

See You There:

**From 9th to 10th
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In Livorno, Italy
At Marina Militare
11st Simposio Livornese
**Hot Topics Clinical
Endocrinology**

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of October**

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USA at the Walt Disney
World Swan and
Dolphin Resort 15th
**International
Thyroid Congress**
(ITC)

**From 29th to 31st
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Annual Meeting**

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AME Associazione
Medici Endocrinologi)
14th National Congress
with AACE Italian
Chapter Joint Meeting

“Laser ablation of thyroid nodules is rapid, safe and effective”

writes Tim Geach, senior editor of Nature Reviews of Endocrinology, basing his statement on the article Pacella, C. M. et al. *Outcomes and risk factors for complications of laser ablation for thyroid nodules. A multicenter study on 1531 patients. J. Clin. Endocrinol. Metab. doi:10.1210/jc.2015-1964*. He sustains that even if many small prospective trials have been completed, there were no real-world data describing the effectiveness of the procedure or the related risks of complications, until the publication of a new retrospective study from eight Italian centres, in which ultrasound-guided laser ablation of thyroid benign nodules was assessed in 1,531 patients. After having reported the excellent results of the study, Tim Geach highlighted that patients treated without local anaesthetic had less pain than those who received local anaesthetic. Moreover he notes that a reduction of the risk of procedural complications might be obtained using the eventual patients' pain during the procedure, because this indicates the clinicians to reposition the LAT apparatus. Tim Geach concludes that LAT is an effective and rapid outpatient procedure.

Tim Geach's article was published online on the 8th of September in the Research Highlight section on Thyroid of Nature Reviews of Endocrinology journal and it is available at <http://www.nature.com/nrendo/journal/vaop/ncurrent/full/nrendo.2015.153.html>.

The abstract of the original article of Pacella C. M. et al. is reported below.

Outcomes and Risk Factors for Complications of Laser Ablation for Thyroid Nodules. A Multicenter Study on 1531 Patients

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Background

Image-guided laser ablation therapy (LAT) of benign thyroid nodules demonstrated favorable results in randomized trials with fixed modalities of treatment. The aim of this retrospective multicenter study was to assess effectiveness, tolerability, and complications of LAT in a large consecutive series of patients from centers using this technique in their routine clinical activity.

Patients

Clinical records of 1,534 consecutive laser-treated nodules in 1,531 patients from eight Italian thyroid referral centers were assessed. Inclusion criteria were: solid or mixed nodules with fluid component up to 40%; benign cytological findings; normal thyroid function.

Methods

LAT was performed with a fixed-power protocol while number of applicators and illumination times were different according to target size. From one to three illuminations with pullback technique and with a total energy delivery based on the nodule volume were performed during the same session. Patients were evaluated during LAT, within 30 days, and 12 months after the procedure.

Results

Total number of treatments was 1,837; 1,280 (83%) of nodules had a single LAT session. Mean nodule volume decreased from 27 ± 24 mL at baseline to 8 ± 8 mL 12 months after treatment ($p<0.001$). Mean nodule volume reduction was $72\pm 11\%$ (range, 48–96%). This figure was significantly greater in mixed nodules ($79\pm 7\%$; range, 70–92%) because they were drained immediately before laser illumination. Symptoms improved from 49% to 10% of cases ($p<0.001$) and evidence of cosmetic signs from 86% to 8% of cases ($p<0.001$). Seventeen complications (0.9%) were registered. Eight (0.5%) patients experienced transitory voice changes that completely resolved at ENT examination within 2–84 days. Nine (0.5%) minor complications were reported. No changes in thyroid function or autoimmunity were observed.

Conclusions

Real practice confirmed LAT as a clinically effective, reproducible, and rapid outpatient procedure. Treatments were well tolerated and risk of major complications was very low.

Comment of Dr C.M. Pacella on US-guided PLA



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US-guided laser thermal ablation is increasingly used in the treatment of symptomatic or steadily growing thyroid nodules which are benign at cytological assessment^[1]. Several randomized controlled trials and a few experts' reviews state that Laser Ablation (LA) is a well tolerated and substantially safe procedure^[1-4]. The present study was based on a consecutive series of unselected benign nodules of variable size and structure. Patients were treated in the participating centers during their usual clinical activity with the same equipment and technique but with a

case-by-case modality of treatment and a total energy delivery based on the initial volume.

This large retrospective series demonstrates that LA induces, mostly with a single treatment, a clinically relevant volume reduction, with a mean nodule decrease that ranges from 48 to 96% (mean $72\pm 11\%$ versus baseline) 12 months after treatment. The volume reduction registered in this study was definitely greater than in previous prospective randomized trials on LA of solid cold nodules^[5-12] (Table 1).

Hospital	Number of Patients M/F	Age Mean \pm SD	Number of Nodules	Volume of Nodules Mean \pm SD	Mean Number of Sessions per patient	Volume Reduction at 12 th month Mean \pm SD	Number of Patients with two or more nodules	Local Anaesthesia	Sedation	Number (%) of Major Complications	Number (%) of Minor Complications	Number (%) of Side Effects
Albano L.	341 110/231	51.5 \pm 13.7	341	13 \pm 12 (2-126)	1,5	67 \pm 10		yes	no	1 (0,3)	1 (0,3)	37 (10.9)
Atri	138	51.5 \pm 13.7	138	13 \pm 9 (1.5-45)	1	76 \pm 8		yes	yes	3 (2.2)	2 (1.4)	20 (14.5)
Alzano L	36 4/32	58.6 \pm 15.0	36	13 \pm 9 (1.5-45)	1	84 \pm 5		yes	yes	0 (0.0)	0 (0.0)	1 (2.8)
Bari	45 10/35	52.0 \pm 13.3	45	13 \pm 9 (1.5-45)	1	92 \pm 13		yes	yes	1 (2.2)	0 (0.0)	13 (28.9)
Cosenza	242 62/180	54.4 \pm 11.8	242	13 \pm 9 (1.5-45)	1	76 \pm 8		yes	no	0 (0.0)	0 (0.0)	54 (22.3)
Livorno	334 111/223	51.6 \pm 31.1	337	13 \pm 9 (1.5-45)	1.4	68 \pm 8	3	no	no	1 (0.3)	0 (0.0)	184 (54.6)
Perugia	58 26/32	58.1 \pm 8.9	58	13 \pm 9 (1.5-45)	1.1	76 \pm 7		yes	yes	2 (3.4)	2 (3.4)	51 (87.9)
Perugia	189 81/108	56.1 \pm 9.9	189	13 \pm 9 (1.5-45)	1.1	73 \pm 11		no	yes	0 (0.0)	4 (2.1)	71 (37.6)
Pisa	148 18/130	52.6 \pm 13.0	148	47 \pm 27 (6-172)	1.1	72 \pm 11		no	yes	0 (0.0)	0 (0.0)	32 (21.6)
Combined Hospitals	1531	54.1 \pm 14.3	1534	27 \pm 24 (1.4-216)	1.2	72 \pm 11	3			8 (0.5)	9 (0.6)	463 (30.2)

Table 1. Patients' data and treatment results.

In the present series the total energy delivery was increased according to the baseline size of the lesion to be ablated. According to other authors [13] these results confirmed that if there is a direct correlation between the amount of energy delivered and the baseline volume of the nodule, a greater volume reduction may be attained.

While various and even severe complications of LA have been described in previous reports [14-17], in this series no damage to the trachea wall or nodule colligation, anecdotally reported in previous case reports, was recorded. These unusual complications were probably due to incorrect positioning of the laser fibre tip by an operator in the initial phase of his learning curve [15] or by delivery an excessive amount of energy [17]. Indeed, liquefactive changes can occur if more energy than needed to induce coagulative necrosis is released in the target tissue.

Major complications of LA were very rare (0.5% of cases). These symptoms resolved within 2–84 days with corticosteroid treatment. Similarly, only nine patients reported minor complications, which were perithyroid haematoma (n = 8) and skin burn (n = 1). However, this burn was an isolated procedural accident. Patient reports of mild, moderate and severe pain were also low (3.3%, 1.9% and 0.4%, respectively). Finally, it should be noted that some centers prefer to treat very large nodules (up to 215 mL) with clear and persistent mechanical and /or cosmetic symptoms (Table 1 and 2).

Type of complications Based on Society of Interventional Radiology criteria		Complications and Side Effects no. (% per session)				Time to Recovery (days)
		Time of Detection				
		Intra-operatively	Immediate post-operative (within 24 h)	Peri-procedural (within 30 days)	Delayed (after 30 days)	
Major						
Voice change	(C)		8 (0.5)			2-84
Minor						
Hematoma	(B)		8 (0.4)			2-10
Skin burn	(B)		1 (0.1)			10
Side Effects						
Pain	(A)					
	mild	194 (10.6)	61 (3.3)			1
	moderate	30 (1.6)	34 (1.9)			1-2
	severe		4 (0.2)			2-3
Vasovagal reaction	(A)	12 (0.7)				
Cough	(A)	1 (0.1)				
Fever (37.5°C-38.5°C)	(A)		141 (7.7)			1-4

Table 2. Complications and Side Effects.

The low rate of major complications in the present series is due to the use of the procedure established since the early 2000s^[18] with multiple heat sources and a pullback technique. The use of thin (21 G) needles allowed a non traumatic positioning of optical fibres into the target and the accurate monitoring of the treatment^[19]. Noteworthy, these results were obtained without the specific methods for the protection of critical structures, such the liquid-isolating region technique or the swallowing of cold water, that are used with the radiofrequency or microwaves ablation^[20-23]. In particular, before inserting microwave (MW) antenna, a mixture of 0.9% lidocaine and physiological saline may be infused into the appropriate area of surrounding thyroid capsule to achieve a liquid-isolating region and to protect the vital structures of the neck (carotid artery, trachea, esophagus and nerves)^[22]. During the multiple imaginary RF ablation units^[24] adjacent to the esophagus, the patient may be asked to swallow cold water^[20]; to prevent skin burns at the electrode puncture site, an ice bag may be applied during the procedure. Finally, because RF current passes through the heart during thyroid RF ablation, the use bipolar electrodes is always suggested to avoid potential complications such as heart attack and arrhythmia in patients with cardiac problems^[20].

In conclusion most benign thyroid nodules are asymptomatic and remain nearly stable over time. However, a fair number

of patients of them (especially in borderline iodine-deficient regions) show a slow but progressive growth that, due to the lack of medical treatments, is the cause of patient concern, repeat medical consultations, and frequently, of thyroid surgery. A single laser treatment performed with a nodule-tailored approach in the outpatient clinic on nodules which are becoming clinically symptomatic is followed in clinical practice by relevant reduction of the nodule volume and by clear improvement of mechanical symptoms and undesirable cosmetic appearance. Volume reduction continues over time until 12 months after initial treatment and remains stable for at least a few years with thyroid function completely maintained^[12]. Indeed, a single LA induces a high rate of volume reduction in solid nodules, with this figure increasing significantly in mixed nodules with fluid component up to 40%. Results, even in large nodules, are comparable to those reported with other techniques in smaller lesions^[24-27]. Due to the use of fine needles, the risk of major complications are lower than that reported with other thermal treatments^[20,23]. Table 3 summarizes the differences among the three techniques, taking into account of emerging techniques with microwave. The data reported are a snapshot of what is known in the literature so far.

Type of complications	MW n (%)		RFA n(%)	LA n(%)
	Feng et al	Yue et al		
Patients (n)	11	222	1459	1531
Nodules (n)	11	477	1543	1534
Sessions (n)	12	477	2197	1837
Major				
Voice change	1 (9.1)	8(3.6)	15 (1.02)*	8 (0.5) [¶]
Nodule rupture			2 (0.14)**	
Nodule rupture with abscess			1 (0.07)***	
Hypothyroidism			1 (0.07) [†]	
Brachial plexus injury			1 (0.07) [°]	
Minor				
Hematoma	4(36.4)		15 (1.02)	8 (0.5) [¶]
Skin burn			4 (0.27)	1 (0.1) [¶]
Vomiting			9 (0.62)	
Side Effects				
Pain				
mild	8 (72.7)			61 (3.3) ^{¶¶}
moderate				34 (1.6) [¶]
severe			38 (2.6)	4 (0.2) [¶]
Vasovagal reaction			5(0.34)	12 (0.7) ^{¶¶}
Cough		12(5.4)	3(0.21)	1 (0.1) ^{¶¶}
Fever (37.5°C-38.5°C)	3 (27.2)			141 (7.7) [¶]

* During and just after the procedure. all patients recovered their voice within 1-90 days except for two who were lost to follow up. In one patient voice change was related to haemorrhage. **Nodule ruptures were detected at 22 and 30 days after RFA and recovered within 30 days. ***The nodule showed delayed rupture with abscess formation 50 days after RFA and underwent surgery. [†] Persistent hypothyroidism was detected 6 months after RFA. [°]Just after ablation and recovered gradually within 2 months. [¶] Detected immediately after LA procedure; ^{¶¶}Detected intraoperatively.

Table 3. Complications and Side Effects associated with Microwave Ablation, Radiofrequency Ablation and Laser Ablation of Thyroid Nodules

In light of the data provided by this study and of the robust evidence of two decades of literature, laser thermal ablation is confirmed as a clinically effective, well-tolerated, and safe minimally invasive technology for non-surgical management of symptomatic benign thyroid lesions.

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Ultrasound-guided percutaneous laser ablation of metastatic lymph node in the neck from papillary thyroid carcinoma: 3 cases report



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[Abstract] Objective

To evaluate the feasibility, safety and effectiveness of ultrasound-guided percutaneous laser ablation (PLA) for metastatic lymph node in the neck from papillary thyroid carcinoma.

Methods

Three patients with a single metastatic lymph node which were diagnosed by fine-needle aspiration cytology underwent ultrasound-guided PLA for local treatment. After treatment, blood flow signals of the lymph nodes were evaluated with Color Doppler ultrasonography, and the ablation extent were assessed by contrast-enhanced ultrasonography (CEUS) immediately and 3 days after PLA. Complications were recorded. All the patients were followed at 30 days after PLA with conventional ultrasonography and serum levels of Thyroglobulin (Tg).

Results

All the 3 patients successfully completed the treatment under local anesthesia. The procedure was well tolerated without serious complications, and the patients required no analgesics. Color Doppler studies demonstrated absence of vascular signals in the treated area, and CEUS showed no blood supply in the three lesions at once and 3 days after PLA. Conventional ultrasonography at 30 days after PLA showed that treatment induced the varying degrees of shrinkage of metastatic lymph nodes in the three patients. Serum Tg levels stably maintained at a relatively low level before treatment and 30 days after treatment.

Conclusions

Ultrasound-guided PLA is a feasible, safe, and effective procedure for the ablation of metastatic lymph node in the neck from papillary thyroid carcinoma.

Key words

Percutaneous laser ablation; Papillary thyroid carcinoma; Lymph node; Ultrasonography.

International School of Thyroid Ultrasonography and Ultrasound-Assisted Procedures Advanced Course



Advanced Course of the **International School of Thyroid Ultrasonography and Ultrasound-Assisted Procedures, "Focus on US-guided diagnostic procedures and laser treatment of thyroid lesions"** that took place on the 17th and 18th of September in Albano Laziale (Rome, Italy) at the Department of Endocrinology and Metabolism, and Department of Diagnostic Imaging and Interventional Radiology of the Ospedale Regina Apostolorum reached a great success.

Medical doctors were from Colombia, Però, Portugal, Spain and Singapore.

During the morning of the first day of course, the attendants were splitted in two groups, one of the groups was followed by Prof. Enrico Papini (Chief of Department of Endocrinology and Metabolism, Ospedale Regina Apostolorum, Albano Laziale Rome, Italy) and the other one was followed by Dr. Giancarlo Bizzarri (Chief of Department of Diagnostic Imaging and Interventional Radiology, Ospedale Regina Apostolorum, Albano Laziale Rome, Italy).

Prof. Enrico Papini performed several ultrasound guided fine needle aspirations (FNA) of thyroid nodules, describing to the attendants the different phases of the operation and illustrating the supporting ultrasound images, in order to explain the interactions between the needle and the anatomical structures.

Dr. Giancarlo Bizzarri performed the ultrasound guided laser ablation of thyroid nodules, explaining the different steps of the operation and describing the best way to perform it, depending on the particular nodule morphology and anatomical structure of the patient. Then the two groups were swapped, so

that everyone could attend both the fine needle aspirations and the laser thermal ablations.

At the end of the morning, both Prof. Papini and Dr. Bizzarri gave additional clarifications and answered to questions of the attendants about the procedures performed.

In the afternoon Prof. Papini and Dr. Bizzarri illustrated through some presentations the main principles of the ultrasound techniques, such as the ultrasound pulse formation, the scanning of the ultrasound beam, how to process the signal and the color Doppler application.

The morning of the second day of the course was dedicated to a practical session in which the attendants could perform US-assisted thyroid FNA and US-guided percutaneous ethanol injection of cystic nodules on a gelatine model, under the assistance of Prof. Papini and Dr. Bizzarri.

After the practical session, a presentation session was performed, in which the attendants were trained on how to recognize US patterns of thyroid nodules suggestive of malignancy. During the last presentation, a list of real cases were presented by Prof. Papini, and the attendants were invited to suggest possible therapies in order to start a discussion on which could be the best approach for each particular case.

The feedback on the course given by the medical doctors was really positive, underlying the great adaptability, ease of use and precision of the percutaneous laser ablation technique, the usefulness of the practical simulation session in which everyone had the chance to perform US-guided thyroid FNA and percutaneous ethanol injection of cystic nodules and the competence and willingness of both Prof. Papini and Dr. Bizzarri.



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