PERCUTANEOUS ETHANOL INJECTION (PEI) TREATMENT OF CISTIC THYROID NODULES

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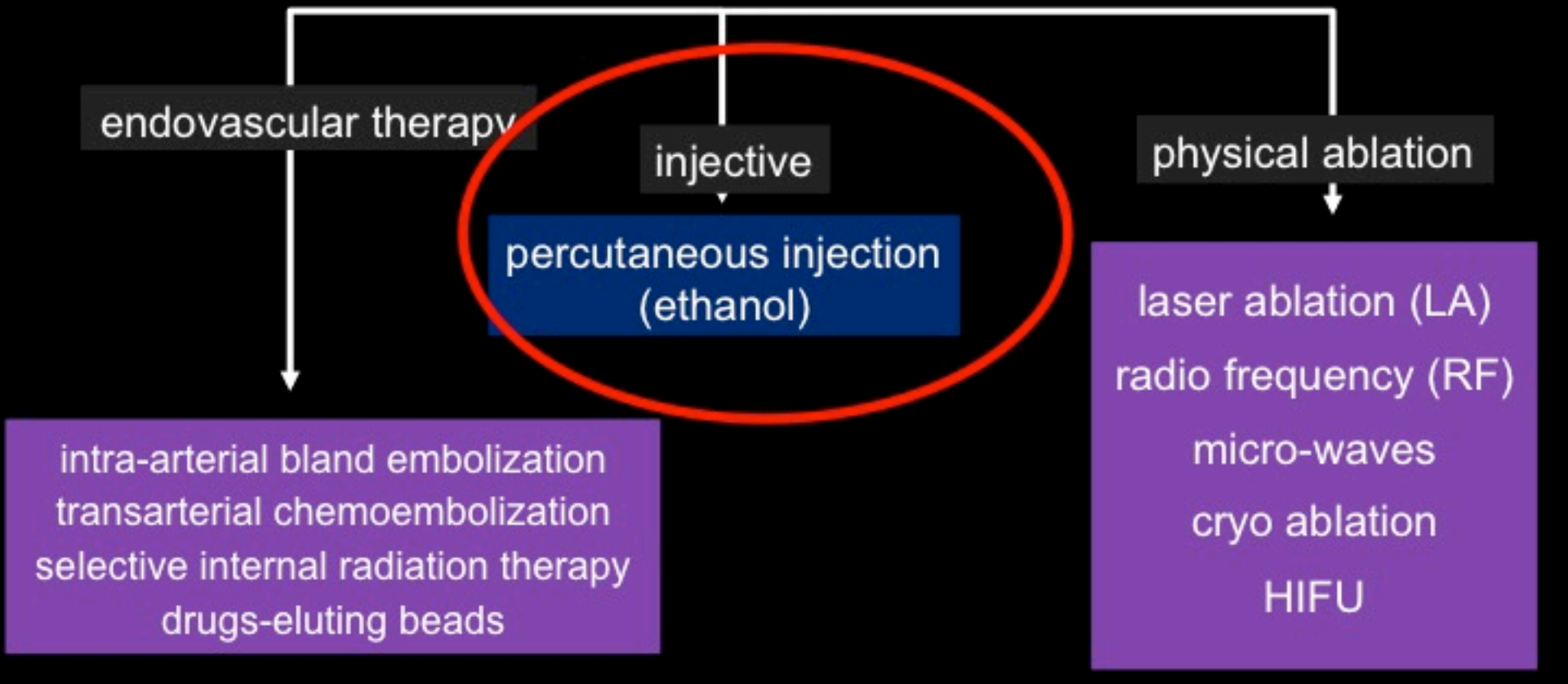
Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni non ho avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

PEI

- fine-needle aspiration biopsy (FNA) is a diagnostic complement of physical and ultrasound (US) examination of thyroid lesions
- percutaneous ethanol injection (PEI) is a non surgical procedure adopted by some medical centers as a therapeutic extension of US-FNA

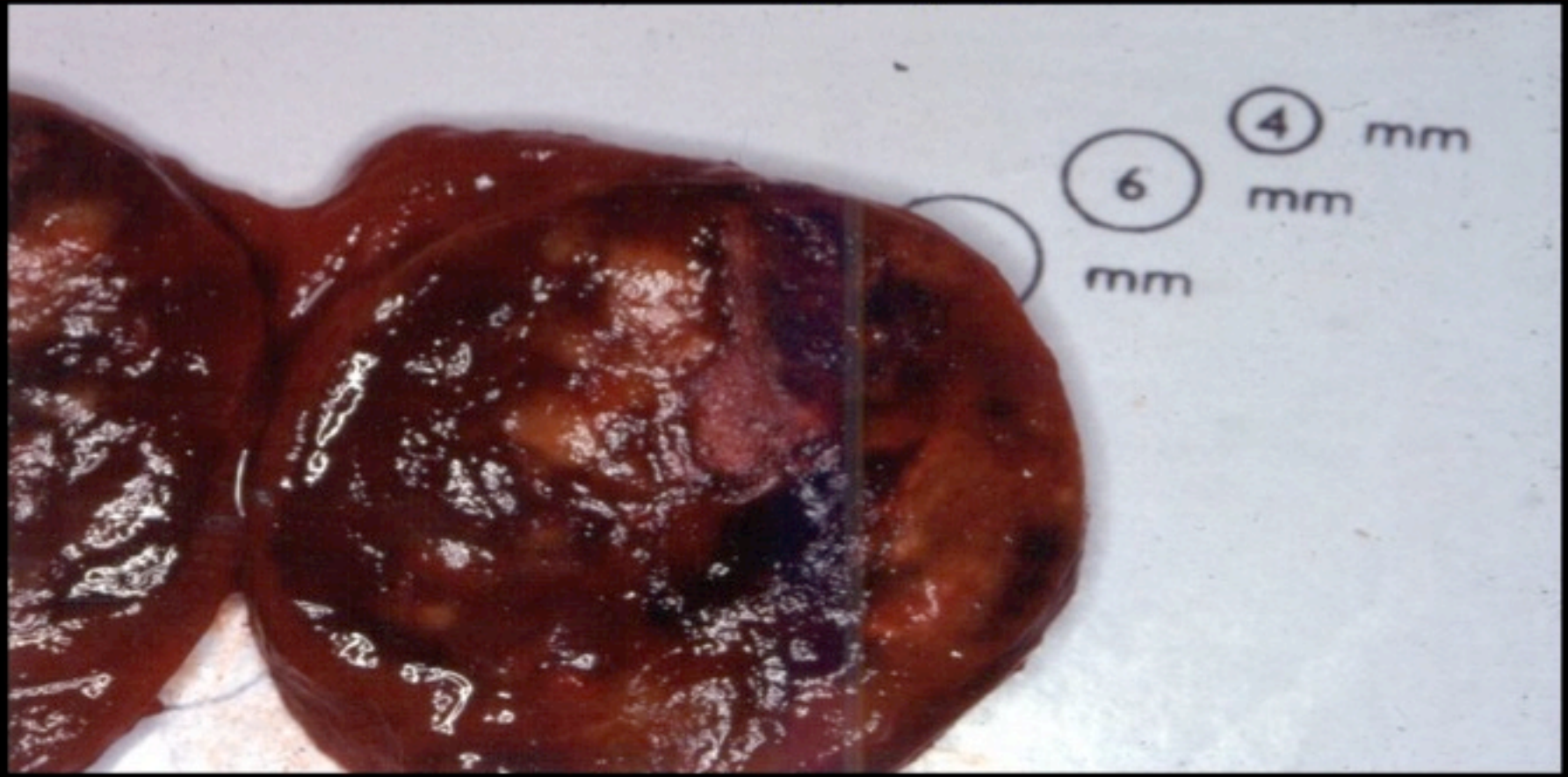
Minimally invasive techniques for tissue ablation



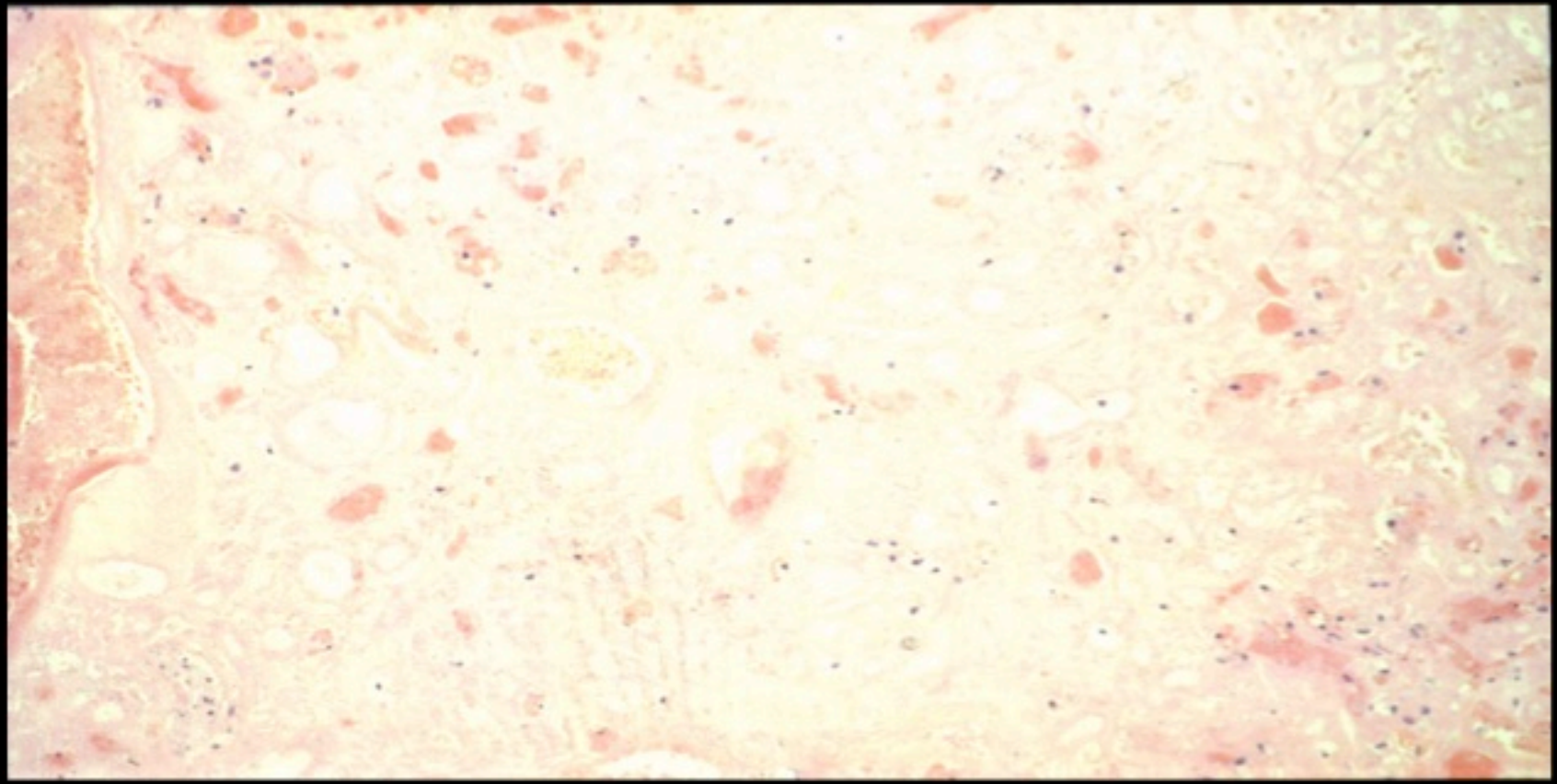
Introduction 2

- ethanol induces in thyroid tissue a complex damage including coagulative necrosis, vascular thrombosis and hemorrhagic infarction
- the treated areas are substituted by granulation tissue which causes scarring and progressive shrinkage of the nodules

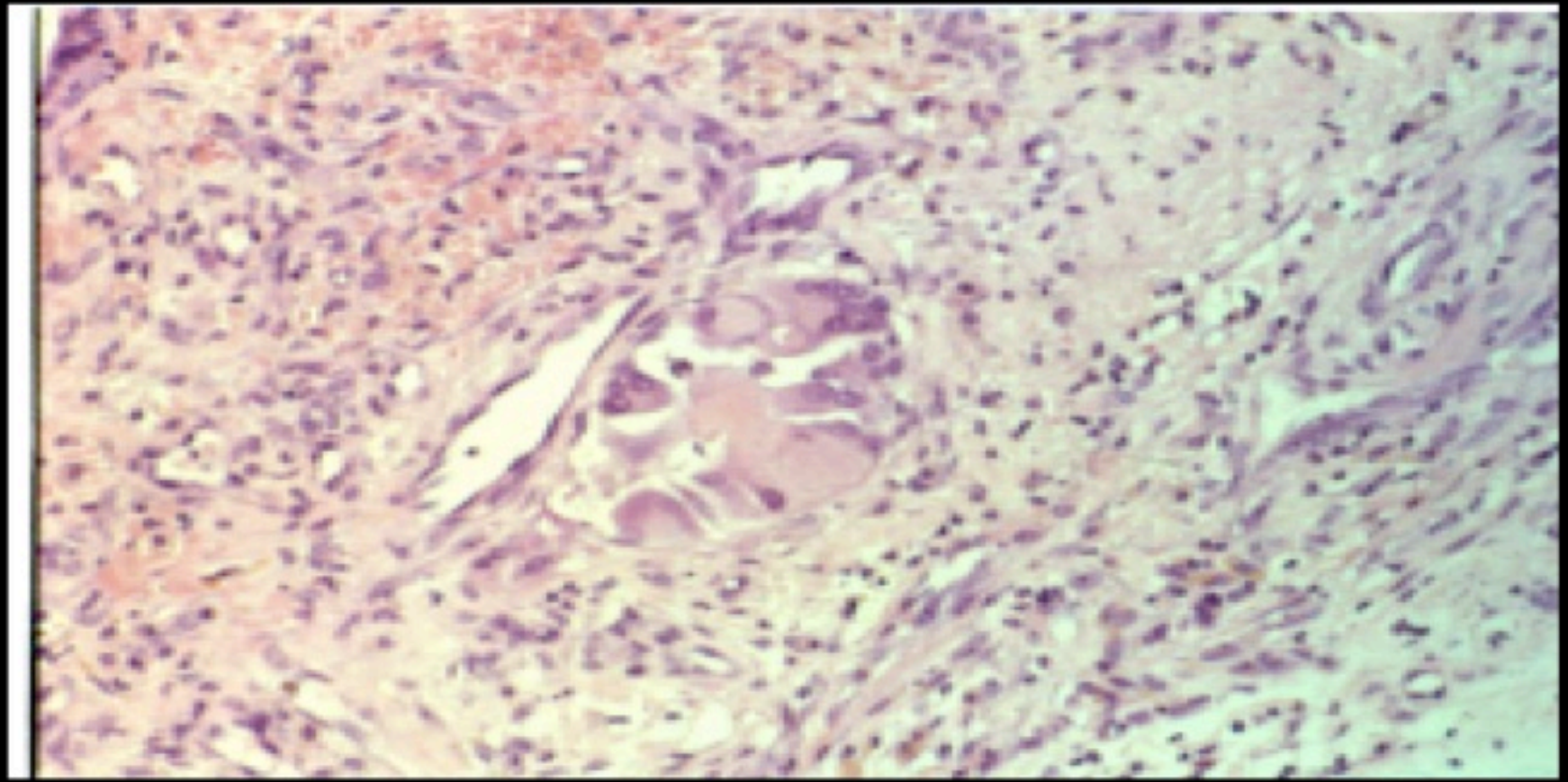
Macroscopic appearance of an AFTN resected after (7 days) PEI



PEI treatment: coagulative necrosis



PEI treatment: granulation tissue



PEI
Indications Proposed

- Hot & Cold benign solid thyroid nodules
- Parathyroid
- PTC Cervical lymph node metastases
- **Cystic thyroid nodules**

PEI in Solid Nodules

- The volume of thyroid tissue ablated by each injection is small and the injection of a large amount of ethanol in solid lesions increases the risk of extracapsular diffusion
- the number of ethanol injections, cost, discomfort and risk of the procedure increase while the probability of persistent therapeutic efficacy decreases

What is actually a Thyroid Cystic Nodule?

- Congenital lesion originate from metaplastic squamous or columnar epithelium coming out from the thyroglossal duct or the fourth bronchial pouch (<5%)

- Lesion caused by degenerative changes of colloid nodules or adenoma

Myer CM et all, Thyroid disease 1990
Salabe GB 1991, Thyroidol Clin Exp 1991

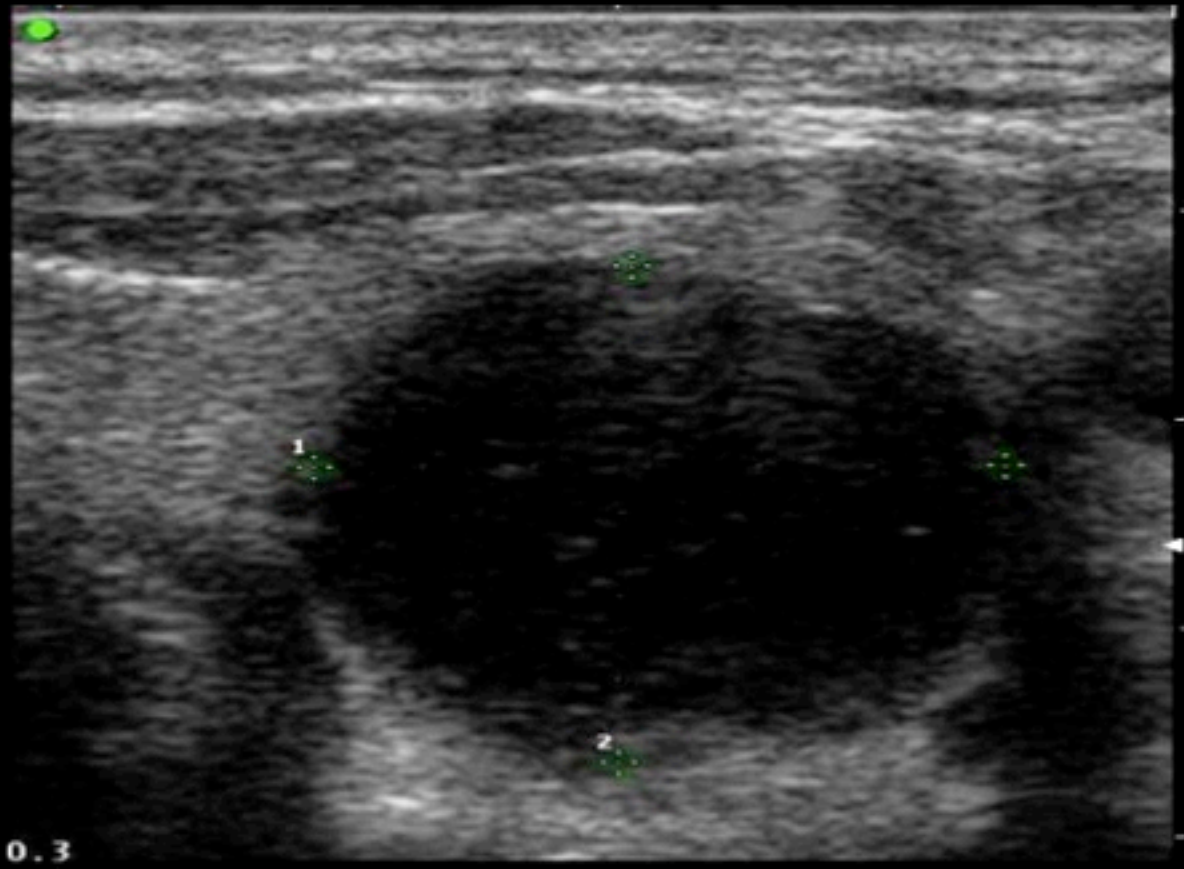
How frequent are Cystic Nodules?

Thyroid nodules are cystic in about 20% of cases

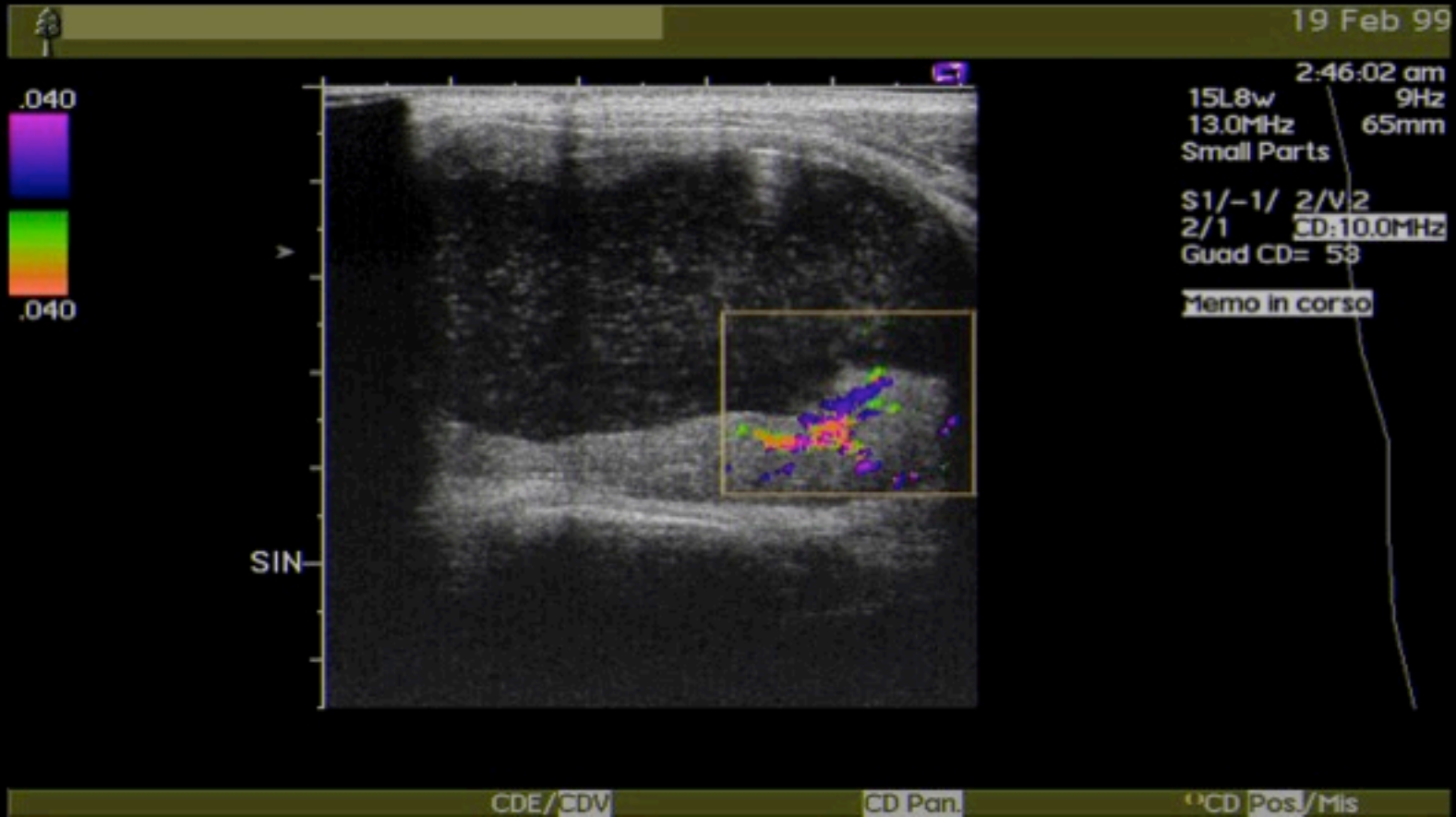
Percentage of fluid is variable
(at least 20% of whole nodule volume)

Recommendations for management of cystic thyroid disease.
McHenry et all, Surgery. 1999 Dec;126(6):1167-71

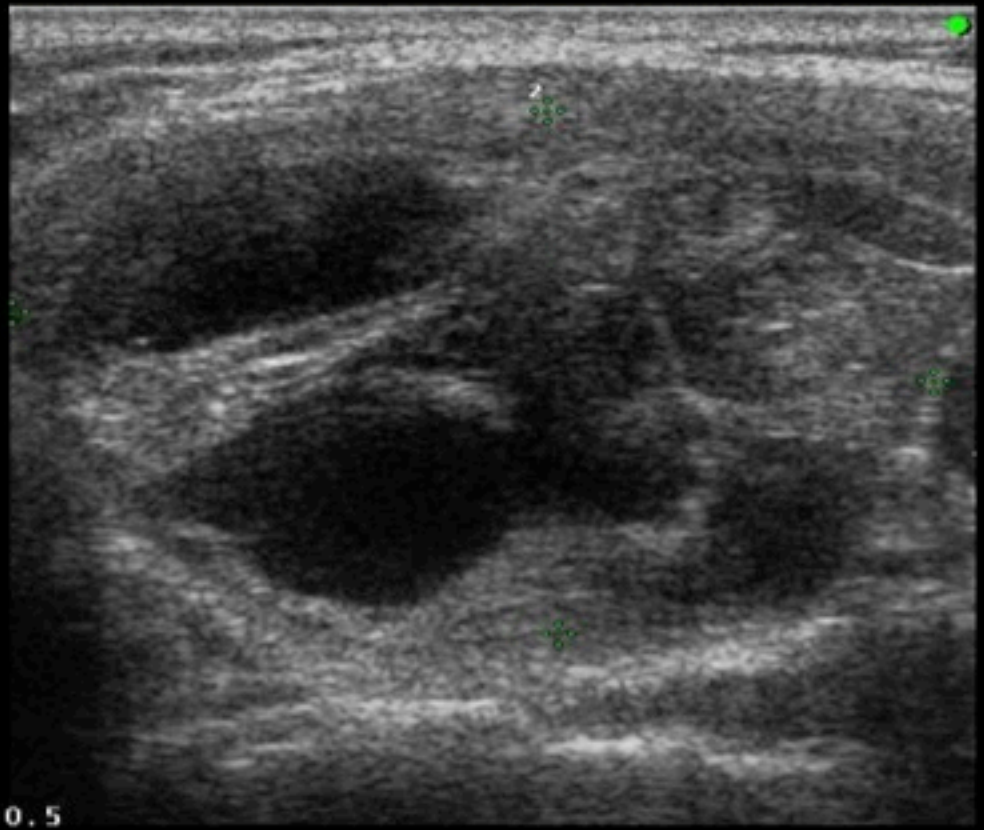
Complete Cystic Nodules



Predominant Cystic Component



Mixed Nodule



Are Cystic Nodules always benign?

The incidence of carcinoma in cytologically benign thyroid cysts

Ghadam Abbas, MD, Keith S. Heller, MD, Ali Khoynezhad, MD, Sanford Dubner, MD, and Laura A. Sawyer, MD, *New Hyde Park, NY*

Table I. Final pathologic findings (number of patients)

Pathologic finding		
Papillary cancer	4	>10%
Adenomas	13	
Multinodular goiter	8	
Colloid cyst	4	
Simple cyst	3	
Hashimoto's disease	2	
Total	34	

SURGERY 1035

Presented at the 22nd Annual Meeting of the American Association of Endocrine Surgeons, Atlanta, Ga, April 28-May 1, 2001.

The incidence of carcinoma in cytologically benign thyroid cysts

Ghulam Abbas, MD, Keith S. Heller, MD, Ali Khoynezhad, MD, Sanford Dubner, MD, *and* Laura A. Snyder, MD, *New Hyde Park, NY*

MEDIAN OF MALIGNANCY: 15%

Presented at the 22nd Annual Meeting of the American Association of Endocrine Surgeons, Atlanta, Ga, April 28-May 1, 2001.

SURGERY 1035

The incidence of carcinoma in cytologically benign thyroid cysts

Ghulam Abbas, MD, Keith S. Heller, MD, Ali Khoynezhad, MD, Sanford Dubner, MD, and Laura A. Snyder, MD, *New Hyde Park, NY*

Some authors have suggested the use of sclerosing agents to prevent the reaccumulation of thyroid cysts.[12,13] Because of the risk of malignancy in these thyroid cysts we caution against this approach because of the possibility that sclerosis might mask but not destroy a thyroid malignancy.

We conclude from this study that thyroidectomy should be considered in all patients with simple thyroid cysts that recur after aspiration, particularly those greater than 3 cm in size.

Presented at the 22nd Annual Meeting of the American Association of Endocrine Surgeons, Atlanta, Ga, April 28-May 1, 2001.

The incidence of carcinoma in cytologically benign thyroid cysts

Ghulam Abbas, MD, Keith S. Heller, MD, Ali Khoynezhad, MD, Sanford Dubner, MD, *and* Laura A. Szuyter, MD, *New Hyde Park, NY*

Dr Robert Udelsman (Baltimore, Md). I want to challenge you a little bit. You conclude that there was a 12% incidence of malignancy in the cystic lesions. But we have to remember this is a surgically based retrospective series. I suggest to you that the vast majority of patients with thyroid cysts are not coming to your practice and do not have recurring illnesses but are being aspirated by the endocrinologists.

I suggest that the incidence of malignancy in a simple thyroid cyst is more in the range of 0.1%. You are reporting a highly selective series by definition since the patients were referred to a surgeon and underwent resection. You might be over-interpreting the data based on the retrospective nature of the study.

Presented at the 22nd Annual Meeting of the American Association of Endocrine Surgeons, Atlanta, Ga, April 28-May 1, 2001.

Is a benign FNAB of cysts as reliable as in solid nodule?

- The answer is **Yes**

- FNABs is generally performed in two stages:

a. the cyst is relieved of the fluid and subsequently
b. material is aspirated under US control from the remaing tissue complex

Efficacy of Ultrasound-Guided Fine-Needle Aspiration Biopsy in the Diagnosis of Complex Thyroid Nodules

MILENA BRAGA, TEREZA CRISTINA CAVALCANTI, LUIZ MARTINS COELHO, AND HANS GRAF

Serviço de Endocrinologia e Metabologia do Pavilhão do Hospital da Clínicas (M.B., H.G.) and Serviço de Anatomia Patológica do Hospital de Clínicas (T.C.C., L.M.C.), Universidade Federal do Paraná, Curitiba 80.060-240, Brasil

proceed directly to biopsy the solid part of the nodule to avoid a non negligible rate of hemorrhage within the cavity of the nodule after partial aspiration:

Diagnostic cytology: >90%

The Journal of Clinical Endocrinology & Metabolism 86(9):4089–4091

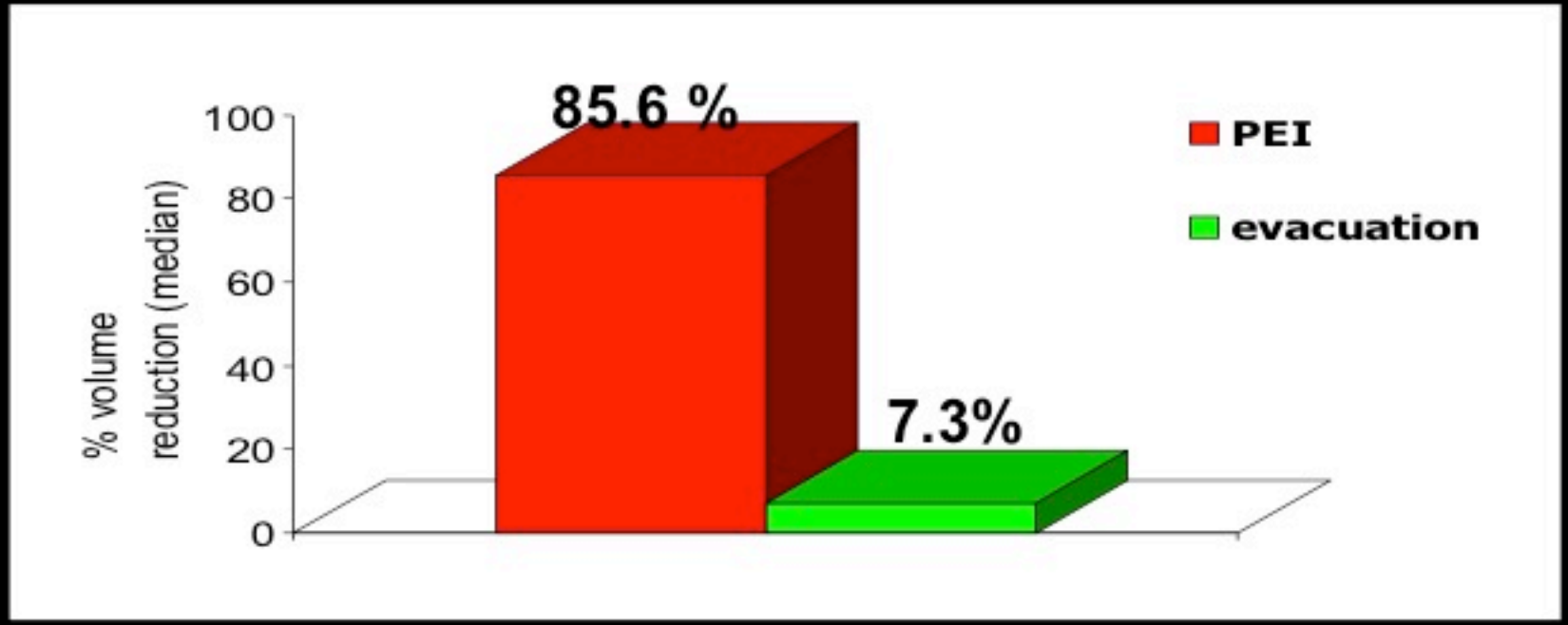
Could Cystic Nodules be cured with simple fluid aspiration?

Cyst resolution occurres in about 10 % patients after FNA

Recommendations for management of cystic thyroid disease. McHenry et all, Surgery. 1999 Dec;126(6):1167-71

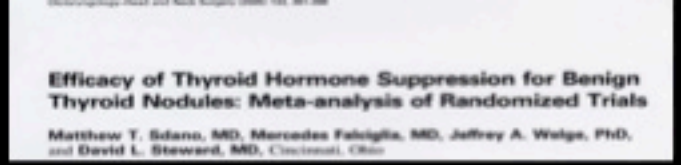
PEI of Cystic Thyroid Nodules

% volume reduction after 1 yr



Valcavi R & Frasoldati A., Endocrine Practice, 2004

Is L-T4 effective in Thyroid Cystic Nodules?



Efficacy of Thyroid Hormone Suppression for Benign Thyroid Nodules: Meta-analysis of Randomized Trials

Matthew T. Sdano, MD, Mercedes Falciglia, MD, Jeffrey A. Welge, PhD, and David L. Steward, MD, Cincinnati, Ohio

Table 1
Studies included in meta-analysis

Study	Length	Patients	Nodule type	TSH (mU/mL)	T4 dose (mcg/kg/d)
Wemeau	18 m	123	Nodules had <20% cystic component	TSH<0.3	T4 ave: 2.24
Larijani	12 m	62	Cystic nodules included	TSH ave: 0.18	T4: 1.5-2
Zelmanovitz	12 m	45	Nodules had <20% cystic component	TSH<0.3	T4: 2.5-3
LaRosa	12 m	45	Cystic nodules excluded	TSH<0.3	T4 ave: 1.8
Papini	12 m	101	Nodules excluded if >1 mL fluid	n/a	T4 ave: 2
Reverter	12 m	40	Solid-cystic nodules included	TSH<0.1	T4 ave: 2.82
Gharib	6 m	53	Cystic nodules included	n/a	T4 ave: 3
Koc	12 m	40	Nodules had <20% cystic component	n/a	T4 ave: 3.2[a] T4 ave: 1.4[b]
Uzunkoy	12 m	100	Cystic nodules excluded	TSH ave: 0.1	T4: 1.5-3

n/a, not available; m, months.
[a]high dose suppression group
[b]low dose suppression group

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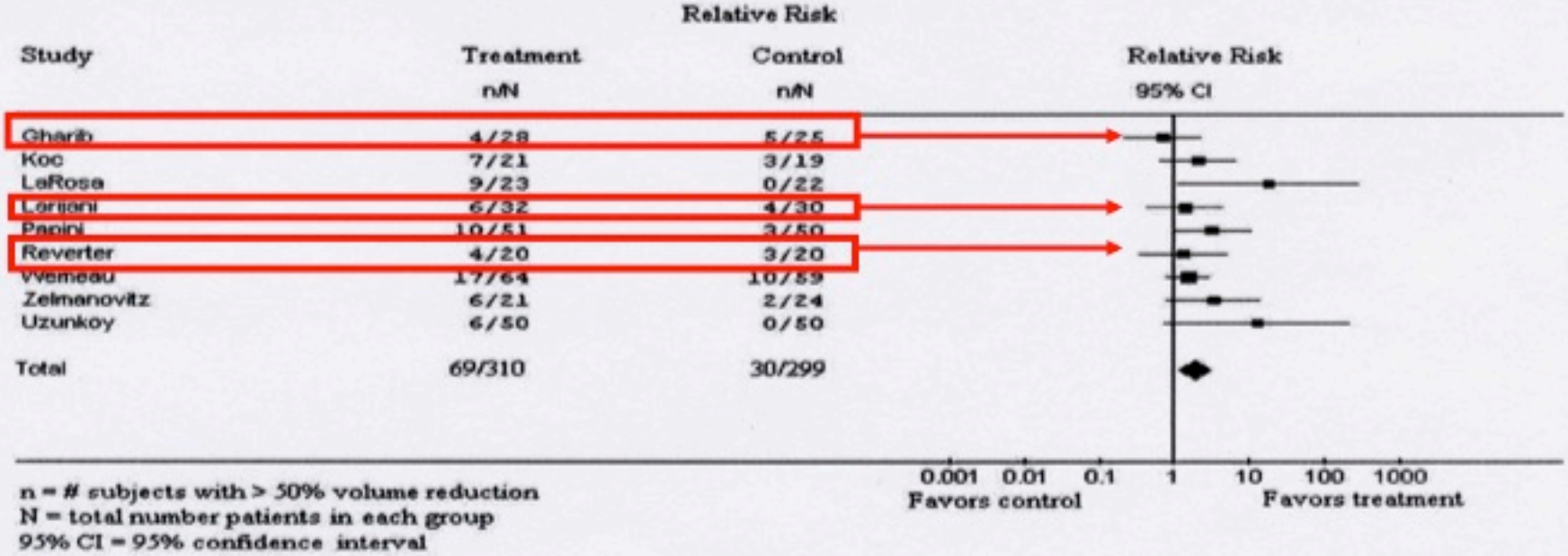


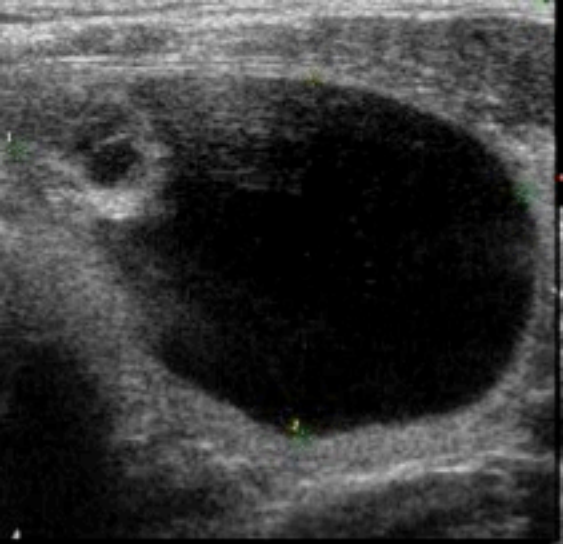
Figure 1 Individual and total relative risk (with 95% confidence intervals) for number of patients having >50% reduction in thyroid nodule volume (using random effects analysis).

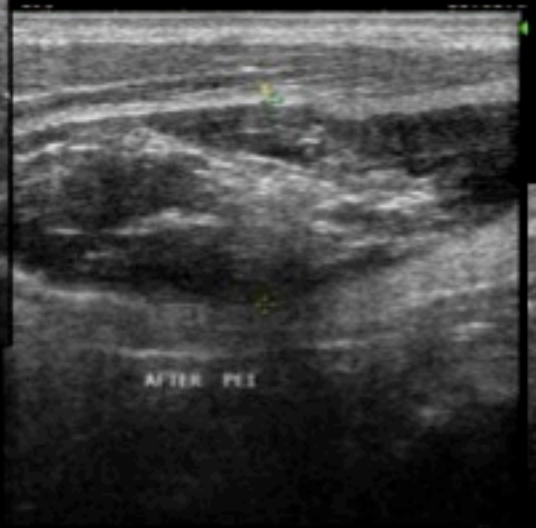
Am J Med. 1980 Jun;68(6):853-5. Links

The role of thyroid therapy in patients with thyroid cysts.

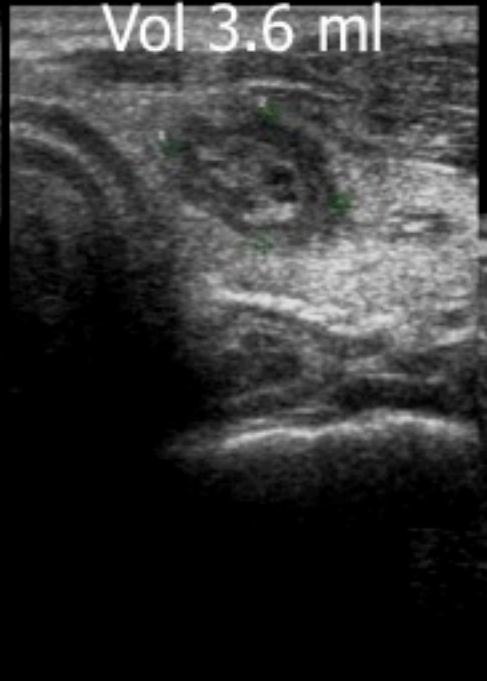
McCowen KD, Reed JW, Fariss BL.

Twenty patients with benign thyroid cysts were studied in a prospective double-blind fashion to determine the effect of thyroid therapy on the recurrence of these cysts after aspiration. When the 10 patients receiving placebo medication were compared with the 10 patients ingesting thyroid hormone, no significant difference was found in the time either group was free of cyst recurrence. **We conclude that thyroid therapy is not effective in preventing the recurrence of benign thyroid cysts after initial aspiration.**

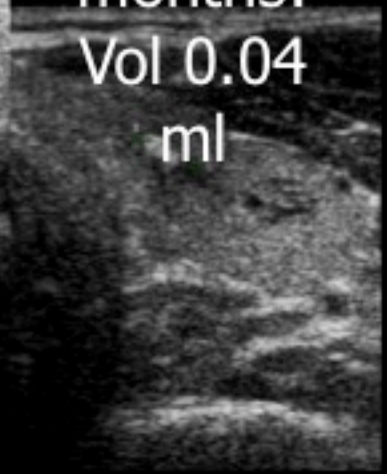


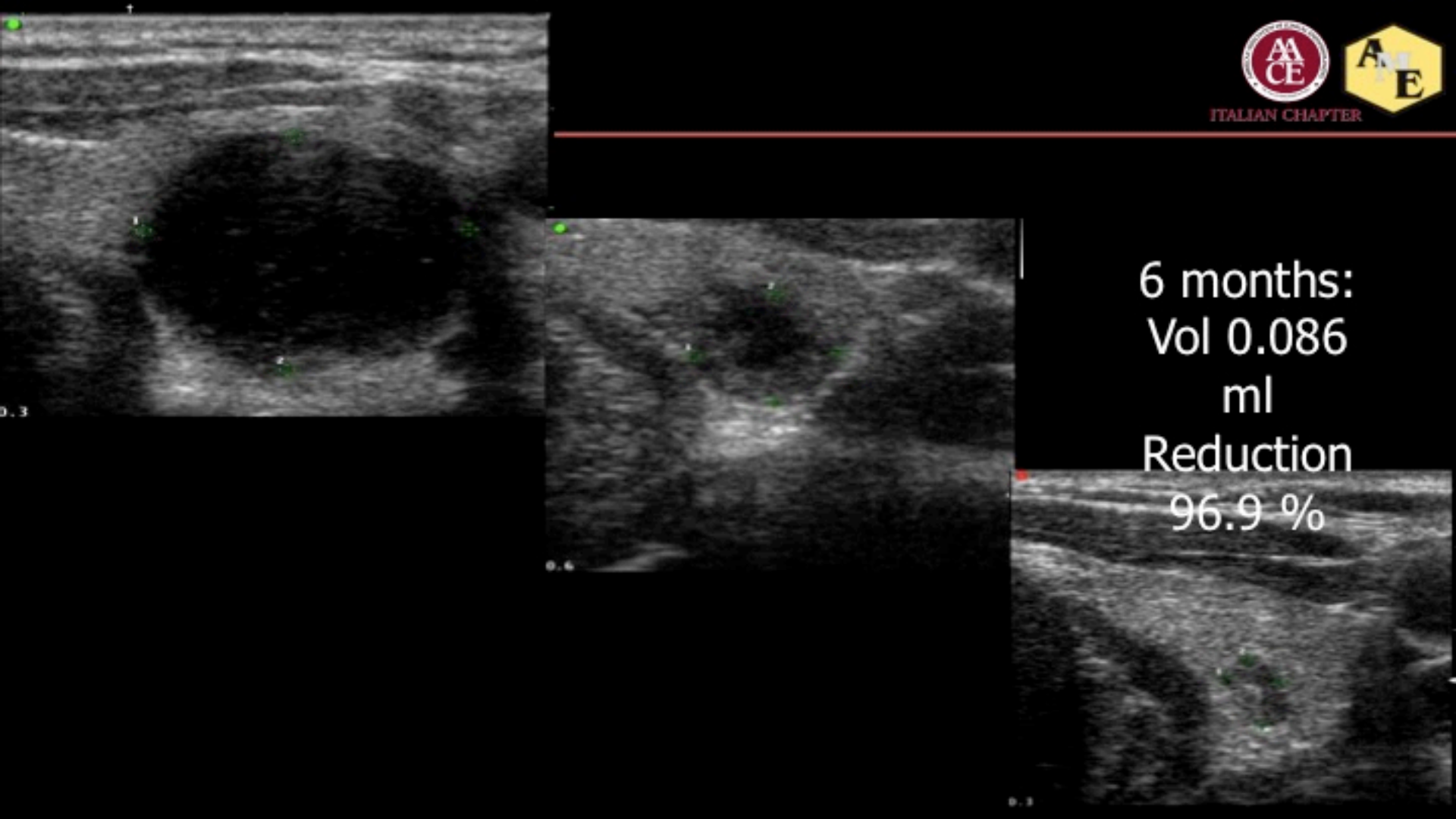


1 month:
Vol 3.6 ml



12 months:
Vol 0.04 ml




ITALIAN CHAPTER
6 months:
Vol 0.086
ml
Reduction
96.9 %

PEI in cystic thyroid nodules volume before and after treatment

	N pts	Pre-PEI Volume (ml) base-line	Post-PEI Volume (ml) 12 months	Post-PEI Volume (ml) 60 months
Zingrillo 1999		33.7±25.3	3.0±2.4*	0.6±0.6*
Verde 1994		14.5 Range 1.5-65.8	2.5* Range 0.4-34.5	-

P<0.001 vs. baseline

Percutaneous Ethanol Injection Treatment in Benign Thyroid Lesions: Role and Efficacy

Rinaldo Guglielmi,[1] Claudio Maurizio Pacella,[1] Antonio Bianchini,[1] Giancarlo Bizzarri,[1] Roberta Rinaldi,[1] Filomena Maria Graziano,[1] Lucilla Petrucci,[1] Vincenzo Toscano,[2] Enzo Patrizi,[1] Maurizio Poggi[3] and Enrico Papini[1]

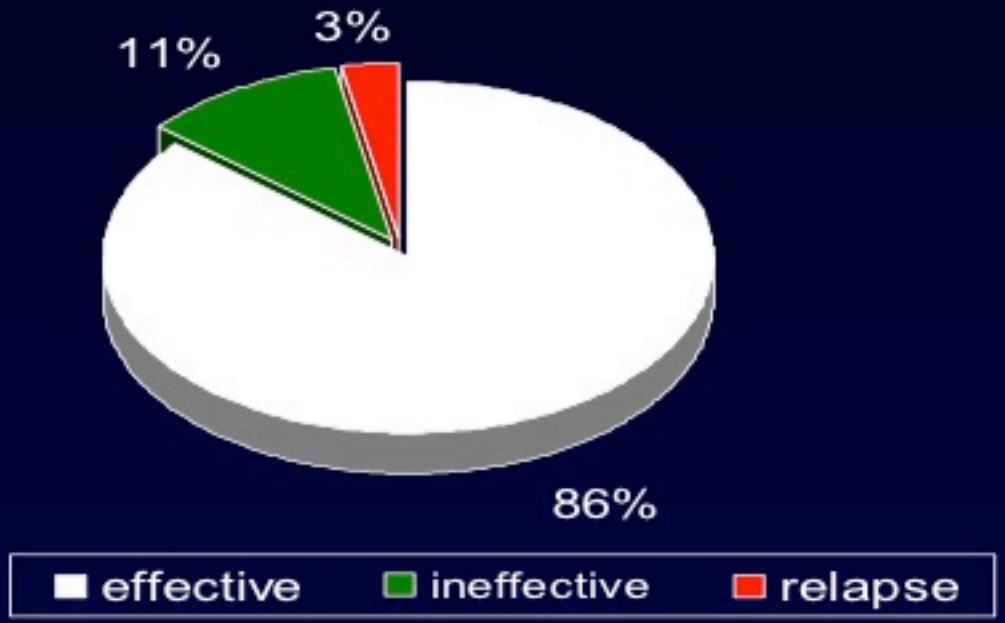
TABLE 1. MAIN OUTCOMES OF PEI IN CYSTIC THYROID NODULES AND TOTAL AFTN FIVE YEARS AFTER TREATMENT

	Cases	*Baseline volume (mL)*	*Ethanol injected (mL)*	*Volume after 5 yrs (mL)*	*Volume reduction (%)*	*Normal serum TSH after 5 yrs (%)*
Cysts	58	13.7 ± 14.0	7.3 ± 5.5	2.3 ± 3.5	86.6 ± 34.3	—
Total AFTN	112	8.5 ± 10.8	10.4 ± 7.4	2.8 ± 7.65	64.2 ± 27.4	56.2 (63/112)

PEI, percutaneous ethanol injection; AFTN, autonomously functioning nodules; TSH, thyrotropin.

Efficacy of PEI treatment
Thyroid Cysts

- cases treated by PEI: 58 (at least 5-years follow-up)
- median number of treatments: 2
- *effective*: volume decrease > 75% and improvement of local symptoms
- *ineffective*: volume decrease < 75% and/or persistence of local symptoms



How safe is percutaneous ethanol injection for treatment of thyroid nodule?

Side-effects caused by ethanol injection are generally few and transient and are related to the injection into solid nodules rather thancysts. Ethanol injection into solid profound nodules may seriously jeopardize subsequent surgery because of perinodular fibrosis

Bennedbaek et al. Eur J Endocrinol., 1997.

Although most complications have been transient in nature we observed ethyl toxic necrosis of the larynx: the patient was admitted to hospital, treated conservatively and ten month later microsurgically.....
The patient must be informed about possible severe complications.
The examiner should have substantial experience in these methods.

Mauz et al., Acta Otolaryngol. 2004

Side effects


Percutaneous Ethanol Injection Treatment in Benign Thyroid Lesions: Role and Efficacy

- **no side effects were registered during the treatment of cystic nodules**
- in two cases (1.8%) of AFTN was observed a transient dysphonia
- The paresis of the homolateral cord appeared immediately after PEI and the recovery (confirmed by laringoscopy) was obtained within one and seven weeks, respectively

Tolerability
Experience of the procedure


Percutaneous Ethanol Injection Treatment in Benign Thyroid Lesions: Role and Efficacy

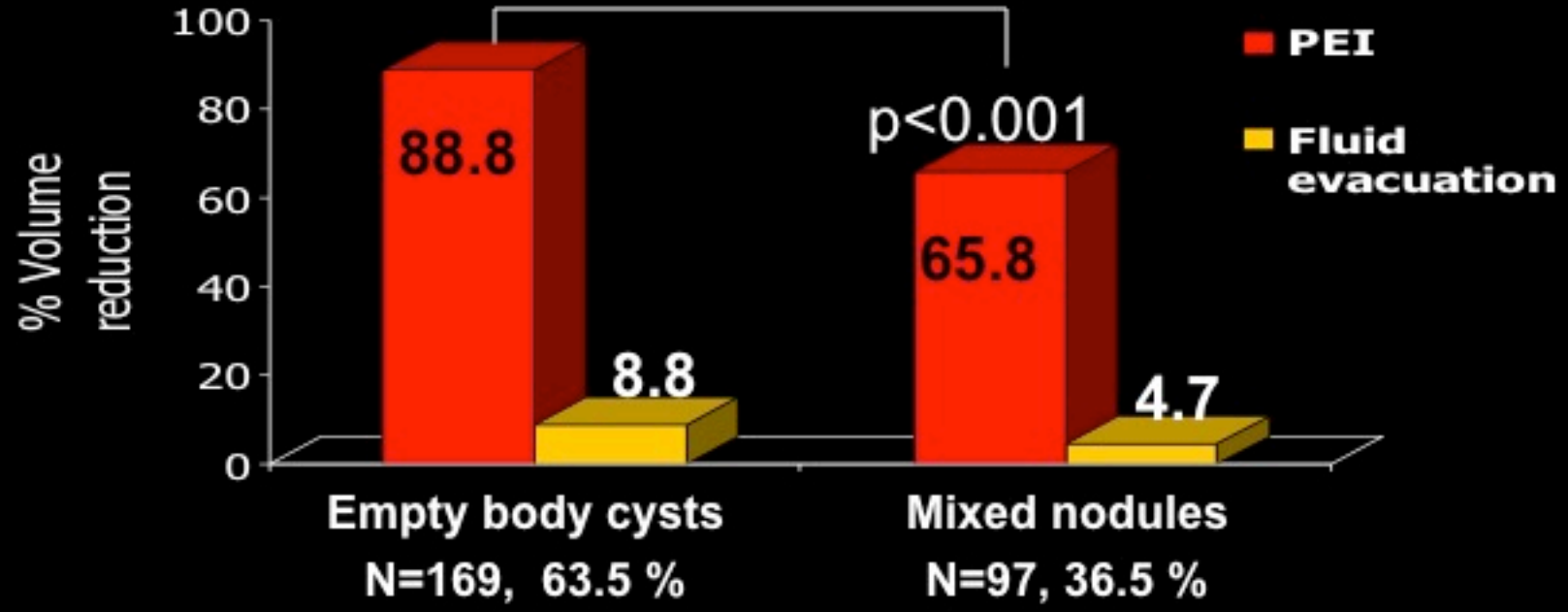
- ***thyroid cysts***
  no patient defined the treatment as very painful and a new session would be accepted without any problem, if needed

- *AFTN*
  30% of patients defined PEI as very painful procedure and a different treatment would be considered if needed

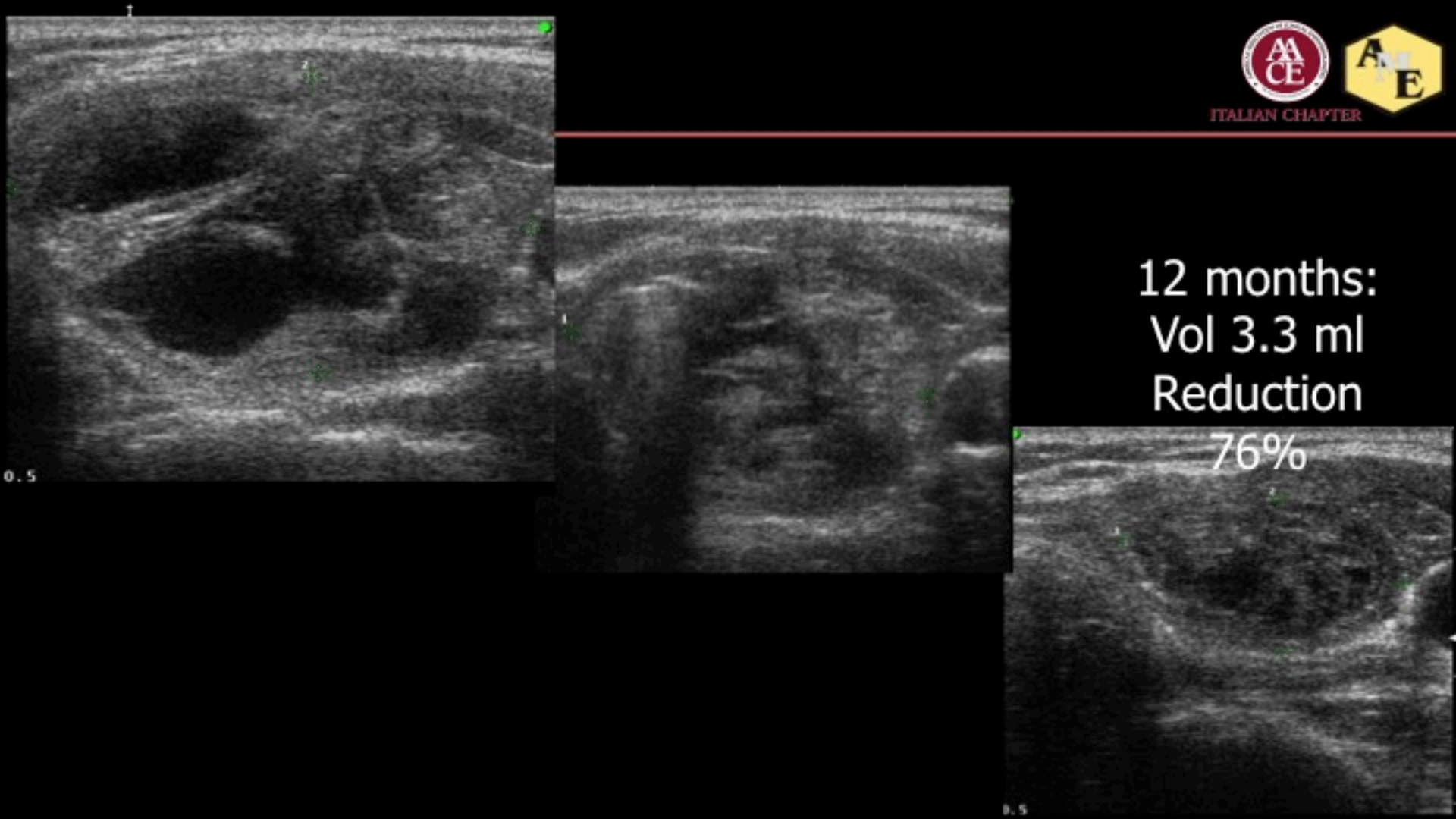
Some further Clinical Problem

Which result with Mixed Thyroid Nodules?

Results of PEI in cystic thyroid nodules
% vol.reduction: empty body vs mixed cysts



Valcavi R & Frasoldati A., Endocrine Practice, 2004


ITALIAN CHAPTER
12 months:
Vol 3.3 ml
Reduction
76%

What to do with Cystic Nodules with Viscous Colloid?

- Stage 1: in case of ineffective aspiration, inject 1 ml di ethanol for each 10 ml of nodule volume
- Stage 2: 2 weeks later, repeat procedure as in stage 1, then use a 20-gauge needle for aspiration. When the cyst is empty do the usual procedure of PEI
- Nodule volume shrinkage reported after 1 yr: **91%**

Zieleznik W et all, Thyroid , 2005
Vol 15, n° 7, pp 683

Is there a maximum nodule volume for PEI treatment?

Thyroid cystic nodules relapse more frequently after PEI if baseline volume is greater than 20 ml and need more number of ethanol injection and longer follow up

Jayesh SR et all
Indian J Radiol Imaging
August 2009

Cost of PEI vs Surgery
Italian National Institute of Health Refunds

Thyroid Cysts

- PEI (9929) two session (DH) = 576 €
- Surgery (conventional) = 3450 €

No Hypothyroidism after PEI

Indications and limitations of PEI
Conclusion 1

- aspiration by itself may cure a few thyroid cysts but relapse is common and surgery is often the final treatment of large recurring lesions
- PEI is highly effective in the treatment of thyroid cysts and of complex thyroid nodules
- the cost of PEI is quite low as the procedure is rapid and needs to be performed an average of 2 times to be effective

Indications and limitations of PEI
Conclusion 2

- PEI treatment of cystic lesions is well tolerated

- surgery is more expensive, time-consuming with risk to produce transient or permanent complications

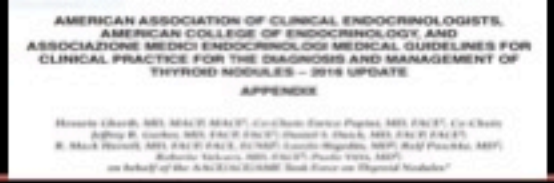

2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer

- **RECOMMENDATION 28**

  Recurrent cystic thyroid nodules with benign cytology should be considered for surgical removal or percutaneous ethanol injection (PEI) based on compressive symptoms and cosmetic concerns. Asymptomatic cystic nodules may be followed conservatively.

  (Weak recommendation, Low-quality evidence)

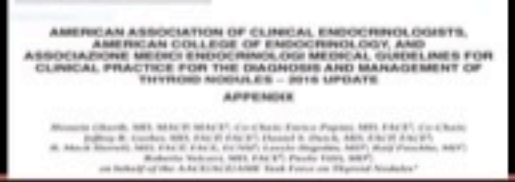

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS, AMERICAN COLLEGE OF ENDOCRINOLOGY, AND ASSOCIAZIONE MEDICI ENDOCRINOLOGI MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND MANAGEMENT OF THYROID NODULES – 2016 UPDATE

APPENDIX

ENDOCRINE PRACTICE Vol 22 (Suppl 1) May 2016 1

7.2.4. *Percutaneous ethanol injection for benign nodules*

- PEI is a safe and effective outpatient therapy for benign thyroid cysts or complex nodules with a large fluid component [BEL 1, GRADE A].


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

APPENDIX

- Carefully sample the solid component of complex lesions and confirm that they are benign before PEI [BEL 3, GRADE B].
- PEI is recommended as the first-line treatment for relapsing benign cystic lesions [BEL 1, GRADE A].

Thank you for your attention