DOTTOR R.CESAREO

ENDOCRINOLOGO

LATINA

RFA

- La tecnica
- Analisi costo/efficacia
- Safety
- La nostra esperienza clinica

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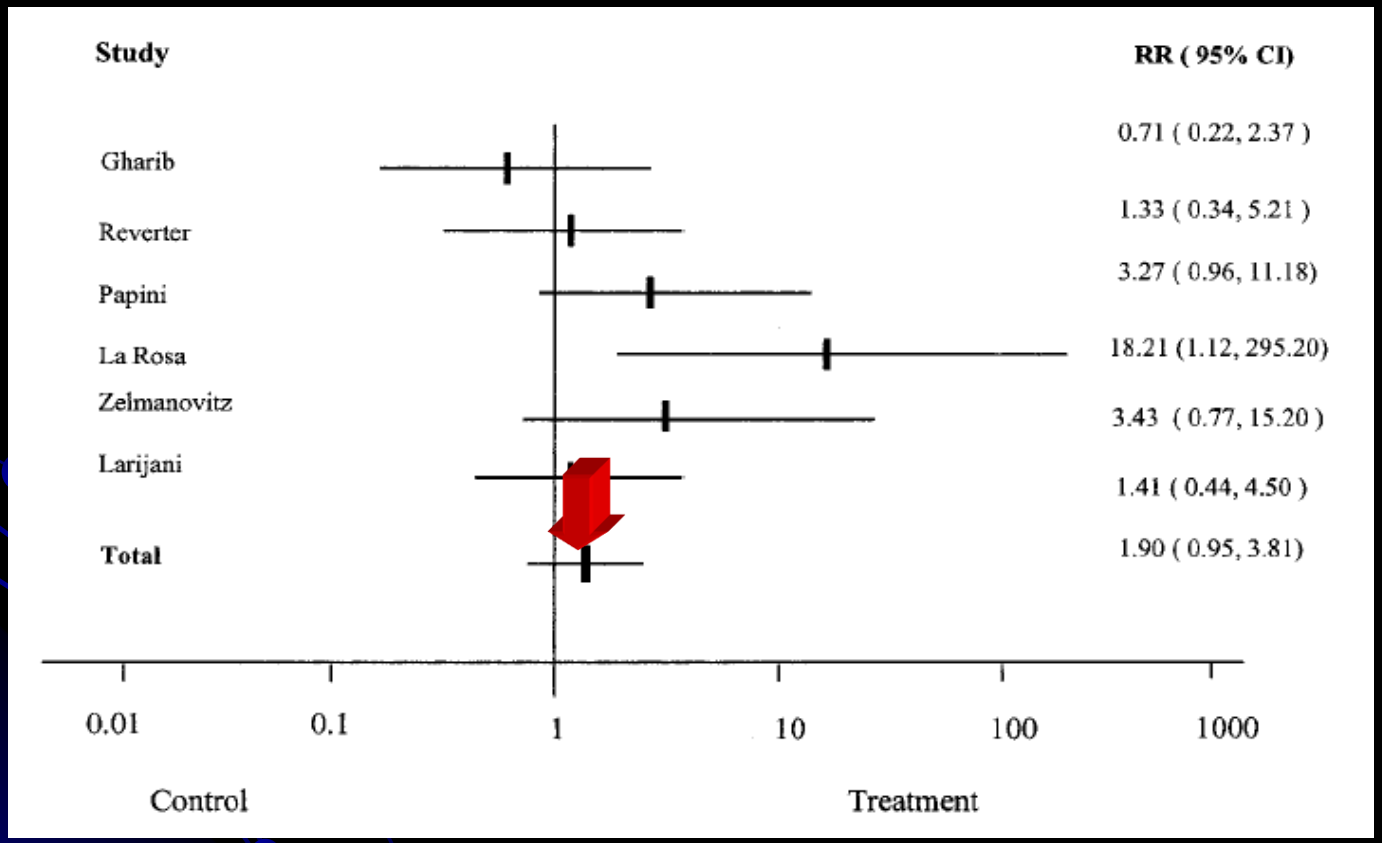
doi: 10.1210/jc.2001-011762

Effectiveness of Thyroid Hormone Suppressive Therapy in Benign Solitary Thyroid Nodules: A Meta-Analysis

M. REGINA CASTRO, PEDRO J. CARABALLO, AND JOHN C. MORRIS



Castro MR et al. J Clin Endocrinol & Metab 2002; 87: 4154-9

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.

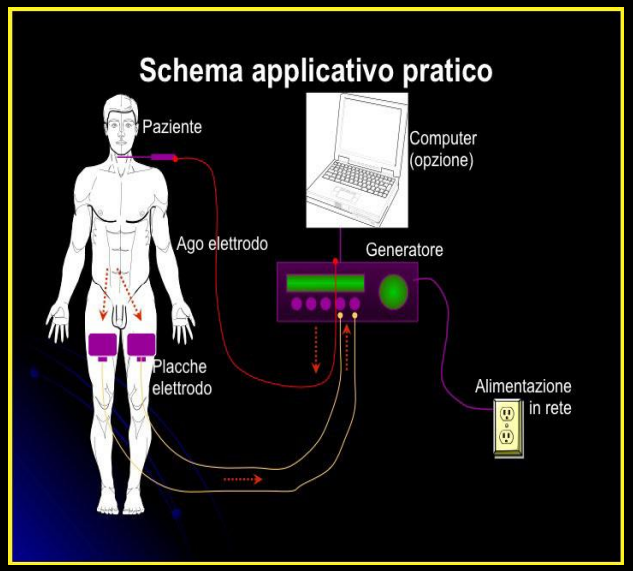
Guidelines 2006

TERMOABLAZIONE CON RADIOFREQUENZA:PRINCIPI FISICI

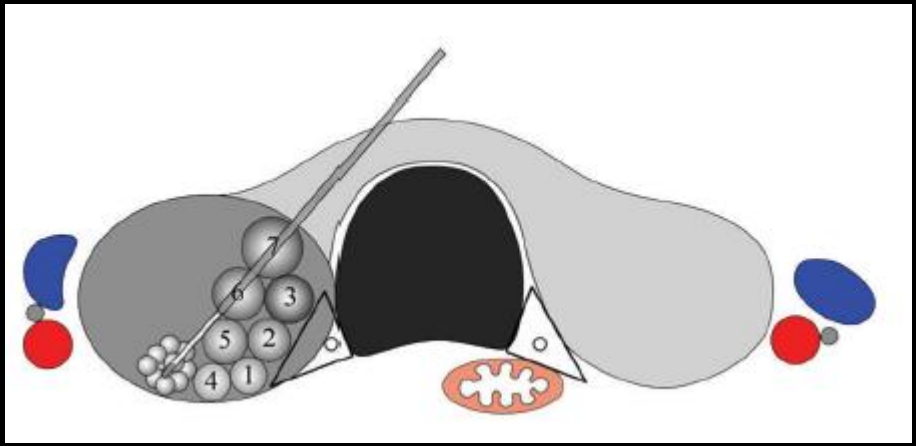
- La termoablazione con radiofrequenza sfrutta le interazioni energia-tessuto per ottenere temperature efficaci a indurre un danno irreversibile alle cellule bersaglio.

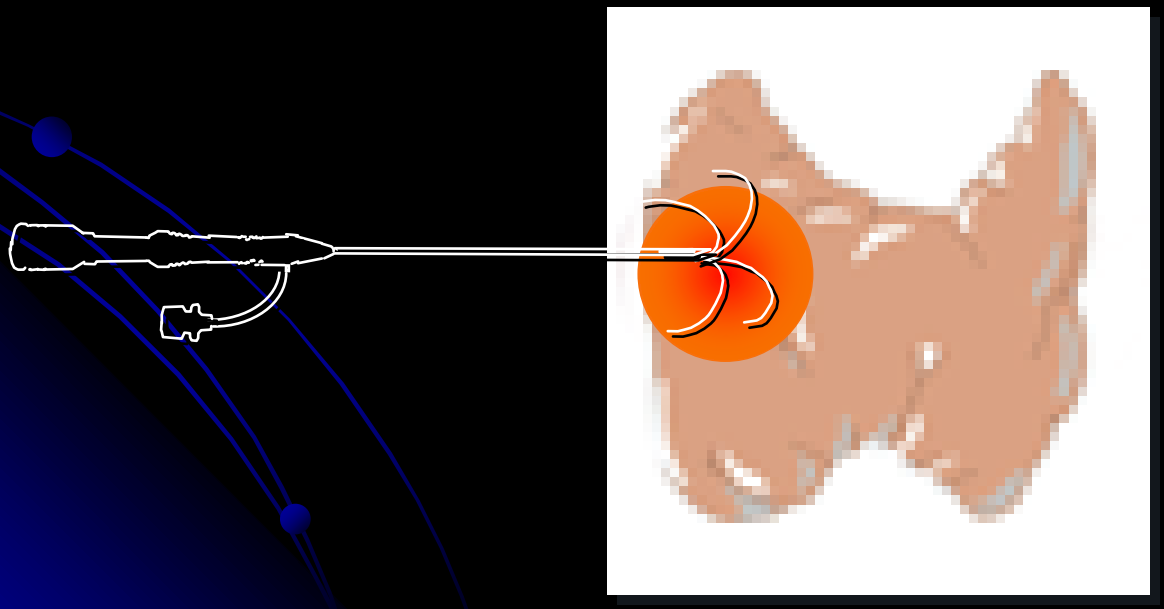
- Le temperature ottimali per ottenere la necrosi coagulativa cellulare devono essere superiori ai 50° C e inferiori ai 100°C per evitare la carbonizzazione dei tessuti.

Il paziente è inserito in un circuito costituito dal GENERATORE, dall'ELETTRODO inserito all'interno del nodulo ed una seconda LARGA ANTENNA ESTERNA, a livello delle coscie (piastra)

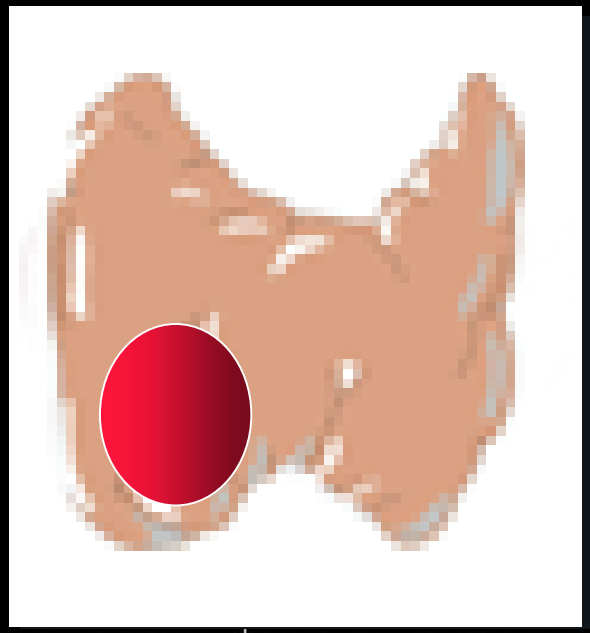


RADIOFREQUENCY
MOVING SHOT AND HOOK UMBRELLA

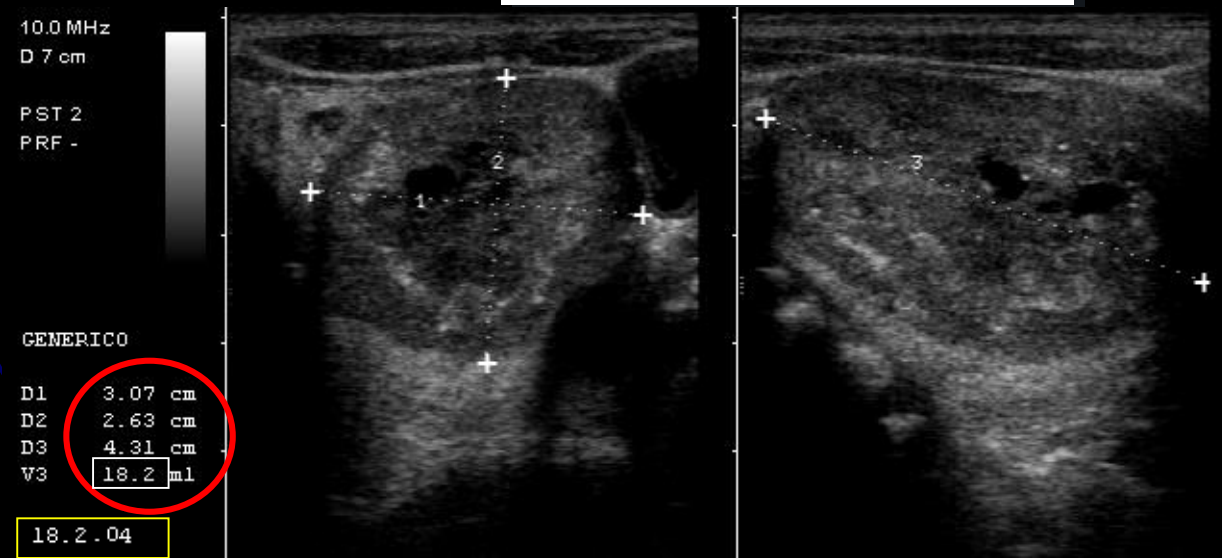




Metodica d'applicazione: tecnica

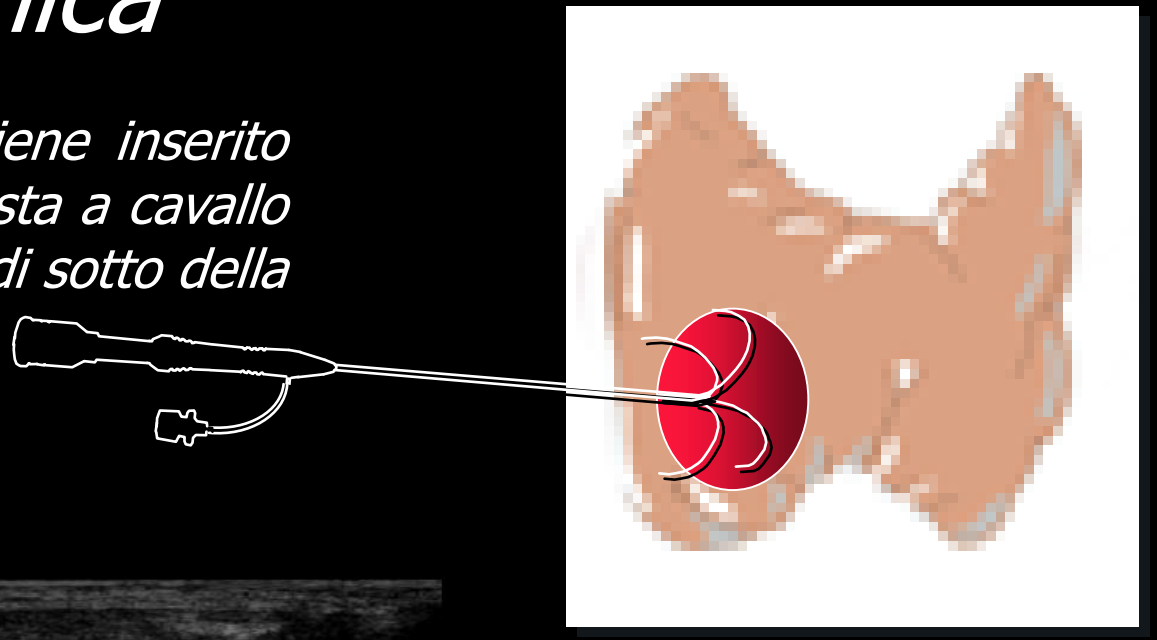


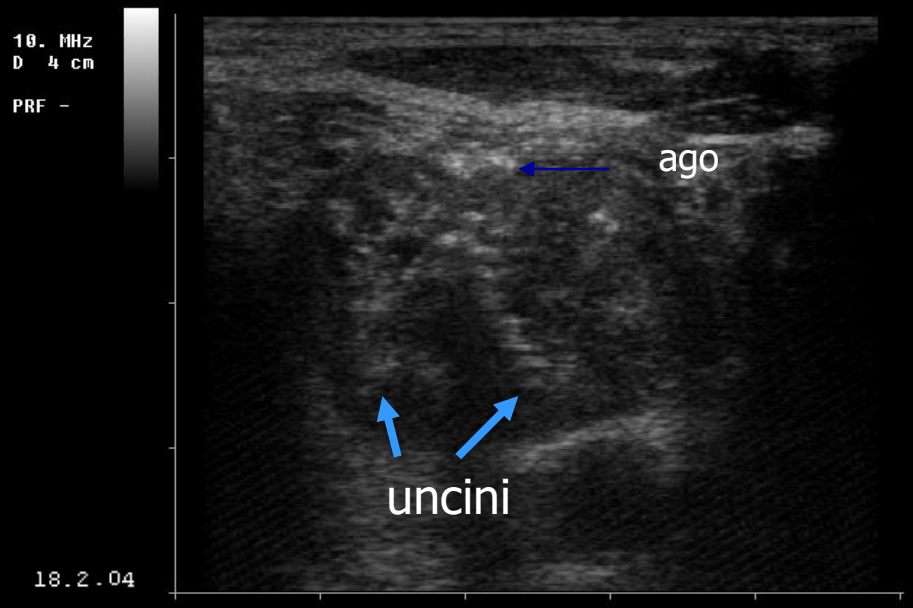
La lesione tiroidea viene localizzata con l'ecografo



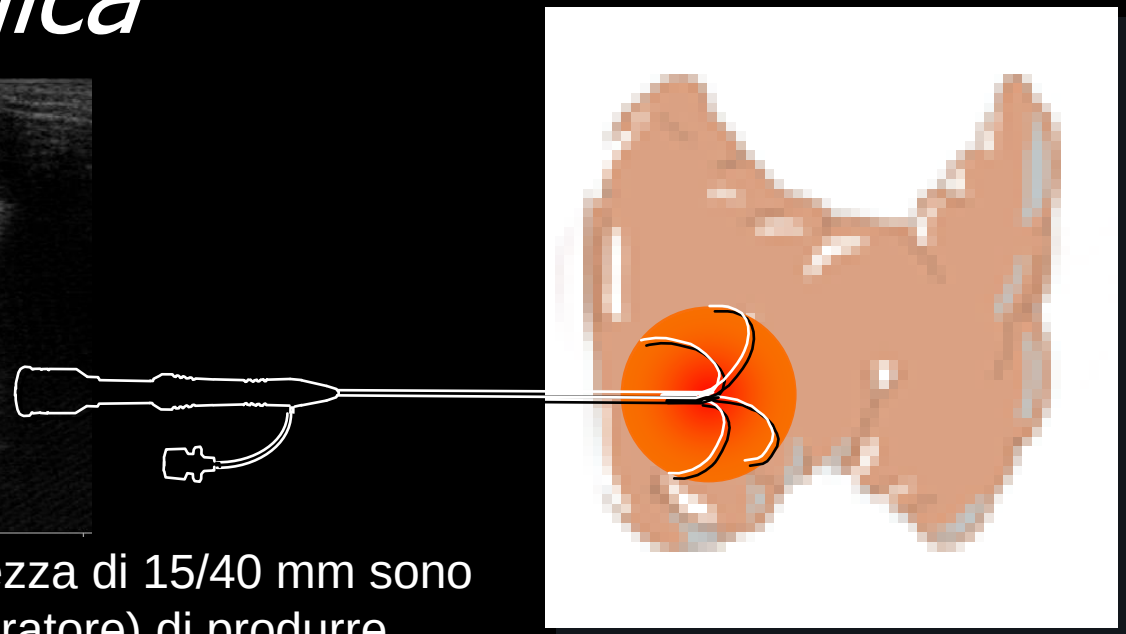
Metodica d'applicazione: tecnica

L'ago elettrodo viene inserito con la parte esposta a cavallo della lesione e al di sotto della capsula



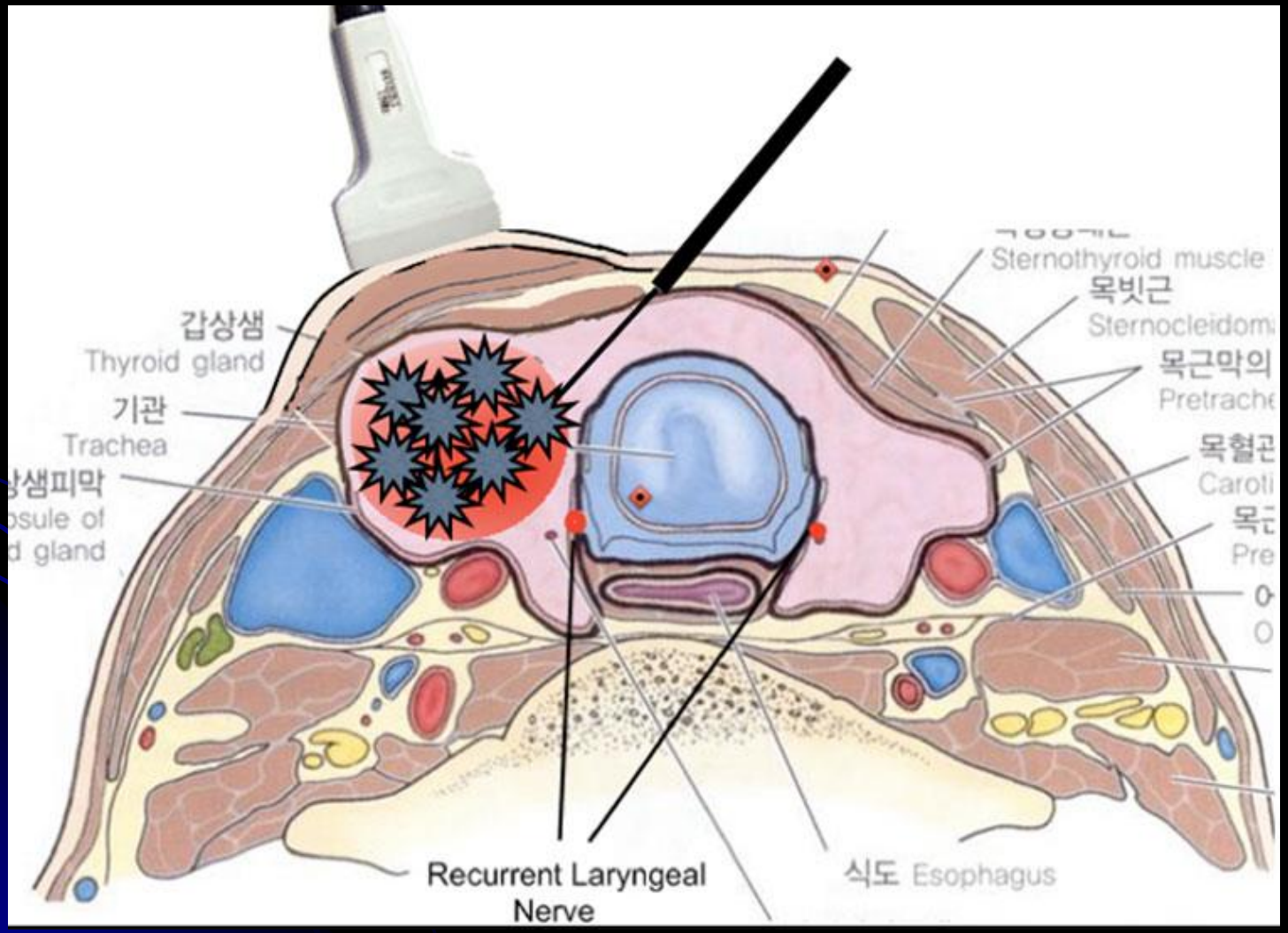


Metodica d'applicazione: tecnica



Gli uncini, della lunghezza di 15/40 mm sono capaci (tramite il Generatore) di produrre energia termica attraverso l'emissione di corrente elettrica a media frequenza (460 khz). Gli stessi uncini contengono delle termocoppie che consentono di rilevare la temperatura e l'impedenza nel tessuto da ablare

Moving shoot technique



Moving-Shot versus Fixed Electrode Techniques for Radiofrequency Ablation: Comparison in an *Ex-Vivo* Bovine Liver Tissue Model

Variable	1 minute		*P*	2 minutes		*P*
	Moving Shot	Fixed Electrode		Moving Shot	Fixed Electrode	
True RF time (sec)*	60	46.7 ± 4.6	< 0.001	120	64.8 ± 4.6	< 0.001
Number of cut-offs	0	1.6 ± 0.5	< 0.001	0	5.5 ± 0.5	< 0.001
Energy (J)	2677.76 ± 83.68	2050.16 ± 209.2	< 0.001	5564.72 ± 5439.2	2970.64 ± 376.56	< 0.001
DV (cm)	3.5 ± 0.7	1.5 ± 0.1	< 0.001	4.1 ± 0.6	1.5 ± 0.1	< 0.001
DT1 (cm)	1.0 ± 0.1	1.1 ± 0.1	0.064	1.3 ± 0.1	1.3 ± 0.1	0.778
DT2 (cm)	1.5 ± 0.3	1.3 ± 0.1	0.054	2.1 ± 0.2	1.4 ± 0.1	0.002
Volume (mL)	2.7 ± 0.3	1.08 ± 0.2	< 0.001	5.6 ± 0.4	1.4 ± 0.2	< 0.001

KJR 2014

LAVORI A CONFRONTO

- L'esperienza dei coreani è stata valutata con

- un ago più sottile (17 g)
- moving shoot
- volume medio **6.13**+/- 9.59 ml

- L'esperienza italiana è stata valutata con

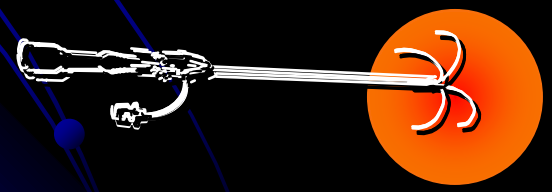
- un ago più spesso (14 g)
- Large single ablation
- - volume medio di **27.4** +/-21.1 ml

Anni 2006-09

US-GUIDED PERCUTANEOUS RADIOFREQUENCY THERMAL ABLATION FOR THE TREATMENT OF SOLID BENIGN HYPERFUNCTIONING OR COMPRESSIVE THYROID NODULES

Table 1. Nodule volume and thyroid function before and after RF ablation

	Enrollment	Time of RTA	1 mo	3 mo	6 mo
Whole group					
Volume (mL)	27.4 ± 21.1	27.7 ± 21.5	19.2 ± 16.2‡	15.9 ± 14.1‡	14.6 ± 12.6‡
Volume variation (%)	−0.1 ± 5.8	—	−32.7 ± 20.0	−46.4 ± 18.8	−50.7 ± 16.5
Cold nodules					
Volume (mL)	38.7 ± 27.2	39.3 ± 27.8	25.2 ± 16.4*	23.1 ± 15.0†	21.4 ± 14.3†
Volume variation (%)	−0.5 ± 3.8	—	−31.7 ± 15.6	−39.8 ± 14.3	−46.3 ± 17.1
TSH (mIU/mL)	0.745 ± 0.490	0.910 ± 0.585	0.880 ± 0.531	0.834 ± 0.476	0.788 ± 0.505
FT4 (pg/mL)	10.7 ± 4.1	11.6 ± 4.5	10.3 ± 3.8	10.8 ± 4.0	11.1 ± 4.2
Hot nodules					
Volume (mL)	22.5 ± 16.1	22.6 ± 16.3	16.6 ± 15.8‡	12.8 ± 12.8‡	11.6 ± 10.7‡
Volume variation (%)	0.1 ± 6.6	—	−33.1 ± 21.9	−49.2 ± 20.1	−52.6 ± 16.3
TSH (mIU/mL)	0.078 ± 0.114‡	0.508 ± 0.339	0.638 ± 1.052	0.661 ± 1.233	0.993 ± 2.033
FT4 (pg/mL)	22.1 ± 4.7‡	10.3 ± 2.9	10.4 ± 3.1	11.7 ± 3.2	10.4 ± 2.4



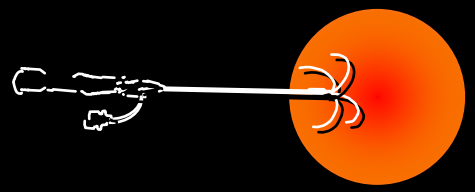
Deandrea M et al 2008

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

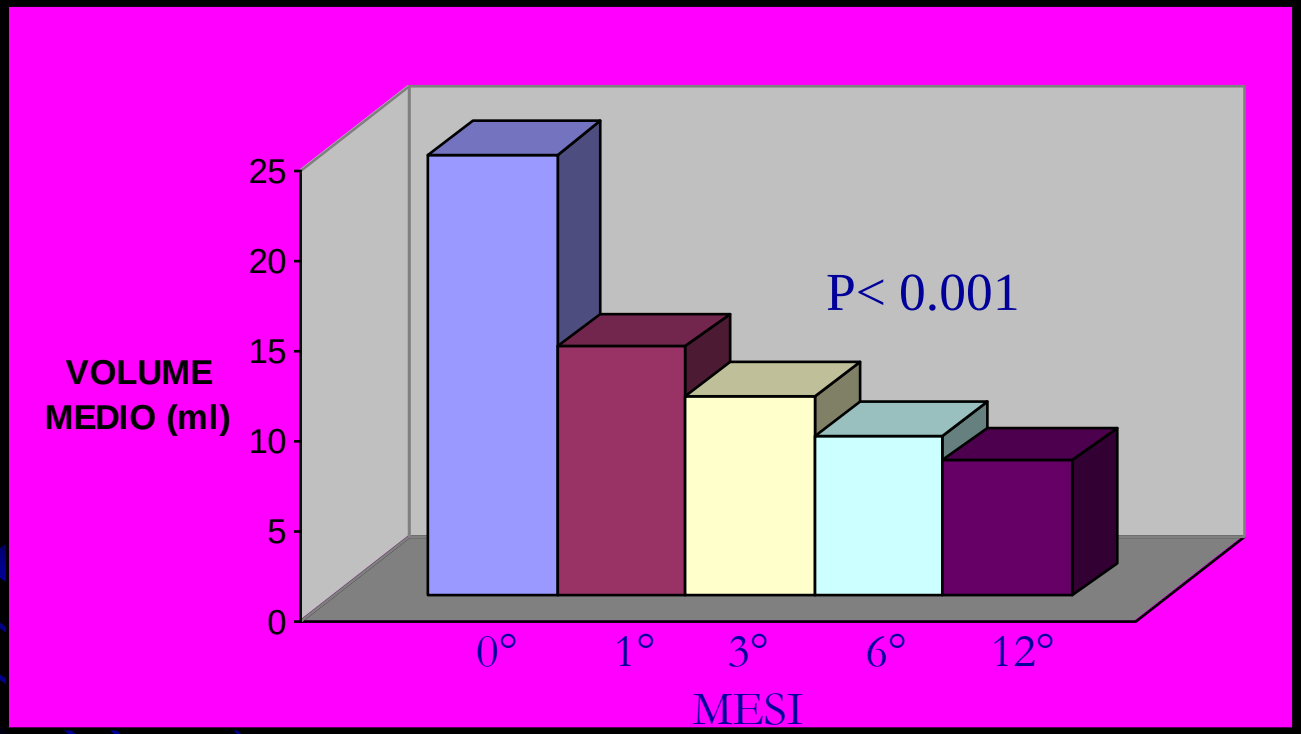
POPOLAZIONE



- 94 pazienti (39 M e 55 F)
- Età media 72 +/-0.5 aa
- Nodulo solido (componenete cistica < 30%)
- Volume **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

Spiezia et al Thyroid 2009

Thyroid Nodules Treated with Percutaneous Radiofrequency Thermal Ablation: A Comparative Study

A. Faggiano, V. Ramundo, A. P. Assanti, F. Fonderico, P. E. Macchia, C. Misso, F. Marciello, V. Marotta, M. Del Prete, E. Papini, G. Lombardi, A. Colao, and S. Spiezia

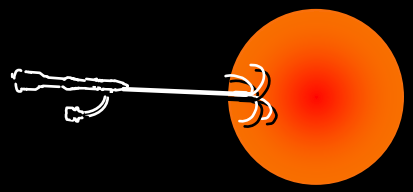


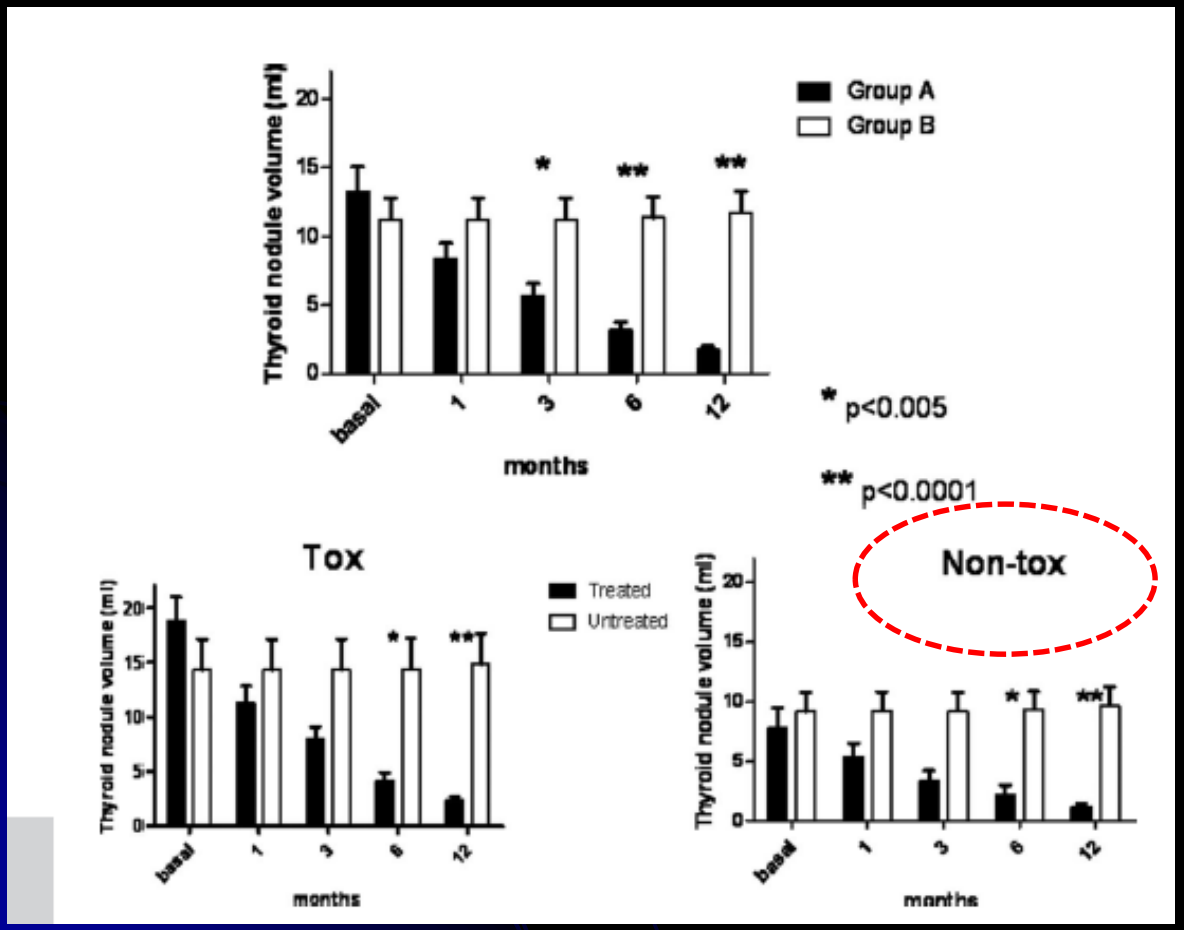
TABLE 1. Baseline characteristics of patients with TNs

Parameter	Group A	Group B	*P*
n	20	20	NS
Sex (males/females)	4/16	5/15	NS
Age in years, mean ± SEM (range)	58.3 ± 4.3 (31–86)	62.1 ± 3.1 (36–85)	NS
TN volume (ml)			
Mean ± SEM	13.3 ± 1.8	11.2 ± 1.5	NS
Median	12.35	7.7	
Range	4–27.9	3.6–25.8	
Patients with nontoxic TNs (n)	10	12	NS
Patients with toxic TNs (n)	10	8	NS
SYS score (range)	3.4 ± 0.3 (1–5)	3.0 ± 0.3 (1–5)	NS

Faggiano dic 2012
JCEM

Thyroid Nodules Treated with Percutaneous Radiofrequency Thermal Ablation: A Comparative Study

A. Faggiano, V. Ramundo, A. P. Assanti, F. Fonderico, P. E. Macchia, C. Misso, F. Marciello, V. Marotta, M. Del Prete, E. Papini, G. Lombardi, A. Colao, and S. Spiezia



13.3 vs *1.8 ml* at baseline
stable in group B 11.7 vs 11.2

- 86%

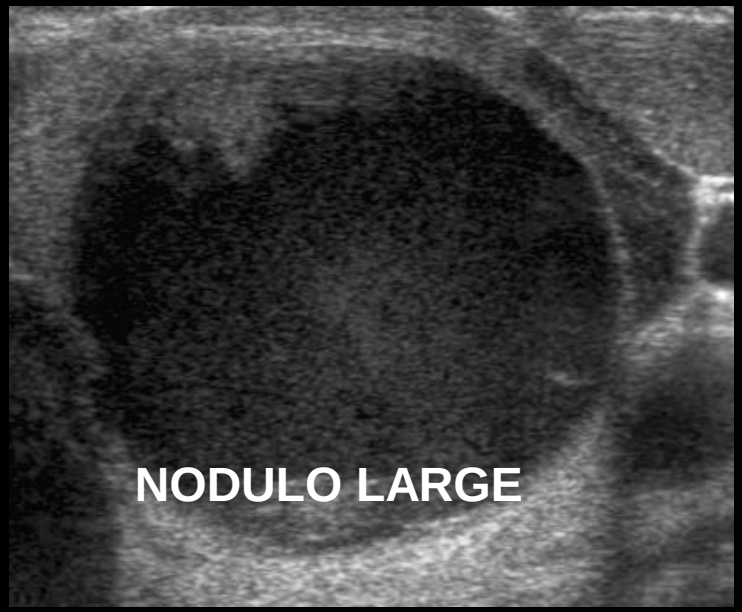
VALUTAZIONI PRE E POST PROCEDURALI

- 2 Agoaspirati ecoguidati (TIR2)
- Valutazione ecocolorDoppler del nodulo
- Volumetria ecografica nodulo
- Dosaggio ormoni tiroidei
- Symptom score (0-10) e Cosmetic grade (1-4)
- Sospensione di farmaci antiaggreganti e anticoagulanti
- Follow-up volumetria ecografica
- Follow-up ormoni tiroidei

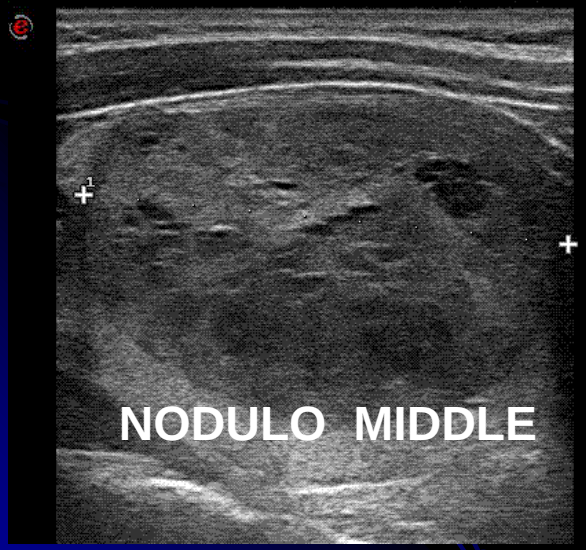
ANALISI COSTO EFFICACIA

CALCOLO DEL VOLUME TIROIDEO

VOLUME 26X25X24 = 8,1 ml



VOLUME 46X34X46 = 37 ml



VOLUME 42X24X36 = 19 ml

CLASSIFICAZIONE VOLUMETRICA

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

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

SAFETY

In letteratura è stata riportata una bassa incidenza di complicanze.

Table 2. Complications and Side Effects of Thyroid RF Ablation from Multicenter Study of Korean Society of Thyroid Radiology (53)

Complications	Number of Complications (%)
Major complications	20 (1.4)
Voice change	15 (1.02)
Nodule rupture	2 (0.14)
Nodule rupture with abscess*	1 (0.07)
Hypothyroidism*	1 (0.07)
Brachial plexus injury	1 (0.07)
Minor complications	28 (1.92)
Hematoma	15 (1.02)
Vomiting	9 (0.62)
Skin burn	4 (0.27)
Side effects	46 (3.15)
Pain	38 (2.6)
Vasovagal reaction	5 (0.34)
Coughing	3 (0.21)

Note.— Number in parentheses is percentage of complications of all patients. *Complications with remaining sequela. RF = radiofrequency

LA NOSTRA ESPERIENZA

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 1. Main characteristics of the study population and clinical data at baseline. Values are reported as mean ± SD

Parameter	Group A	Group B	*p*
N	42	42	
Sex (males/females)	15/27	18/24	ns
Age in years	56 ± 14 (24 - 80)	53 ± 12 (30 - 76)	ns
Thyroid nodule volume (mL)	24.5 ± 19.6 (3.4 - 89)	27.5 ± 22.1 (3.2-90)	ns
TSH(mIU/mL)	2.1 ± 0.9 (0.6 – 4.1)	2.3 ± 1.1 (0.6 - 4.4)	ns
FT3 (pg/mL)	2.7 ± 0.6 (1.2 – 3.7)	2.6 ± 0.6 (1.8 – 3.6)	ns
FT4 (pg/mL)	1.2 ± 0.3 (0 – 1.7)	1.2 ± 0.4 (0 – 1.7)	ns
Cosmetic score	2.6 ± 0.9 (1 – 4)	2.6 ± 1 (1 – 4)	ns
Symptom score	2.8 ± 3.3 (0 – 10)	2.7 ± 3 (0 – 8)	ns

JCEM 2015

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.
$^*p \leq 0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

JCEM 2015

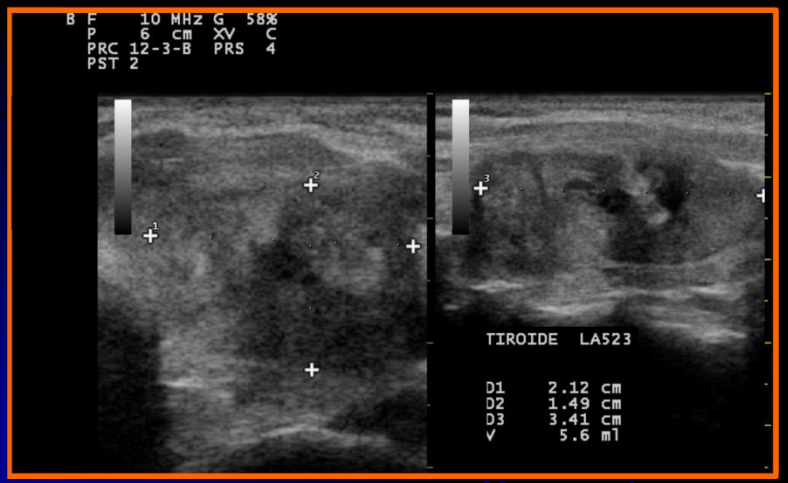
RADIOFREQUENZA
TEMPI DI TRATTAMENTO

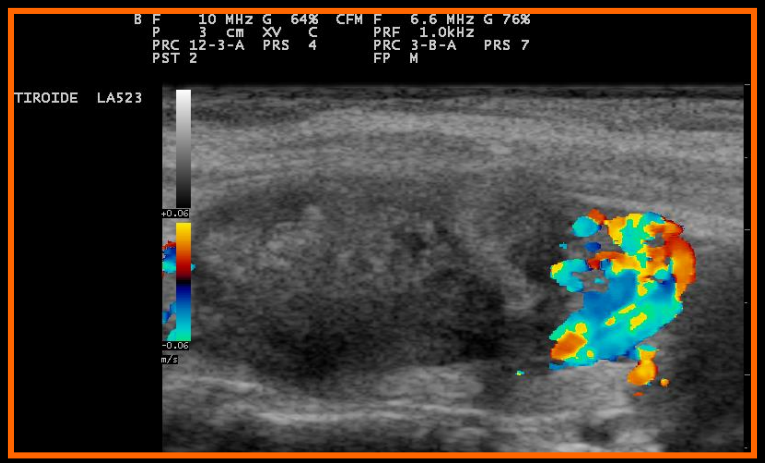
TABLE 3. Thyroid treatment time (minutes). Values are reported as mean ± SD (min-max)

	Time
Whole group	37 ± 17.4 (17-85)
Small	20.7 ± 2.8 (17-25)
Medium	31.9 ± 6.7 (24-45)
Large	61.6 ± 12.5 (48-85)

JCEM 2014 in print

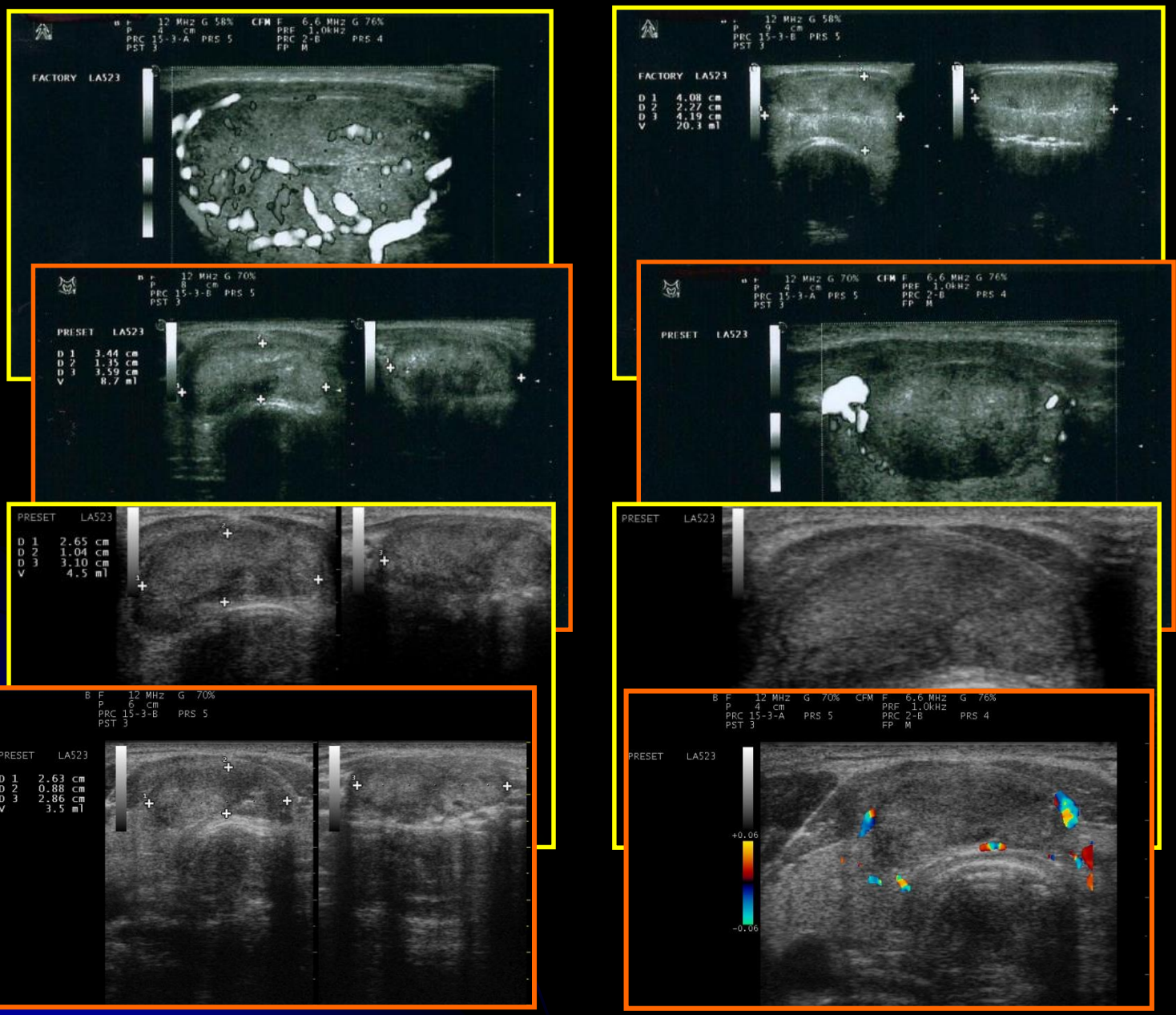
PRE RF





12 MESI
RIDUZIONE
DEL 82%

CASISTICA “SANTA MARIA GORETTI” LATINA



PRE RF

1 MESE
RIDUZIONE DEL
57%

6 MESI
RIDUZIONE DEL
78%

12 MESI
RIDUZIONE DEL
83%

Nodule Size as Predictive Factor of Efficacy of Radiofrequency Ablation in Treating Autonomously Functioning Thyroid Nodules.

Cesareo R et al

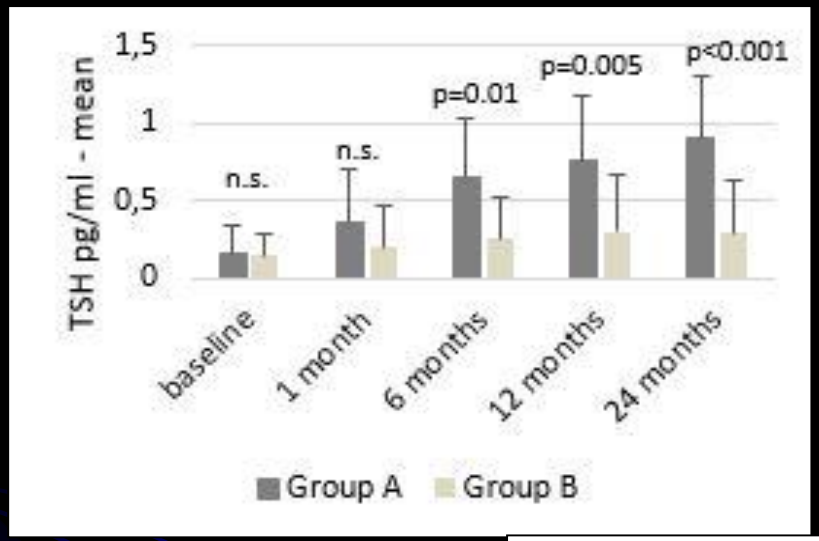
Thyroid nodule volume (ml).

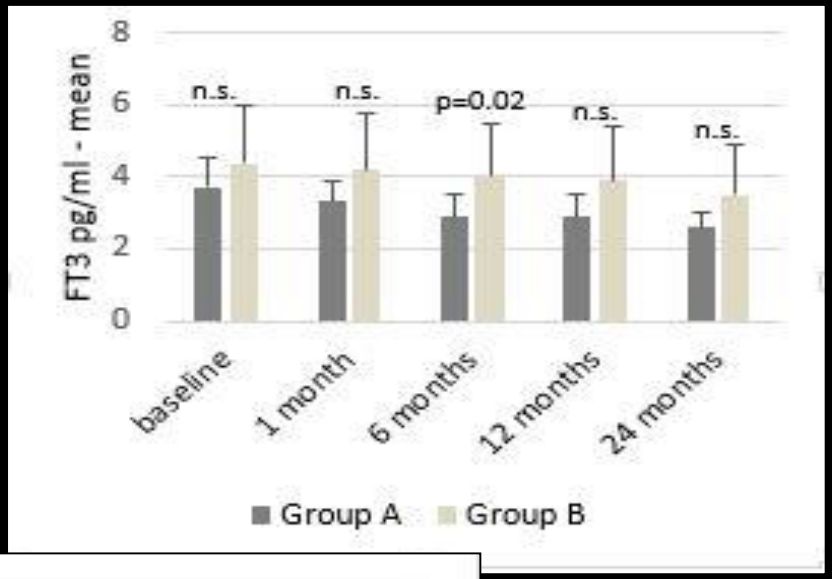
	Baseline	1 month	6 months	12 months	24 months	p vs baseline
Whole group (n)	29	29	29	29	26	
TN vol.	11.5 ± 7.5	5 ± 4.4*	3.9 ± 3.7*	3.4 ±3.2*	2.9 ± 3.3*	<0.001
TN vol. reduction (%)		61 ±10	68 ±15	75 ± 10	77 ± 11	<0.001
Group A (n)	15	15	15	15	15	
TN vol.	**5.2 ± 1.8**	1.7 ± 0.6*	1.3 ± 0.6*	0.9± 0.4*	0.8 ± 0.4*	<0.001
TN vol. reduction (%)		68 ± 6	75 ± 8	82 ± 6	84 ± 6	<0.001
Group B (n)	14	14	14	14	11	
TN vol.	**18.3 ± 4.7**	8.6 ± 3.8*	6.6 ± 3.6*	6 ± 2.6*	5.7 ± 3.3*	<0.004
TN vol. reduction (%)		54 ± 8	61 ± 18	67 ± 8	68 ± 11	=0.001

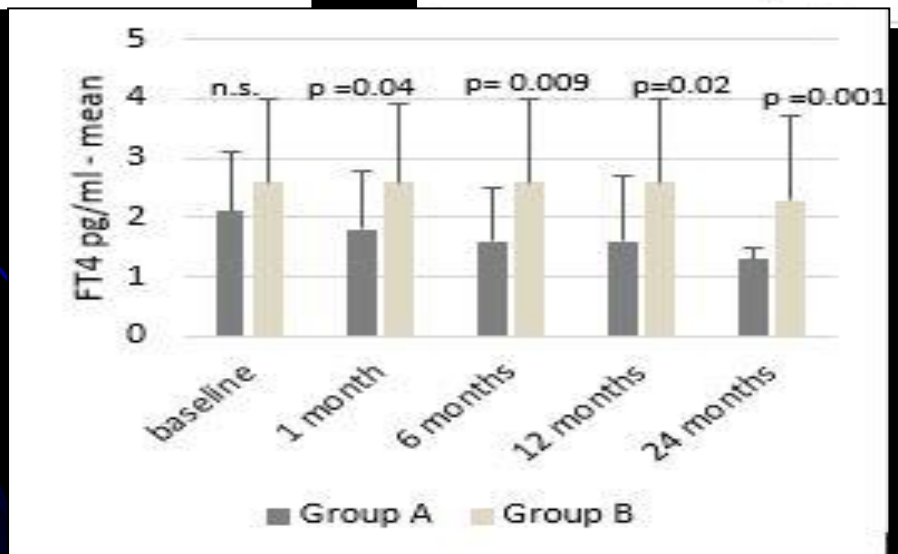
Differences in mean volumes are considered vs baseline.

Int J Hypert 2018

NODULE SIZE AS PREDICTIVE FACTORT OF EFFICACY FOR RADIOFREQUENCY ABLATION ON AUTONOMOUSLY FUNCTIONING THYROID NODULES

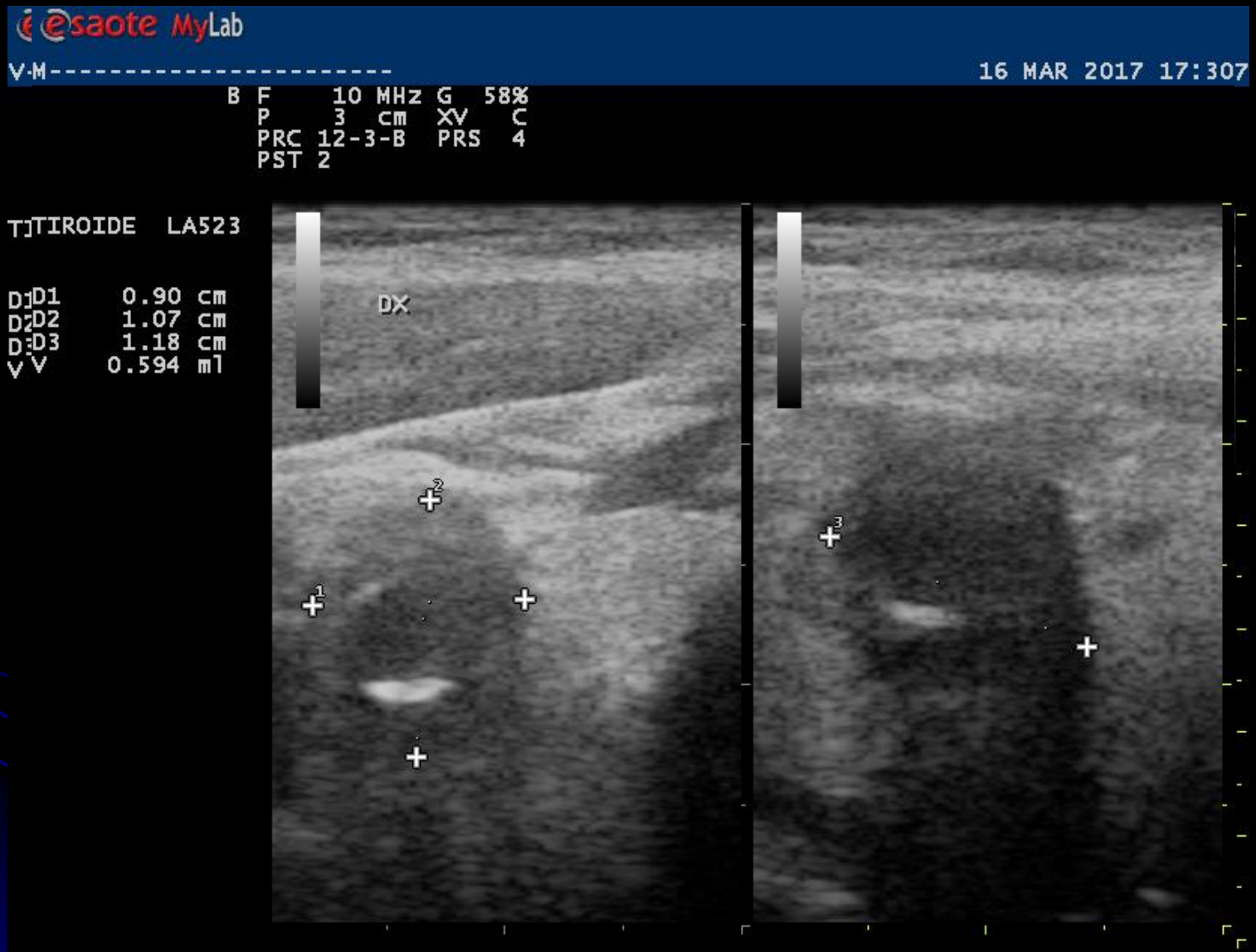




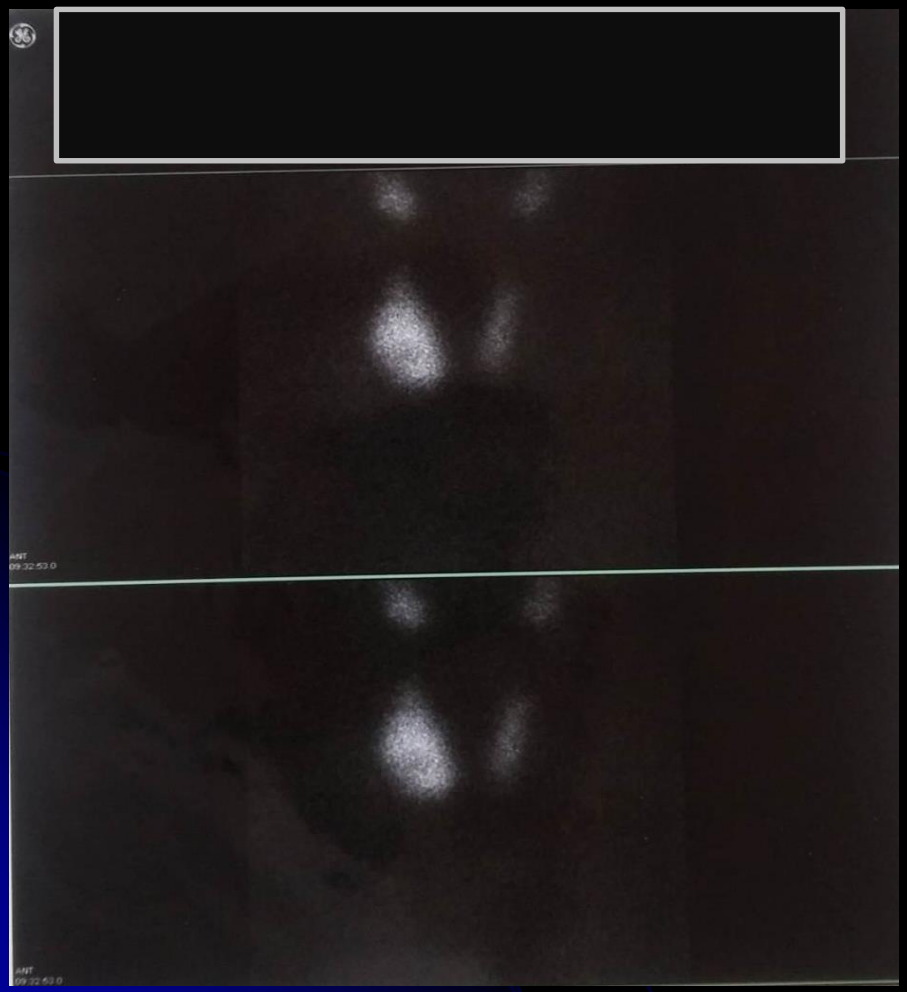


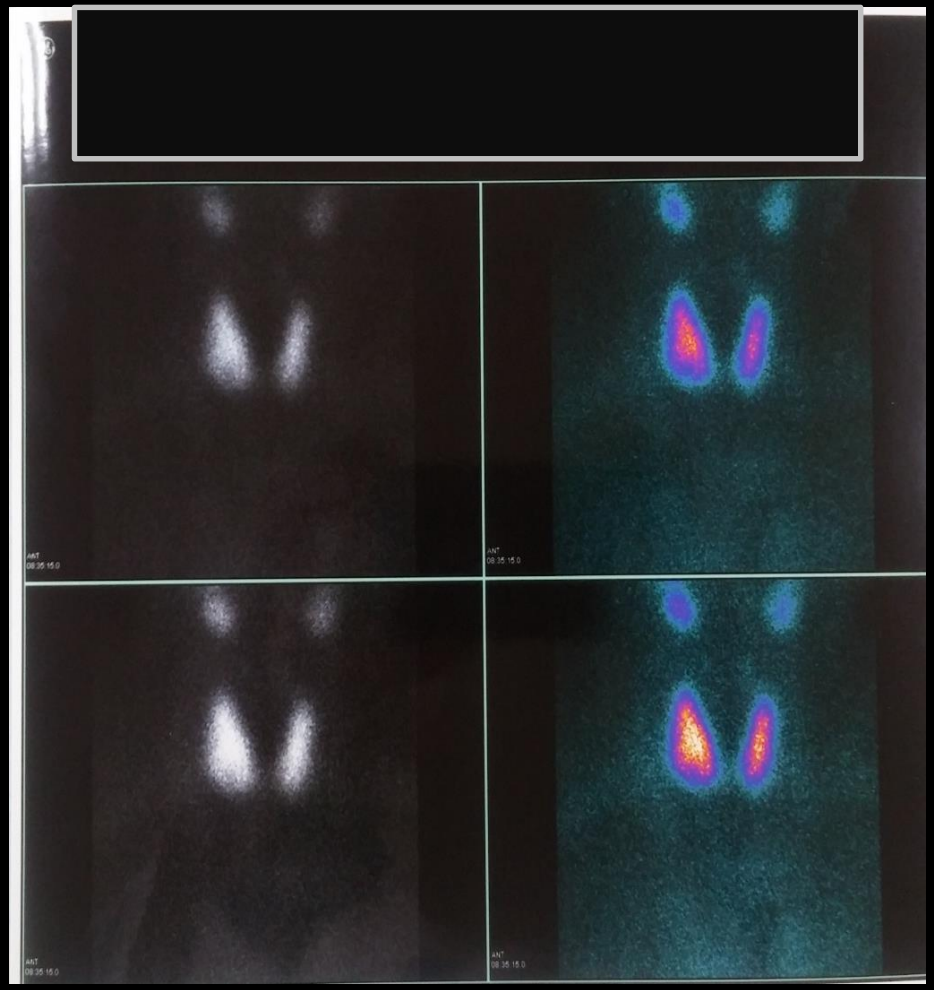
NODULE SIZE AS PREDICTIVE FACTORT OF EFFICACY FOR RADIOFREQUENCY ABLATION ON AUTONOMOUSLY FUNCTIONING THYROID NODULES

		Scintigrafia_t0		scintigrafia_t24		
		hot	cold	Drop-out	hot	cold
VOLUME NODULO	<12	15	0	1	2	**12**
	>12	14	0	3	9	**2**


esaote MyLab
V·M----------
16 MAR 2017 17:307
B F 10 MHz G 58%
P 3 cm XV C
PRC 12-3-B PRS 4
PST 2
TTIROIDE LA523
D1 D1 0.90 cm
D2 D2 1.07 cm
D3 D3 1.18 cm
V V 0.594 ml
DX

5 ML NODULE
SCINTI-SCAN BEFORE AND AFTER RFA





ESPERIENZA “SANTA MARIA GORETTI” COMPLICANZE 250 procedure eseguite

MAGGIORI:

- 2 disfonie transitorie risolte in 48 ore
- 1 paralisi della corda vocale destra con disfonia trasitoria risolta in 15 giorni; permanenza di stridor alla respirazione
- 1 pz ha sviluppato ipertiroidismo autoimmune

MINORI:

- 6 reazioni vasovagali
- **18%** ha riferito dolore periprocedurale (dolore al collo, dolore alla mandibola, dolore sternale) un solo paziente riferiva dolore severo

Radiofrequency ablation for the management of thyroid nodules: A critical appraisal of the literature

Roberto Cesareo[1*] | Andrea Palermo[2*] | Valerio Pasqualini[3] | Roberto Cianni[3] | Gianluigi Gaspa[4] | Silvia Manfrini[2] | Claudio Maurizio Pacella[5]

a) Which are the nodules that better respond to RFA treatment? In particular, is it cost-effective to treat large benign nonfunctioning nodules?

b) How many small and medium nodules can cause compressive symptoms or cosmetic discomfort?

c) Is it cost-effective to treat autonomously functioning thyroid nodules with RFA compared to radiometabolic treatment?

Cesareo et al Clin End 2017

TAKE HOME MESSAGES

- RF è tecnica operatore dipendente e che necessita una accurata learning curve
- Le complicanze sono senz'altro inferiori all'intervento di tiroidectomia
- I dati di effectiveness vanno correlati ai costi e pertanto al numero di procedure attese per il raggiungimento del goal terapeutico
- L'indicazione al trattamento di noduli small (< 12 ml) si giustifica secondo la nostra esperienza solo per i noduli hot
- E' auspicabile in futuro determinare delle curve di valutazione clinica più affidabili in merito a quelle attualmente in uso (cosmetic score e symptom score)

GRAZIE!!!