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Современные технологии визуализации и термоаблации очагов гиперпаратиреоза

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АННОТАЦИЯ

Патология околощитовидных желёз по частоте встречаемости находится на третьем месте среди эндокринных болезней, уступая сахарному диабету и заболеваниям щитовидной железы. На сегодняшний день в клинической практике широко применяются только два метода лечения гиперпаратиреоза — консервативный и хирургический. Однако в последние время помимо них появились способы транскутанной термодеструкции (абляции), основанные на прицельном физическом воздействии — лазерном, радиочастотном, микроволновом, ультразвуковом. Настоящий обзор посвящён критическому анализу современного арсенала методов локальной термодеструкции гиперфункции околощитовидных желёз при гиперпаратиреозе. Цель обзора — показать возможности современных неинвазивных и малоинвазивных методов лечения гиперпаратиреоза без противопоставления их хирургическому методу. В обзор включены данные рандомизированных клинических исследований за период с 2012 по 2021 г., найденных в Google Scholar, Pubmed. Общее количество пациентов — 1938 (лазерная абляция — 216, радиочастотная абляция — 225, микроволновая абляция — 1467, абляция ультразвуком высокой плотности — 30). Получены критерии применимости методов термодеструкции. Составлен алгоритм по лечению гиперпаратиреоза. Таким образом, в качестве альтернативы хирургическому вмешательству проанализированы четыре современных метода термодеструкции патологически изменённых околощитовидных желёз, каждый из которых имеет преимущества и недостатки, свой профиль эффективности и безопасности. Как показывает анализ существующей доказательной практики, наибольшей популярностью среди клиницистов пользуется метод микроволновой абляции, однако более эффективным методом термодеструкции гиперфункционирующих околощитовидных желёз является лазерная абляция.

Ключевые слова: гиперпаратиреоз; термодеструкция; абляция околощитовидных желёз; лазерная абляция; радиочастотная абляция; микроволновая абляция; HIFU-абляция.

Как цитировать

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Methods of medical visualization and thermal ablation as a new approach to treatment of hyperparathyroidism

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ABSTRACT

The pathologies of parathyroid glands are widespread among endocrine system diseases, excluding diabetes and thyroid pathology. There are only two methods that are used to treat hyperparathyroidisms, such as surgery and conservative therapy. However, transracial thermal destruction methods (ablation) have recently appeared in clinical practice. The methods have good precision and connect with physical phenomena, such as interaction laser, radiofrequency, microwave, and HIFU irradiation with bio substance. The review is dedicated to critically analyze the modern methods for local thermal destruction of the hyper-functioning parathyroid glands. The review includes data from randomized clinical trials from 2012 to 2021. The studies were from Google Scholar and Pubmed with a total number of 1,938 patients (laser ablation — 216 patients, radiofrequency ablation — 225, microwave ablation — 1467, high-density ultrasound ablation — 30 patients). Recommendations methods of thermal destruction application were obtained during the review. Furthermore, we have designed some algorithms for hyperparathyroidism treatment. Moreover, thermal destruction methods were observed. There are four modern methods of thermal destruction which have been analyzed like alternatives to surgery. Each of them has advantages and disadvantages, its profile of safety and effectiveness. After processing information from a proven database, the most popular among specialists is methods of microwave ablation. However, laser ablation is more effective than other ways.

Keywords: hyperparathyroidism; thermal destruction; ablation of parathyroid glands; laser ablation; radiofrequency ablation; microwave ablation; HIFU ablation.

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甲状旁腺功能亢进病灶可视化和热消融的现代技术

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简评

甲状旁腺病理学在内分泌疾病中居第三位，仅次于糖尿病和甲状腺疾病。　目前，只有两种治疗甲状腺功能亢进的方法被广泛应用于临床：保守的和手术的。然而，最近还出现了基于激光、射频、微波等目标物理效应的跨层热分解（消融）方法，超声波。本综述致力于对甲状腺功能亢进的局部热分解方法的现代武库进行批判性分析。本综述的目的是展示现代无创和微创方法治疗甲状旁腺功能亢进的可能性，同时又不反对手术方法。 该综述包括2012年至2021年期间在谷歌学者（Google　Scholar，PubMed）中发现的随机临床研究数据。患者总数-1938人（激光消融216人，射频消融225人，微波消融1467人，高密度超声消融30人）。获得了热分解方法的适用性标准。建立了治疗甲状腺功能亢进的算法。因此，作为手术干预的替代方法，已经分析了四种现代热破坏病理改变的甲状旁腺方法，每种方法都有优点和缺点，其自身的有效性和安全性。　对现有循证实践的分析表明，最受临床医生欢迎的是微波消融方法，而激光消融是一种更有效的热破坏功能亢进的甲状旁腺的方法。

关键词：甲状旁腺功能亢进；　热破坏；　甲状旁腺消融；　激光烧蚀；　射频消融；　微波消融；　HIFU 消融。

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INTRODUCTION

Hyperparathyroidism (HPT) is an autonomous hyperfunction of one or more parathyroid glands. Primary HPT (PHPT) results from primary autonomous hyperfunction, mostly of a single parathyroid gland of neoplastic nature. Secondary (SHPT) and tertiary HPT, which are most common with multiple hyperfunctioning parathyroid glands, occur in response to chronically low blood calcium concentrations due to chronic renal failure [1].

PHPT is characterized by excessive secretion of parathyroid hormone (parathormone) with upper normal or increased blood calcium concentrations due to primary parathyroid gland pathology. The worldwide PHPT prevalence ranges between 1–40 cases per 100,000 population [2]. In addition, PHPT is more common in the working age. In the age group of up to 45 years, the probability of developing the disease is equal for both genders, whereas after 45 years, this pathology becomes more typical for women [3].

SHPT results from a compensatory increased parathormone production in response to decreased serum calcium concentrations [4] and is most frequently observed in the end-stage renal disease. Up to 75% of patients with renal failure have clinically evident SHPT; of these patients, 5% require surgical treatment [5].

The main methods for diagnosing HPT are biochemical blood test (parathyroid hormone, calcium, phosphorus, creatinine, and vitamin D concentrations) and a 24 h urine test (calcium). Once the diagnosis is confirmed, and if radical treatment is indicated, instrumental examinations (ultrasound (US), contrast-enhanced X-ray computed tomography, and radioisotope scanning) are performed, including hybrid methods of molecular imaging (planar scintigraphy and single-photon emission computed tomography/computed tomography [SPECT/CT]) with technetril staining (^{99m}Tc-MIBI) or 18F-choline positron emission tomography/CT (PET/CT) [6, 7].

Currently, two methods of HPT treatment are widely used in clinical practice, that is, conservative therapy and surgery (Table 1). Conservative therapy includes drug treatment [8] to reduce hypercalcemia and prevent hypercalcemic crises and fractures. This method lacks a radical HPT treatment and is used mostly in mild, uncomplicated HTP forms, the impossibility of parathyroidectomy, or refusal of the patient to undergo surgery. The surgical treatment can radically eliminate parathormone hyperproduction; however, this method is associated with hospitalization, anesthesia, risk of surgical complications, scarring on the neck, and recovery period [9, 10].

The introduction of new algorithms for imaging parathyroid glands in HPT into surgical practice improved the topical differential diagnosis, increased the precision, and reduced the number of surgical injuries. [11]. Endoscopic technologies, intraoperative neuromonitoring, and fluorescence imaging of the periothyroid glands allow improved efficiency and safety of interventions [12]. The efficiency of surgical treatment is 92%–94% [13]. However, not all patients are willing to be operated on, and others have no opportunity to undergo surgery (contraindications and risk to life with anesthesia and surgery).

Thus, in the study by B. Wu et al. [14], surgical HPT treatment was performed in only 29% of patients with absolute indications. Most frequently, patients aged up to 60 years undergo surgery, whereas in older age groups, the proportion of surgical interventions decreases by 1.5–3 times every decade.

Table 1. Conventional HPT treatments

Treatment	Indications	Approach	Imaging
Conservative therapy	• Correction of hypercalcemia • Prevention of hypercalcemic crises • Prevention of low traumatic fractures	• Palliative • Symptomatic	-
Surgery	• Serum total calcium concentration of 0.25 mmol/L (1 mg%) exceeding the laboratory norm • Decreased glomerular filtration rate (<60 mL/min/1.73 m^2) • Visceral PHPT manifestations (ICD) • Daily calcium excretion (>400 mg/10 mmol per day) • Decreased bone mineral density in radius, femur, or vertebrae (<–2.5 SD by T-criterion) • A history of low traumatic fractures and/or radiologically detectable vertebral body fractures (based on MSCT or MRI) • Age of <50 years	• Radical	• US, scintigraphy (SPECT/CT, PET/CT) • Contrast-enhanced CT, PET/CT

Note. PHPT (ICD), primary hyperparathyroidism; MSCT, multispiral computed tomography; MRI, magnetic resonance imaging; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography.

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In this regard, the development of alternative methods of destruction (ablation) of hyperfunctioning parathyroid glands is necessary.

In addition to surgical treatment, methods of transcutaneous thermal destruction (ablation) based on targeted physical effects (laser, radio frequency, microwaves, and US), appeared in clinical practice (Table 2) [15–17].

According to the Google Scholar database, microwave ablation was used in the largest number of papers on thermal destruction of hyperfunctioning parathyroid glands, whereas high-intensity focused US (HIFU) ablation was used in the smallest number (Fig. 1).

Radiofrequency and laser ablation occupy an intermediate position. The high popularity and accumulated wide experience of microwave ablation is due to the leading position among all currently known methods for thermal destruction of the parathyroid glands.

CURRENT PREOPERATIVE IMAGING AND INTRAOPERATIVE NAVIGATION OPTIONS

Before considering alternative surgical methods of parathyroid gland destruction in HTP, the current possibilities of their imaging at the preoperative and intraoperative stages should be highlighted.

Preoperative parathyroid gland imaging

US is the standard, most accessible, and safe method for preoperative imaging in HTP (Fig. 2).

In addition to US, either single-isotope biphasic scintigraphy with ^{99m}Tc-MIBI or dual-isotope scintigraphy in SPECT/CT mode with ^{99m}Tc-MIBI and $^{99m}TcO_4$ (pertechnetate) is performed [18, 19] (Fig. 3).

Table 2. Characteristics of different methods for thermal destruction of hyperfunctioning parathyroid glands in verified HPT (based on international recommendations)

Ablation	*n*	Applicability criteria	Operating mode	Efficiency	Side effects
Laser	216	• Lesion diameter (≤30 mm) • Contraindications to surgery • Restrictions on ectopia • Age over 18 years	3 W 6–10 min	92%	8% (dysphonia)
Radio frequency	225	• Parathormone (≥800 ng/mL) • Number of parathyroid hyperplasias (<4) • Uncontrolled SHPT with drug treatment • No serious clotting disorders, heart failure, or uncontrolled hypertension	10–50 W 1–2 min	83,6%	2,1% (transient hypocalcemia, transient hoarseness)
Microwaves	1467	• Renal failure with hyperparathyroidism • Inefficient conservative treatment (despite adequate drug therapy) • Parathormone concentrations (≥600 pg/mL) • At least one enlarged parathyroid gland • Minimum gland diameter (≥6 mm) • Not applicable for surgical resection • Parathyroid glands in an area that is difficult to access for resection	30 W 3–5 min	89,4%	6% (hoarseness)
High-intensity focused US	30	• Serum calcium concentrations (≥2.60 mmol/L) • A cytologically proved lesion of parathyroid origin • Adenoma depth (<23 mm) between posterior margin and skin surface • Adenoma thickness (>8 mm) • Distance from trachea (>3 mm), distance from esophagus and carotid artery (>2 mm) • No significant macrocalcifications at <10 mm distance from the target • Age over 18 years	5 W 2–3 min	Complete remission in 23% after one year; good control of the disease in 69%	Temporary side effects included impaired vocal cord mobility (23.1%), subcutaneous swelling (23.1%), and combined effect (15.2%)

Note. *n*, the total number of patients treated at the date of writing.

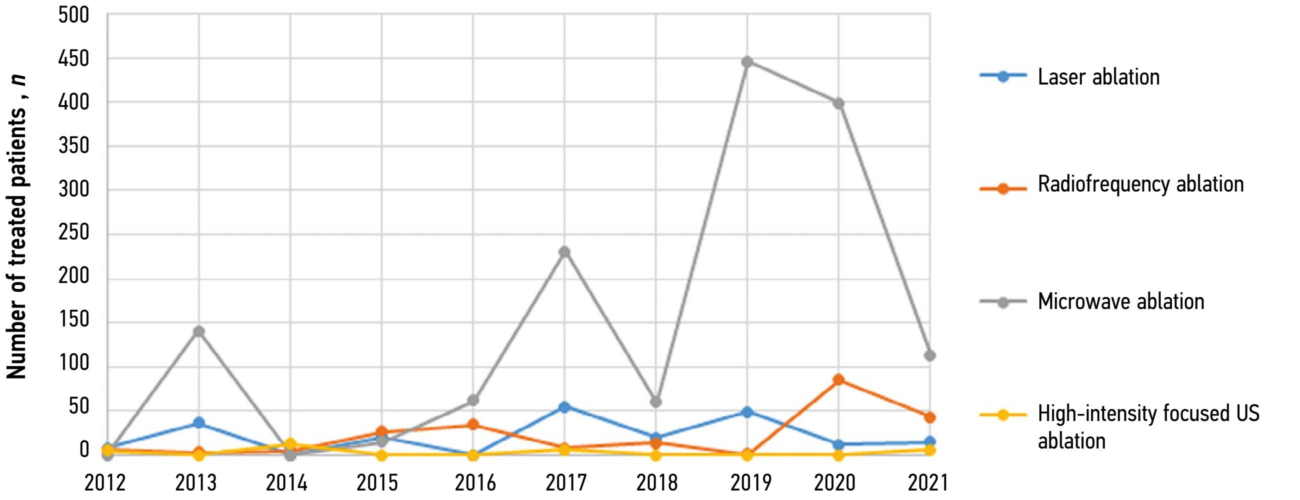

Fig. 1. Dynamics of publications on the use of alternative methods for periothyroid gland destruction.

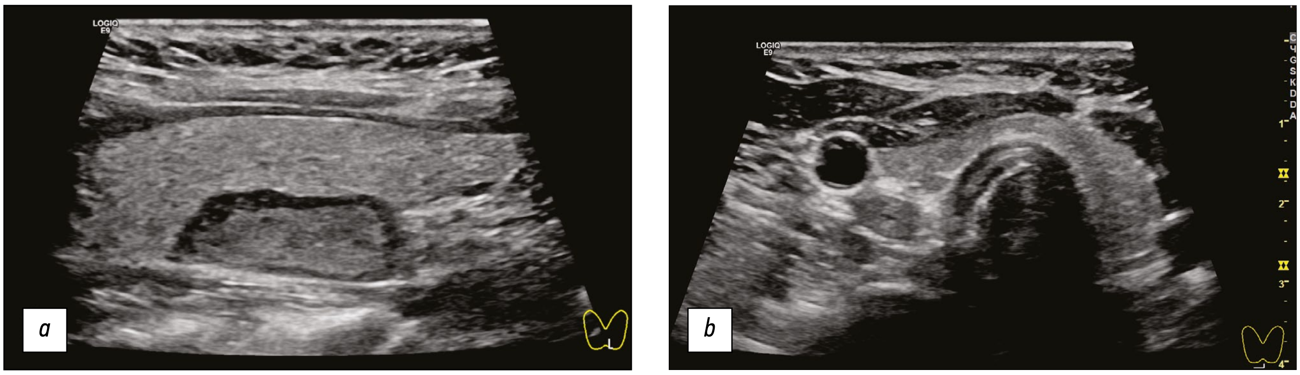

Fig. 2. US imaging of hyperfunctioning parathyroid glands in HPT: *a*, PHPT; *b*, SHPT.

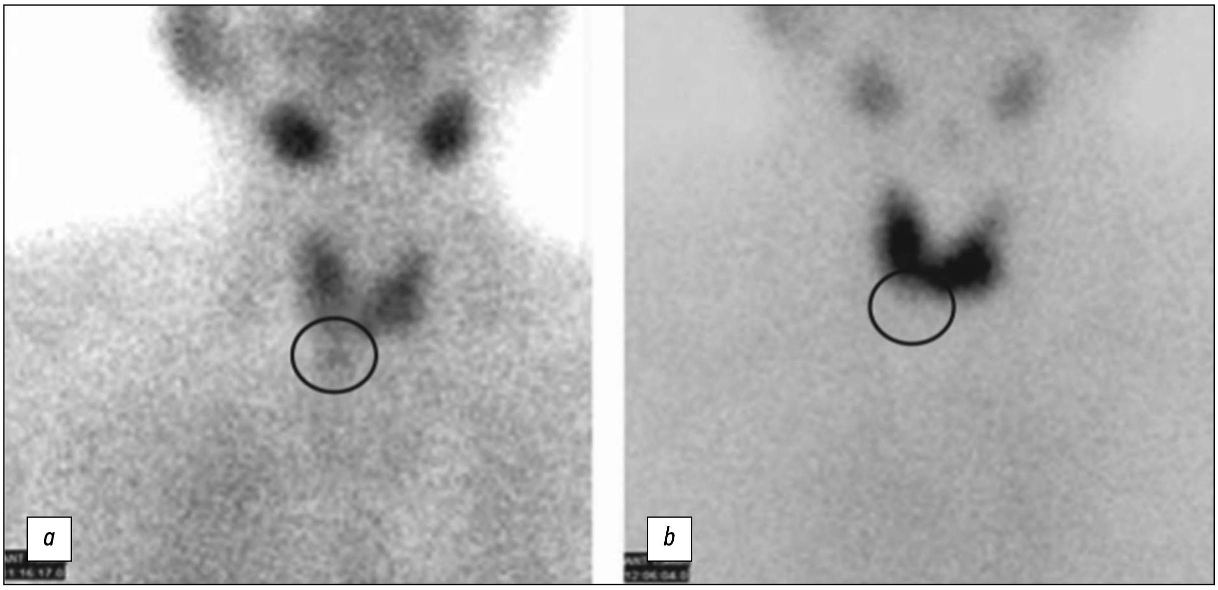

Fig. 3. Dual-isotope scintigraphy: *a*, ^{99m}Tc-MIBI scintigraphy; *b*, ^{99m}Tc-TcO4 scintigraphy.

The most informative method for topical HPT diagnosis is ^{99m}Tc-MIBI radionuclide diagnostics, especially in SPECT/CT mode (Fig. 4). On average, the sensitivity of the method reaches 88% (with a positive prognostic value of 96%) [20].

According to the literature, the sensitivity of ^{99m}Tc-MIBI studies in patients with PHPT is 88% [21], whereas a combination of diagnostic methods gives better results. Thus, a combination of ^{99m}Tc-MIBI scintigraphy and US has a sensitivity of 95% compared with the 80% and 87% for US and separate radionuclide diagnosis, respectively [22].

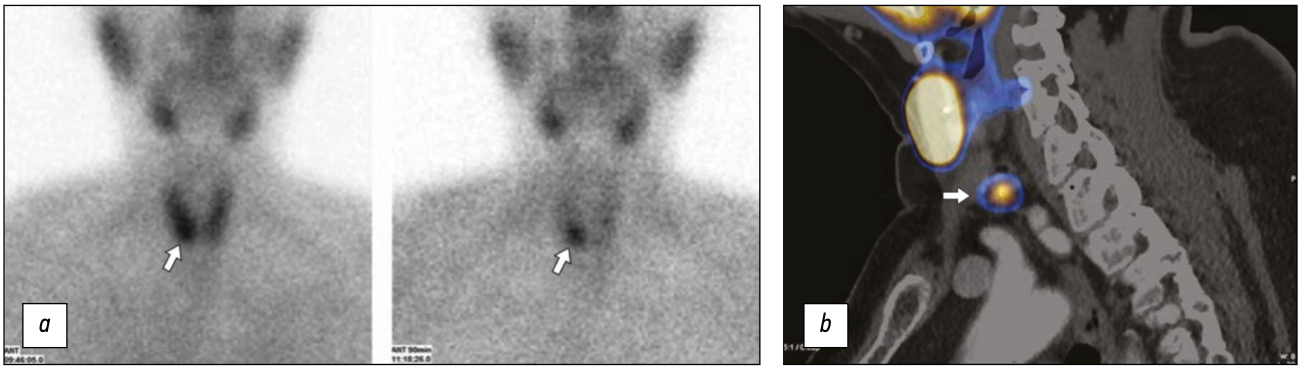

Fig. 4. ^{99m}Tc-MIBI radionuclide examinations (technetril): *a*, dual-phase planar scintigraphy (early and delayed scans). A parathyroid mass is visualized in the right lobe projection (arrows) with preserved and increased accumulation of radiopharmaceuticals on the delayed scan; *b*, ^{99m}Tc-MIBI SPECT/CT. A periothyroid mass is visualized behind and downward from the lower pole of the left lobe (arrow), which accumulates radiopharmaceuticals.

Intraoperative imaging for minimally invasive parathyroid removal techniques

The complementarity of preoperative and intraoperative imaging methods is an important factor for the localization of pathological structures when using minimally invasive techniques for the removal of parathyroid glands (Fig. 5).

Among intraoperative imaging methods, US is most commonly used to obtain real-time information about the region

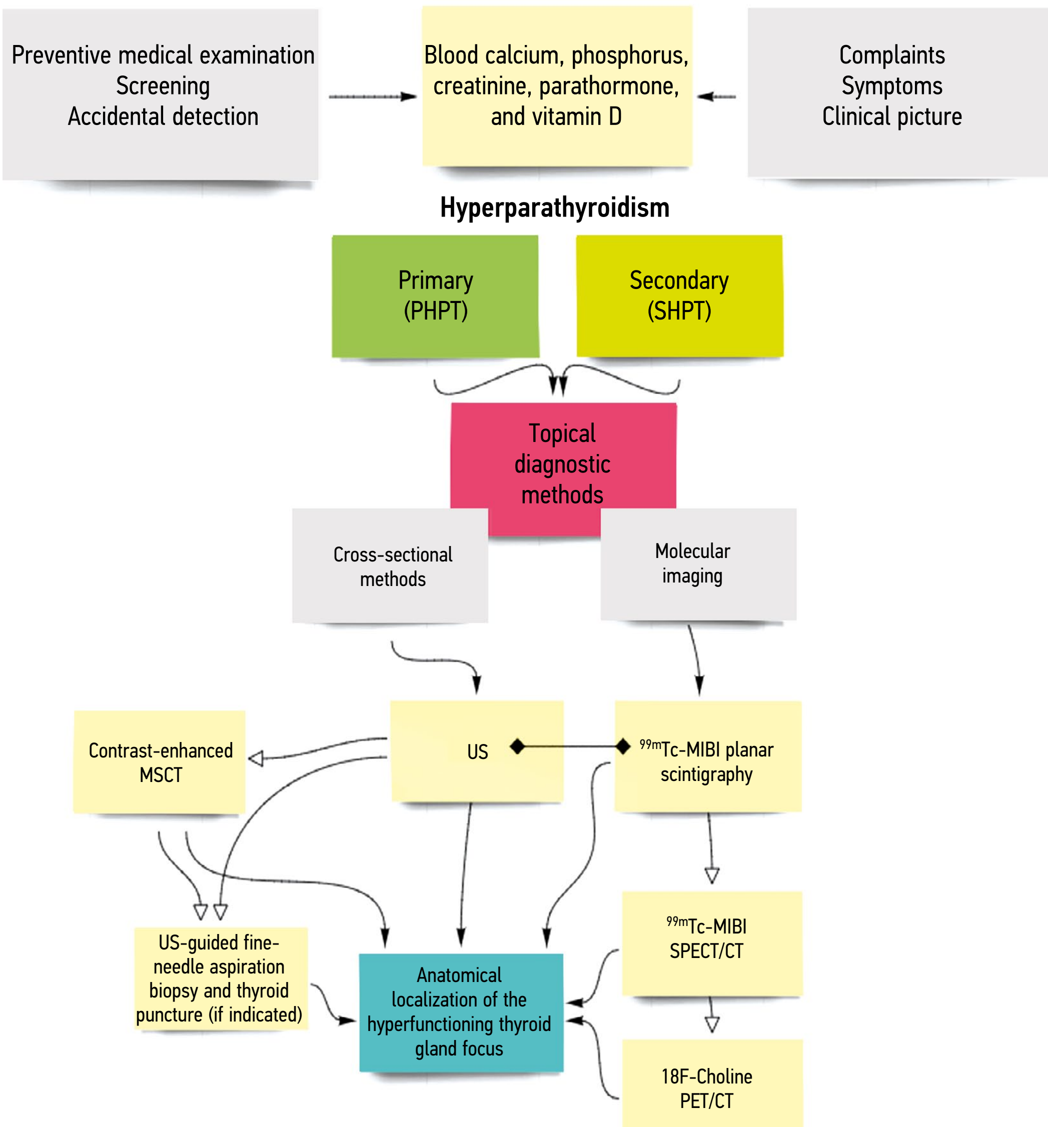

Fig. 5. Hyperparathyroidism diagnosis algorithm.

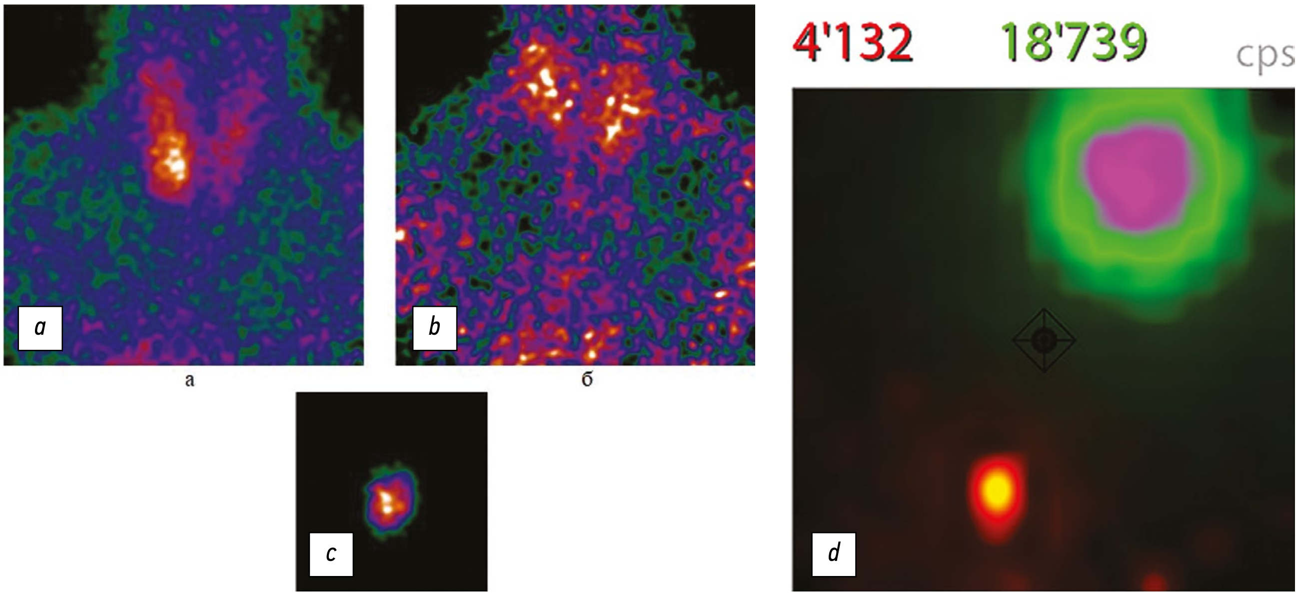

Fig. 6. Images obtained with Sentinella-102 (*a–c*) and CrystalCam (*d*) multichannel gamma probes.

of interest. However, with advances in technologies, multichannel gamma probes, including portable (Sentinella-102) and handheld (CrystalCam) gamma cameras, may be used in addition to US (Fig. 6).

These devices are based on the same physical principles. However, they implement different technical solutions, which make the use of handheld gamma cameras more promising (Table 3). Given the better characteristics, CrystalCam provides higher-quality (contrast) images as opposed to Sentinella-102.

Thus, intraoperative imaging techniques allow to control the thyroid bed area and use parathyroid gland destruction methods, which are alternatives to parathyroidectomy.

MINIMALLY INVASIVE THERMAL ABLATION OF HYPERFUNCTIONING PARATHYROID GLANDS

Thermal ablation has uncontrolled effects on surrounding tissues to varying degrees, and the location of the parathyroid glands may be adjacent to the recurrent laryngeal nerve. The need to assess the risk of recurrent laryngeal nerve damage during thermal ablation creates additional difficulties in the choice of treatment, given that the loss of vocal function is a highly undesirable complication. The more focused and controlled the thermal exposure, the lower the risk of surrounding tissue damage. For example, the MRgFUS method (InSightec, Israel) uses MR-guided focused US by heating the object of thermal destruction (see below). Currently, no sufficient evidence exists for the full comparison of thermal ablation and surgical treatment in terms of risk of recurrent laryngeal nerve damage. However, the evidence base will continually grow.

Laser destruction (ablation)

The invention of the ruby crystal laser by the American physicist Theodore H. Maiman in 1960 ushered in an era of using this technology in various fields of human life, including medicine [23]. The laser found its first practical application in medicine for microadhesion during retinal surgery in 1962. Historically, lasers were originally used in ophthalmology, given that the eye and its interior are among the

Table 3. Characteristics of gamma probes

Parameters	Installation	
	Portable gamma camera	Handheld gamma camera
Model	Sentinella-102	CrystalCam
Sensitivity, count rate, MBq	300–200	5000
Count rate, 10^6	1,7	6,2
Spatial resolution with collimator (native), mm	4–10 at 10 cm distance with different collimators	5,4–9,2
Energy resolution, %	16	<7
Dynamic range of detectable energies, keV	50–200	40–250

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most accessible organs due to their transparency. The first procedure that may be called laser ablation was performed at the National Medical Laser Centre in London in 1984. A patient with skin cancer underwent a 10 min surgery using Nd-YAG laser radiation with a 20 W output power [24].

Laser ablation is based on heating pathological biostructures by the application of energy to cause irreversible damage at the cellular level (tissue necrosis due to fluid heating in cells and its subsequent evaporation). Typically, tissues are heated to a temperature of 50 °C–54 °C to achieve coagulation within the region of interest.

Currently, laser ablation is increasingly used to remove parathyroid glands. The technique is based on the US-guided introduction of fibers into the periothyroid gland (Fig. 7). Then, the laser is switched on, and energy is brought in through the fiber to further coagulate the tissue. For laser ablation, a hybrid system is commonly used (EchoLaser X4, Esaote, Genova, Italy), and it combines US with a linear sensor and four independent fibers to deliver laser radiation to the periothyroid gland. The radiation is generated by a diode laser with a wavelength of 1064 nm, a beam diameter of 0.3 mm, and an output power level of 1–7 W. Optical fibers 1.5 m long with a 300 μm core are inserted percutaneously into the target using a 21G needle.

The use of laser ablation to treat patients with functional adenomas of parathyroid glands demonstrates high levels of sustained complete response with a clinically significant follow-up period within 24 months. Clinical HPT symptoms disappeared by 6 months. Alternatively, persistent serologic normalization of parathormone and calcium was observed by the same period [25].

Radiofrequency ablation

The capability of radiofrequency waves to pass through biological tissues was discovered in 1891. However, an increase in tissue temperature did not result in neuromuscular excitation. Thus, this discovery became the starting point for the development of the radiofrequency ablation method [26]. For a long time, scientists faced the problem of tissue necrosis expansion during exposure to radiofrequency waves and after its solving, had difficulties associated with the uncontrollable form and unpredictability of necrosis development. This problem was solved only by the end of the XX century, with the invention of a special electrode type that allowed the prediction of necrosis in tissues more accurately [27].

The physical basis of the method is resistive heating through an electrically conductive pathway (exposure to alternating current on the tissue), which consists of tissue molecules with most of the particles being water molecules. The dipole moments of the molecules, while attempting to remain aligned in the direction of the current, are forced to oscillate when the alternating current is rapidly applied and transmit the oscillations to neighboring molecules. Energy losses due to friction between adjacent molecules lead to local energy release and temperature increase above 50 °C, which activates the subsequent tissue necrosis. Radio waves are generated in the frequency range of 450–500 kHz. The main physical limitation of the method is its use in tissues with low electrical conductivity [28].

Radiofrequency ablation is used for various tumors, including those of lungs, kidneys, breasts, bones, thyroid glands, and liver [29–31]. Recently, studies have been conducted to verify the efficiency and safety of this technique in PHPT treatment and consider it as an alternative to open parathyroidectomy [32]. The procedure is US guided. A probe is inserted into the adenoma through a puncture, and the total power delivered to the adenoma varies from 10 W to 70 W, depending on the mass size [33].

The method is an alternative to open parathyroidectomy for patients with comorbidities and a single adenoma that is visible on US and SPECT/CT. Large adenomas that cause discomfort in the neck or cosmetic problems are also good candidates. If periothyroid glands are suspected for a malignancy (US signs of local invasion, size >3 cm, laboratory parathormone >300 pmol/L, and albumin-corrected calcium >3 mmol/L), the procedure is contraindicated. If periothyroid

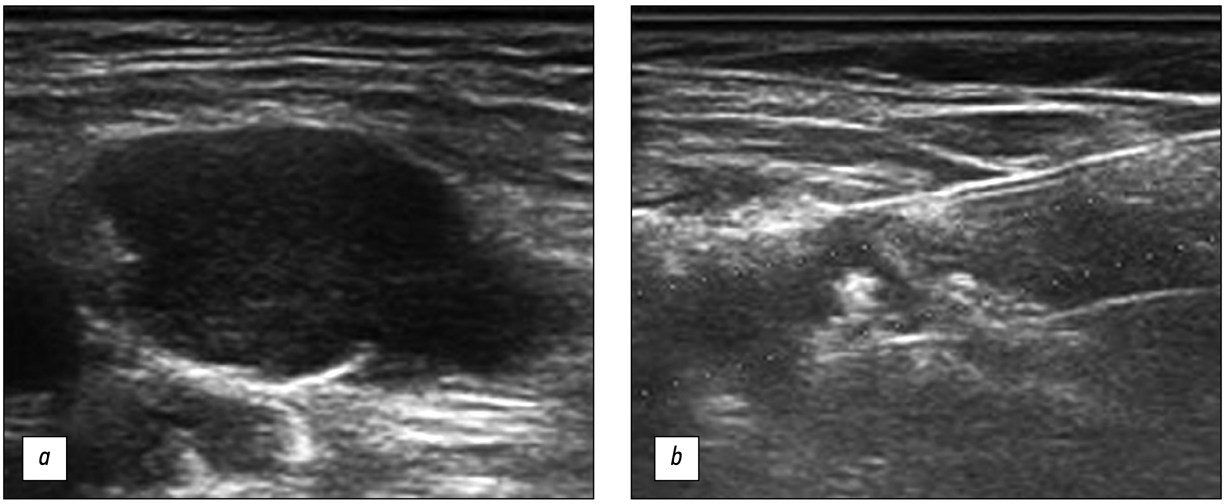

Fig. 7. Laser ablation in primary hyperparathyroidism: *a*, parathyroid adenoma; *b*, two laser fibers and a periothyroid area after ablation.

carcinoma is suspected, then surgical removal and pathomorphologic verification are recommended.

Microwave ablation

Microwave ablation is the "youngest" method. The first references to the use of microwave ablation date back to the 1980s. However, generators applicable for this procedure began to be produced commercially in the XXI century, which largely pushed the development of this area [34].

The mechanism of microwave ablation is based on the effect of electromagnetic fields with high frequencies (915 MHz to 2.45 GHz). This type of radiation is between infrared radiation and radio waves. Water molecules are polar, that is, electric charges on molecules are asymmetrical. The part of molecules that contains two hydrogen atoms is positively charged, whereas that with oxygen is negatively charged. Molecules function as small electric dipoles that rapidly rotate back and forth in spatial orientation and attempt to align with charges of opposite polarity. Polar molecules in the tissue are forced to continuously rearrange with the oscillating electric field and increase their kinetic energy and consequently, the temperature of the tissue. Tissues with a high-water content (such as solid organs and tumors) are the most favorable for this type of heating. When temperatures reach 50 °C–100 °C, protein and enzymatic degradation and denaturation of histone complexes, which are necessary to maintain the tertiary DNA structure, are activated. After exposure to these cytotoxic temperatures, cell death through coagulation necrosis eventually occurs [35].

Microwave ablation for PHPT is US-guided. The surgeon creates access through a 17G needle to bring the applicator antenna to the periothyroid gland. At the end of the applicator, a field is formed through which energy is transmitted to the tissue. Ablation is performed in a fractionation mode with an input power of 30 W for 25–30 s for each point in the volume. The duration of the procedure is 3–5 min, and it is performed until a hypoechogenic picture is obtained on the US image [36].

According to the literature, the incidence of recurrent and persistent HPT after parathyroidectomy was 0.83%–26% and 0.4%–15%, respectively [37]. When microwave ablation was used to remove the parathyroid glands, the rates of local recurrence and new cases were 8.8% and 11.8%, respectively. Ablation implicitly differed from surgical treatment; however, the long-term efficiency was not inferior to parathyroidectomy [38]. The use of microwave ablation as a radical method for treatment in patients with PHPT is safe and effective, whereas the long-term follow-up period showed no increase in the number of complications.

High-intensity focused ultrasound ablation

R.W. Wood and A.L. Loomis first introduced the thermal properties of high-intensity US in 1927. Subsequently, J.G. Lynn described the use of a focused US generator in 1942, and this generator can induce *ex vivo* focal thermal ablation of liver and brain samples through intermediate areas of the skull and cerebral membranes without skin damage [39]. In the 1950s, brothers William and Francis Fry developed a transcranial system based on high-intensity US, and it can be used after craniotomy in animals to target deep parts of the brain, contributing to the development of interest in this type of ablation for the treatment of movement disorders such as Parkinson's disease [40].

The earliest cases of high-intensity US ablation therapy were described in the early 1990s in patients with prostate diseases, and further improvements in imaging techniques (US and MRI) allowed the treatment of a wide range of benign and malignant tumors [41]. Currently, the HIFU method is used to remove benign functionally active nodular neoplasms of the thyroid gland, hyperfunctioning parathyroid glands, and in prostate cancer [42–44].

The formation of ultrasonic waves occurs as a result of the inverse piezoelectric effect. The generator supplies an alternating voltage to the plate covers, which are applied to the piezoelectric crystal (quartz crystal). Consequently, the crystal lattice is deformed when exposed to the electric field, and forced oscillations occur. Resonance of oscillations is observed when the change frequency in the electric field voltage and the natural frequency of the crystal oscillation coincide. As a result, with a decrease in the crystal thickness, rarefaction is developed in the adjacent layers of the surrounding medium, and with its increase, the medium particles thicken. Thus, an ultrasonic wave arises in the medium, and it propagates in the direction perpendicular to the piezoelectric crystal surface.

Ultrasonic waves are generated in the frequency range from 20 kHz to 1 THz. Therapeutic US has an intensity of >5 W/cm^2, which may result in coagulation tissue necrosis and is most commonly used for ablation. Protein denaturation and coagulation necrosis usually occur at 56°C and have a 1 s exposure time, whereas temperatures above 43° for 1 h make tissues more susceptible to chemotherapy and radiation. The increase in temperature of biological tissues, which results from the absorption of ultrasonic radiation, is linearly proportional to sound intensity.

Currently, EchoPulse (Theraclion, Paris, France) is the only system available for high-intensity US ablation in PHPT. The device contains a diagnostic US unit for intraoperative imaging (7.5 MHz) and a therapeutic US component (3 MHz) for delivering the energy to the target volume. A special cooling circuit reduces the temperature between successive pulses. A pulse of therapeutic US creates an elliptical ablation area with the semi-major and semi-minor axes of 4.5 and 1 mm, respectively. After preplanning the procedure, several pulses are delivered to perform ablation. Safe boundaries of the treated area from the trachea, carotid artery, and skin are 3, 2 mm, 5 mm, respectively. The maximum treatable depth from the skin surface is 28 mm. The procedure is usually performed under sedation, during which the patient is conscious, and local anesthesia is rarely required.

Thus, the size of parathyroid glands and parathyroid hormone level decrease significantly after one month of therapy, whereas the calcium concentrations slowly decrease. Complete remission is noted in 23% after a year, good disease control is achieved in 69%, and the procedure is considered unsuccessful in 8% of the treated patients. The number of sessions largely depends on the therapeutic response [45].

Despite the encouraging results of these studies, high-intensity US therapy still has limiting factors. The procedure is time consuming, and the patient must remain immobile during the entire ablation period because the treatment will have to be restarted when they move. Moreover, additional procedures are needed to treat large and deep lesions, given that the maximum depth at which the method works is only 28 mm from the skin. If scars or moles are present between the transducer and the skin, performing ablation is not possible. Thus, larger studies are needed to introduce HIFU ablation into clinical practice.

DISCUSSION

Importantly, the quality of HPT destruction when using the above-mentioned methods may vary significantly. Adenomas or hyperplasia of parathyroid glands function by every cell, and destruction of only a part of the gland may not give the proper effect. In this regard, the most significant controversy is the determination of destruction volume to achieve the best result and consider the likelihood of complications. In the articles included in this review, the destruction volume was determined under US guidance and compared with the preoperative SPECT/CT data. Persistent complications were either not observed, or the authors did not specify these data in their findings, which further emphasizes the need for direct comparative and randomized clinical studies devoted to this issue.

Practically, the HPT nature must be considered and separately, the use of thermal ablation techniques in PHPT and SHPT (renal origin), when determining the destruction volume. These diseases are different, and the tactics of using minimally invasive techniques therefore may differ. Morphological changes in PHPT and SHPT are fundamentally different; therefore, the destruction volume in these diseases may vary.

A separate concern is the long-term efficiency of thermal ablation methods compared with surgical treatment. In the majority of the analyzed articles, a positive attitude toward the use of alternative treatment methods was observed, and these methods are rarely extremely and critically compared with traditional (radical) ones. However, insufficient data have been accumulated recently on the long-term follow-up of patients after thermal ablation in comparative studies to assess the efficiency in comparison with traditional methods. Therefore, the viability of alternative methods should mainly be considered at this stage, but only if traditional methods cannot be used.

Based on the analyzed information, the algorithm for HPT treatment, which considers the potential of alternative methods, was developed (Fig. 8). This algorithm differs from the clinical PHPT treatment guidelines approved by the Russian Ministry of Health and the recommendations for SHPT treatment proposed by Kidney Disease: Improving Global Outcomes) [46] and Kidney Disease Outcomes Quality Initiative [47]. However, the formulated algorithm is based on more recent data and the results of the latest studies with applications that are described in the technology review, which make them relevant for further discussion without changing or compromising other algorithms.

Thus, the review analyzed four methods of thermal HPT destruction as an alternative to surgical intervention. (Fig. 9). These methods use different physical principles of thermal ablation, and considerable clinical experience in their application has been accumulated. The HPT cause is determined by using functional and topical diagnostic

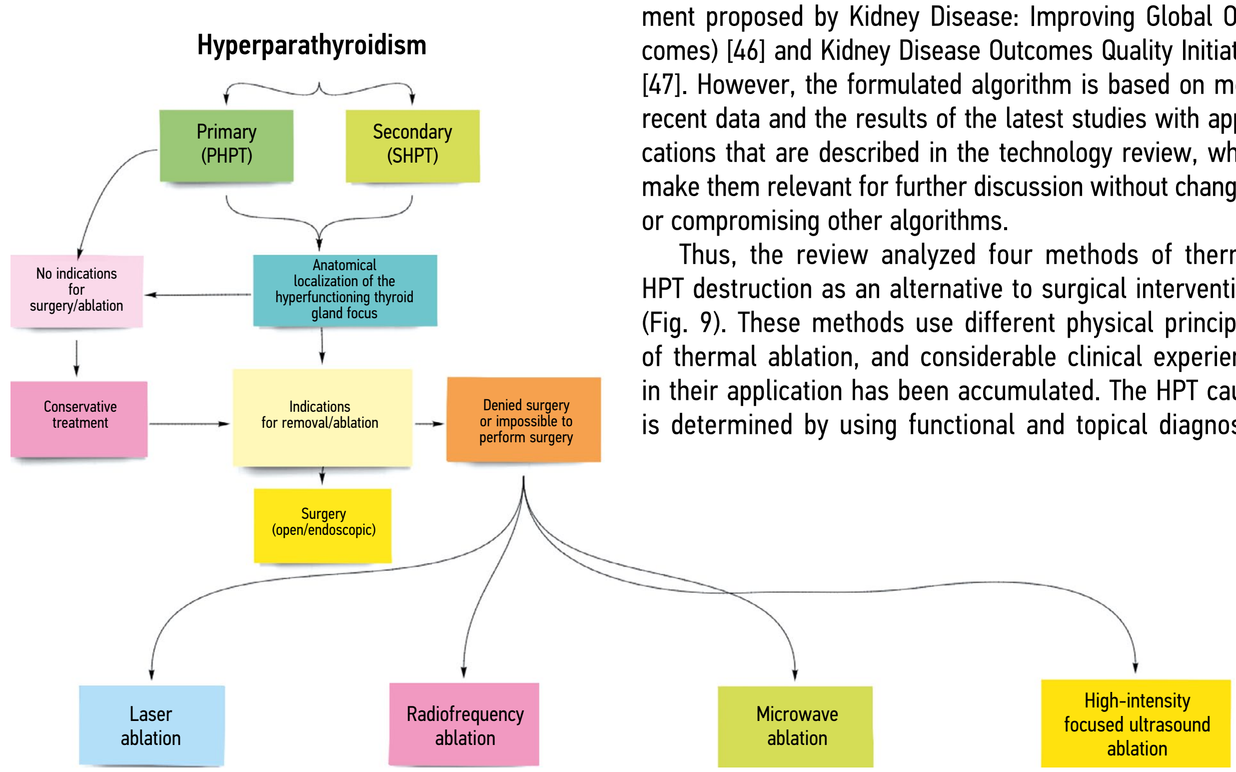

Fig. 8. Hyperparathyroidism treatment algorithm.

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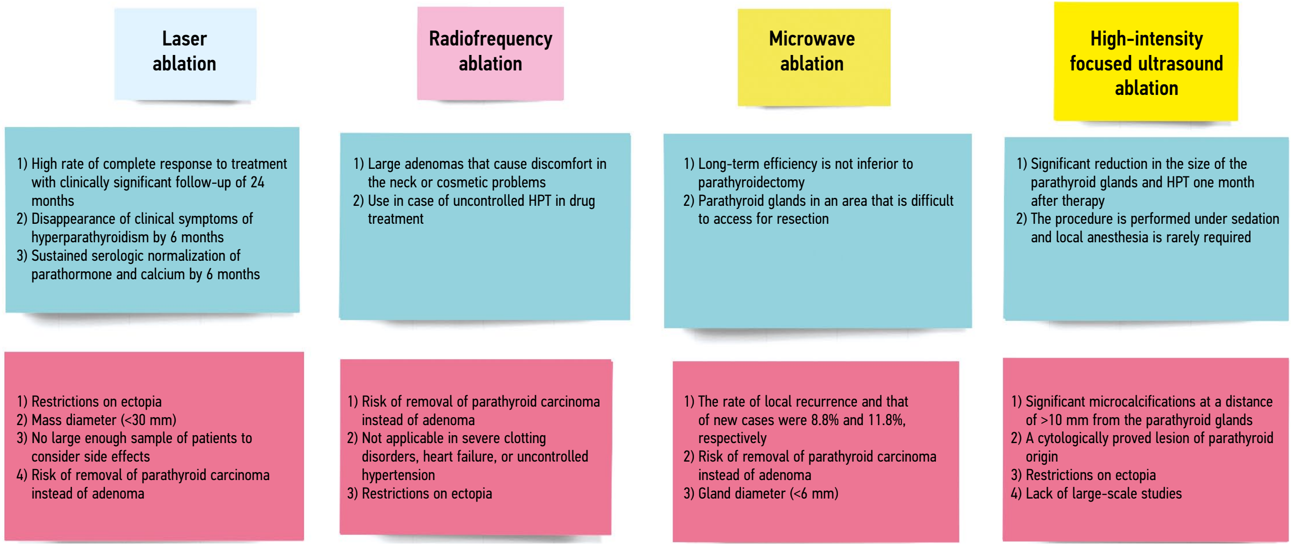

Fig. 9. Summary of the advantages (green) and disadvantages (red) of the methods for thermal destruction of the parathyroid glands.

methods. The current algorithm for preoperative topical HTP diagnosis, including US, MSCT, SPECT/CT, and PET/CT, allows to achieve 95% detection of hyperfunctioning parathyroid glands.

CONCLUSIONS

Thus, any of the selected methods of thermal destruction requires monitoring (US and MRI) of the thermal effect and highly qualified and experienced specialists. Each basic method of thermal destruction of hyperfunctioning parathyroid glands has its advantages and disadvantages, efficiency, and safety profile. The analysis of clinical practice shows that microwave ablation is the most popular (the first and best known) method at present. However, laser ablation is potentially more effective and safer primarily due to the technical capability of the method to perform more targeted and US-guided thermal destruction.

Not all patients with indications for surgical HPT treatment may be operated on. Hence, the interest in improving alternative nonsurgical treatment methods will increase.

ADDITIONAL INFORMATION

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