

Mini-Invasive Treatments for Thyroid Lesion



PERCUTANEOUS ETHANOL INJECTION (PEI)

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PEI

percutaneous ethanol injection (PEI) is a non surgical procedure adopted by some medical centers as a therapeutic extension of US-FNA

Non surgical techniques for thyroid tissue ablation



Post-ablative histological changes

coagulative necrosis

 endoarteritis and vascular thrombosis

• granulation tissue, scarring and shrinkage of the area.



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



PEI treatment: immunohistochemical changes (SDH stain)



PEI Clinical Indications

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

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Treatment of Large Cold Benign Thyroid Nodules Not Eligible for Surgery with Percutaneous Ethanol Injection

MATTEO ZINGRILLO, DANIELA COLLURA, MARIA ROSARIA GHIGGI, VINCENZO NIRCHIO, AND VINCENZO TRISCHITTA



Effect of Percutaneous Ethanol Injection Therapy *Versus* Suppressive Doses of L-Thyroxine on Benign Solitary Solid Cold Thyroid Nodules: A Randomized Trial*

FINN NOE BENNEDBÆK, LARS KJÆR NIELSEN, AND LASZLO HEGEDÜS

Percutaneous ethanol injection therapy administered as a single small dose results in a satisfactory clinical response in ~50% of patients by halving the nodule volume. The thyroid nodule-reducing effect of L-T₄ suppressive therapy is insignificant, but a subjective satisfactory clinical response is seen in a subgroup of patients, probably explained by the concomitant reduction of perinodular thyroid volume. (J Clin Endocrinol Metab 83: 830–835, 1998)

PEI halves nodule volume in 50% of patients

Hot Thyroid Nodule treated by PEI









Percutaneous Ethanol Injection of Hyperfunctioning Thyroid Nodules: Long-Term Follow-Up in 125 Patients AJR:190, March 2008

Luciano Tarantino^{1,2} Giampiero Francica³ Ignazio Sordelli⁴ Pasquale Sperlongano⁴ Domenico Parmeggiani¹ Carmine Ripa¹ Umberto Parmeggiani⁴

TABLE I: Results of Percutaneous Ethanol Injection (PEI) and Follow-Up

Volume Range (mean) (mL)	Patients (Nodules)	Mean Injected Ethanol per Nodule (mL)	Mean No. Sessions per Patient	Complete Ablation (% Nodules)	Partial Cure (% Patients)	Major Complications (Time to Resolution)	Recurrences (Time at Follow-Up)
≤ 10 (2.5)	66 (67)	4.0	2.2	63/67 (94)	4/66 (6)	Two transient vocal chord paresis (24 h and 2 wk, respectively); one abscess (10 d)	
$> 10 \text{ to} \le 30 \text{ (13.8)}$	35 (35)	15.6	4.8	32/35 (91.4)	3/35 (8.6)	One transient vocal chord paresis (2 mo)	Two (18 and 48 mo) with low to normal TSH and normal FT3 and FT 4
> 30 to \le 60 (35.9)	18 (19)	36.0	7.6	17/19 (89.5)	2/18 (11)	One large hematoma (3 wk)	Two (12 and 18 mo) with low TSH and normal FT3 and FT4 in both
> 60 to maximum 90 (72.0)	3 (3)	81.0	10.3	3/3 (100)	0/3 (0)		
Overall (12.5)	122 (124)	14.0	3.9	115/124 (92.7)	9/122 (7.4)	4/480 PEI sessions (0.8%)	4/122 patients (3.3%)

Note—Three (2.4%) of 125 patients refused treatment after the first PEI session and were considered treatment failures. This table includes only the 122 patients with 124 nodules who underwent at least one complete cycle of PEI sessions. TSH = thyroid-stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine.

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

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AFTN > 5 ml

AFTN < 5 ml

Percutaneous Ethanol Injection plus Radioiodine Versus Radioiodine Alone in the Treatment of Large Toxic Thyroid Nodules

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Therapeutic options for toxic thyroid nodules (TTNs) are surgery, radioiodine (RAI), and percutaneous ethanol injection (PEI). Surgery is generally considered for TTNs larger than 4

Key Words: toxic thyroid nodules; radioiodine treatment; alcohol ablation; interventional procedures

J Nucl Med 2003; 44:207-210

NV and Thyro	TABLE 2 Did Function in the 2 Subgroups at the 1	12th Month
Characteristic	Subgroup A: 11 subjects (RAI)	Subgroup B: 11 subjects (PEI + RAI)
Nodulo volumo (ml.)	210 ± 12 2 (0.1 41 E)	
Percentage of NV reduction	57.2 ± 16.3 (30.0–82.9)	79.3 ± 14.7* (56.0–96.5)
515	2.3 ± 0.6 (1-4)	1.4 ± 0.3 (0-4)
FT ₄ (pmol/L)	12.7 ± 2.7 (8.6–18.3)	14.5 ± 1.9 (12.4–19.2)
FT ₃ (pmol/L)	$4.4 \pm 0.9 (3.0 - 5.9)$	4.2 ± 0.7 (3.1–5.7)
TSH (mU/L)	3.64 ± 5.52 (0.01–18.4)	$1.9 \pm 1.2 (0.2 - 4.2)$

*P < 0.01 vs. group A.

Modified percutaneous ethanol injection of parathyroid adenoma in primary hyperparathyroidism

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Table 1 Laboratory findings before each injection and during follow-up (case 1)

	l Step				II Step	Follow-up		
	1°	2°	3°	4°	5°		1st month	45th month
Serum calcium (mg/dl)	10.4	9.9	10.3	10.1	10.4	10.3	8.0	8.9
lonized calcium (mg/dl) Intact PTH (pg/ml)	6.2 186	5.9 145	6.1 157	6.1 163	6.3 177	6.2 162	1.0 35	4.7 49

 Table 2
 Laboratory findings before each injection and during follow-up (case 2)

	I Step							II Step	Follow-up
	1°		3°	4°	5°	6°	7°		(17th month)
Serum calcium (mg/dl) Ionized calcium (mg/dl) Intact PTH (pg/ml)	12.6 7.2 401	10.3 6.2 162	12.2 7.0 393	12.2 7.0 363	11.7 6.9 405	12.0 7.0 374	12.1 6.9 359	11.6 6.0 362	8.4 4.5 42

The Coming of Age of Ultrasound-Guided Percutaneous Ethanol Ablation of Selected Neck Nodal Metastases in Well-Differentiated Thyroid Carcinoma

Ian D. Hay and J. William Charboneau



Efficacy of Ultrasound-Guided Percutaneous Ethanol Injection Treatment in Patients with a Limited Number of Metastatic Cervical Lymph Nodes from Papillary Thyroid Carcinoma

Arne Hello, Eva Sigstad, Kristin Holgersen Fagerlid, Olav Inge Håskjold, Krystyna Kotanska Grøholt, Aasmund Berner, Trine Bjøro, and Lars H. Jørgensen



Nonsurgical, Image-Guided, Minimally Invasive Therapy for Thyroid Nodules

Hossein Gharib, MD, Laszlo Hegedus, MD, Claudio Maurizio Pacella, MD, Jung Hwan Baek, MD, and Enrico Papini, MD

PEI was the first mini-invasive procedure proposed for nonsurgical control of thyroid cancer metastases.

Possible limitations of PEI are the difficulty of inducing a predictable area of necrosis, the risk of ethanol leakage, and the need of repeated injections for a complete ablation (2, 13).

Limits of PEI. 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

Jin Hyoung Kim¹ Ho Kyu Lee¹ Jung Hyun Lee¹ II Min Ahn² Choong Gon Choi¹

Efficacy of Sonographically Guided Percutaneous Ethanol Injection for Treatment of Thyroid Cysts Versus Solid Thyroid Nodules

AJR:180, June 2003

- 20 simple or complex thyroid cysts
- 22 solid cold nodules
- 6-month follow-up



RESULTS. The mean volume reduction rate for cysts (65%) was greater than that for solid nodules (38.3%) ($p \le 0.01$, Student's *t* test). The volume of the instilled ethanol correlated significantly with the volume reduction rate of cysts but not with that of solid nodules ($p \le 0.01$, Student's *t* test). **CONCLUSION.** Sonographically guided percutaneous ethanol injection is more effective for thyroid cysts than for solid thyroid nodules.



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

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













Are Cystic Nodules always benign?

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. Sznyter, 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. Sznyter, MD, New Hyde Park, NY

MEDIANA MALIGNITA': 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. Sznyter, 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 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

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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 Copyright © 2001 by The Endocrine Society 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

Am J Med. 1980 Jun;68(6):853-5. Links The role of thyroid therapy in patients with thyroid cysts. <u>McCowen KD, Reed JW, Fariss BL</u>.

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 the recurrence of benign thyroid cysts after initial aspiration.

Resolution of Recurrent Thyroid Cysts With Tetracycline Instillation LTC Gary L. et all

Nine patients with recurrent purely cystic thyroid nodules after one or two previous cyst aspirations were treated with repeat cyst aspiration and instillation of intracystic tetracycline hydrochloride. All but two of the patients' cysts resolved completely and have not recurred after a follow-up period of 12 to 50 months (mean=40). The remaining patients had a partial response that left them with clinically insignificant lesions. The procedure was well tolerated and obviated the need for further therapy in all patients. **Cyst aspiration and tetracycline instillation is a safe and effective treatment of recurrent purely cystic thyroid nodules that eliminates the need for surgical excision.**

Arch Intern Med. 1983;143(12):2285-2287

Sclerotherapy with OK-432 for Recurrent Cystic Thyroid Nodule

Hang-Seok Chang, Jong Ho Yoon, Woung Youn Chung, and Cheong Soo Park

We have adopted OK-432 as a sclerosing agent in the treatment of cystic predominant thyroid nodules and have analyzed our findings to assess the efficacy of intralesional instillation of OK-432. From 1992 through 1993, 48 patients with recurrent or progressive cystic thyroid nodules after 2 or 3 aspirations alone, and whom were cytologically negative for malignancy, were used for this study. The OK-432 solution was prepared by dissolving 0.1 mg of OK-432 in 2 ml of physiologic saline and it was instilled in the amount of 1/10-to-1/5 of the aspirated cystic fluid. A repeated course of therapy was given up to 3 times when sufficient resolution was not obtained 4-to-6 weeks after treatment. The mean number of treatment sessions per patient was 1.5. Throughout the follow-up period from 30-to-45 months (mean, 38 months), 32 (66.7%)

> Yonsei Medical Journal Vol. 39, No. 4, pp. 367~371, 1998





PEIT: materials



PEI Procedure

- a disposable 22-G needle is inserted (without anesthesia) into the lesion.
- fluid is nearly completely removed.
- aspirating syringe is substituted with a syringe containing ethanol .

Procedure (2)

- 95% sterile ethanol (volume: 35 50% of the aspirated fluid) is slowly injected.
- needle is withdrawn during the injection of 0.5 ml of xylocaine.
- a neck dressing is applied without pressure on the lesion.



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	40	33.7±25.3	3.0±2.4*	0.6±0.6*
Verde 1994	32	14.5 Range 1.5-65.8	2.5* Range 0.4-34.5	_

*P<0.001 vs. baseline

Efficacy of PEI treatment Thyroid Cysts

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

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Some Clinical Problems

Which result with Mixed Thyroid Nodules?

Complex nodules: volume changes after PEIT



Results of Percutaneous Ethanol Injection (PEI) in cystic thyroid nodules % vol.reduction: empty body vs mixed cysts



Valcavi R & Frasoldati A., Endocrine Practice, 2004

What to do with Cystic Nodules with Viscous Colloid?

- <u>Stage 1:</u> in case of ineffective aspiration, inject 1 ml di ethanol for each 10 ml of nodule volume
- <u>Stage 2:</u> 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

Nonsurgical, Image-Guided, Minimally Invasive Therapy for Thyroid Nodules

Hossein Gharib, MD, Laszlo Hegedus, MD, Claudio Maurizio Pacella, MD, Jung Hwan Baek, MD, and Enrico Papini, MD

While many do not report side-effects at all, there is agreement on most patients having mild to severe transient pain, lasting for minutes, and many have low grade fever. Serious side-effects are rare, but recurrent nerve palsy with transient dysphonia, Graves' disease, Graves' orbitopathy, Horner's syndrome, facial dysesthesia with increased tear flow, necrosis of the larynx and skin, as well as impairment of post-PEIT surgery, due to local fibrosis, have been reported (5). These, and other side-effects, are most likely linked to seepage of alcohol along the needle tract, and not only due to insufficient training.

J Clin Endoorin Metab. First published ahead of print August 18, 2013

Tolerability Experience of the procedure

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- thyroid cysts

 no patient defined the treatment as very
 painful and a new session would be accepted
 without any problem
- AFTN

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

Risk- and cost-benefit ratio of PEIT

Advantages:

- Effective volume reduction
- No cosmetic damage
- Mild or absent pain
- No hypothyroidism
- Negligible cost
- No heavy technology
- No general anesthesia
- Outpatient clinics (15 minutes).

Disadvantages:

- Nodule persistence
- Operator with experience in US-guided FNA
- Complications: rare and transitory (learning period)
- Repeated treatments in large or multilocular cysts.

AACE/AME/ETA Guidelines



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

7.6.2.4. US-Guided PEI

- PEI is effective in the treatment of benign thyroid cysts and complex nodules with a large fluid component (Grade B; BEL 1)
- PEI should not be performed in solitary solid nodules, whether hyperfunctioning or not, or in MNGs (Grade C; BEL 3)

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

> The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

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RECOMMENDATION 15

Recurrent cystic thyroid nodules with benign cytology should be considered for surgical removal or PEI based on compressive symptoms and cosmetic concerns. Recommendation rating: B

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Thank you for your attention

