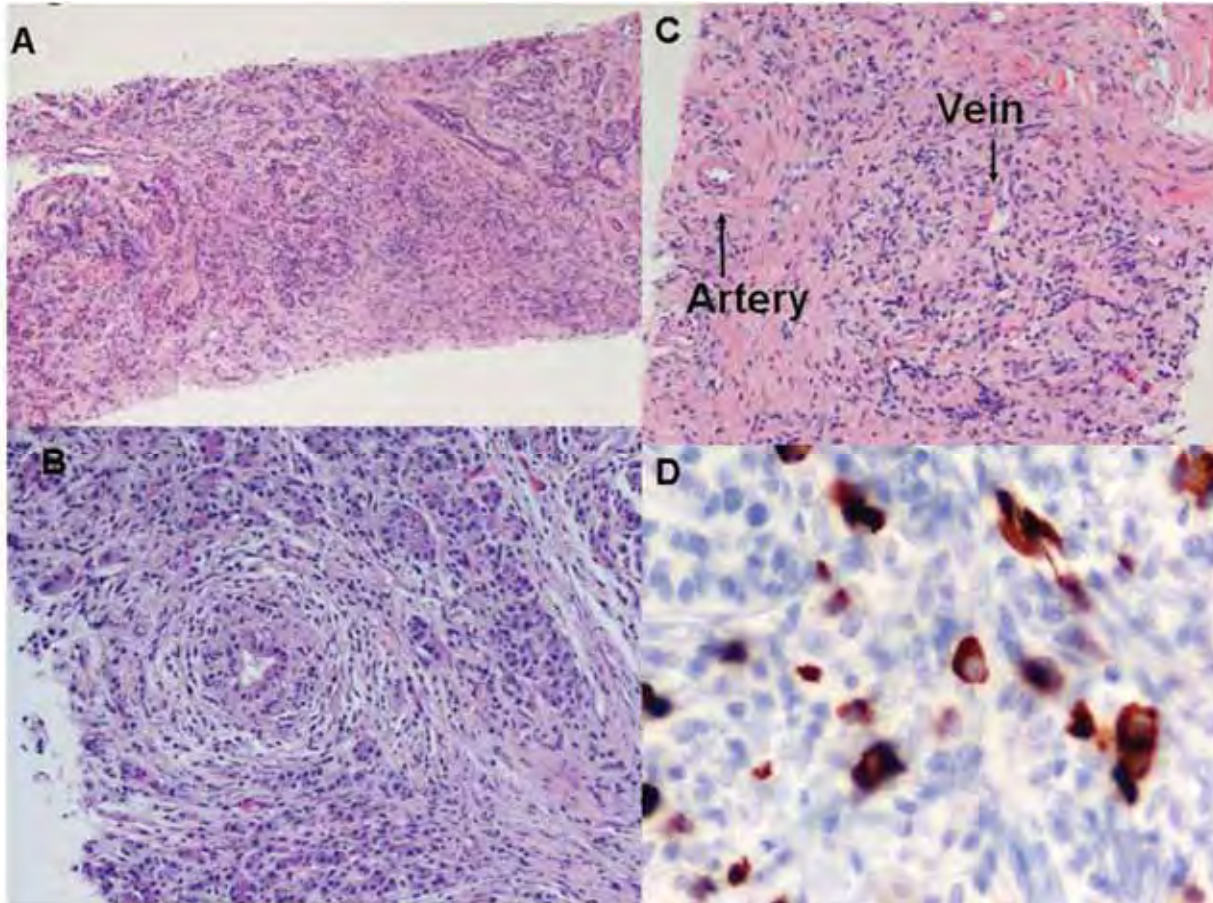


IgG4硬化性疾患と 橋本自己免疫性甲状腺炎

和歌山県立医科大学 人体病理学 覚道 健一

Autoimmune pancreatitis



Histopathological features:

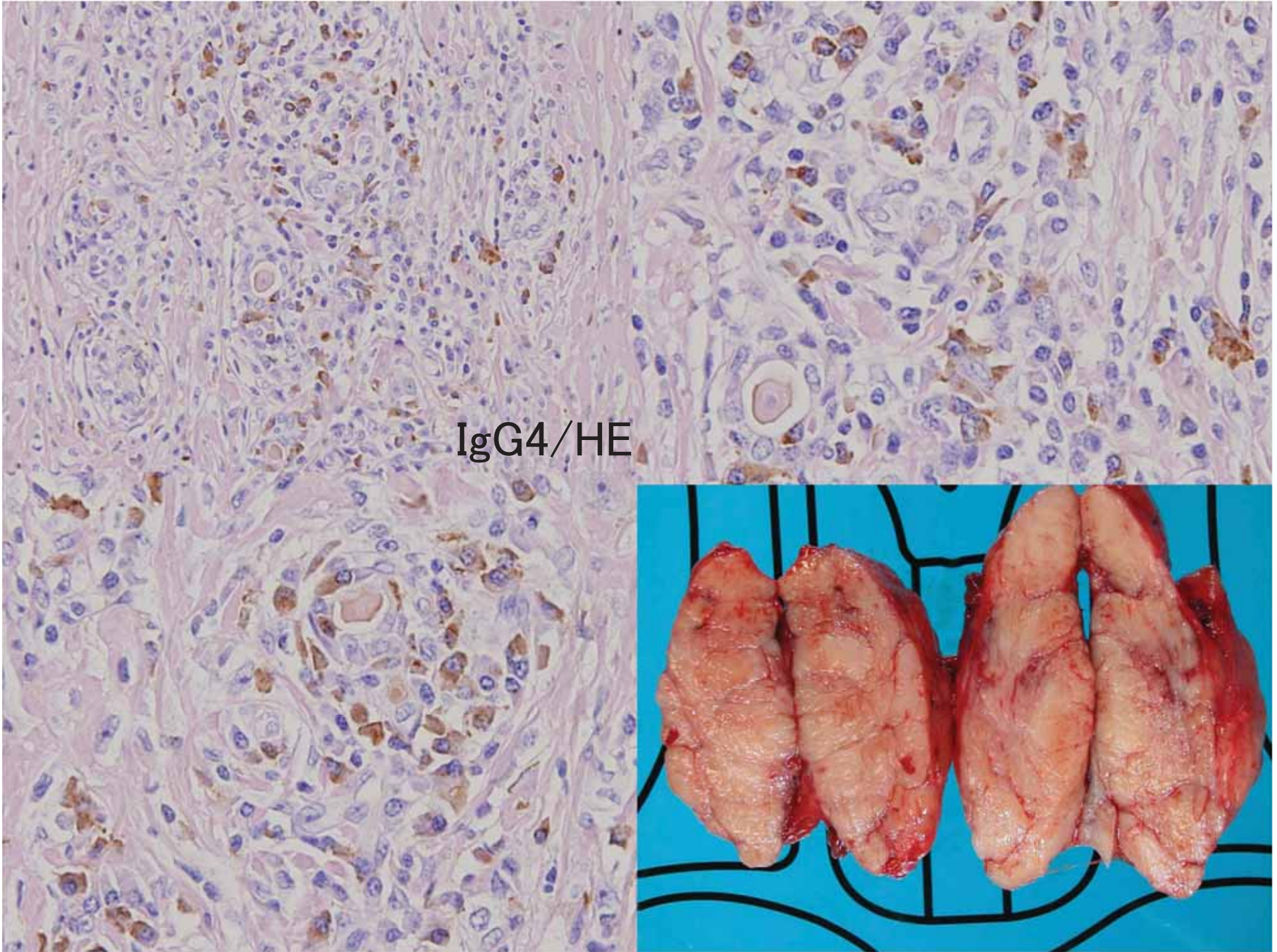
- Diffuse lymphoplasmacytic infiltration
- Stromal fibrosis
- Acinar atrophy
- Obliterative phlebitis

1. Hamano et al reported that serum IgG4 levels were specifically elevated in patients with autoimmune pancreatitis (AIP). (N Engl J Med, 2001,344: 732-738)
2. Hamano et al found abundant infiltration of IgG4-positive plasma cells in pancreatic lesion of patients with AIP. (Lancet, 2002, 359:1403-1404)
3. Park DH et al: Recent advances in autoimmune pancreatitis. GUT, 2009, 12: 1680-1689

IgG4 positive plasma cells and thyroiditis

- ◆ 類似の炎症性、腫瘤形成性甲状腺疾患には橋本甲状腺炎とRiedel甲状腺炎が推定される。
- ◆ The IgG4-positive plasma cell rich group was termed as: *IgG4 thyroiditis*; IgG4-positive plasma cell poor group was termed as: *non-IgG4 thyroiditis* (Cut-off value: $>20/\text{HPF}$ IgG4-positive plasma cells and $>30\%$ IgG4/IgG ratio).

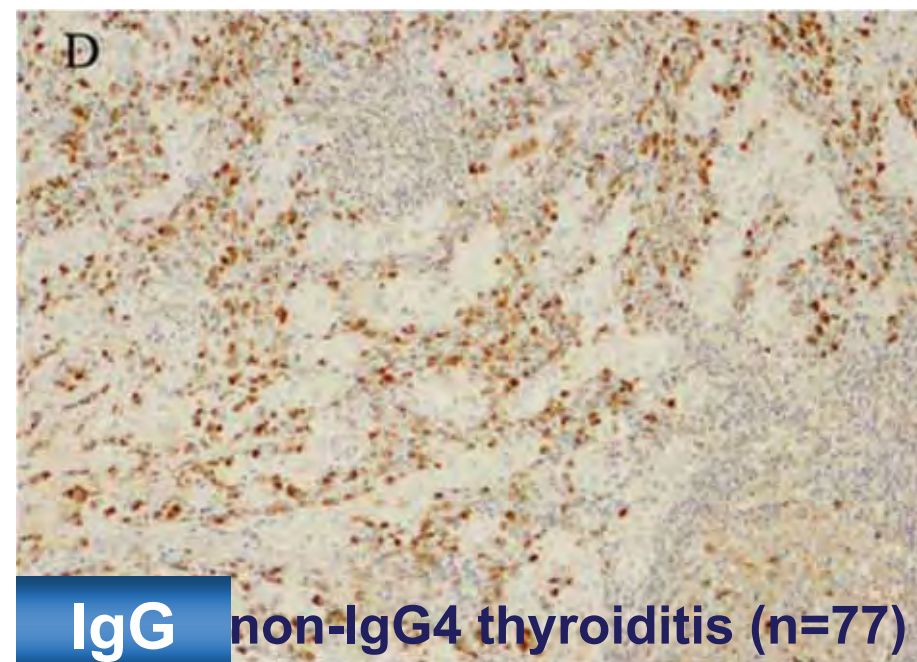
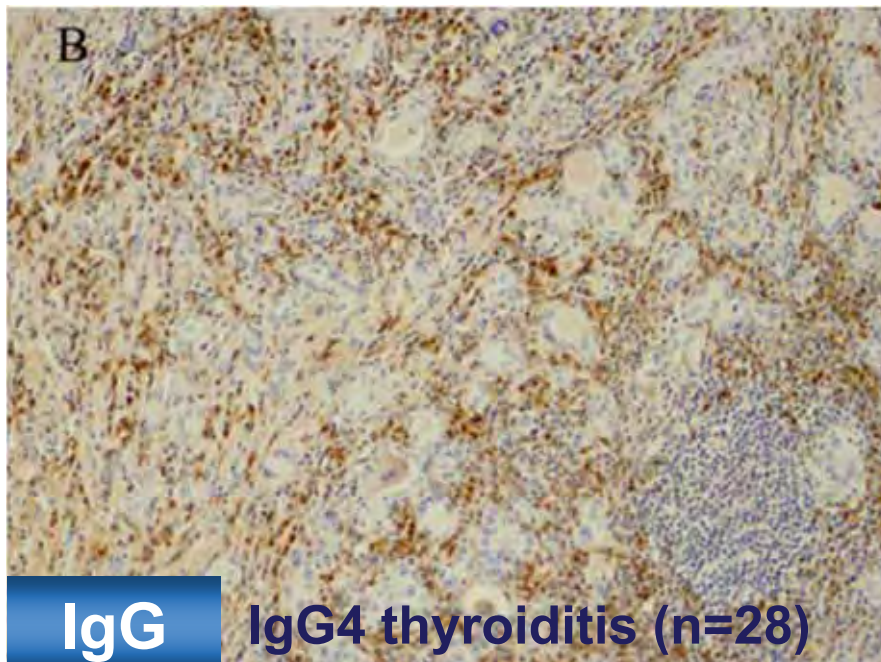
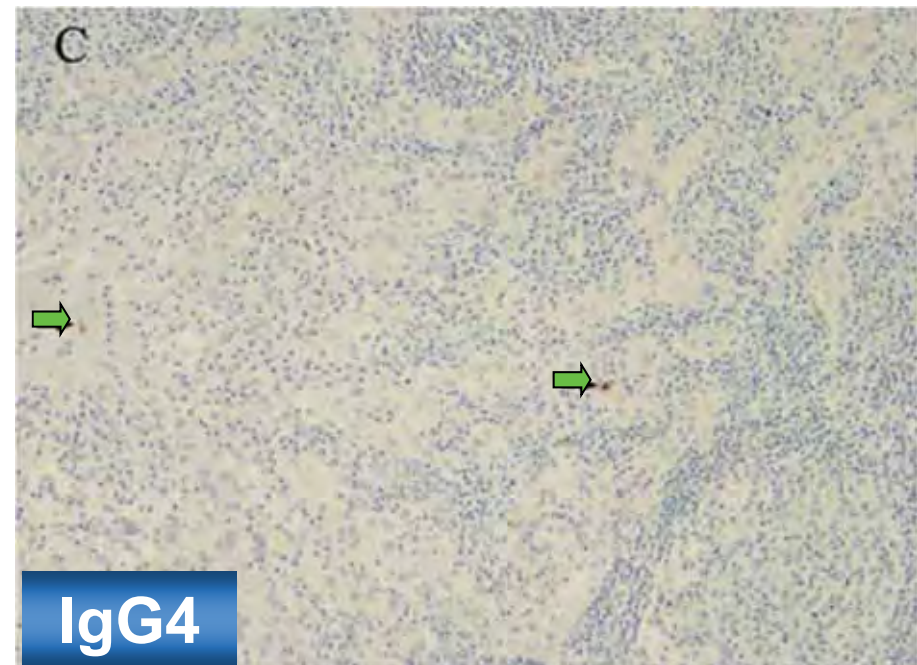
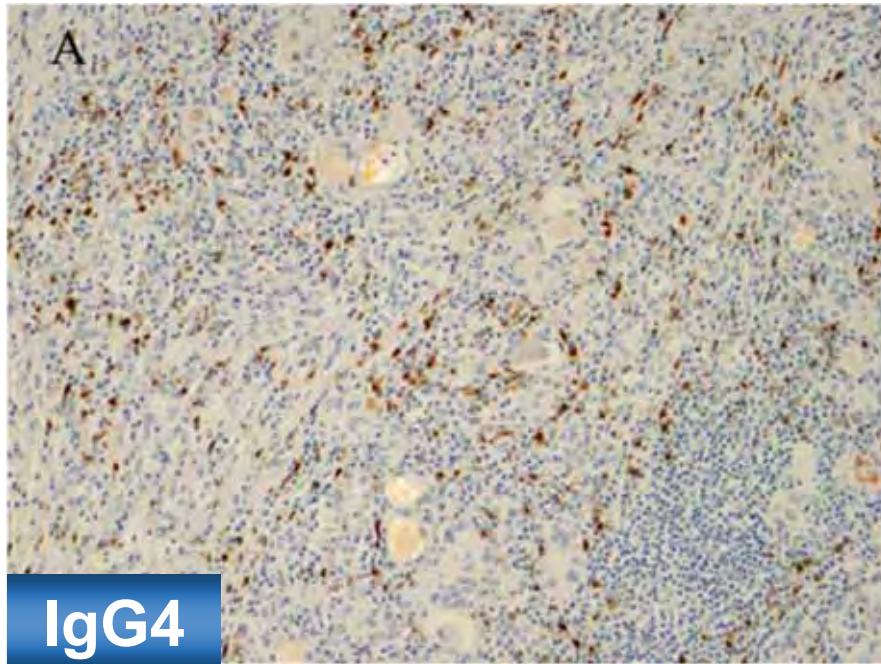
Yaqiong Li et al. Immunohistochemistry of IgG4 can help subclassify Hashimoto's autoimmune thyroiditis. *Pathology International* 2009; 59: 636-641



症例と方法

1. 隈病院で切除術を受けた105例の甲状腺橋本病（自己免疫性甲状腺炎）病理組織標本を用い、線維化の程度、濾胞細胞の変性の程度を検討した。
2. 免疫組織化学的にtotal IgG, IgG4陽性細胞の分布、高倍率5視野での絶対数、IgG4/ total IgG比率について検討した。
3. 血清保存のある22例については術前、術後のIgG4値を測定した。

>20/HPF IgG4-positive plasma cells and >30% IgG4/IgG ratio



IgG4-positive plasma cell infiltrate: A marker of more fibrotic disease in HT

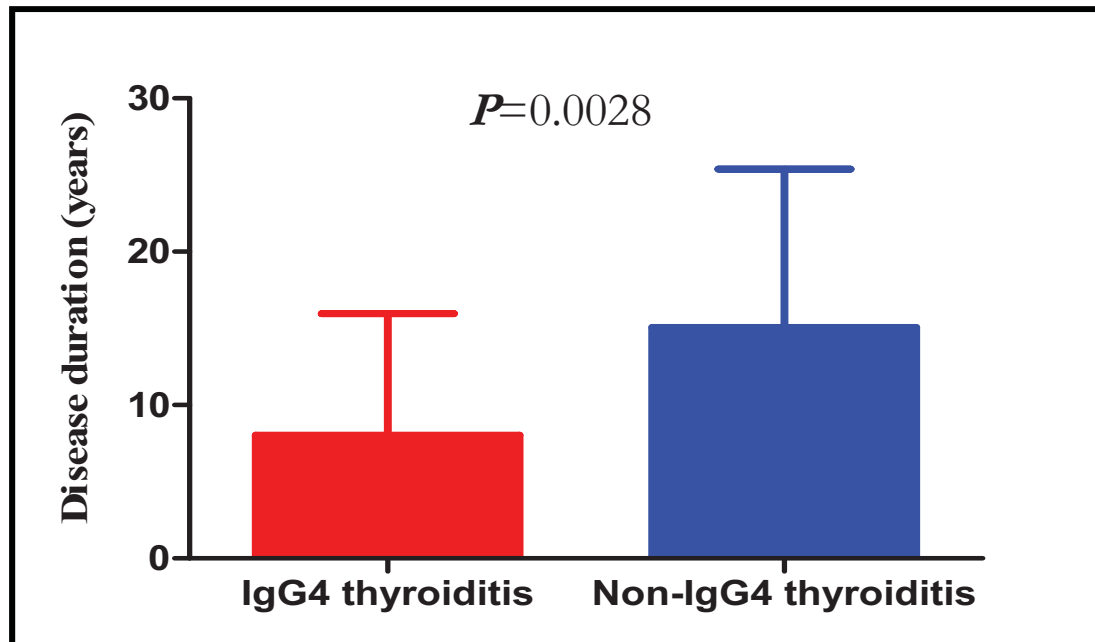
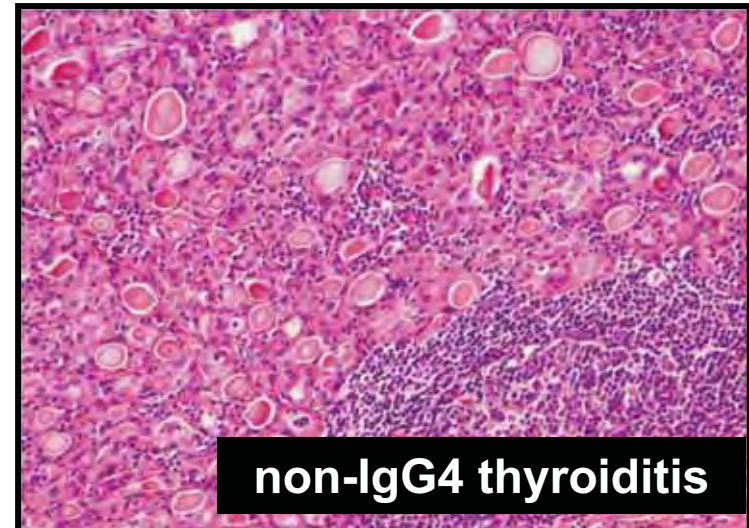
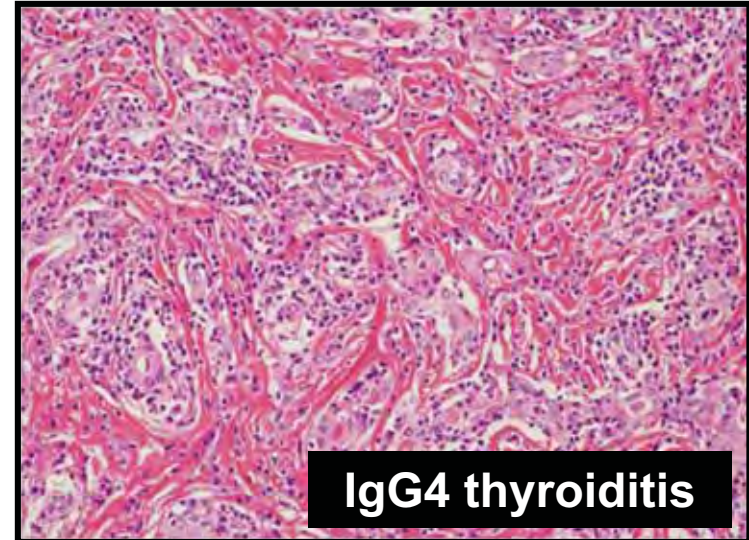
Hashimoto's autoimmune thyroiditis (HT)

	IgG4 thyroiditis (n=28)	non-IgG4 thyroiditis (n=77)	P value
Number of IgG4+ plasma cells per HPF	53.89 ± 30.51	7.497 ± 6.687	-
Number of IgG+ plasma cells per HPF	101.9 ± 28.78	68.64 ± 31.12	-
IgG4/IgG plasma cells (%)	52.26 ± 17.97	11.21 ± 9.752	-
Stromal fibrosis (3+, 2+, 1+, 0)	17/7/4/0	10/19/34/14	< 0.0001
Lymphoplasmacytic infiltration (3+, 2+, 1+, 0)	24/4/0/0	24/21/32/0	< 0.0001
Follicular cell degeneration (3+, 2+, 1+, 0)	21/5/2/0	13/21/34/9	< 0.0001
Lymphoid follicle formation (3+, 2+, 1+, 0)	3/12/13/0	15/17/45/0	0.6025

Comparison of clinical, serological and sonographic features ②

Disease duration

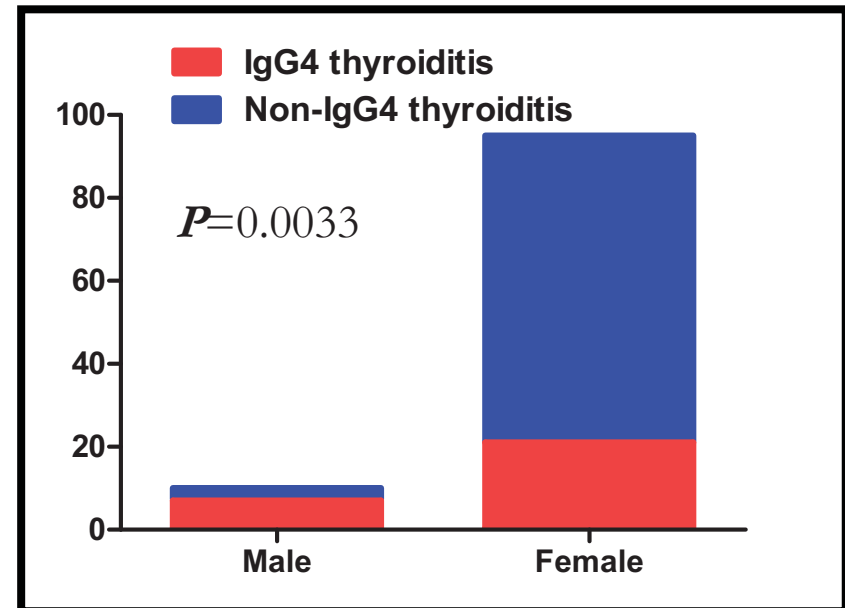
Disease duration (years)	Hashimoto's thyroiditis	
	IgG4 thyroiditis	non-IgG4 thyroiditis
	8.042 ± 7.915	15.07 ± 10.31



Comparison of clinical, serological and sonographic features ①

Gender

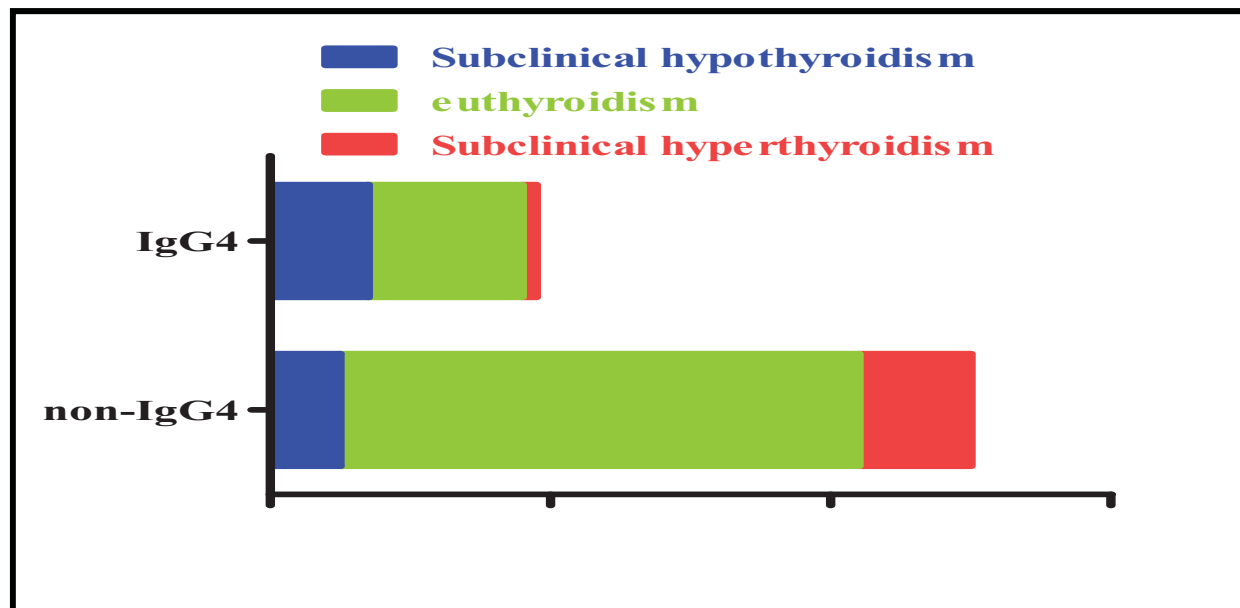
Gender	Hashimoto's thyroiditis	
	IgG4 thyroiditis	non-IgG4 thyroiditis
Male	7	3
Female	21	74



Comparison of clinical, serological and sonographic features ③

Thyroid functional status*

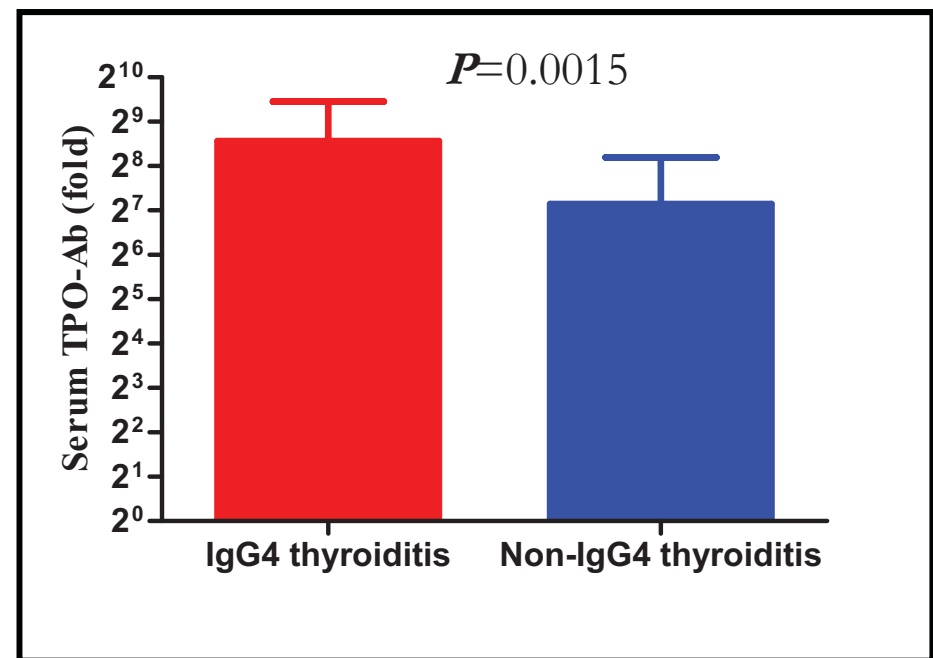
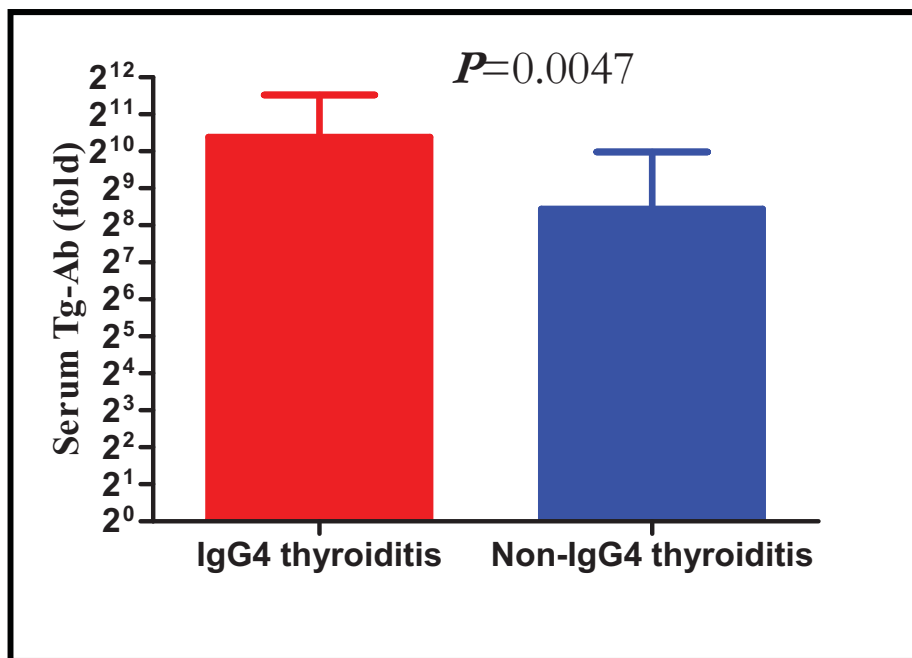
Hashimoto's thyroiditis		
	IgG4 thyroiditis	non-IgG4 thyroiditis
Weight of thyroid gland (g)*	202.5 (110.8; 232.0)	188.0 (115.4; 225.5)
L-T4 (ug/day)*	75 (50; 100)	50 (0; 100)
Thyroid functional status*	6/11/1	5/36/8



Comparison of clinical, serological and sonographic features ④

Thyroid autoantibodies

Thyroid autoantibodies	Hashimoto's thyroiditis	
	IgG4 thyroiditis	non-IgG4 thyroiditis
Tg-Ab (fold)	1341 ± 1610	348.0 ± 663.2
TPO-Ab (fold)	377.1 ± 326.4	141.8 ± 152.1



IgG4 thyroiditis and non-IgG4 thyroiditis:

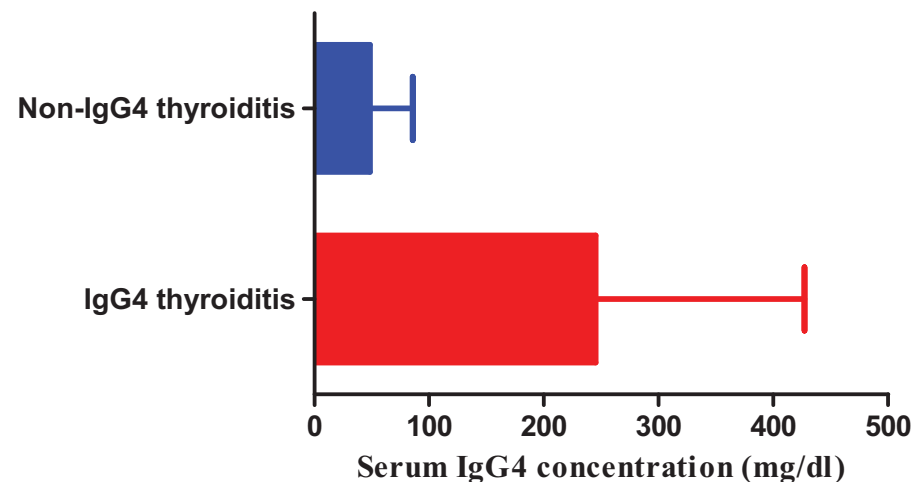
Distinct clinical, serological and sonographic characteristics

Hashimoto's autoimmune thyroiditis (HT)			
	IgG4 thyroiditis (n=28)	non-IgG4 thyroiditis (n=77)	P value
Age (yr)	53.24 ± 10.61	59.11 ± 10.02	0.0775
Gender (Male/Female)	7/21	3/74	0.0033
Disease duration (yr)	8.042 ± 7.915	15.07 ± 10.31	0.0028
Thyroid functional status* (Subclinical hypo-/Eu- /Subclinical hyper)	6/11/1*	5/36/8*	0.0243
ESR (mm/hr)	25.72 ± 23.50	21.43 ± 20.84	0.8939
Tg-Ab (fold)	1341 ± 1610	348.0 ± 663.2	0.0047
TPO-Ab (fold)	377.1 ± 326.4	141.8 ± 152.1	0.0015
Echogenicity (ultrasound) (diffuse low/coarse)	19/9	19/52	0.0002

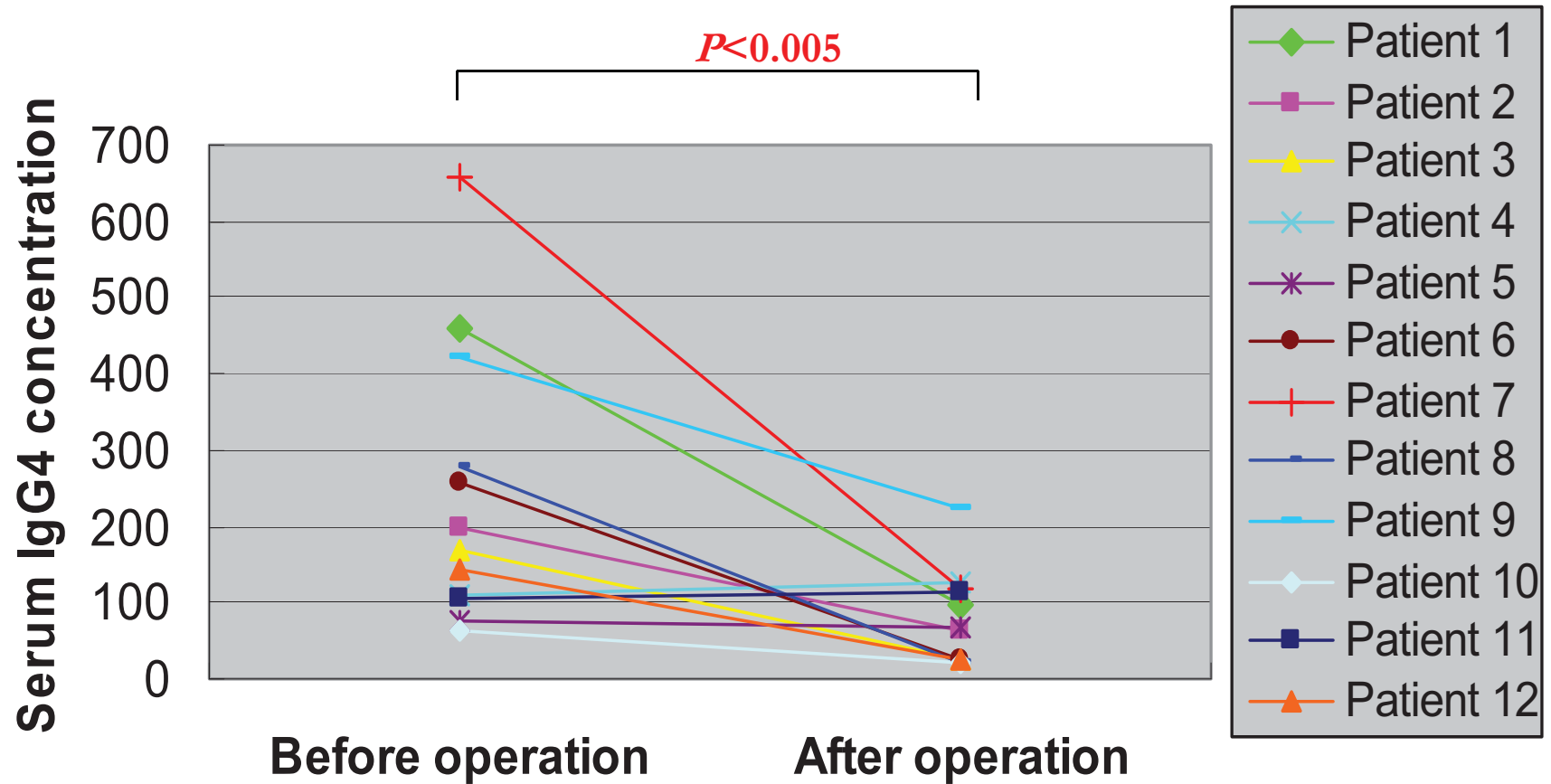
Serum concentrations of IgG subclasses in IgG4 thyroiditis (12 cases) and non-IgG4 thyroiditis (10 cases)

	IgG4 thyroiditis (n=12)	non-IgG4 thyroiditis (n=10)	<i>P</i> value
Serum IgG subclasses			
IgG1 (mg/dl)	1487 ± 528.2	1111 ± 545.5	0.0602
IgG2 (mg/dl)	1083 ± 471.1	720.2 ± 357.6	0.0697
IgG3(mg/dl)	74.03 ± 33.05	98.97 ± 86.16	0.8689
IgG4 (mg/dl)	245 ± 182.1	48.49 ± 37.31	<i>P</i><0.001

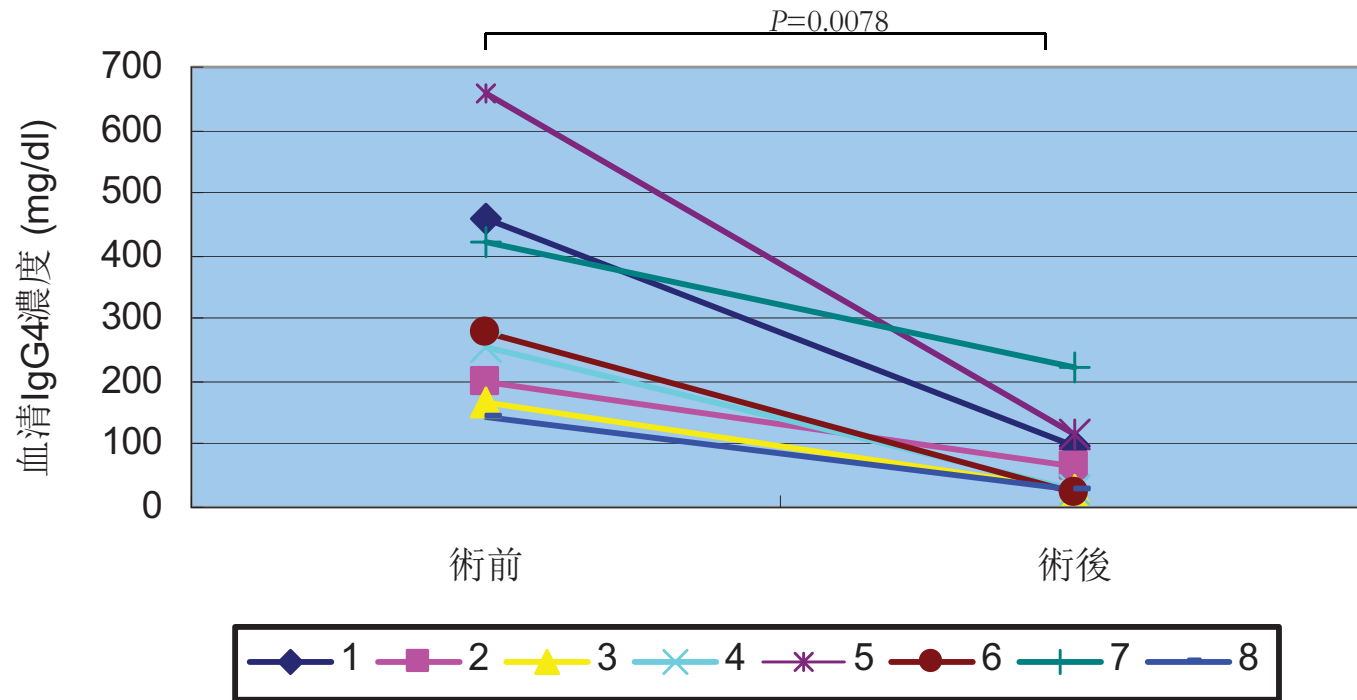
*Reference value of serum IgG4 concentration: **4.8-105 mg/dl**



Comparison of serum IgG4 concentration before operation and after operation



術前、術後血清のIgG4変動



Riedel甲状腺炎について

◆ Dahlgren M, Khosroshahi A, Nielsen GP, Deshpande V, Stone JH: Riedel's thyroiditis and multifocal fibrosclerosis are part of the IgG4-related systemic disease spectrum. Arthritis Care Res (Hoboken)62:1312-1318, 2010. の3例での報告がある。

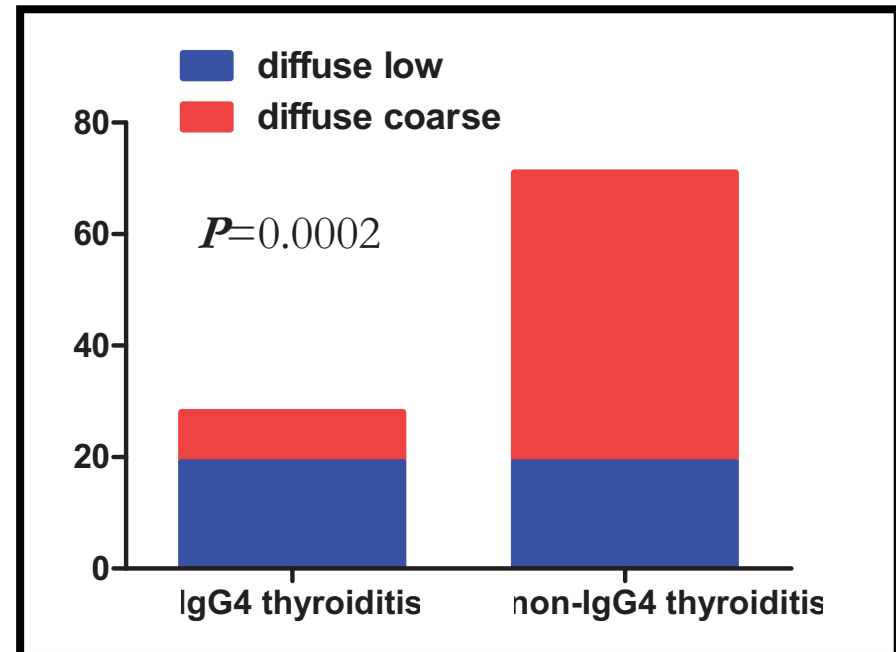
我々の経験(1例)では、IgG4陽性細胞は多くないが、上記論文を否定するものではない。

◆ Dahlgrenの1例では全身のIgG4硬化性疾患を合併する例があることから、IgG4甲状腺炎は全身型(systemic)の1部として甲状腺に現れた場合、Riedel甲状腺炎として、また臓器特異的に発症した時には橋本病(線維化型)として、みられるのではないかと解釈している。

Comparison of clinical, serological and sonographic features ⑤

Difference in Echogenicity

Echo - genicity	Hashimoto's thyroiditis	
	IgG4 thyroiditis	non-IgG4 thyroiditis
Diffuse low	19	19
Diffuse coarse	9	52

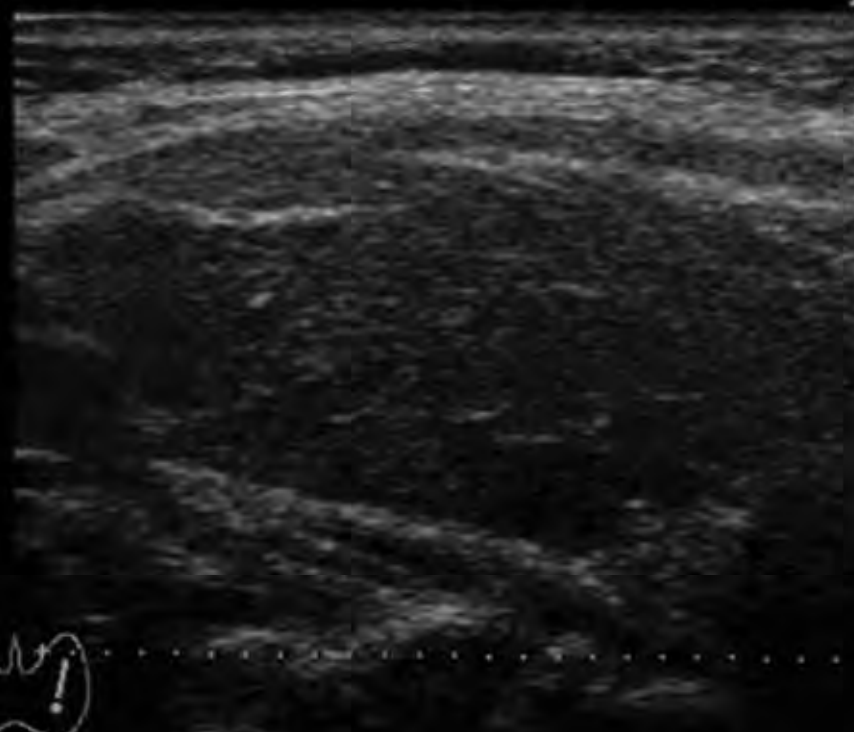


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