TERAPIE ABLATIVE NELLA GESTIONE DEL NODULO TIROIDEO

ROBERTO CESAREO
RESPONSABILE UO MALATTIE METABOLICHE
OSPEDALE S.M. GORETTI
LATINA

Energia
Onde elettromagnetiche

- Onde radio (radiofrequenza)
- Microonde
- Radiazioni infrarosse (laser)
- Raggi X
- Raggi γ

Differiscono tra loro per la lunghezza d'onda e, di conseguenza, per la differente frequenza di emissione

ABLAZIONE CON ONDE TERMICHE

- *Temperatura locale tra 40 e 45°C*

  ➔ *I danni sono reversibili se il tempo di esposizine è meno di 30 minuti*

- *Temperatura locale tra 45 and 99°C*

  ➔ *il tessuto coagula a differenti tempi dipendendo dalla temperatura (1 secondo a 60° C)*

- *Temperatura locale > 99°C*

  ➔ *il tessuto vaporizza con successiva carbonizzazione e necrosi coagulativa*

- Area necrotica con cavità circondata da un'area sede di necrosi coagulativa
- dopo 4 settimane una capsula di tessuto connettivo ricopre la lesione

Pacella CM et al. Eur Radiol 1993

Thermal ablation procedures

Percutaneous

- Radiofrequency ablation (RFA)
- Laser ablation (LA)
- Microwave ablation (MWA)

Transcutaneous

- High-intensity focused ultrasound (HIFU)

TRATTAMENTO LASER

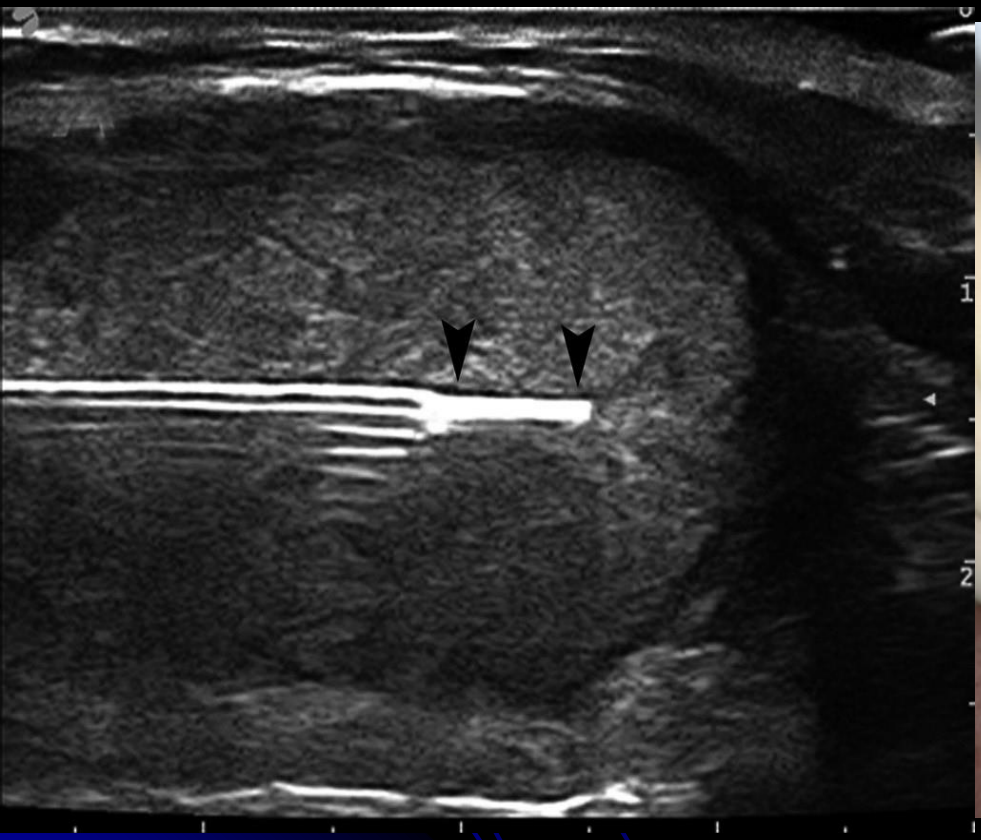
Consiste nel posizionare lungo l'asse maggiore del nodulo uno o più aghi sottili (fino a 4), da 21 G in relazione alle dimensioni del nodulo.

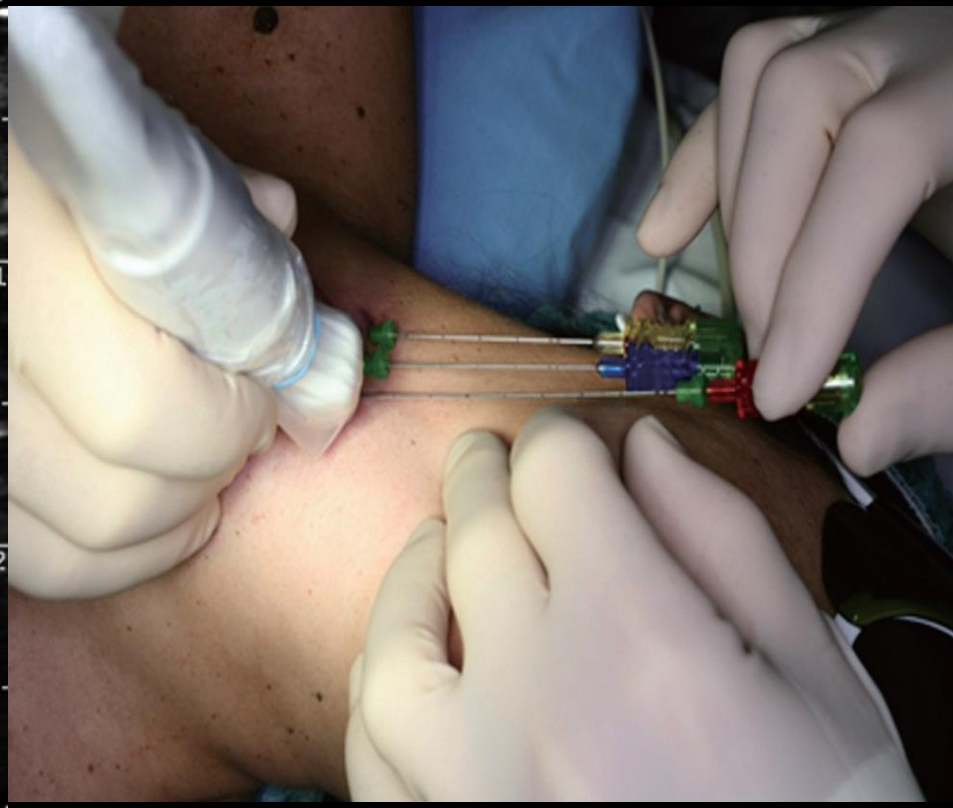
La punta della fibra deve essere a una distanza di sicurezza di 15 mm dalle strutture critiche del collo quali vasi epiaortici e trachea.

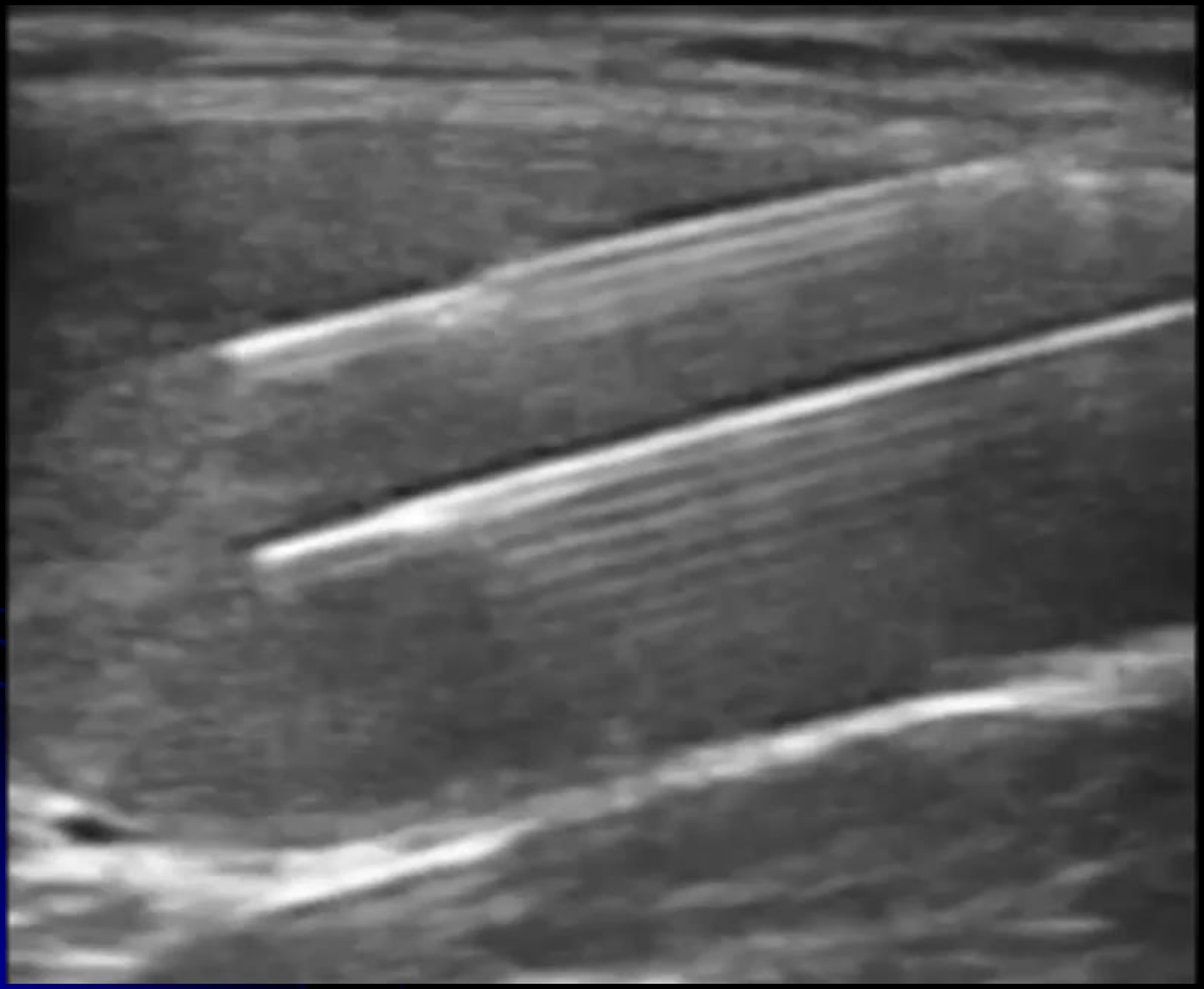
Il trattamento ha una durata variabile da 6 a 30 minuti.

La massima estensione dell'area trattata si ottiene a 72 ore per successivi fenomeni trombotici dei piccoli vasi che irrorano il tessuto tiroideo.

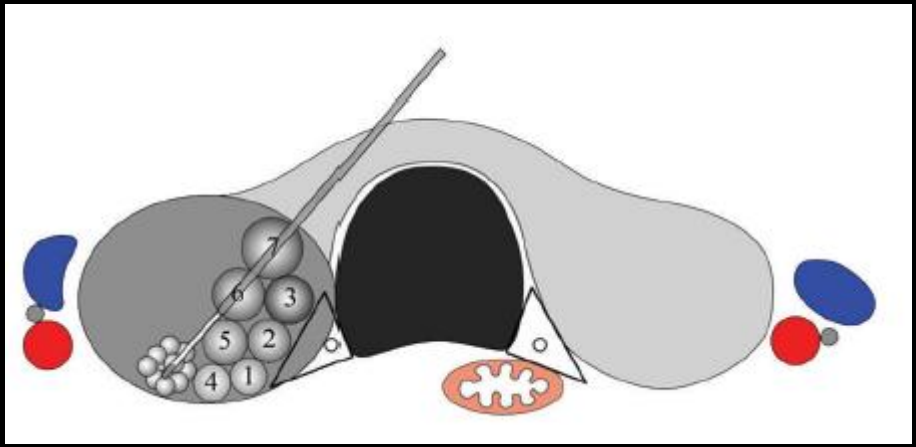
LASER

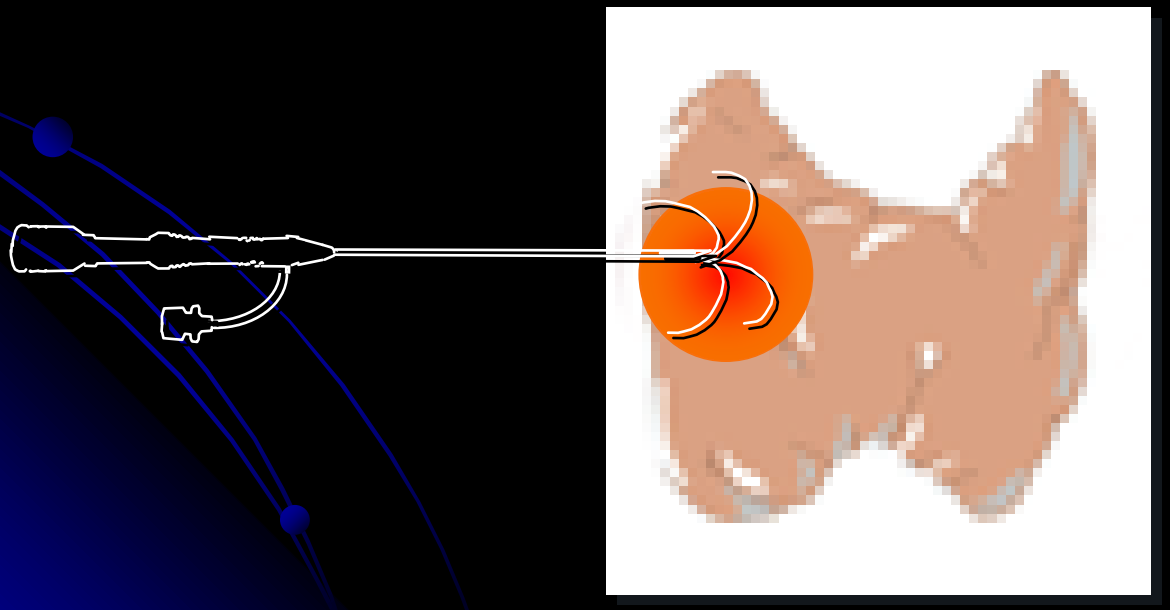






RADIOFREQUENZA
MOVING SHOT AND HOOK UMBRELLA





TECNICA RF

Dopo l'niziale utilizzo di un ago uncinato , di calibro maggiore,(14 G) Beak, ha proposto un'ago non uncinato, di calibro minore,(17G) con punta esposta di 1 cm ed usando la tecnica moving-shot; cioè suddividendo idealmente il nodulo in multiple piccole unità e di eseguire la RF in ogni singola unità muovendo l'elettrodo.

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND ASSOCIAZIONE MEDICI ENDOCRINOLOGI MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND MANAGEMENT OF THYROID NODULES

AACE/AME Guidelines

Candidates for LT_4 Treatment. Currently, routine LT_4 treatment in patients with nodular thyroid disease is not recommended (72). LT_4 therapy may be considered in patients from iodine-deficient geographic areas, in young patients with small thyroid nodules and colloid features at cytologic sampling, and in those who have nodular goiters with no evidence of functional autonomy. The use of LT_4 should be avoided in patients with large thyroid nodules or long-standing goiters, if the TSH level is <1 μIU/mL, in postmenopausal women or in men older than 60 years, and in patients with osteoporosis, cardiovascular disease, or systemic illnesses.

Guidelines 2006

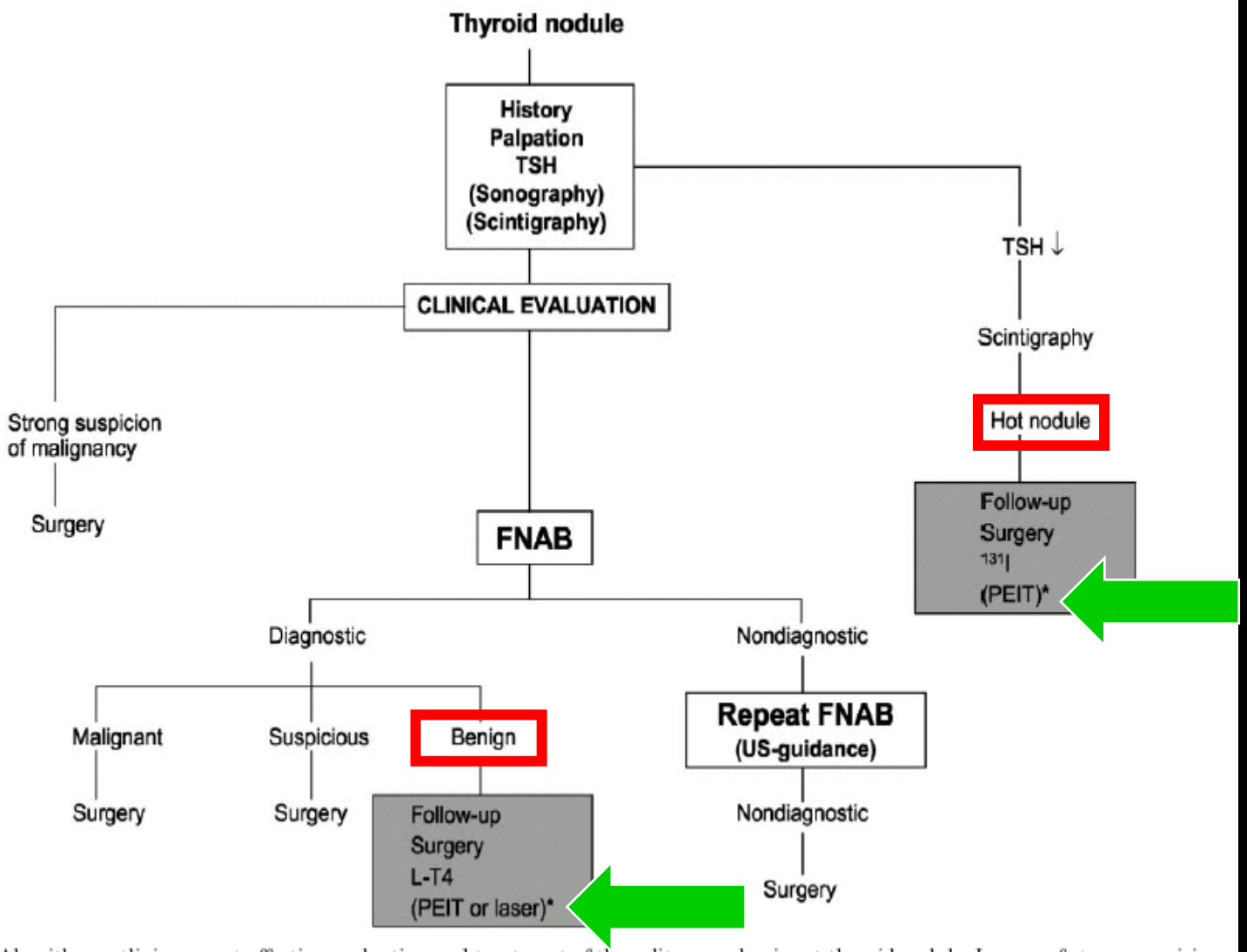


FIG. 2. Algorithm outlining a cost-effective evaluation and treatment of the solitary or dominant thyroid nodule. In case of strong suspicion of malignancy, surgery is advised irrespective of FNAB results. In case of a nondiagnostic result, repeat FNAB yields a satisfactory aspirate in 50%. FNAB guided by US (US-guidance) allows sampling from the periphery of a solid nodule or solid part of a mixed solid-cystic nodule, increasing the sufficiency rate. The options in case of a diagnostic FNAB cover both solid and cystic nodules. In case of recurrent cysts, the possibilities are reaspiration, surgery, or ethanol injection. The *shaded boxes* indicate treatment options. *, PEIT or ILP.

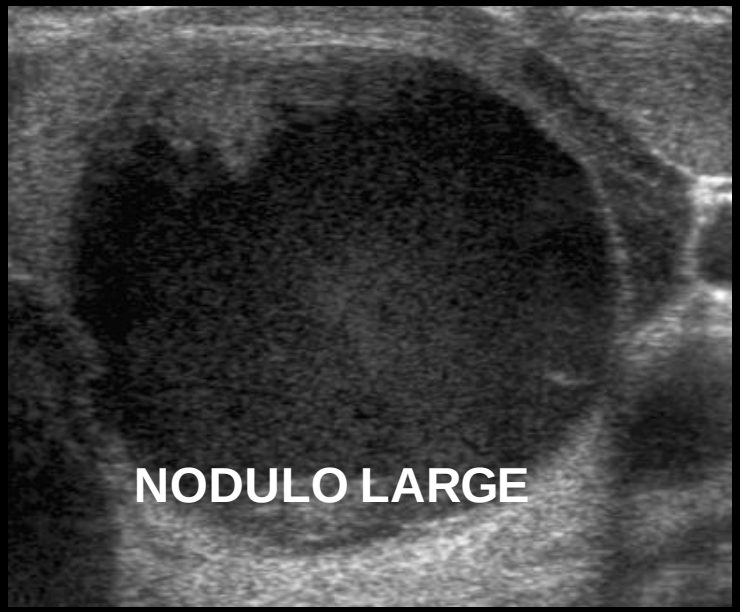
Minimally Invasive Ablation Techniques (AACE/AME GUIDELINES 2008)

TERMOABLAZIONE
Nodulo tiroideo

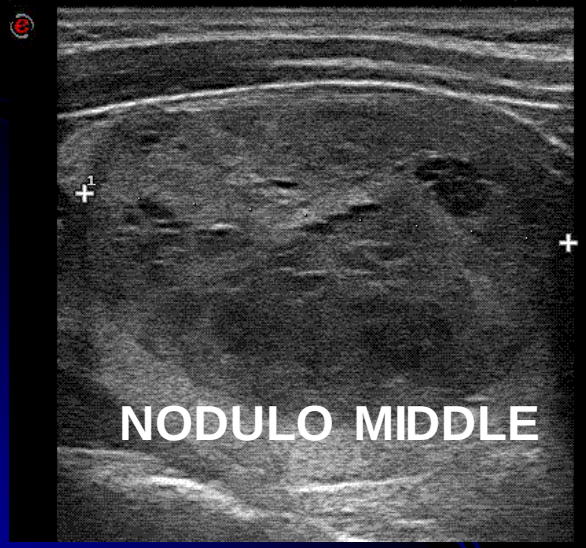
CHI/QUANDO/PERCHE' TRATTARE

CALCOLO DEL VOLUME TIROIDEO

VOLUME 20X18X21 = 4,1 ml



VOLUME 46X34X46 = 37 ml



VOLUME 2.8X2.8X3.2 = 13 ml

CLASSIFICAZIONE VOLUMETRICA

Nodulo small	<12 ml
Nodulo Middle	12 e 30ml
Nodulo Large	>30 ml

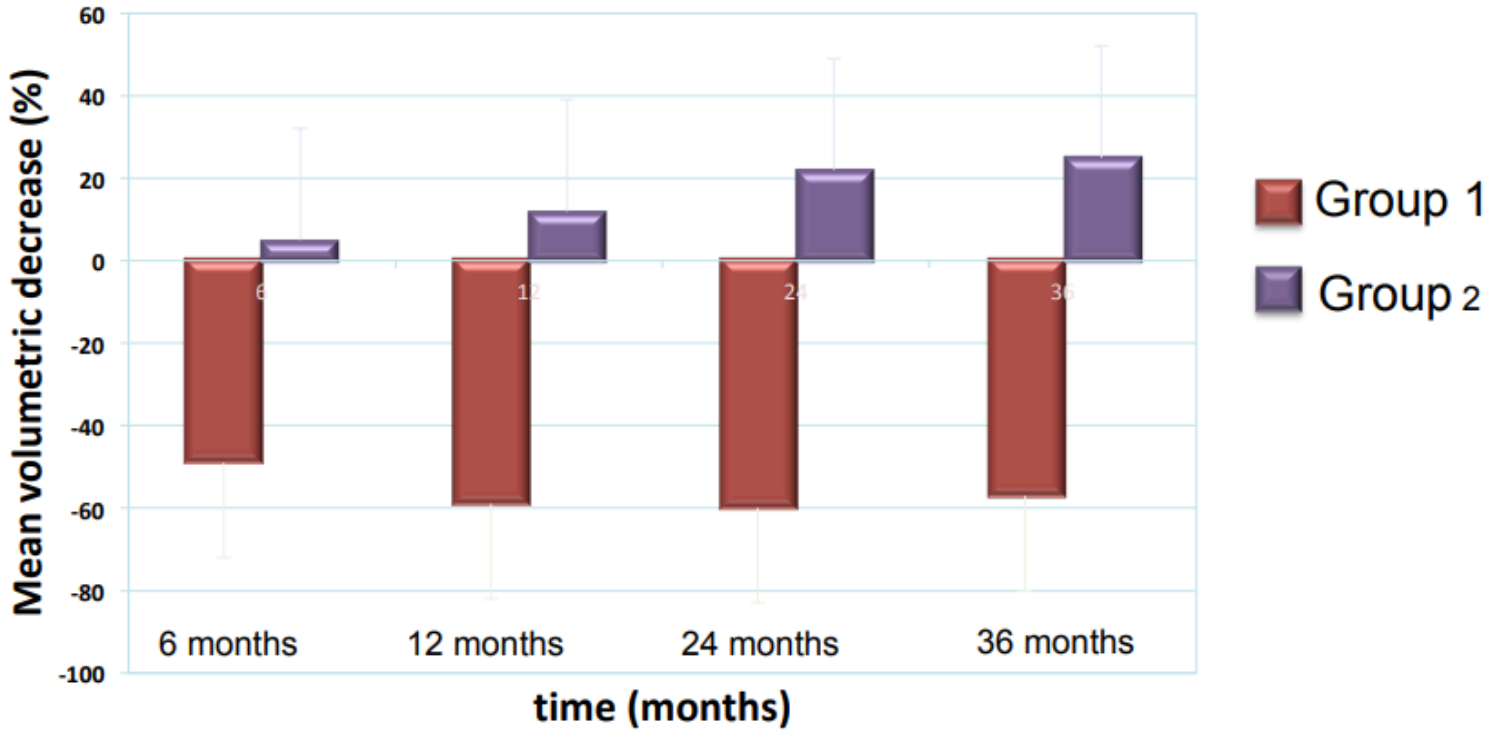
TERMOABLAZIONE
DATI DI EFFICACIA

- LASER: evidenze su nodulo ipocatante
- RF: evidenze cliniche su nodulo ipocaptante

- LASER: evidenze su nodulo ipercatante
- RF: evidenze cliniche su nodulo ipercaptante

2014: Italian Multicenter Study on Laser Ablation of Cold Thyroid Nodules. Three-Year Results

Mean volume changes (%) at 6, 12, 24, and 36 months respect to baseline values in Group 1 (active treatment, 101 cases) and Group 2 (99 controls).



JCEM 2014

2015: Large scale trials

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

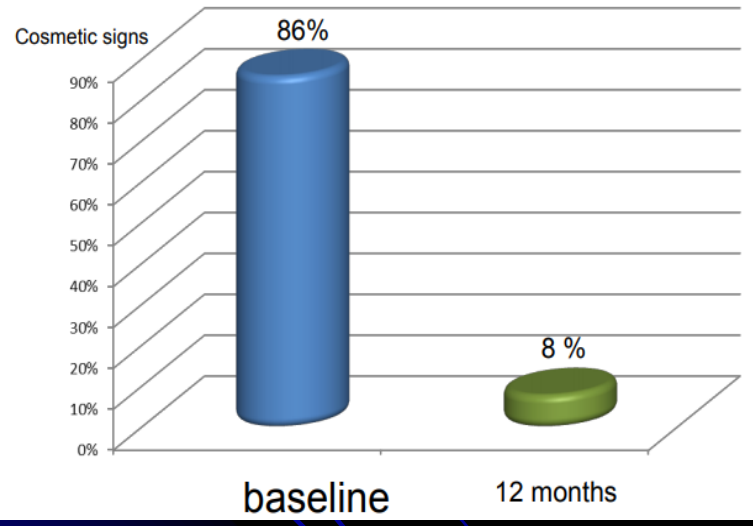
Pacella CM*, Mauri G°, Achille G°°, Barbaro D°°°, Bizzarri G*, De Feo P**, Di Stasio E+, Esposito R, Gambelunghe G**, Misischi I***, Raggiunti B, Rago T, Patelli GL#, D'este S #, Vitti P, and Papini E***

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±8mL 12 months after treatment ($p<0.001$). Mean nodule volume reduction was 72±11% (range, 48–96%). This figure was significantly greater in mixed nodules (79±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.

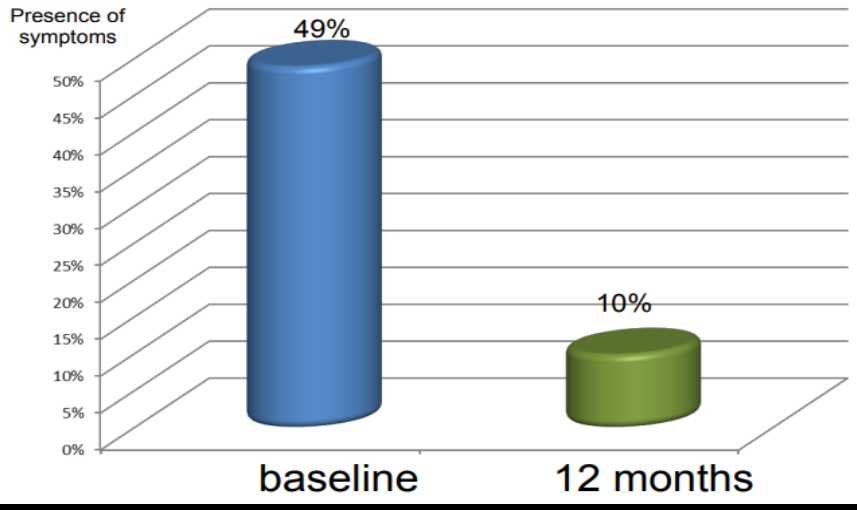
- **mean nodule volume decrease: 70%**
  (multiple treatments)
- **complication rate: 0.5%**

JCEM 2015

COSMETIC SIGNS (NODULE VISIBILITY) CHANGES: 12 MONTHS VS BASELINE



LOCAL SYMPTOMS CHANGES: 12 MONTHS VS BASELINE

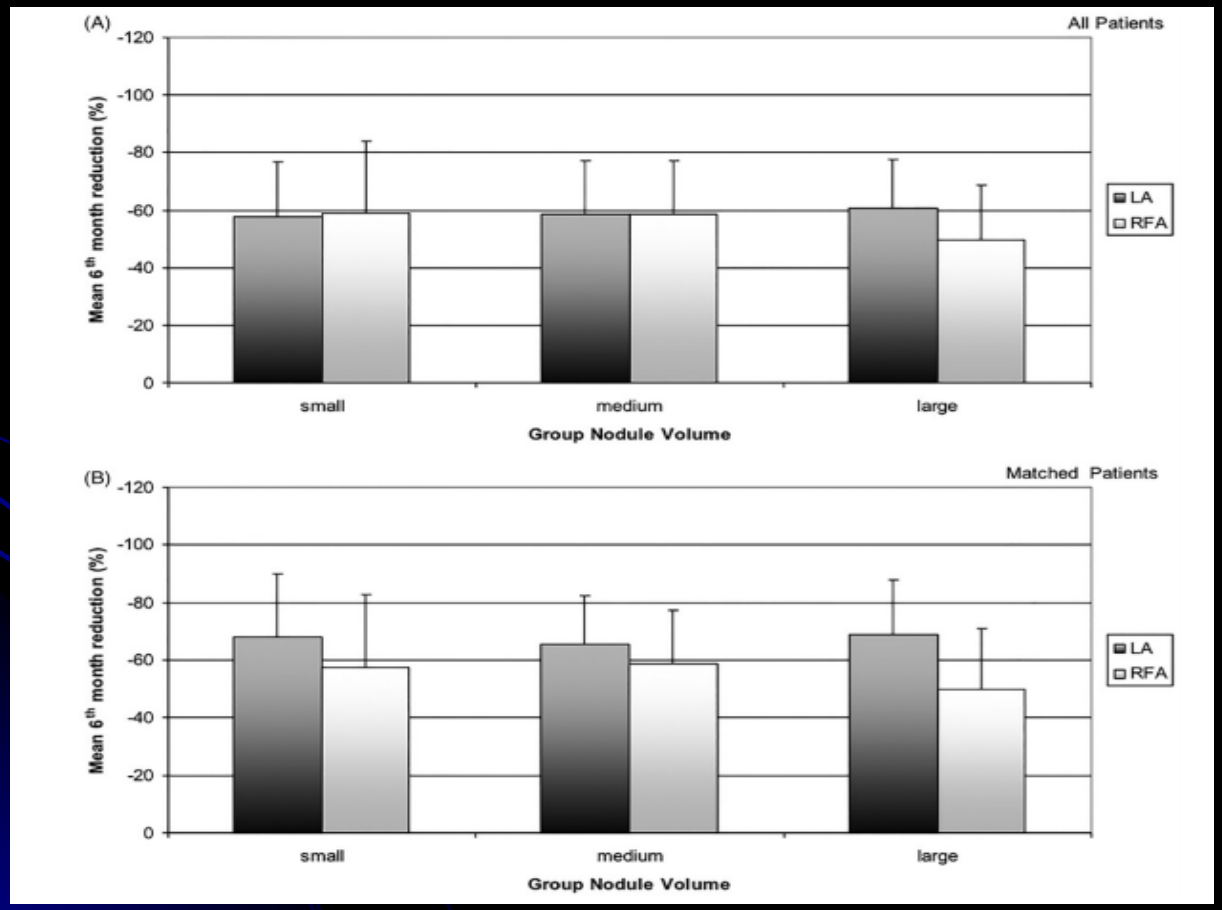


JCEM 2015

Journal
International Journal of Hyperthermia
Volume 0, - Issue ja

A Comparison of Laser with Radiofrequency Ablation for the Treatment of Benign Thyroid Nodules A Propensity Score Matching Analysis

Claudio Maurizio Pacella, Giovanni Mauri, Roberto Cesareo,

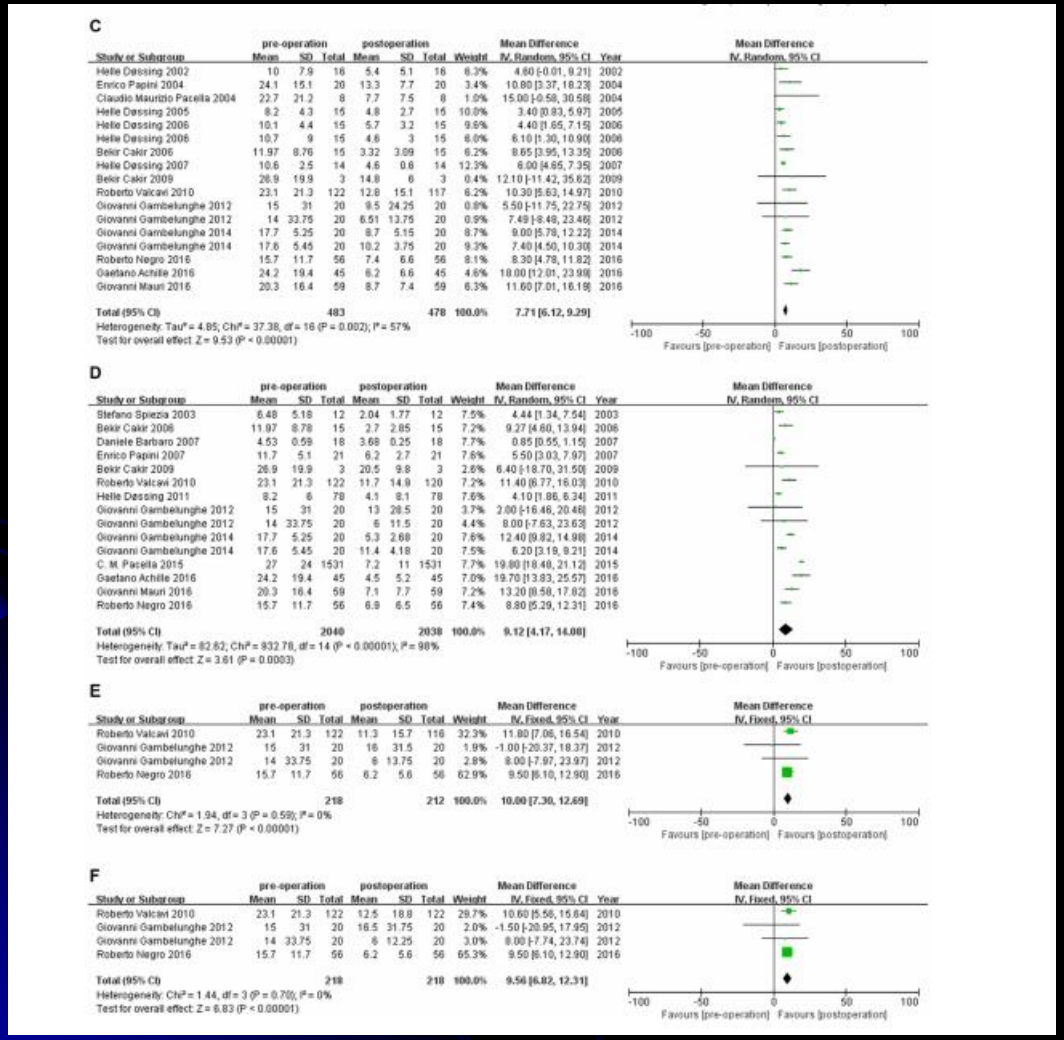


Int J Hypert 2017

Percutaneous laser ablation for benign thyroid nodules: A meta-analysis

Wei Fan Sui[1], Jian Yun Li[1] and Jian Hua Fu[1]

[1]Department of Interventional Radiology, The Affiliated Renmin Hospital of Jiangsu University, Zhenjiang, 212002, China



Larger number of high-quality prospective studies still needs to be performed.

Oncotarget, Advance Publications 2017

TERMOABLAZIONE
DATI DI EFFICACIA

- LASER: evidenze su nodulo ipocatante
- RF: evidenze cliniche su nodulo ipocaptante

- LASER: evidenze su nodulo ipercatante
- RF: evidenze cliniche su nodulo ipercaptante

Benign Predominantly Solid Thyroid Nodules: Prospective Study of Efficacy of Sonographically Guided Radiofrequency Ablation Versus Control Condition

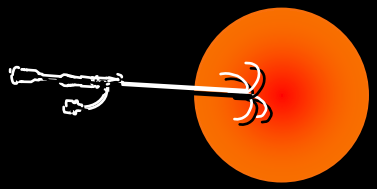


TABLE 1: Baseline Characteristics

Characteristic	Control Group	Radiofrequency Ablation Group	*p*
Sex (M/F)	3/12	3/12	1.00
Age (y)	47.47 ± 9.01 (34–66)	40.87 ± 11.08 (29–66)	0.06
Follow-up period (mo)	6.87 ± 0.99 (6–9)	6.43 ± 0.62 (6–8)	0.31
Triiodothyronine (ng/dL)	113.18 ± 18.51 (72–149)	104.59 ± 13.81 (79–124)	0.11
Free thyroxine (ng/dL)	1.49 ± 0.31 (0.90–1.90)	1.52 ± 0.22 (0.90–1.80)	0.84
Thyrotropin (μIU/L)	1.50 ± 0.82 (0.81–3.67)	1.50 ± 0.61 (0.47–2.35)	0.41
Solidity (%)	88.67 ± 13.30 (60–100)	81.67 ± 15.77 (50–100)	0.14
Volume (mL)	6.9 ± 4.0 (2.7–16.1)	7.5 ± 4.9 (1.7–20.0)	0.84
Symptom score	3.13 ± 1.51 (0–6)	3.33 ± 0.90 (2–5)	0.60
Cosmetic grade	3.47 ± 0.64 (2–4)	3.60 ± 0.51 (3–4)	0.68

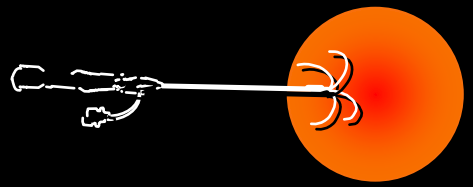
Baek Am J R 2010

Thyroid Nodules and Related Symptoms Are Stably Controlled Two Years After Radiofrequency Thermal Ablation

OBIETTIVI

Valutare l'efficacia a lungo termine della RTA nel trattamento dei noduli benigni della tiroide ad ecostruttura solida in pazienti anziani con sintomi compressivi

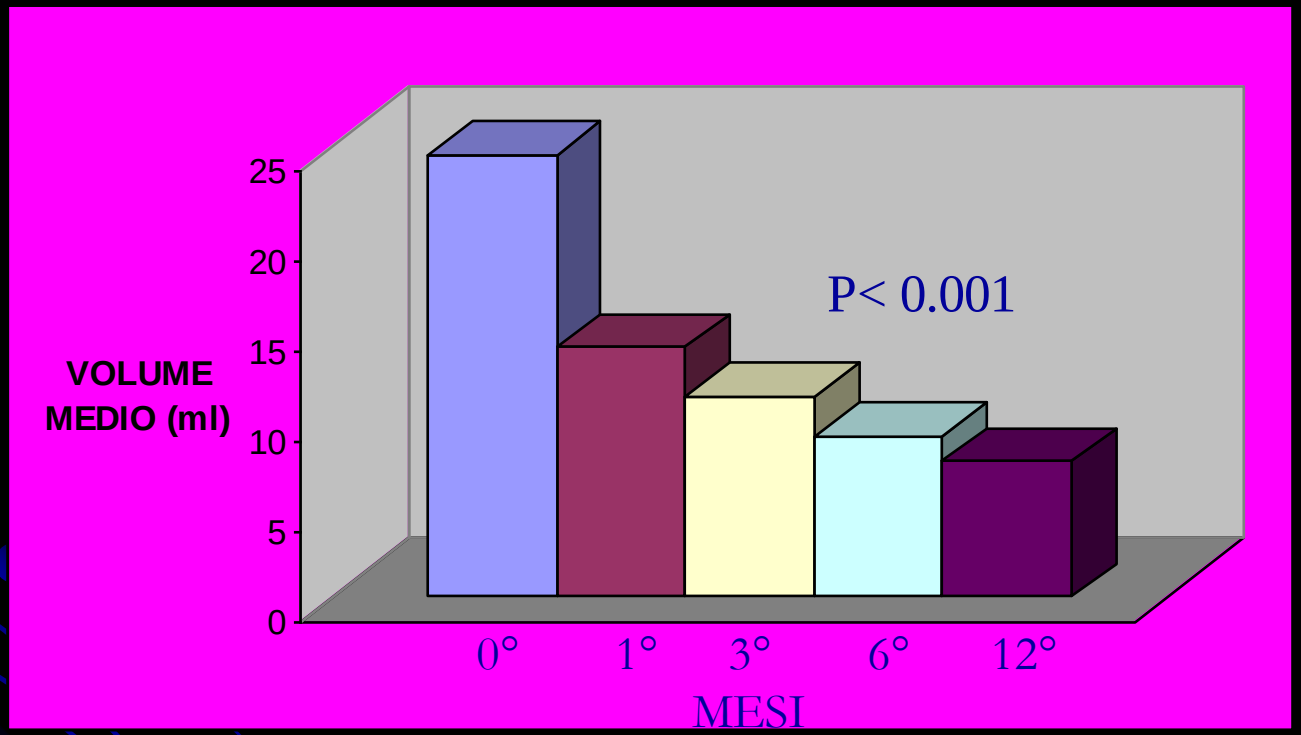
POPOLAZIONE



- 94 pazienti (39 M e 55 F)
- Età media 72 +/-0.5 aa
- Nodulo solido (componenete cistica < 30%)
- Volume > 4 ml (MEDIA 24.5 ml)
- 30% pazienti con nodulo pre-tossico o tossico)

Spiezia Thyroid 2009

Thyroid Nodules and Related Symptoms Are Stably Controlled Two Years After Radiofrequency Thermal Ablation



DOPO 1 ANNO RIDUZIONE DEL 78% RISPETTO AL BASALE
DOPO 2 ANNI RIDUZIONE DEL 79.4% RISPETTO AL BASALE
Al termine del follow-up la funzione tiroidea è risultata normale nel 100% dei pazienti con gozzo pretossico e nel 53% di quelli con gozzo tossico

Thyroid Nodules and Related Symptoms Are Stably Controlled Two Years After Radiofrequency Thermal Ablation

Dopo 2 anni 83/94 pazienti (88%)
Presentava completa risoluzione
dei sintomi e segni di tipo compressivo

median number of RTA treatments necessary to achieve complete necrosis of the treated nodule was 1 (range, 1–3). Thirty-four percent of patients required more than one RTA treatment (two treatments in 25 patients, three treatments in 7 patients); their TN volume before RTA treatment was $\geq$20 mL.

Radiofrequency ablation of benign non-functioning thyroid nodules: 4-year follow-up results for 111 patients

Characteristics	
Largest diameter (cm)	3.3±1.0 (2–6)
Volume (ml)	9.8±8.5 (2–43)
Volume ≤10 ml	81
Volume > 10 ml to≤20 ml	28
Volume >20 ml	17
Proportion of solid component (%)	65.1±32.9 (5–100)
Solidity ≤50 %	45
Solidity >50 %	81
Vascularity	1.7±0.7 (1–4)
Cosmetic score	3.2±0.8 (1–4)
Symptom score	4.3±1.6 (0–10)

Eur Radiol 2013

Radiofrequency ablation of benign non-functioning thyroid nodules: 4-year follow-up results for 111 patients

Table 4 Number of sessions and last VRR according to initial nodule volume

Initial nodule volume	0–10 ml (n=81)	10–20 ml (n=28)	> 20 ml (n=17)
Number of session	1.7±0.9	2.8±1.7	3.8±1.5
P value	0.001	0.023	
Last VRR (%)	94.5±9.6	93.6±9.7	88.2±20.4
P value	0.928	0.297	

Values are presented as mean ± SD (%)

E ur Radiol 2013

DIAGNOSIS OF ENDOCRINE DISEASE

Thyroid ultrasound (US) and US-assisted procedures: from the shadows into an array of applications

Enrico Papini[1,†], Claudio M Pacella[2] and Laszlo Hegedus[3]

Progressively growing benign thyroid lesions that reach to a volume over 12 ml seem to be especially suited for minimally invasive procedures. Less appropriate indications are large nodular goitres, multinodular thyroid disease or deeply positioned lesions.

European Journal of Endocrinology
(2014) 170, R133–R146

Prospective study of effectiveness of ultrasound-guided radiofrequency ablation versus control group in patients affected by benign solid thyroid nodules

Roberto Cesareo, MD*- Valerio Pasqualini, MD**- Carla Simeoni*** M. Sacchi, MD[§] - E. Saralli, MD§ - G. Campagna, MD[§§] - Roberto Cianni, MD **

TABLE 2. Thyroid nodule volume (ml) in Radiofrequency ablation Group. Values are reported as mean ±SD

	Baseline	1 month	6 months
Whole group (n=42)			
TN vol.	24.5 ± 19.6	12.7 ± 11.8 ***	8.6 ± 9.5 ***
TN vol. variation (%)		-49.7±14.5	-68.6±13.5
Small (n=10)			
TN vol.	7.4 ± 2.7	3 ± 1.2**	1.6 ± 1**
TN vol. variation (%)		-57.5 ± 8.6	-78.2 ± 10.7
Medium (n=21)			
TN vol.	18.1 ± 4.4	9.3 ± 3***	5.9 ± 2.5***
TN vol. variation (%)		-47 ± 15	-67 ± 12.2
Large (n=11)			
TN vol.	52.3 ± 17.5	27.8 ± 13.7*	20.1 ± 12.1**
TN vol. variation (%)		-47.7 ± 16.3	-62.8 ± 14.8

Differences in mean volumes are considered between value at 1 month and 6 month vs baseline.
$^*p \leq 0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Cesareo et al JCEM 2015

Efficacy and safety of a single radiofrequency ablation of solid benign non-functioning thyroid nodules

Roberto Cesareo[*1] MD, Andrea Palermo*[*2] MD, Valerio Pasqualini[3] MD, Carla Simeoni[4], Alessandro Casini[1], Giuseppe Pelle[2], Silvia Manfrini[2] MD, Giuseppe Campagna[1] MD, Roberto Cianni[2] MD.*

Table 2. Thyroid nodule volume (ml) in Radiofrequency ablation group.
Values are reported as mean ±SD

	Baseline	6 month	12 months
Whole group (n=48)			
TN vol.	23.5±18.6	8.5±9.0***	7.6±8.7***
TN vol. variation% from baseline		-66.8±13.6	-71.1±14.3
TN vol. variation % from 6 months			-13.7±17.1
Small (n=12)			
TN vol.	7.4±2.6	2.0 ±1.1***	1.6±0.9 *
TN vol. variation (%) from baseline		-73.5±10.8	-78.7±1
TN vol. variation % from 6 months			-18.7±18.8
Medium (n=24)			
TN vol.	18.3±42	6.2 ±2.6***	5.6±2.7***
TN vol. variation (%) from baseline		-65.8±13.7	-69.0±14.4
TN vol. variation % from 6 months			-10.8±13.4
Large (n=12)			
TN vol.	49.8±18.4	19.7±11.6***	17.5±12.3 *
TN vol. variation (%) from baseline		-62.0±14.3	-67.7±15.9
TN vol. variation % from 6 months			-14.7±21.8

Differences are considered between baseline and 6 months and between 6 and 12 months.
*p≤0.05, ***p≤0.001

Cesareo et al Arch End Met 2017

COMPLICATIONS OF RF ABLATION CLINICAL STUDIES

Tabella 2. Complicazioni ed effetti collaterali su 1459 pazienti che hanno subito ablazione dei noduli tiroidei con radiofrequenza

	N	Tempo del rilevamento (giorni dall'ablazione)	Recupero funzionale (giorni dall'ablazione)
Principali	20 (1.4%)	1-180	1-90
Cambiamento di voce	15 (1.02%)	1-2	1-90
Rottura di un nodulo	2 (0.14%)	22-30	< 30
Rottura nodulo con ascesso	1 (0.07%)	50	Nessuno
Ipotiroidismo	1 (0.07%)	180	Nessuno
Lesione del plesso brachiale	1 (0.07%)	1	60
Secondari	28 (1.92%)	1-2	1-30
Ematoma	15 (1.02%)	1	< 30
Vomito	9 (0.62%)	1-2	1-2
Ustioni	4 (0.27%)	1	< 7
Effetti collaterali	46 (3.15%)	1	1-2
Dolore	38 (2.6%)	1	1-2
Reazione vaso-vagale	5 (0.34%)	1	1
Tosse	3 (0.21%)	1	1

Radiology 2011

Efficacy of thermal ablation in benign non-functioning solid thyroid nodule: A systematic review and meta-analysis

Pierpaolo Trimboli[1] · Marco Castellana[2] · Luca Maria Sconfienza[3,4] · Camilla Virili[5] · Lorenzo Carlo Pescatori[6] · Roberto Cesareo[7] · Francesco Giorgino[2] · Roberto Negro[8] · Luca Giovanella[1,9] · Giovanni Mauri[10]

Table 3 Volume reduction rate of BNFSTN with all thermal treatments, RFA or laser ablation, according to follow-up and number of sessions

	6-month assessment			12-month assessment			24-month assessment			36-month assessment		
	Number of BNFSTN (number of studies)	VRR (%)	I^2	Number of BNFSTN (number of studies)	VRR (%)	I^2	Number of BNFSTN (number of studies)	VRR (%)	I^2	Number of BNFSTN (number of studies)	VRR (%)	I^2
Overall results of thermal ablation												
All studies	1479 (19)	60	97	2960 (17)	66	99	598 (7)	62	99	370 (5)	53	99
Single session treatment	1123 (16)	57	97	1034 (12)	59	99	323 (5)	51	98	289 (4)	44	94
Radiofrequency ablation												
All studies	1120 (11)	68‡	98	1023 (8)	75‡	98	315 (3)	87†‡	85	–	–	–
Single session treatment	779 (8)	67‡	97	631 (4)	71‡	98	–	–	–	–	–	–
Laser ablation												
All studies	359 (8)	48‡	11	1937 (9)	52‡	97	283 (4)	45‡	96	289 (4)	44	94
Single session treatment	344 (8)	47‡	0	403 (8)	49‡	86	283 (4)	45	96	289 (4)	44	94

†$p < 0.05$ versus previous assessment with the same technique

‡$p < 0.05$ for RFA versus laser ablation at the same follow-up

Endorcine 2019

Laser Ablation Versus Radiofrequency Ablation for Benign Non-Functioning Thyroid Nodules: Six-Month Results of a Randomized, Parallel, Open-Label, Trial (LARA Trial)

Roberto Cesareo,[1] Claudio Maurizio Pacella,[2,†] Valerio Pasqualini,[3] Giuseppe Campagna,[4] Mario Iozzino,[2] Andrea Gallo,[5] Angelo Lauria Pantano,[6] Roberto Cianni,[7] Claudio Pedone,[8] Paolo Pozzilli,[9] Chiara Taffon,[10] Anna Crescenzi,[10] Silvia Manfrini,[9,*] and Andrea Palermo[9,*]

The primary endpoint was to evaluate the difference in nodule volume reduction between RF and LA group at six months.

The co-primary endpoint was the difference between groups in the rate of nodules (%) greater than the 50% baseline volume reduction, 6 months after the treatment (success rate)

As secondary endpoint we explored the hypothesis, never tested so far, that histopathological features of thyroid nodules could predict the volumetric response to treatment

Cesareo et al Thyroid 2020

METHODS

LARA is a six-month, single-use, randomized, superiority, open-label, parallel trial.

We enrolled subjects with a solitary BNTN or dominant nodule characterized by pressure symptoms/cosmetic problems.

Patients were randomly assigned (1:1) to receive treatment with either LA or RFA

Nodules underwent core needle biopsy (CNB) to evaluate the histological architecture.

Setting : *Unit of metabolic diseases, "S. M. Goretti" Hospital, Latina, Italy*

Trial registration: *Clinical trials: LA vs RFA for BTN; NCT02714946;*

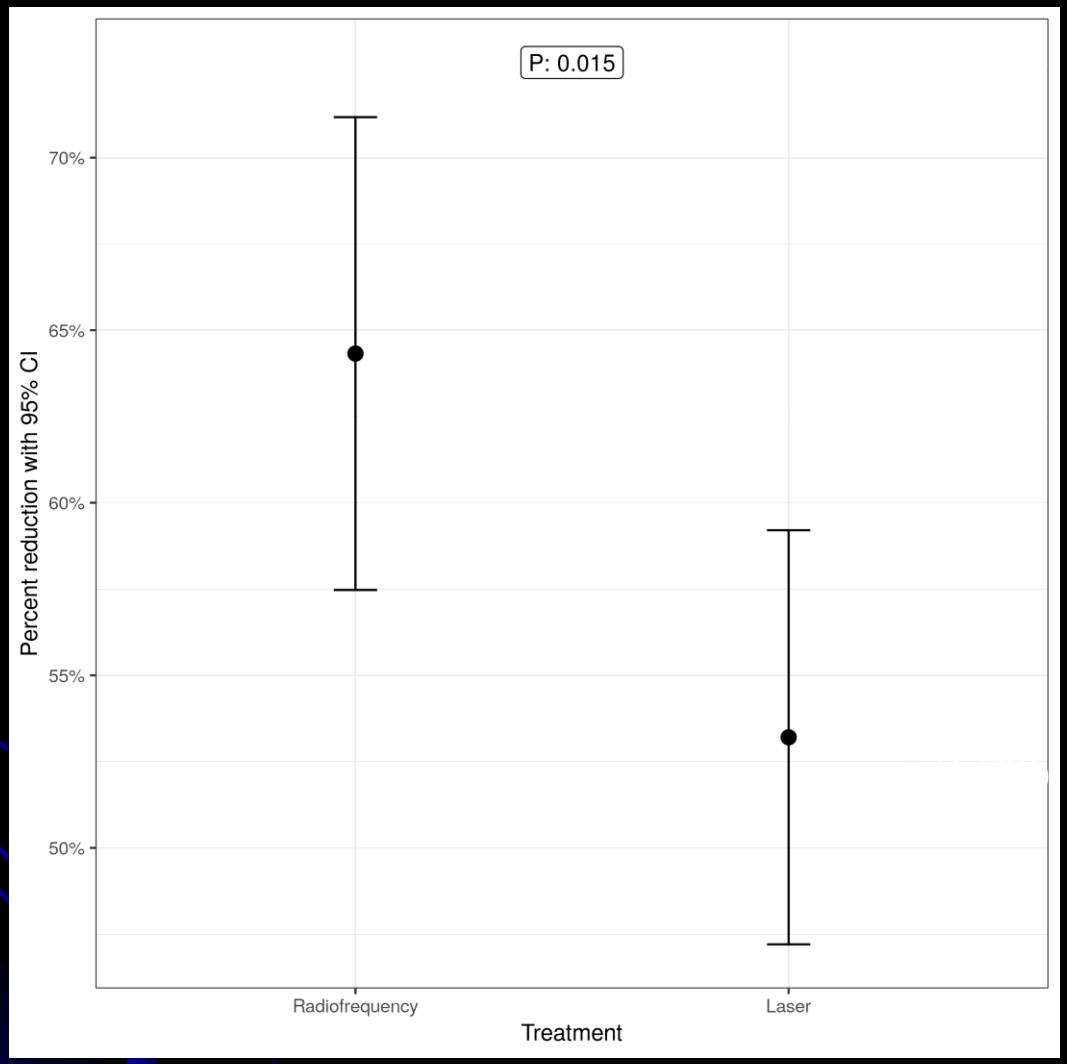
BASELINE CHARACTERISTICS

	Laser (SD)	RFA (SD)	P-value
Age (yrs)	59·3 (11·7)	53·3 (14·3)	0·08
Baseline volume (mL)	24·7 (24)	26 (20·9)	0·82
Cellular component (%)	49·2 (18)	50·1 (18)	0·85
Colloidal component (%)	31·7 (13·8)	31·3 (12·8)	0·92
Fibrotic component (%)	19·8 (18·8)	18·6 (18·7)	0·82
Symptoms score	4·5 (2·1)	4·5 (2·5)	1·00
Cosmetic score	3·4 (0·5)	3·4 (0·6)	0·82
TSH (μU/mL)	1·75 (0·6)	1·98 (0·8)	0·52
FT4 (ng/dL)	1·29 (0·22)	1·25 (0·279)	0·54
Necrosis volume (mL)	16·2 (10·4)	21·0 (14·5)	0·15
Total Energy (J)	9540 (3573)	53898 (47494)	<0·001
Energy delivered/volume (J/mL)	496 (209)	2011(95)	0·01
Time (minutes)	23 (8)	16 (13)	0·13

SD, standard deviation; RFA, radiofrequency ablation; TSH, thyrotropin; FT4, free thyroxine

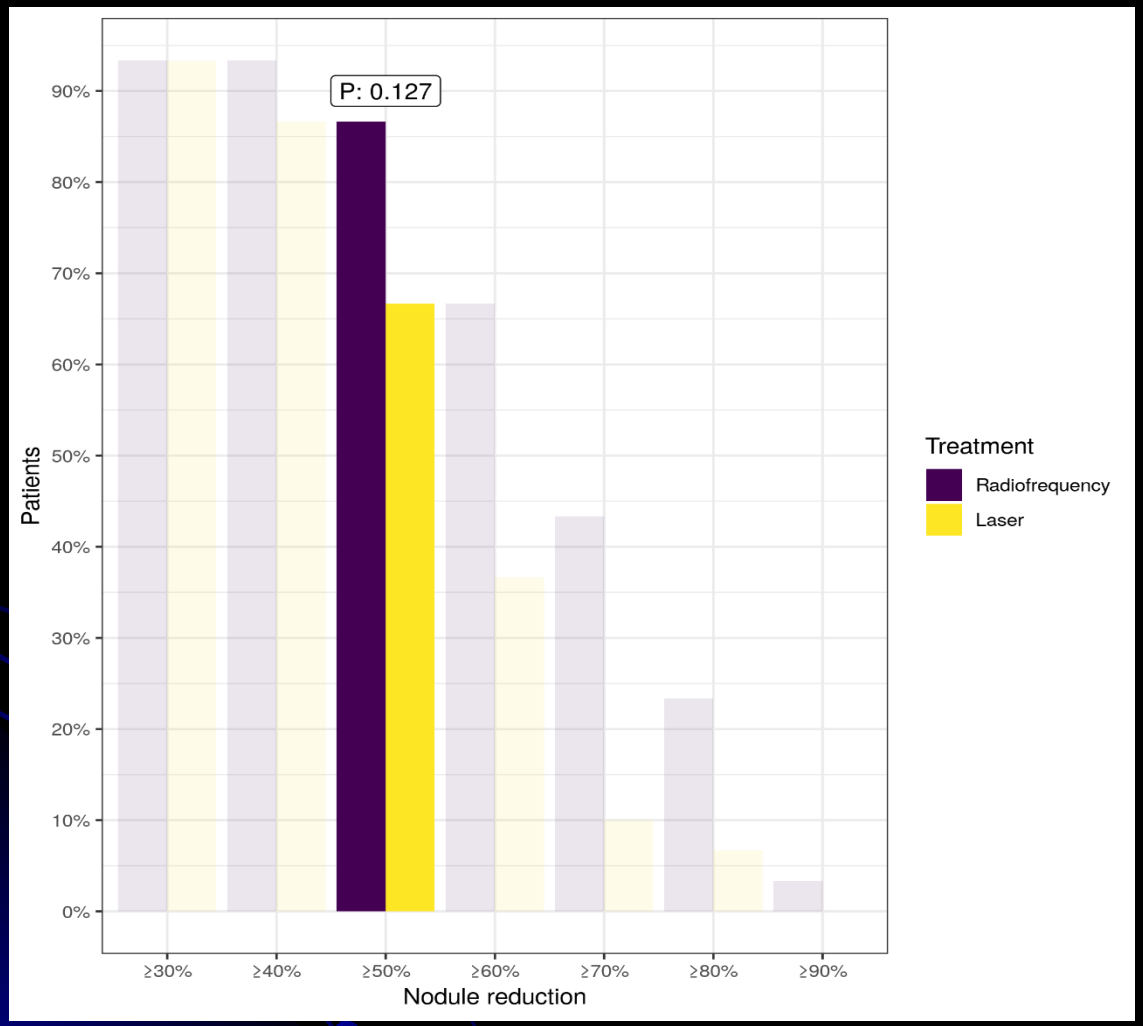
Cesareo et al Thyroid 2020

VOLUME REDUCTION RATE AT SIX MONTHS



Cesareo et al Thyroid 2020

SUCCESS RATE AT SIX MONTH
(nodules with greater than 50% basal volume reduction)



Cesareo et al Thyroid 2020

Correlation between nodule characteristics and volume reduction at 6 months

	RFA *r* coefficient (P-value)	Laser *r* coefficient (P-value)
Baseline volume	0·177 (0·35)	0·296 (0·11)
Coagulative necrosis volume	0·069 (0·72)	0·145 (0·45)
Cellular component (%)	-0·41 (0·03)	-0·066 (0·76)
Fibrotic component (%)	0·366 (0·06)	0·192 (0·38)
Colloidal component (%)	0·042 (0·83)	-0·213 (0·32)

RFA, radiofrequency ablation

Cesareo et al Thyroid 2020

Complications and side effects no. (%) time of detection										
	Intra-procedural		Immediate post-procedural (within 24 h)		Peri-procedural (within 30 days)		Delayed (after 30 days)		Maximum Time to recovery (days)	
Type of complications (SIR Class) [a]	LA	RFA	LA	RFA	LA	RFA	LA	RFA	LA	RFA
Major										
Dysphonia	1 (3·3)	1 (3·3)							14	14
Hyperthyroidism					1 (3·3)		1 (3·3)	1 (3·3)	90	90
Minor										
Hematoma	2 (6.6)	3 (10)							10	10
Side effects										
Local pain	5 (17)	6 (20)							1	1
Headache				1(3·3)						1
Fever			3 (10)						60	

a. Society of Interventional Radiology (SIR) guidelines criteria;

The adverse event rates **(local pain, dysphonia, <u>thyrotoxicosis,</u> fever, haematoma)** were 37% (n=11) and 43% (n=13) for RFA and LA, respectively, with no requirement for hospitalization.

Five-Year Results of Radiofrequency and Laser Ablation of Benign Thyroid Nodules: A Multicenter Study from the Italian Minimally Invasive Treatments of the Thyroid Group

Stella Bernardi,[1,2] Fabiola Giudici,[1–3] Roberto Cesareo,[4] Giovanni Antonelli,[5] Marco Cavallaro,[6]

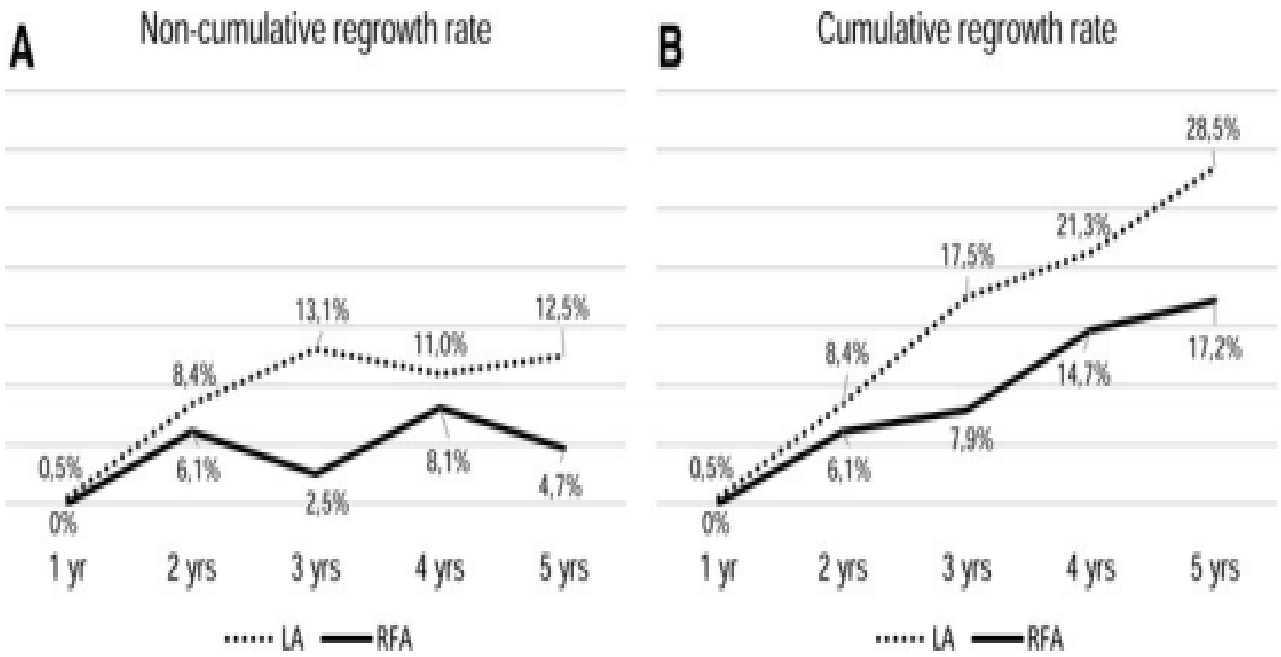
TABLE 1. NODULE VOLUMES AND NODULE VOLUME REDUCTION

	Baseline	*1 Year*	*2 Years*	*3 Years*	*4 Years*	*5 Years*
All patients						
Nodule volume (mL)	14.3 (0.4 to 179.0)	5.2* (0.0 to 242.0)	4.8* (0.0 to 214.0)	4.3* (0.0 to 96.0)	4.2* (0.0 to 88.7)	4.0* (0.0 to 62.0)
VRR (%)	—	63.3 (−50.0 to 99.7)	67.5 (−80.4 to 99.9)	68.3 (−63.5 to 1.0)	68.7 (−54.9 to 1.0)	70.4 (−50.0 to 1.0)
Number (cumulative) of patients not retreated	406	406	387	363	353	334
Number (cumulative) of patients retreated (%)	0	0	19 (4.7)	43 (10.3)	53 (13.1)	72 (17.7)
Surgery			12	13	4	14
MITT			5	9	6	4
MITT + surgery			2	1		
^{131}I				1		1
RFA group						
Nodule volume (mL)	17.2 (0.4 to 179.0)	4.9* (0.0 to 242.0)	4.7* (0.0 to 214.0)	4.4* (0.0 to 96.0)	4.0* (0.0 to 89.0)	3.9* (0.0 to 62.0)
VRR (%)	—	72.4 (−35.2 to 99.7)	74.6 (−24.9 to 99.9)	75.9 (−48.2 to 1.0)	76.3 (−34.5 to 1.0)	77.1 (−34.5 to 1.0)
Number (cumulative) of patients not retreated	216	216	208	203	197	190
Number (cumulative) of patients retreated (%)	0	0	8 (3.7)	13 (6.0)	19 (8.8)	26 (12.0)
Surgery			*4*	*2*	*2*	*5*
MITT			*2*	*3*	*4*	*2*
MITT + surgery			*2*			
LA group						
Nodule volume (mL)	12.2 (1.7 to 86.0)	5.5* (0.3 to 52.0)	4.8* (0.2 to 39.0)	4.3* (0.2 to 46.8)	4.2* (0.2 to 39.7)	4.1* (0.1 to 35.0)
VRR (%)	—	54.9 (−50.0 to 95.7)	58.3 (−80.0 to 97.0)	58.8 (−63.5 to 93.8)	57.5 (−54.9 to 1.0)	56.7 (−50.0 to 97.8)
Number (cumulative) of patients not retreated	190	190	179	160	156	144
Number (cumulative) of patients retreated (%)	0	0	11 (5.8)	30 (15.8)	34 (18.4)	46 (24.2)
Surgery			8	11	2	9
MITT			3	6	2	2
MITT + surgery				1		
^{131}I				1		1

THYROID 2020

Five-Year Results of Radiofrequency and Laser Ablation of Benign Thyroid Nodules: A Multicenter Study from the Italian Minimally Invasive Treatments of the Thyroid Group

Stella Bernardi,[1,2] Fabiola Giudici,[1–3] Roberto Cesareo,[4] Giovanni Antonelli,[5] Marco Cavallaro,[6]



THYROID 2020

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS, AMERICAN COLLEGE OF ENDOCRINOLOGY, AND ASSOCIAZIONE MEDICI ENDOCRINOLOGI MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND MANAGEMENT OF THYROID NODULES – 2016 UPDATE

EXECUTIVE SUMMARY OF RECOMMENDATIONS

7.2.5. *Image-guided thermal ablation for benign nodules*

- Consider laser or radiofrequency ablation for the treatment of solid or complex thyroid nodules that progressively enlarge or are symptomatic or cause cosmetic concern [BEL 2, GRADE C].

ENDOCRINE PRACTICE 2016

2017 Thyroid Radiofrequency Ablation Guideline: Korean Society of Thyroid Radiology

Recommendation 1-1

Radiofrequency ablation is indicated for patients with benign thyroid nodules complaining of symptomatic or cosmetic problems.
(strong recommendation, moderate-quality evidence)

KRJ 2017

Minimally-invasive treatments for benign thyroid nodules: a Delphi-based consensus statement from the Italian minimally-invasive treatments of the thyroid (MITT) group

Enrico Papini, Claudio Maurizio Pacella, Luigi Alessandro Solbiati, Gaetano Achille, Daniele Barbaro, Stella Bernardi, Vito Cantisani, Roberto Cesareo, Arturo Chiti, Luca Cozzaglio, Anna Crescenzi, Francesco De Cobelli, Maurilio Deandrea, Laura Fugazzola, Giovanni Gambelunghe, Roberto Garberoglio, Gioacchino Giugliano, Livio Luzi, Roberto Negro, Luca Persani, Bruno Raggiunti, Francesco Sardanelli, Ettore Seregni, Martina Sollini, Stefano Spiezia, Fulvio Stacul, Dominique Van Doorne, Luca Maria Sconfienza & Giovanni Mauri

Statement #5. Thermal ablation may be proposed as a first-line treatment for solid nonfunctioning thyroid nodules that are benign at cytology when they become symptomatic.

INT J HYPERT 2019

2020 European Thyroid Association Clinical Practice Guideline for the Use of Image-Guided Ablation in Benign Thyroid Nodules

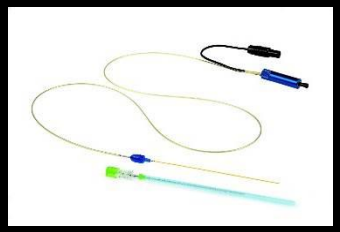
Recommendation 1	In adult patients with benign thyroid nodules that cause pressure symptoms and/or cosmetic concerns and decline surgery, image-guided thermal ablation (TA) should be considered as a cost- and risk-effective alternative option to surgical treatment or observation alone (1, ØØOO)
Recommendation 2	We recommend against the use of TA for asymptomatic lesions (1, ØØØO)
Recommendation 3	Before TA of thyroid lesions, a benign cytological diagnosis is needed; a repeat FNA is suggested for cytologically benign nodules with the exception of spongiform nodules and pure cystic lesions (EU-TIRADS Class 2); we recommend against TA for nodules with high-risk US features (EU-TIRADS Class 5; 1, ØØØO)

Eur Th J 2020

TERMOABLAZIONE
DATI DI EFFICACIA

- LASER: evidenze su nodulo ipocatante
- RF: evidenze cliniche su nodulo ipocaptante

- LASER: evidenze su nodulo ipercatante
- RF: evidenze cliniche su nodulo ipercaptante

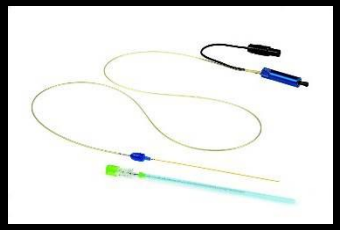


Laser Ablation and 131-Iodine: A 24-Month Pilot Study of Combined Treatment for Large Toxic Nodular Goiter

In group (LAT131I), however, **normalization of TSH** occurred in nine of 15 patients **(60%)** already 1 month after LAT; in particular, in three of these patients radioiodine was not necessary

Combined treatment determined **faster volume reduction and relief of symptoms, and faster control of hyperthyroidism.**

J Clin Endocrinol Metab 2014



EFFICACY AND SAFETY OF A SINGLE SESSION OF LASER ABLATION OF TOXIC THYROID NODULES: THE PERUGIA EXPERIENCE

For Review Only

Table 2. volume reduction at different times

Volume (ml)	Pre-LTA	3 months	6 months	1 year	3 years
Median	12	7.5	5.1	5.1	5
Minimum	5	1.1	1.2	1.2	1.2
Maximum	118	47	39	39	40

Table 3. Correlation between initial volume of toxic nodule and therapeutic response (suspension of methimazole)

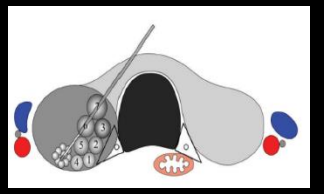
0-5ml (n= 6)	5-15 ml (n= 51)	15-25 ml (n= 18)	> 25 ml (n= 7)
6/6 (100%)	46/51 (90.2%)	11/18 (61.1%)	2/7 (28.5%)

Int J Hypert 2017

TERMOABLAZIONE
DATI DI EFFICACIA

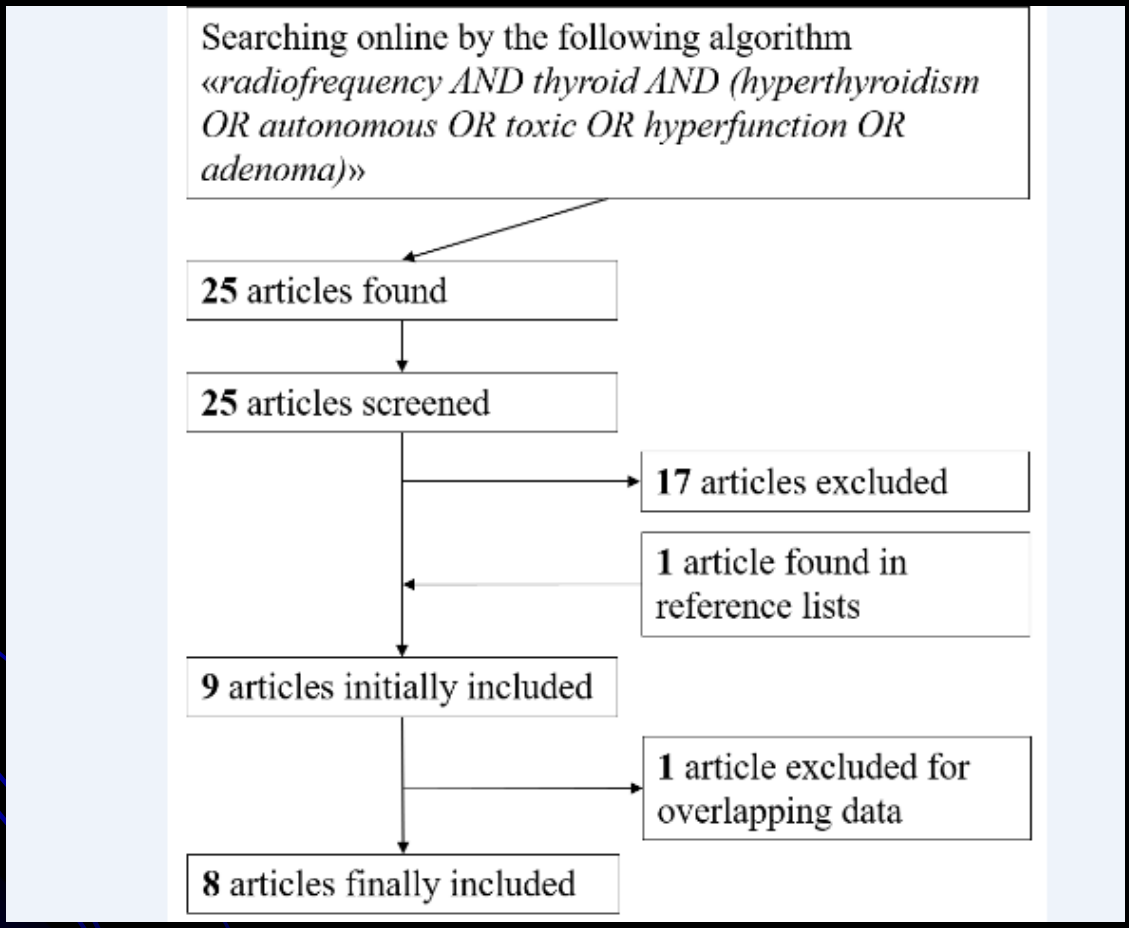
- LASER: evidenze su nodulo ipocatante
- RF: evidenze cliniche su nodulo ipocaptante

- LASER: evidenze su nodulo ipercatante
- RF: evidenze cliniche su nodulo ipercaptante

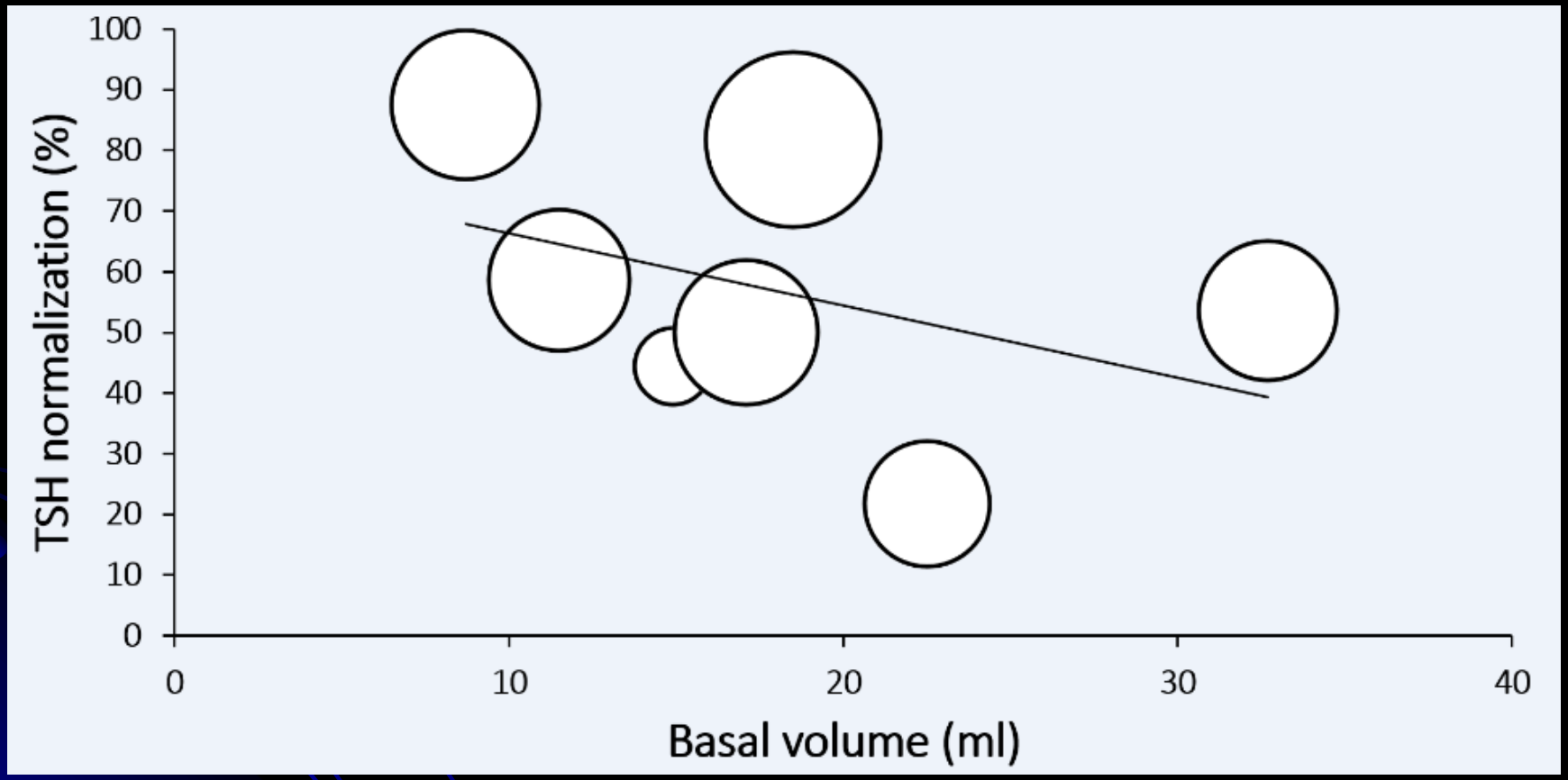


Efficacy of radiofrequency ablation in autonomous functioning thyroid nodules. A systematic review and meta-analysis.

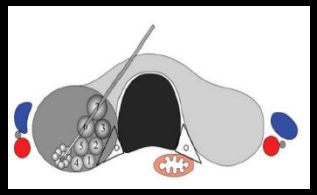
R. Cesareo* [1], A. Palermo* [2], D. Benevenuto[3], E. Cella[3], V. Pasqualini[4], S. Bernardi[5], F. Stacul[6], S. Angeletti[7], G. Mauri[8], M. Ciccozzi[3], P Trimboli[9]



Cesareo et al Rev Endocr Metab Dis 2019



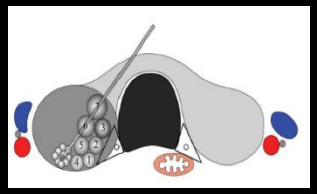
Under Rev 2019



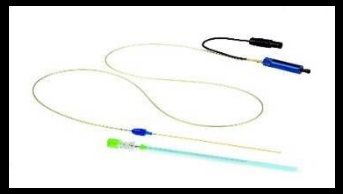
2017 Thyroid Radiofrequency Ablation Guideline: Korean Society of Thyroid Radiology

Key Questions	Recommendations	Evidence Level	Delphi Score	Grading of Recommendations	References
1. What are indications for RFA for benign thyroid nodules?	1-1. RFA is indicated for patients with benign thyroid nodules complaining of symptomatic or cosmetic problems	Moderate	9	Strong	4, 9, 10, 12, 18
	1-2. Thyroid nodules should be confirmed as benign on at least two US-guided FNA or CNB before RFA	Moderate	8	Strong	27, 43-45
	1-3. Single benign diagnosis on FNA or CNB is sufficient when nodule has US features highly specific for benignity (isoechoic spongiform nodule or partially cystic nodules with intracystic comet tail artifact)	High	8	Strong	27, 43-45
	1-4. Single benign diagnosis on FNA or CNB is sufficient for confirmation of a benign nodule in AFTN	Low	8	Weak	49
	1-5. RFA can be indicated for AFTN, either toxic or pre-toxic	Moderate	8	Weak	4, 7, 53-59
2. What are indications for RFA for recurrent thyroid cancers?	2. RFA can be performed for curative or palliative purposes in recurrent thyroid cancers at thyroidectomy bed and cervical lymph nodes for patients at high surgical risk or who refuse surgery	Moderate	9	Strong	64, 66, 68-74

Korean J Radiol 2018



Minimally-invasive Treatment of Benign Thyroid Nodules: Statements from the Italian MITT Group



Statement #3. A double cytological confirmation of benignity should be obtained prior to image-guided thermal ablation of thyroid nodules. However, a single cytological sample can be considered adequate to confirm nodule benignity if US appearance is of low risk of malignancy (≤ EU-TIRADS 3) and in autonomously functioning nodules.

Level of evidence: 2

Level of agreement: strong (agree, n=28; abstain, n=0; disagree, n=1)

Int J Hypert 2019

Statement #8. Thermal ablation may be proposed as a treatment option for AFTN in patients who refuse or cannot undergo traditional treatments with radioiodine or surgery.

Level of evidence: 2

Level of agreement: strong (agree, n=27; abstain, n=1; disagree, n=1)

Statement #9. Small size AFTN can be treated with thermal ablation when the sparing of normal thyroid tissue is a priority and it is reasonable to expect an at least 80% nodule volume ablation.

Level of evidence: 3

Level of agreement: strong (agree, n=27; abstain, n=1; disagree, n=1)

Clinical Study

Radiofrequency Ablation Compared to Surgery for the Treatment of Benign Thyroid Nodules

RFA		hEMItx		Short-stay	
		Preprocedural costs			
Radiological visit	25.30	Surgical visit	25.30	Surgical visit	25.30
Laboratory tests	100.20	Laboratory tests	291.10	Laboratory tests	291.10
US	41.70	ECG	14.40	ECG	14.40
Otolaryngological visit	1.70	Chest X-ray	26.90	Chest X-ray	26.90
Anaesthesiological visit	34.50	Otolaryngological visit	34.50	Otolaryngological visit	34.50
		Anaesthesiological visit	34.50	Anaesthesiological visit	34.50
		Procedural costs			
		(A) Equipment			
Needle	1,240.70	Operating theatre	1,920.00	Operating theatre	1,980.00
US machine	3.00	Tools	197.60	Tools	197.60
Drugs	1.70	Drugs	664.00	Drugs	664.00
		(B) Personnel			
Radiologist	57.00	Surgeon (×2)	202.60	Surgeon (×2)	207.60
Nurse (×2)	45.50	Theatre nurse	41.50	Theatre nurse	42.50
Anaesthetist	57.00	Nurse (×2)	82.90	Nurse (×2)	85.00
		Anaesthetist	101.30	Nurse (×2)	103.80
		(C) Hospitalization			
Hospital day	—	>24 hours hospital stay	862.50	<24 hours hospital stay	375.00
		Follow-up costs			
Laboratory tests	11.50	Laboratory tests	22.70	Laboratory tests	22.70
US	41.70	Otolaryngological visit	34.50	Otolaryngological visit	34.50
Total	€1661.50	Total	€4556.30	Total	€4139.40

Int J of Endocrinol 2014

TAKE HOME MESSAGES

- Le tecniche termoablative costituiscono un valido strumento applicativo al fine di ottenere una significativa riduzione volumetrica del nodulo tiroideo
- Radiofrequenza (RF) e Laser (LA) sono le tecniche che hanno i migliori dati di evidence-based
- La riduzione volumetrica sia nel breve che nel lungo periodo ed i relativi tassi di recurrence lasciano preferire il trattamento termoablativo con RF anche se l'una o l'altra tecnica possono essere utilizzate in base anche a numerose variabili da prendere in considerezione (learning-curve dell'operatore, disponibilità della metodica, etc)
- Le complicanze seppur rare vanno sempre considerate ed il paziente va sempre edotto in merito ad i dati di efficacy/safety con apposito consenso informato

GRAZIE!!!