

# Alternative Therapieansätze: Alkoholinstillation in die Schilddrüse

Alexander Becherer

LKH Feldkirch, Abteilung für Nuklearmedizin



# Perkutane Ethanol-Injektion

## PEI



← Previous Article

June 1990  
Volume 175, Issue 3

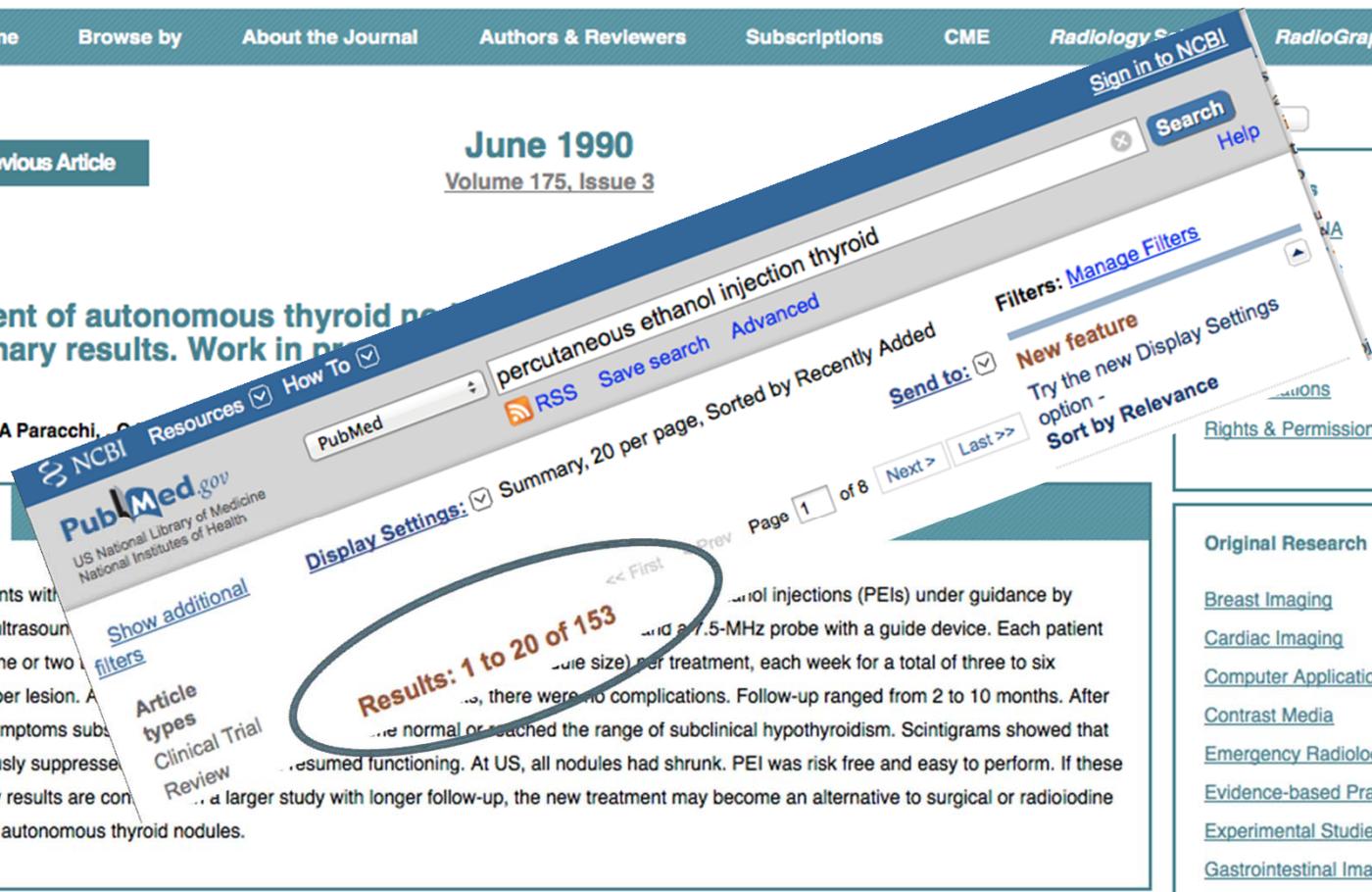
## Treatment of autonomous thyroid nodules with percutaneous ethanol injection thyroid ablation: preliminary results. Work in progress

T Livraghi, A Paracchi, et al.

### Abstract

Eight patients with autonomous thyroid nodules were treated with percutaneous ethanol injections (PEIs) under guidance by means of ultrasound. Each patient received one or two PEIs (1-2 mL ethanol per lesion). After therapy, symptoms subsided, and the previously suppressed thyroid function resumed functioning. At US, all nodules had shrunk. PEI was risk free and easy to perform. If these preliminary results are confirmed in a larger study with longer follow-up, the new treatment may become an alternative to surgical or radioiodine ablation of autonomous thyroid nodules.

Results: 1 to 20 of 153



# Wirkung (lokal)

- Thrombose kleiner Gefäße
- Koagulationsnekrosen
- Knotenverkleinerung
- Wachstumsstopp
- Normalisierung der SD-Funktion
- Verhinderung des Zystenrezidivs

# Heiße Knoten

Clinical Endocrinology (1997) 46 9–15

## **Five-year follow-up of percutaneous ethanol injection for the treatment of hyperfunctioning thyroid nodules: a study of 117 patients**

**Fabio Monzani, Nadia Caraccio, Orlando Goletti\*,  
Piero V. Lippolis\*, Arturo Casolaro, Paolo Del Guerra,  
Enrico Cavina\* and Paolo Miccoli\***  
*Institute of Internal Medicine 2 and \*Department of  
Surgery, University of Pisa, Italy*

# Patienten

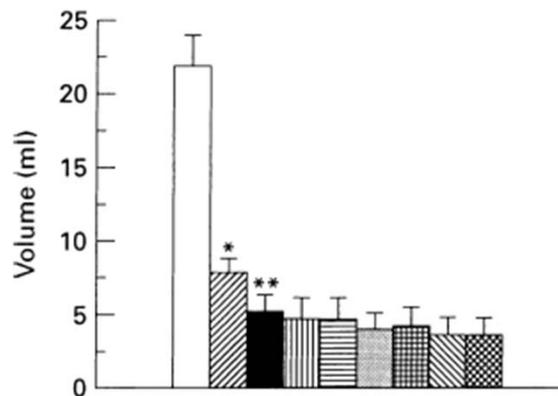
- 117 Pt., Rekrutierung 1990-1995
- Knoten > 3 cm mit hohem Op-Risiko, Pat. < 40a, die die Op ablehnten (RJT damals nicht < 40a!)
- Rezidivknoten nach Op
- Ablehnung anderer Therapieformen
- 40 Pt. subklin. Hyperthyreose (=prätox. Adenom), 77 Pt. manifeste H. (=tox. Adenom)
- Mittleres f/u 2,5a, bis zu 5a

*Monzani, et al. Clin Endocrinol (Oxf) 1997*

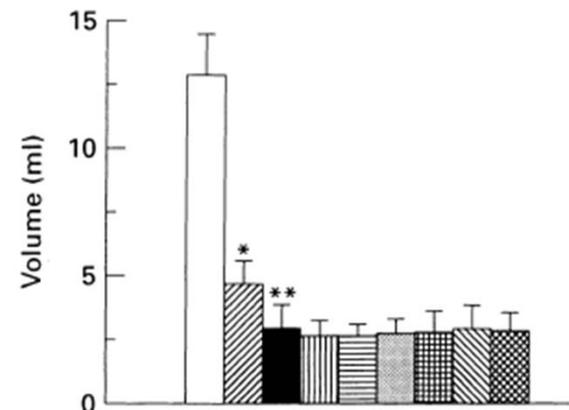
# Nebenwirkungen

- Lokales Brennen 30'-60', evtl. retroaurikuläre Ausstrahlung (30%)
- Temp. bis 38% 12-24h (10% tox. A, 3% prätox. A.)
- Transiente Rekurrensparese (1-4w, 3 Pt., 1990/1991)

*Monzani, et al. Clin Endocrinol (Oxf) 1997*



**Fig. 1** Nodule volumes (ml) of toxic thyroid adenoma before percutaneous ethanol injection treatment and at follow-up. Data are expressed as mean  $\pm$  standard error of the mean.  $\square$ , Pretreatment;  $\text{▨}$ , end of treatment;  $\blacksquare$ , 3 months;  $\text{▤}$ , 6 months;  $\text{▥}$ , 1 year;  $\text{▦}$ , 2 years;  $\text{▧}$ , 3 years;  $\text{▨}$ , 4 years;  $\text{▩}$ , 5 years. \* $P = 0.0001$  vs pretreatment; \*\* $P = 0.0003$  vs treatment.



**Fig. 2** Nodule volumes (ml) of pretoxic thyroid adenoma before percutaneous ethanol injection treatment and at follow-up. Data are expressed as mean  $\pm$  standard error of the mean. Key as Fig. 1. \* $P = 0.0001$  vs pretreatment; \*\* $P < 0.001$  vs pretreatment.

Monzani, et al. Clin Endocrinol (Oxf) 1997

**Table 4** Patients with toxic adenoma with complete and partial cure or failure to PEI treatment divided on the base of pretreatment nodule volume range

Pretreatment volume range (ml)	Complete cure (n = 60)	Partial cure (n = 7)	Failure (n=10)
≤10	14	1	0
>10 ≤ 20	29	3	3
<20 ≤ 30	8	1	4
>30 ≤ 40	5	1	0
>40	4	1	3

Monzani, et al. Clin Endocrinol (Oxf) 1997

*Clinical Radiology* (2001) **56**: 895–901

doi:10.1053/crad.2001.0787, available online at <http://www.idealibrary.com> on **IDEAL**<sup>®</sup>



## **Percutaneous Ethanol Injection of Autonomous Thyroid Nodules With a Volume Larger than 40 ml: Three Years of Follow-up**

SALVATORE DEL PRETE\*, DOMENICO RUSSO\*, MICHELE CARAGLIA†,  
GAIA GIUBERTI†, MONICA MARRA†, GIOVANNI VITALE‡, GIOVANNI LUPOLI‡,  
ALBERTO ABBRUZZESE†, ELENA CAPASSO\*

*\*Unità Operativa di Oncologia, Ospedale 'S. Giovanni di Dio', Frattamaggiore, Italy, †Dipartimento di Biochimica e  
Biofisica 'F. Cedrangolo', Seconda Università di Napoli, Napoli, Italy and ‡Dipartimento di Endocrinologia ed Oncologia  
Molecolare e Clinica, Università degli Studi di Napoli 'Federico II', Napoli, Italy*

# Patienten

- 34 Pt., autonome Adenome >40 mL (41-180), manifeste Hyperthyreose, thyreostat. Vorbehandlung
- 1-11 Ethanolinjektionen mit 3-14 mL/Sitzung (kumulativ bis 125 mL)
- Beurteilung der Wiederherstellung der  $^{99m}\text{Tc}$ -Speicherung 3m nach Behandlungsende
- Beurteilung des Knotenvolumens bis 3a nach Behandlungsende

*Del Prete, et al. Clin Radiol 2001*

# Resultate

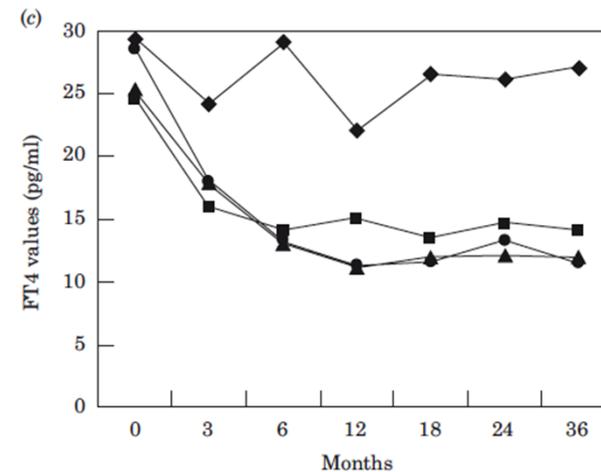
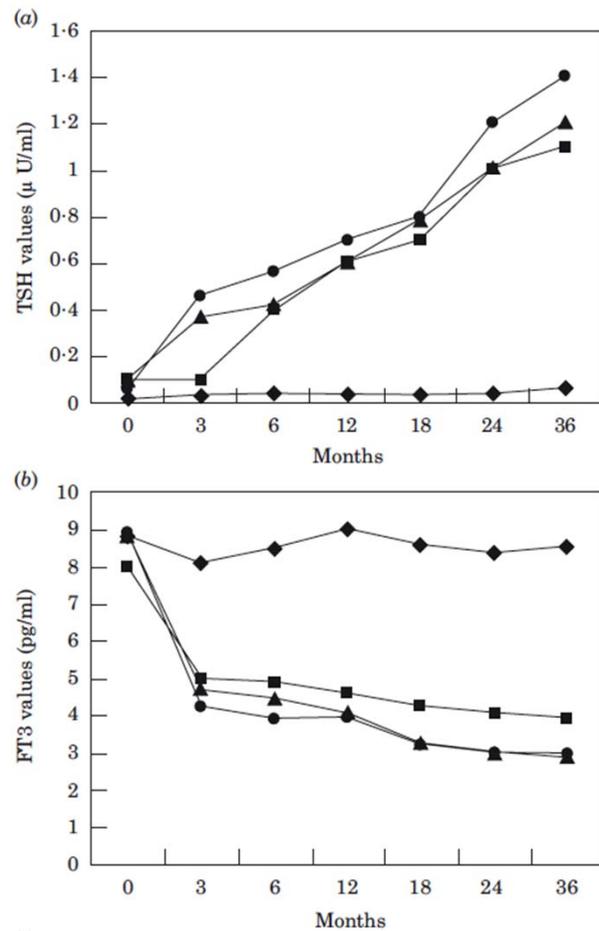


Fig. 1 – (a) TSH, (b) FT3 and (c) FT4 serum levels. The serum values of thyroid hormones were determined before treatment and at 3-, 6-, 12-, 18-, 24- and 36-month intervals from the beginning of PEI sessions. The points are the means of the values for each group of patients divided according to their responsiveness to PEI. TC (●); PC (▲); HR (■); F (◆). TC = total cure; PC = partial cure; HR = hormonal remission; F = failure.

Therapieerfolg bei 30/34 Pt.

*Del Prete, et al. Clin Radiol 2001*

# Resultate

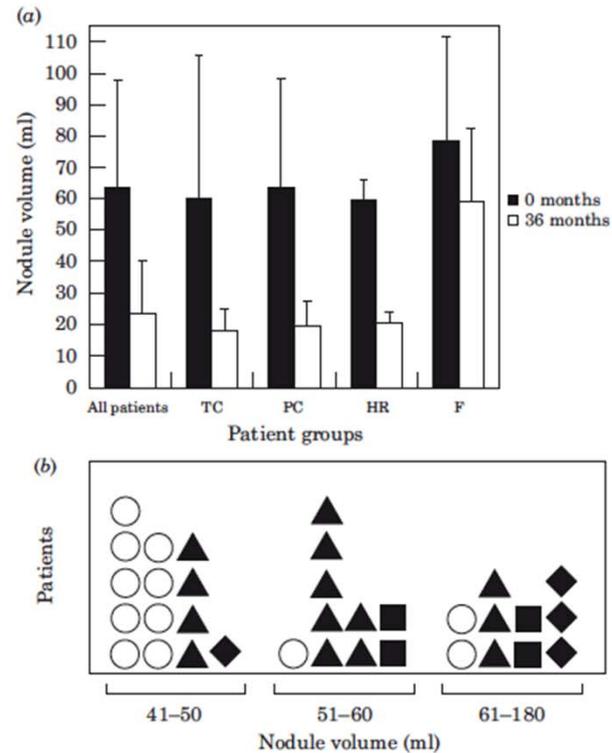


Fig. 2 – Nodule volume shrinkage after PEI at a 36-month follow-up period. (a) The patients were evaluated for their mean nodule volume with US before (■) and after 36 months from (□) the beginning of PEI. The patients are divided on the basis of their responsiveness to therapy. Bars: averages  $\pm$  SDs. (b) The clinical results achieved in PEI-treated patients are represented in relation to the initial nodule volume. TC (●); PC (▲); HR (■); F (◆).

*Del Prete, et al. Clin Radiol 2001*

**Table 1 – Patient characteristics\***

Clinical outcome	No. of patients	Age (years)	Sex	Initial volume	Final volume	% reduction	Volume of alcohol injected	No. of sessions
TC	12	57 ± 11	F 10 M 2	60 ± 40.5	17.8 ± 7.1	70.3	54.3 ± 28.8	4.8 ± 2.1
PC	14	57 ± 14	F 10 M 4	63.4 ± 35.5	19.3 ± 8.1	69.7	74.4 ± 38.2	6.9 ± 3.2
HR	4	49 ± 20	F 3 M 1	59.7 ± 6.9	18.7 ± 3.2	66.1	91.2 ± 14.9	6.2 ± 2.2
F	4	52 ± 9.3	F 4 M 0	78.7 ± 34.2	59.73 ± 24.3	24.1	37.7 ± 9.6	7.2 ± 0.9

\*The values are expressed as mean ± SD.

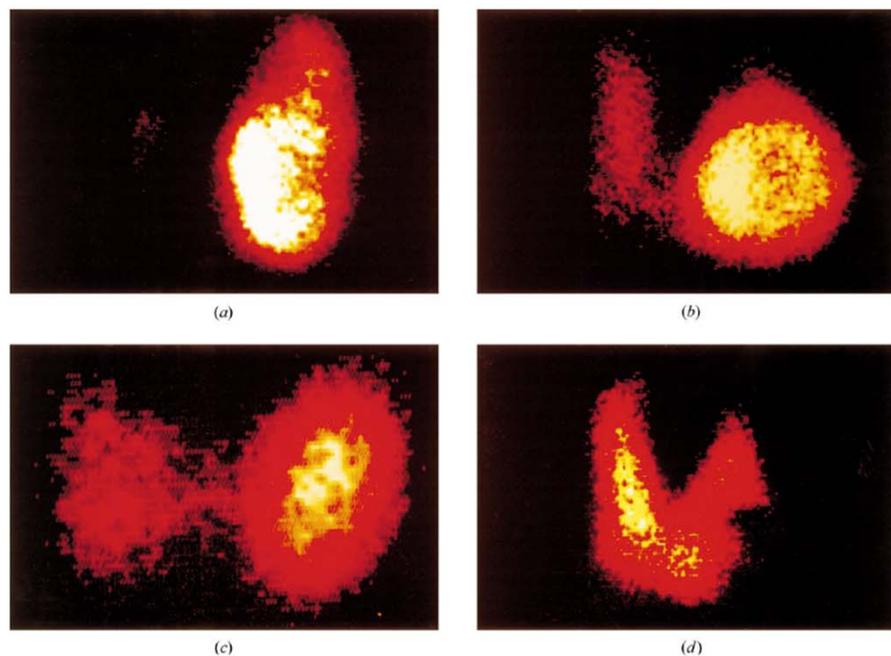


Fig. 4 – Anterior images of the thyroid of patient 10 obtained at scintigraphy performed with <sup>99m</sup>Tc pertechnetate. (a) Image shows exclusive uptake in the nodule and complete inhibition in the normal thyroid parenchyma. (b) After five sessions of PEI (45 ml ethanol) the image shows the central part is still hyperfunctioning. (c) After a further three sessions (30 ml ethanol) uptake in the contralateral lobe is reappearing and (d) after three sessions (31 ml ethanol) complete necrosis of the nodule (cold area) and re-uptake within the normal thyroid tissue.

*Del Prete, et al. Clin Radiol 2001*

# Kalte Knoten

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Printed in U.S.A.

## **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

*Department of Endocrinology, Odense University Hospital, DK-5000 Odense C, Denmark*

# Patienten

- 50 Pt. einschließbar, symptomat. Knoten, randomisiert 1:1
- Gruppe 1: 1,5 µg L-T4/kg KG, Ziel-TSH 0,10-0,40
- Gruppe 2: Einzelinjektion Ethanol. abs. (20-50% des initialen Knotenvol.)
- f/u über 12m

*Bennedbaek, et al. JCEM 1998*

**TABLE 3.** Questionnaire

Self-estimated ratings	PEIT <sup>a</sup>		L-Thyroxine	
	Initially	12-month evaluation	Initially	12-month evaluation
<b>Pressure symptoms</b>				
Severe	3	1	2	1
Moderate	9	2	11	7
Mild	10	8	9	9
None	3	14	3	8
<b>Cosmetic symptoms</b>				
Severe	1	1	1	1
Moderate	5	2	7	3
Mild	7	4	5	4
None	12	19	13	17

Values shown are the number of patients.  
<sup>a</sup> Final evaluation at 6 months in two patients.

**TABLE 4.** Association between subjective and objective findings

Variable	Subjective scores at the final evaluation <sup>a</sup>					
	PEIT <sup>b</sup>			L-T <sub>4</sub>		
	Complete relief	Partial relief	No relief	Complete relief	Partial relief	No relief <sup>c</sup>
No. of patients in each group.	14	5	6	8	5	12
Initial nodule vol (mL)	8.1 [5.6;10.9]	6.9 [3.6;18.4]	12.6 [11.3;13.7]	8.6 [4.5;15.5]	4.5 [1.8;19.0]	7.0 [3.3;12]
Median change in nodule vol (%)	51 [42;64]	53 [36;69]	10 [-40;59]	33 [12;40]	7 [-31;36]	-4 [-45;13]
Ethanol dose/nodule vol (%)	24 [20;31]	20 [14;30]	15 [8;23]			

Values are medians, with 95% confidence intervals in *brackets*, or numbers of cases.

<sup>a</sup> Relief of pressure symptoms or cosmetic complaints.

<sup>b</sup> Two patients evaluated at 6 months.

<sup>c</sup> Worsening in one patient.

*Bennedbaek, et al. JCEM 1998*

THYROID  
Volume 7, Number 5, 1997  
Mary Ann Liebert, Inc.

## Is Percutaneous Ethanol Injection a Useful Alternative for the Treatment of the Cold Benign Thyroid Nodule? Five Years' Experience

NADIA CARACCIO,<sup>1</sup> ORLANDO GOLETTI,<sup>2</sup> PIERO VINCENZO LIPPOLIS,<sup>2</sup> ARTURO CASOLARO,<sup>1</sup>  
ENRICO CAVINA,<sup>2</sup> PAOLO MICCOLI,<sup>2</sup> and FABIO MONZANI<sup>1</sup>

- 54 Pt., 27 Pt. PEI, 27 Pt. L-T4 (suppressiv)
- Knotenvol. Ø 21 mL (5-55)
- Äthanol 4-13 wöchentliche Injektionen, Ø 7,4 (1,3±0,6 mL/mL Knotenvolumen)
- Knotenvol. nach Therapieende
  - PEI: Ø 7,7±5,5 mL; (4,4±3,8 nach 1a)
  - L-T4: alleine keine sig. Reduktion

*Caraccio, et al. Thyroid 1997*

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

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

Division of Endocrinology, Diabetes, Metabolism, and Nutrition (H.G.), Mayo Clinic College of Medicine, Rochester, Minnesota 55905; Department of Endocrinology and Metabolism (L.H.), Odense University Hospital, 5000 Odense, Denmark; Department of Radiology (J.H.B.), University of Ulsan College of Medicine, Seoul 138–736, Korea; Regina Apostolorum Hospital (C.M.P.), 00041 Rome, Italy; and Endocrinology Department (E.P.), Regina Apostolorum Hospital, Albano Laziale, 00041 Rome, Italy

doi: 10.1210/jc.2013-1806

J Clin Endocrinol Metab, October 2013, 98(10):3949–3957

[jcem.endojournals.org](http://jcem.endojournals.org)

# Nebenwirkungen der PEI von soliden Knoten

– schwere NW sind selten

- Schmerzen
- Rekurrensparesen
- Horner Syndrom
- Dysästhesien im Gesichtsbereich
- Hautnekrosen
- Larynxnekrose
- Erschwerung einer späteren SD-Chirurgie

*Gharib, et al. JCEM 2013*

## Ethanolinjektion 2013 (2014)

...The use in benign solid thyroid tumors is on the wane due to availability of alternatives with a better ratio between efficacy and side effects (6). The same is true for the use in benign parathyroid tumors (5, 6). Most expert centers, those introducing it in the first place, have abandoned this technique during the last decade for solid thyroid as well as parathyroid tumors. The exception is benign cysts and predominantly cystic thyroid nodules, where it has become the recommended standard therapy (7)...

*Gharib, et al. JCEM 2013*

# SD-Zysten

- Meist benigne
- Rezidivrate bis 80%
- Tetrazyklin nicht besser als NaCl (*Hegedüs, et al. Arch Intern Med 1988*)
- Reine Zysten: konservatives Vorgehen, keine FNA  
(*Revised ATA Guidelines. Thyroid 2009: Recommendation Rating: C = expert opinion*)

*Gharib, et al. JCEM 2013*

THYROID  
Volume 6, Number 5, 1996  
Mary Ann Liebert, Inc.

## Percutaneous Ethanol Injection of Large Thyroid Cystic Nodules

MATTEO ZINGRILLO,<sup>1</sup> MASSIMO TORLONTANO,<sup>1</sup> MARIA ROSARIA GHIGGI,<sup>1</sup>  
LEONARDO D'ALOISO,<sup>1</sup> VINCENZO NIRCHIO,<sup>2</sup> MICHELE BISCEGLIA,<sup>2</sup> and  
ANTONIO LIUZZI<sup>1</sup>

- 20 Pt., symptomat. Zysten > 10 mL, 14 Rezidive nach 2 kompletten Evakuierungen  
6 visköse Zysten, nicht evakuierbar
- 1-4 PEI-Sitzungen, bei viskösen Knoten 1. PEI zur Verflüssigung
- 6m:
  - 7/20 Pt. <10% Rest
  - 2/20 Pt. 10-50% Rest
  - 1/20 Pt. idem nach 3 PEI
- Knotenvol. Basis  $39 \pm 24$  mL vs.  $10,9 \pm 13,3$  ( $p < 0,001$ ) nach 6m
- Restknoten überwiegend solide, Kalzifikationen

*Zingrillo, et al. Thyroid 1997*

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Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 88(12):5773–5777  
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## **Treatment of Recurrent Thyroid Cysts with Ethanol: A Randomized Double-Blind Controlled Trial**

FINN NOE BENNEDBÆK AND LASZLO HEGEDÜS

*Department of Endocrinology, Odense University Hospital, DK-5000 Odense C, Denmark*

**TABLE 4.** PEI in cystic thyroid nodules: listing of published studies

Author	Yr of publication	No. of patients treated	Follow-up (months)	Study design	No. of treatments	Success rate <sup>a</sup> (%)
Rozman (17)	1989	13	8	Open	1	77
Yasuda (18)	1992	61	6	Open	1-4	72
Monzani (19)	1994	20	12	Open	1-2	95
Verde (20)	1994	10	1	Randomized	1	80
		10 <sup>b</sup>	1		1	30
Antonelli (21)	1994	32	12	Open	1	80
		26	12	Open	1-5	77
		44 <sup>c</sup>	12		1	36
Zingrillo (22)	1996	20	6	Open	1-4	95
Zingrillo (23)	1999	43	24	Open	1-4	93
Cho (24)	2000	22	1-10	Open	1-6	64
Del Prete (25)	2002	98	115	Open	1-4	94

<sup>a</sup> Near disappearance or marked (>50%) size reduction of cystic lesion.

<sup>b</sup> Treated with simple aspiration.

<sup>c</sup> Control group treated with saline.

*Bennedbaek, et al. JCEM 2003*

**TABLE 2.** Treatment characteristics and response

	PEI	NaCl	P
Treatment-volume (ml)	3.5 [2;5]	3.0 [2;5]	0.7
% Treatment-volume	36 [25;48]	36 [27;50]	0.4
No. of treatments	1 [1;2]	3 [2;5]	0.0002
Cure after			
1 treatment	21	6	
2 treatments	4	7	0.006
3 treatments	2	3	
Failure	6	17	
% Cyst volume-reduction	100 [83;100]	68 [21;94]	0.001

Values are medians (with quartiles) or number of cases.

**TABLE 3.** Effect of variables on treatment response

Variable	Multivariate effects on treatment success				Univariate OR
	OR	P	CI		
Ethanol vs. saline	27.752	0.005	2.699	285.357	4.781
Previous aspirations	0.058	0.005	0.008	0.419	0.380
Gender	2.495	0.524	0.157	37.740	0.373
Age	1.026	0.561	0.940	1.121	0.969
Months from diagnosis	1.039	0.179	0.983	1.098	0.987
Cystic vs. complex	0.855	0.873	0.125	5.867	0.648
Additional nodules	7.820	0.127	0.559	109.432	0.344
Cyst volume	0.830	0.005	0.728	0.945	0.886
Thyroid volume	0.921	0.052	0.847	1.001	0.951

OR, Odds ratio; CI, confidence interval.

*Bennedbaek, et al. JCEM 2003*

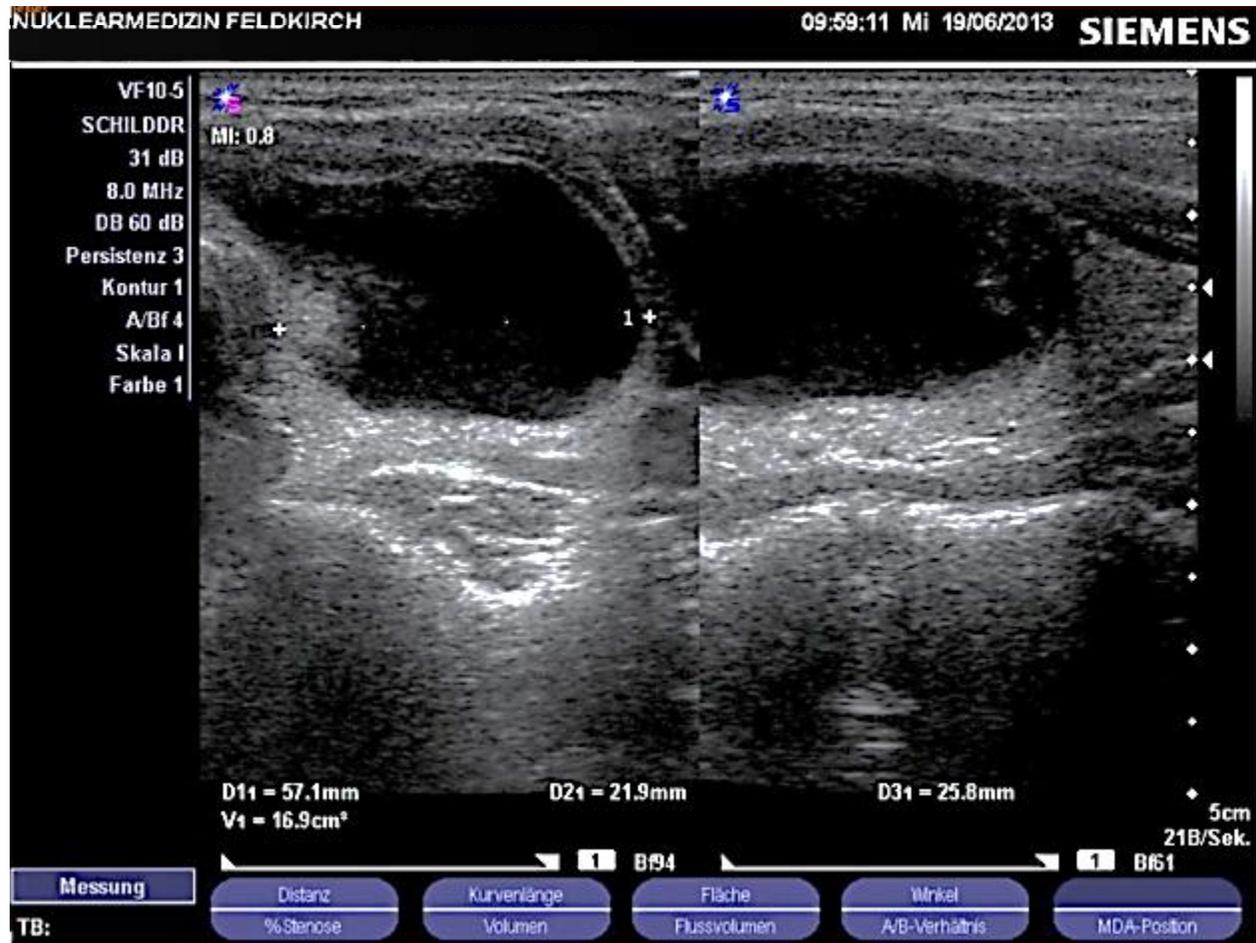
# Technik

- Ultraschallgezielte Zystenpunktion
  - Schallkopf quer gehalten (Überblick)
- Spritze 10 mL
  - 20 mL-Spritze bereithalten für visköse Zysten)
- Nadel: 20G (0,8 mm x 40 mm) grünes Ansatzstück
  - Abschrägung zum Schallkopf gedreht
- Subtotale Evakuierung der Zyste
  - Nadelspitze soll noch im Zysteninhalt erkennbar sein

# Technik

- Ohne Nadelwechsel Injektion von Ethanol 95%, Vol.= $\frac{1}{2}$  -  $\frac{2}{3}$  des evakuierten Zystenvol. (US-Kontrolle)
- 3 Min. warten (ohne Spritzen- und Nadelwechsel)
- Möglichst komplette Evakuierung des Zysteninhalts

# Zyste vor Ethanol



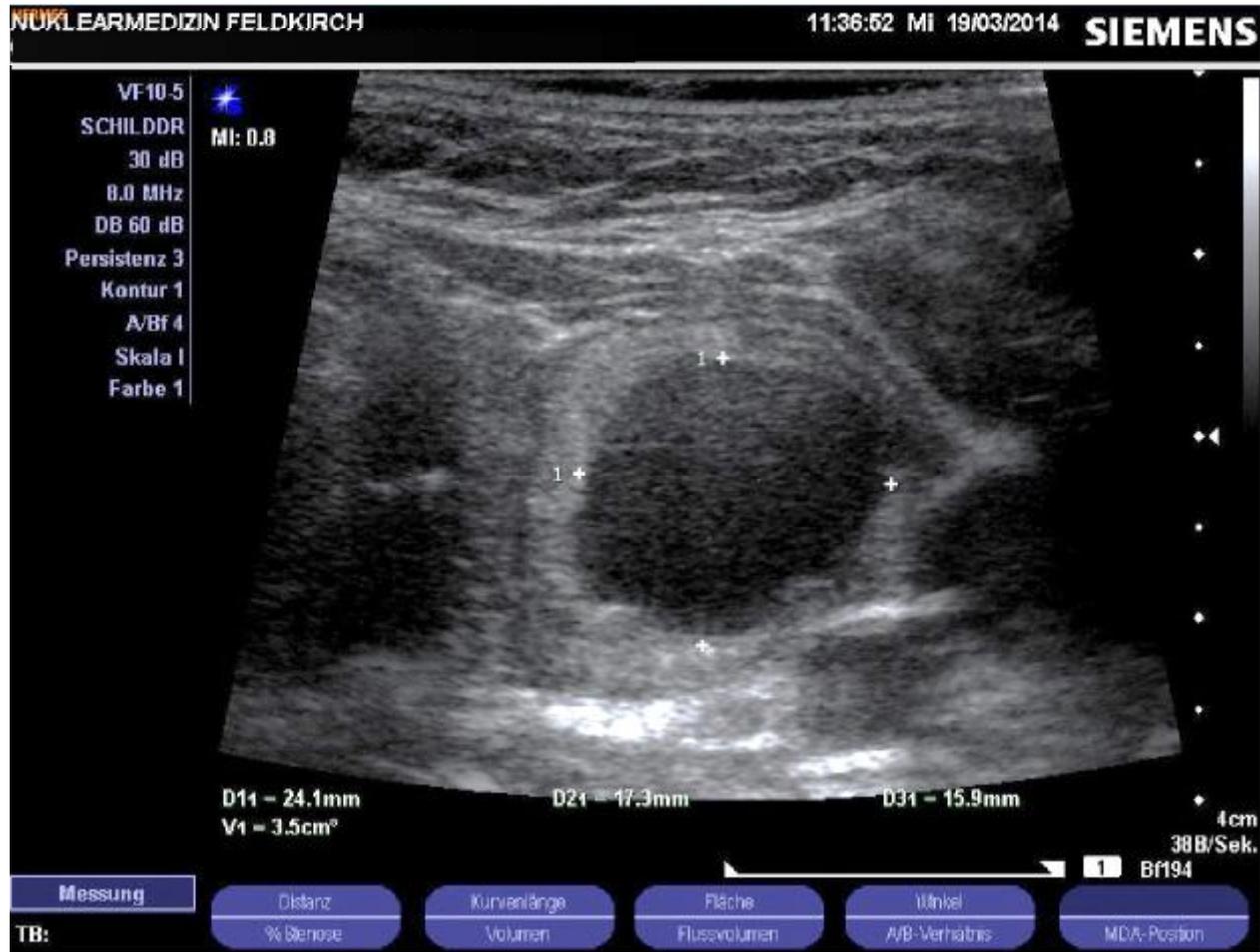
# Zyste mit Ethanol



# Zyste post Ethanol



# Zyste vor Ethanol



# Zyste mit Nadel



# Zyste mit Nadel und Ethanol



# Zyste nach Ethanol

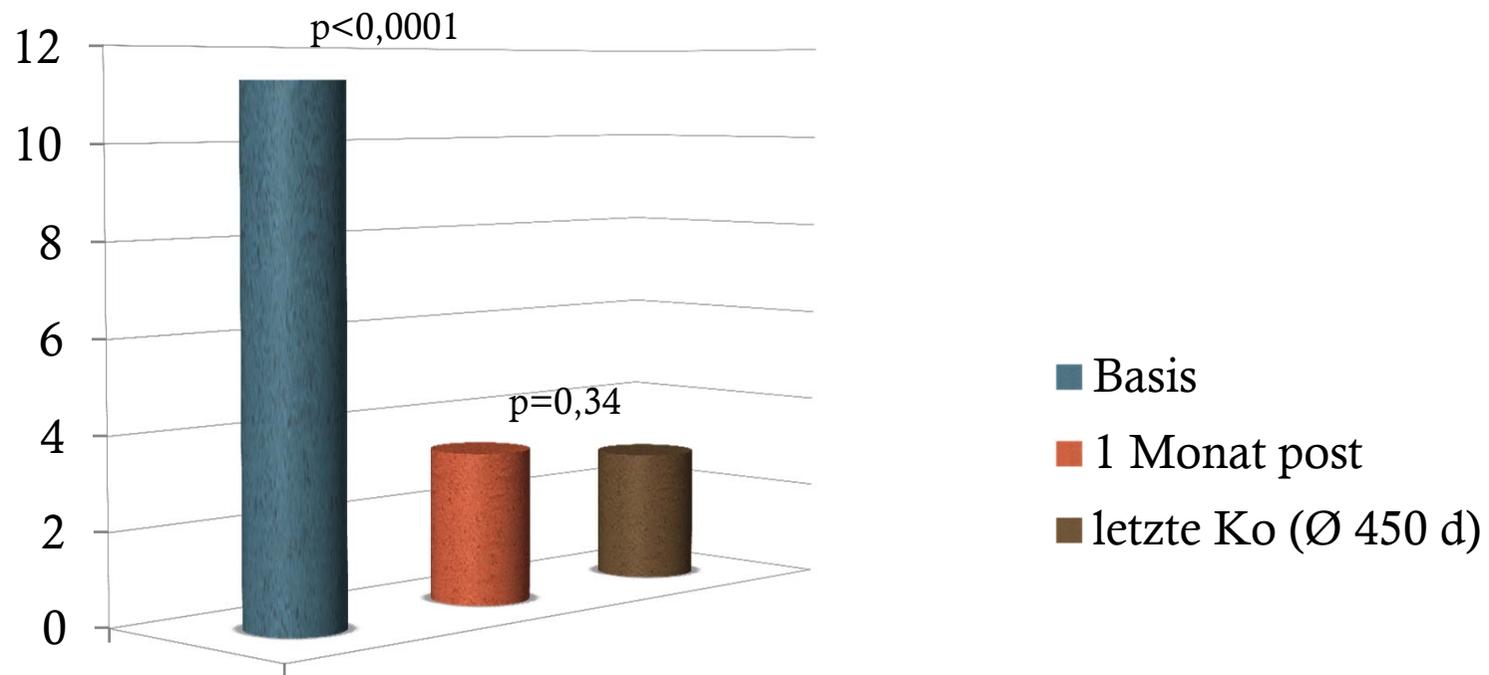




# Eigene Daten

- 43 Punktionen, 42 Zysten, 41 Pt., w/m=31/10
- Zystenlok.: 7\*Isth., 19\*li., 17\*re.
- Vorpunkt. (Pt.-bez.) 21\*0, 11\*1, 7\*2, 1\*3, 1\*4
- Vol. vor Ethanol  $\bar{\varnothing} 11,3 \pm 15,9$  mL (0,7-100)
- Vol. nach Ethanol  $\bar{\varnothing} 3,3 \pm 11,4$  mL (0-70)  
= Red. um 2/3
- NW: 2/43 Pkt. starke Schmerzen, 1 Pt. bis 2 Tage danach, sonst vzt. leichtes lokales Brennen für Min.

# Volumina (mL)



# Schlussfolgerung

Four controlled studies demonstrated a 75–85% success rate after PEI compared with a 7–38% success rate in controls treated by simple cyst evacuation or saline injection. Success was achieved after an average of two PEI treatments. Complications included mild to moderate local pain, flushing, dizziness, and dysphonia (90–93)

- **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

*Revised ATA Guidelines. Thyroid 2009*