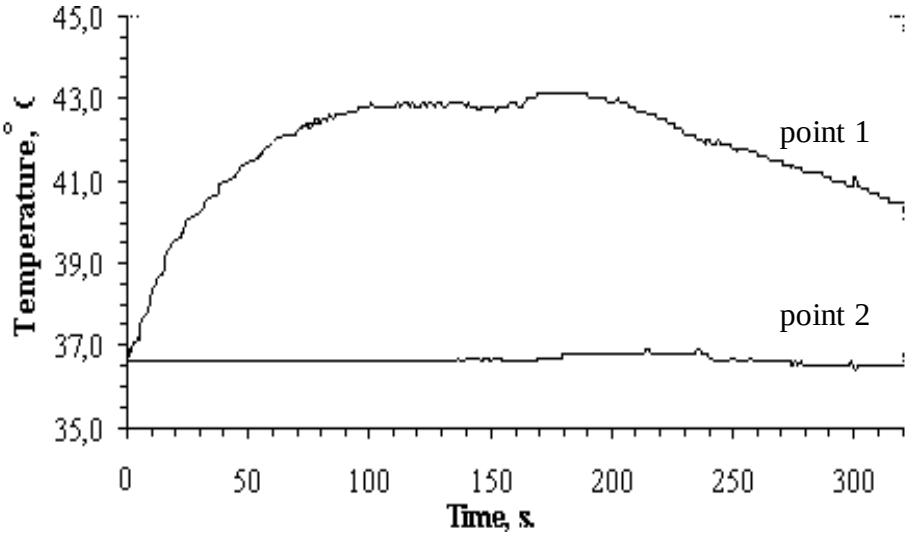

Fig. 3. Temperatures of tissue in two points (indicated on fig. 1) during LITT of thyroid gland node.

Morphological investigation of the preparations taken from the nodes during trepanobiopsy under US control revealed that in the zone of laser action on the 2nd – 3d day there was abundant neutrophilic infiltration (fig.4b), and on the 5th – 7th day there appeared the layers of connective tissue (fig.4c). In a month in hyperthermy zone a scar formed (fig.4d).

In conclusion we present a clinical case.
Patient B., 44 years old, female, was ill with multinodular endemic euthyroid goiter since 1984. She was operated on 13.01.1997. At inspection of the left lobe of thyroid gland the soft elastic nodes of 0.5– 2.0 cm diameter were found. There was performed subtotal resection of the left lobe within limits of healthy tissue, keeping thyroid tissue (up to 2cm^3) on the side surface of trachea. Postoperative course was smooth. Histological conclusion – multinodular medium-macrofollicular colloidal goiter. In January, 1998, on the control examination there was found a node of 1.5 cm diameter in the right lobe. Ultrasonic monitoring revealed that right lobe of 19x25x48 mm (volume 12.1 cm^3) has a heterogeneous node of 12x14x25 mm (volume 2.1 cm^3). TTH =3.2Mc/ml. L-thyroxin was assigned in 100 μg./day. In March, 1998, there was another control examination, palpation and ultrasonic monitoring revealed that the node in right lobe became larger (15x20x30 mm; volume 4.8 cm^3). Taking into account negative dynamics, the patient was subjected to 2 procedures of LITT on 24.03.98 and on 07.05.98 with diode laser (λ = 980 nm, P = 3 W, exposure 1 and 3 min.). During further dynamic observation there was marked the gradual decrease of the node within 8 months. Since 1999 node sizes are 6x7x8 mm (volume 0.2 cm^3), node is not determined at palpation, the level of T4 is 14.5ng/ml, TTH=2.4 Mc/ml. Patient is taking L-thyroxin. 50 μg/day

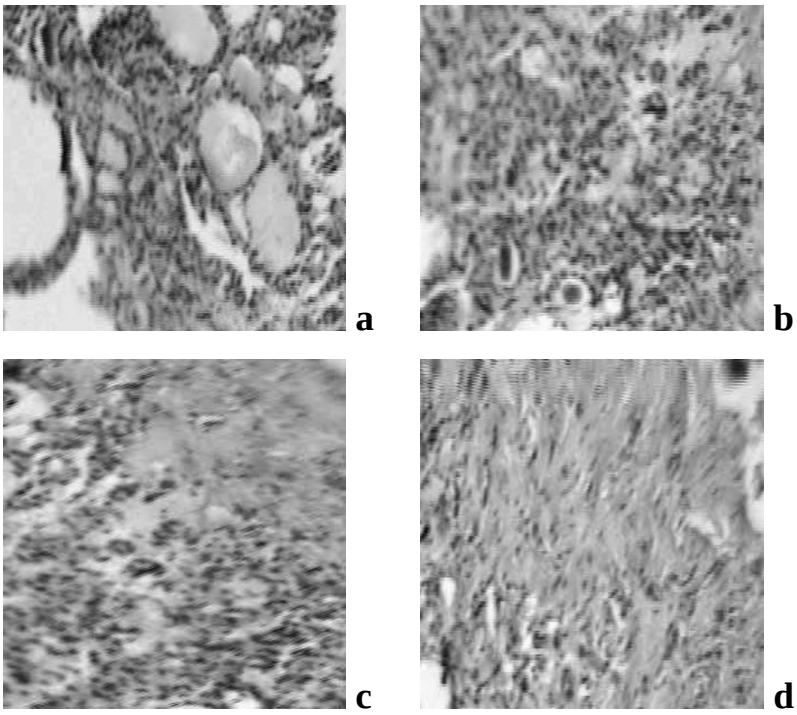

Fig. 4. Histological changes of thyroid gland node tissue after LITT
a) node tissue of the ordinary micro- mediumfollicular structure (before LITT);
b) abundant infiltration of the node tissue with neutrophiles (2^{nd} –3^{d} day);
c) together with marked neotrophilic infiltration there appear layers of connective tissue (5^{th} – 7^{th} day);
d) large scar with the single atrophied follicles (in a month).

4. CONCLUSION

The results of our investigation show that LITT is effective and safe method of nodular goiter treatment. The efficiency of application of LITT to the neoplasm treatment requires further study.

REFERENCES

1. V.A. Privalov, O.V. Seliverstov, J.A. Revel-Muroz, A.V. Lappa, R.U. Giniatulin, and A.I. Kozel, "Transcutaneous laser-induced interstitial thermotherapy of nodular goiter", proccedings of SPIE vol. 3907, pp.278-288, 2000.
2. A.V. Lappa, A.A. Kazakov, S.I. Veresov, V.A.Privalov et al., "Contact thermometry in intensive fields of laser radiation", *Thermal Therapy, Laser Welding, and Tissue Interaction*, Stephen G. Bown et al., proceedings of SPIE vol. 3565, pp. 90-100, 1998.