RESEARCH

Thyroid ^{18}F-fluorocholine uptake in patients with chronic autoimmune thyroiditis

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Abstract

Objective: ^{18}F-Fluorocholine (^{18}FCH) PET/CT has high sensitivity for parathyroid adenoma detection and can reliably exclude malignancy in thyroid nodules with indeterminate cytology. Data regarding ^{18}FCH uptake in chronic autoimmune thyroiditis (CAT) are scarce. We aimed to assess thyroid ^{18}FCH uptake in CAT with biological and histological correlation.

Methods: This is an ancillary study from the Chocolate trial (NCT02784223) that prospectively enrolled 107 patients planned for thyroid surgery. ^{18}FCH PET/CT acquisitions were performed 20 and 60 min after injection. ^{18}FCH uptake in the thyroid gland was assessed by measuring maximum (SUVmax) and mean (SUVmean) standardized uptake values. Thyrotropin, free thyroxine (FT4), thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies were collected. The intensity of thyroiditis and the degree of fibrosis were assessed on pathology.

Results: CAT was evidenced in 19/107 (18%) patients. Of these, 13 (68%) displayed an increased and diffuse ^{18}FCH thyroid uptake. This uptake pattern was not observed in patients without CAT. SUVmax and SUVmean were higher in patients with CAT than in those without ($P < 0.001$). At both acquisition times, SUVmax showed a monotonic relationship with the intensity of thyroiditis (Spearman $\rho = 0.44$ and 0.51, respectively, $P < 0.001$) and with the degree of fibrosis (Spearman $\rho = 0.55$ and 0.62, respectively, $P < 0.001$). SUVmax showed a linear relationship with TPOAb titers at 20 min (Pearson $r = 0.54$, $P < 0.05$; Spearman $\rho = 0.59$, $P = 0.03$).

Conclusions: More than two-thirds of the patients with CAT present high and diffuse thyroid ^{18}FCH uptake. This uptake pattern is highly specific to CAT and is correlated with pathology and TPOAb titers.

Key Words

- 18-Fluorocholine PET/CT
- ^{18}FCH PET/CT
- choline
- chronic autoimmune thyroiditis
- diffuse thyroid uptake
- diffuse ^{18}FCH uptake
- thyroid imaging

Introduction

^{18}F-Fluorocholine (^{18}FCH) PET/CT is a common imaging modality for patients with prostate cancer in countries with limited access to radiolabelled prostate-specific membrane antigen ligands. Over the past 5 years, many studies have shown that ^{18}FCH PET/CT is also highly sensitive (i.e. >90%) for the detection of parathyroid adenomas in patients with primary hyperparathyroidism (PHPT) (1, 2). Recently, we reported that ^{18}FCH PET/CT is an interesting

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imaging tool in thyroid nodules with indeterminate cytology, enabling malignancy in ^{18}FCH-negative nodules to be reliably excluded (3).

Some cases of increased and diffuse ^{18}FCH uptake in the thyroid gland have been described in the imaging workup of patients with prostate cancer and were related to chronic autoimmune thyroiditis (CAT) (4, 5). Diffuse thyroid uptake is also a well-known pattern in patients with CAT on ^{18}F-Fluorodeoxyglucose (^{18}FDG) PET/CT (6, 7). Although some authors showed that thyroid antibody (Ab) titers were associated with maximum standardized uptake values (SUVmax) (8), others did not find such associations (6).

So far, the relationship between thyroid ^{18}FCH uptake and CAT has not been studied. Furthermore, data are lacking in female patients. Therefore, we aimed to assess thyroid ^{18}FCH uptake in CAT in a series including both female and male patients, taking into account biological and histological parameters.

Materials and methods

Patients

This study was ancillary to the single-center Chocolate prospective trial (EUDRACT 2015-005017-71; ClinicalTrials.gov identifier: NCT02784223) that we conducted in 107 enrolled patients who gave their written informed consent (3). Inclusion criteria were the following: patients with a thyroid nodule ≥15 mm with a cytology scored class III (atypia of undetermined significance/follicular lesion of undetermined significance), IV (follicular neoplasm/suspicious for follicular neoplasm or Hürthle-cell neoplasm), or V (suspicious for malignancy) according to the Bethesda classification in the 6 months before inclusion, and for whom thyroid surgery had been recommended. Exclusion criteria were the following: patients with a hot nodule on thyroid scintigraphy.

^{18}F-Fluorocholine PET/CT

As previously described (3), ^{18}FCH PET/CT images were acquired on a Biograph 6 TrueV PET/CT system (Siemens Medical Solutions, Erlangen, Germany) with an extended field-of-view of 21.6 cm. A PET acquisition of 10 min (one-bed position) covering the neck and upper chest was performed in 3D list-mode 20 and 60 min after intravenous injection of 1.5 MBq/kg of ^{18}FCH. For each acquisition, a low-dose CT (CAREdose ref. mAs 100, 130 kV, slice 3 mm, pitch 1.0) was performed. For clinical interpretation, PET raw data at 20 and 60 min were reconstructed with the point spread function (PSF) reconstruction algorithm (HD; TrueX, Siemens Medical Solutions; 3 iterations and 21 subsets) without filtering, with matrix size 256 × 256 and zoom 1.0. Scatter and attenuation corrections were applied. To fulfill EARL guideline requirements (9), an EARL1 reconstruction was generated with the same parameters and a postfiltering Gaussian filter of 6 mm was applied.

PET/CT image analysis

All anonymized ^{18}FCH PET/CT data sets were reviewed by a board-certified nuclear medicine physician on a digital workstation (IntelliSpace, Philips Healthcare). PET/CT acquisitions were blindly reviewed in random order. For each acquisition, the reviewer had knowledge of the localization of the thyroid nodule studied in the Chocolate trial. On visual analysis, a diffusely increased ^{18}FCH uptake in the thyroid gland was sought. For quantitative analysis, a circular region of interest (ROI) with a fixed diameter of 15 mm was placed over the region of highest intensity in the contralateral thyroid lobe of the nodule studied in the Chocolate trial. CT scan and, if necessary, US data were used to ensure that the ROI did not contain nodules. ^{18}FCH uptake in the thyroid gland was assessed by measuring SUVmax, $SUVmax_{EARL}$, and SUVmean.

Laboratory data

Serum for thyrotropin (TSH), free thyroxine (FT4), thyroid peroxidase antibodies (TPOAb), and thyroglobulin antibodies (TgAb) were collected for measurements using Roche Cobas 6000 Tg electrochemiluminescent immunoassays (Roche Diagnostics). The normal reference ranges are 12–22 pmol/L for FT4, 0.27–4.2 mIU/L for TSH, 0–34 IU/mL for TPOAb, and 0–115 IU/mL for TgAb.

Pathology

All pathological slides were blindly reviewed by two experienced pathologists to assess thyroid parenchyma. The intensity of thyroiditis was scored as follows: absent, mild, moderate, or intense (Fig. 1). The degree of fibrosis was scored in patients with thyroiditis as follows: absent, mild, moderate, or intense (Fig. 2).

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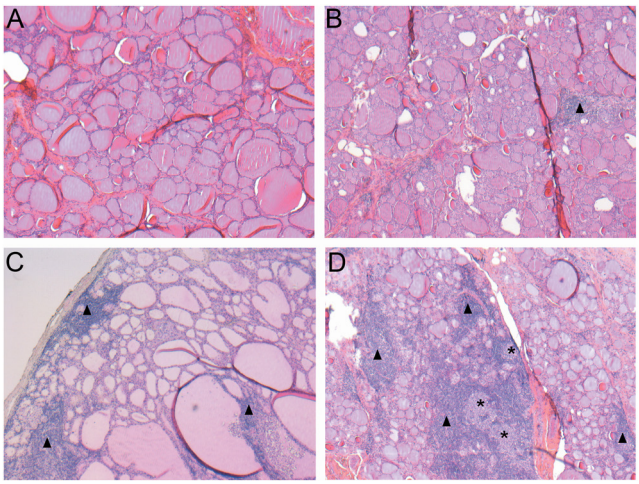

Figure 1
Representative slides of lymphocytic infiltrate displaying (A) negative, (B) mild, (C) moderate, and (D) intense thyroiditis (hematoxylin–eosin–saffron staining, ×5). Black arrowheads, lymphocytic infiltrate; asterisks, germinal center formation.

Chronic autoimmune thyroiditis

The diagnosis of CAT was defined by the presence of positive thyroid Ab (i.e. TPOAb and/or TgAb) and thyroiditis on pathology (10, 11).

Statistical analysis

Quantitative variables were described by means (±S.D.), and qualitative variables by frequencies and percentages. Patient characteristics were compared according to the presence of CAT by the Student's *t*-test for quantitative variables (or by the non-parametric Wilcoxon–Mann–Whitney test if non-gaussian distributions) and by the chi-square test for qualitative variables. Linear and monotonic associations between quantitative variables were assessed by computing the Pearson (r) and the Spearman rank correlation coefficient (ρ), respectively. Association between quantitative and qualitative ordinal variables was assessed by computing the Spearman rank correlation coefficient. Each of these correlation coefficients was provided with *P*-value testing absence of correlation ($r=0$ or $\rho=0$). For all tests, a two-tailed *P*-value of 0.05 or less was considered statistically significant. The analyses were conducted using R version 4.0.2.

Results

Patients

Among the 107 patients (mean age, 55 ± 14 years; female, 75%), 19 (18%) had positive thyroid Ab, including 14 with positive TPOAb and 14 with positive TgAb. All these 19 patients (including 17 women) had thyroiditis on pathology and formed the group of patients with CAT. Characteristics of the patients are presented in Table 1. Of these 19 patients, four were on levothyroxine (LT4) for replacement therapy. They had been on LT4 for 6 months, 5 years, 7 years and 15 years, respectively.

Biology

TSH level was higher in the 19 patients with CAT than in the 88 without (2.51 ± 1.99 mIU/L vs 1.40 ± 0.76 mIU/L, $P=0.02$). Likewise, TSH level was higher in the 14 patients with positive TPOAb than in the 93 without (3.09 ± 2.02 mIU/L vs 1.37 ± 0.75 mIU/L, $P<0.001$). TSH level did not statistically differ between the 14 patients with positive TgAb and the 88 without (2.50 ± 2.28 mIU/L vs 1.46 ± 0.8 mIU/L, $P=0.25$). Among patients with CAT, TSH level was similar in those with or without LT4 therapy ($P=0.5$). In addition, TSH levels did not differ statistically according to the intensity of thyroiditis (1.86 ± 0.02 mIU/L, 1.64 ± 0.60 mIU/L, and 2.89 ± 2.45 mIU/L in mild, moderate, and intense thyroiditis, respectively; $P=0.7$).

Thyroid gland uptake on ^{18}FCH PET/CT

$SUVmax_{EARL}$ was not available in three patients for whom EARL1 reconstruction was missing. Visual analysis showed an increased and diffuse ^{18}FCH thyroid uptake both at 20 and 60 min (SUVmax=7.69 ± 1.43 and 7.91 ± 1.71,

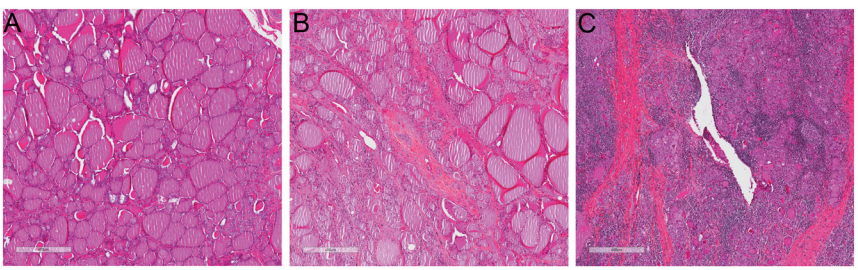

Figure 2
Representative slides displaying (A) mild, (B) moderate, and (C) intense fibrosis.

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Table 1 Patient characteristics according to diagnosis of chronic autoimmune thyroiditis (CAT), *n* = 107.

	No CAT (*n* = 88)	**CAT** (*n* = 19)	***P* value**
Age (years), mean (S.D.)	55 (14)	57 (14.8)	0.65
Sex (female) (*n*, %)	63 (72%)	17 (89%)	0.15
Biology			
TSH (mIU/L), mean (S.D.)	1.4 (0.76)	2.51 (1.99)	0.019
FT4 (pmol/L), mean (S.D.)	16.11 (2.13)	15.37 (2.67)	0.21
Positive TPOAb, *n* (%)	0	14 (74%)	<0.001
Positive TgAb, *n* (%)	0	14 (74%)	<0.001
Pathology			<0.001
No thyroiditis	47 (54%)	0	
Thyroiditis, mild	32 (36%)	2 (11%)	
Thyroiditis, moderate	7 (8%)	4 (21%)	
Thyroiditis, intense	2 (2%)	13 (68%)	
^{18}FCH PET/CT			
Thyroid uptake, 20 min p.i.			
SUVmax	3.93 (0.87)	6.66 (2.02)	<0.001
$SUVmax_{EARL}$	3.04 (0.67)	5.08 (1.34)	<0.001
SUVmean	2.48 (0.6)	3.74 (1.01)	<0.001
Thyroid uptake, 60 min p.i.			
SUVmax	3.78 (0.94)	6.82 (2.27)	<0.001
$SUVmax_{EARL}$	2.85 (0.64)	5.07 (1.52)	<0.001
SUVmean	2.28 (0.61)	3.64 (1.1)	<0.001

FT4, free thyroxine; ^{18}FCH, ^{18}fluorocholine; SUV, standardized uptake value; TSH, thyrotropin; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies.

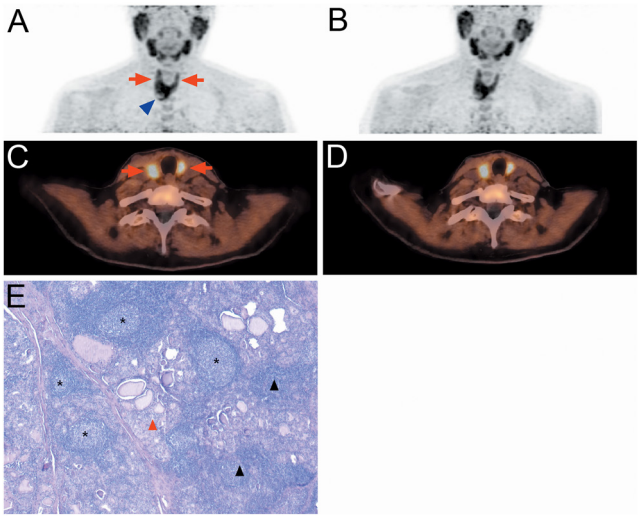

Figure 3
Clinical example of a 50-year-old female patient with CAT. PET/CT displayed diffusely increased ^{18}FCH uptake in the thyroid gland (red arrows) at 20 (A, maximum intensity projection (MIP); C, fused axial image) and 60 min (B, MIP; D, fused axial image). She was referred for surgery for a 35-mm nodule in the right thyroid lobe (^{18}FCH-negative, blue arrowhead) with indeterminate cytology (Bethesda IV) (patient 10 in Table 2). (E) Pathology showed extensive lymphocytic infiltrate (black arrowheads) with germinal center formation (asterisks) and atrophic follicles with abundant Hürthle cells (red arrowhead) (hematoxylin–eosin–saffron staining, ×5). Thyroiditis was scored intense.

respectively) in 13 out of 19 patients (68%) with CAT. The four patients on LT4 were included in the 13. One patient with such ^{18}FCH thyroid uptake is presented in Fig. 3. In contrast, none of the 88 patients without CAT exhibited increased and diffuse ^{18}FCH thyroid uptake.

TSH level was higher in the 13 patients with diffusely increased thyroid uptake than in the remaining 94 (2.97 ± 2.23 vs 1.40 ± 0.75 mIU/L, $P = 0.008$). Likewise, TSH level was higher in these 13 patients than in the 88 patients without CAT (2.97 ± 2.23 vs 1.4 ± 0.76 mIU/L, $P = 0.007$).

Quantitative analysis of ^{18}FCH uptake in the thyroid gland of the 19 patients with CAT is presented in Tables 1 and 2. SUVmax and SUVmean were higher in the 19 patients with CAT than in the 88 without at both acquisition times ($P < 0.001$). Among patients with non-specific thyroiditis, SUVmax was similar in those with mild intensity and in those with moderate/high intensity (SUVmax = 4.02 ± 0.87 vs 4.16 ± 1.12, $P = 0.8$). SUVmax was higher in patients with CAT of moderate/high intensity than in those with non-specific thyroiditis of moderate/high intensity (SUVmax = 6.89 ± 1.94 vs 4.16 ± 1.12, $P < 0.001$). SUVmax and SUVmean were also higher in the 19 patients with positive thyroid Ab than in those without, both at 20 min (6.66 ± 2.02 vs 3.93 ± 0.87, $P < 0.001$ and 3.74 ± 1.01 vs 2.48 ± 0.6, $P < 0.001$, respectively) and 60 min (6.82 ± 2.27 vs 3.78 ± 0.94, $P < 0.001$ and 3.64 ± 1.10 vs 2.28 ± 0.61, $P < 0.001$, respectively). Likewise, positive TPOAb and positive TgAb were associated with both higher SUVmax and SUVmean.

At both acquisition times, SUVmax showed a monotonic relationship with the intensity of thyroiditis in the 107 patients ($\rho = 0.44$, $P < 0.001$ and $\rho = 0.51$, $P < 0.001$, respectively) (Fig. 4). Furthermore, SUVmax showed a monotonic relationship with the degree of fibrosis at both acquisition times in the 60 patients with thyroiditis on pathology (Spearman $\rho = 0.55$ and 0.62, respectively, $P < 0.001$) (Fig. 5). SUVmax showed a linear relationship with TPOAb titers at 20 min ($r = 0.54$, $P < 0.046$ and $\rho = 0.59$, $P = 0.029$) (Fig. 6), and with a trend to a monotonic association at 60 min, but not linear ($r = 0.36$, $P = 0.21$ and $\rho = 0.51$, $P = 0.064$). No relationship was observed between SUVmax and TgAb titers at 20 and 60 min (all $P > 0.05$). Furthermore, no significant relationship was found between SUVmax and TSH level in patients with CAT.

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Table 2 Characteristics of 19 patients with chronic autoimmune thyroiditis (CAT).

							^{18}FCH PET/CT						
							Acquisition 20 min p.i.			Acquisition 60 min p.i.			Pathology
Pt	**Age** (year)	**Sex** (F/M)	**TSH** (mIU/L)	**TPOAb** (IU/L), *n* ≤**34**	**TgAb** (IU/L), *n* ≤**115**	**LT4**	SUVmax	$SUVmax_{EARL}$	SUVmean	SUVmax	$SUVmax_{EARL}$	SUVmean	Thyroiditis
1	80	F	0.88	6	334	N	3.38	2.66	2.13	3.97	2.82	2.24	+++
2	75	F	1.83	72	34	N	6.32	4.6	3.51	6.23	4.13	2.97	+
3	51	F	4.55	656	2483	Y	9.78	6.12	4.21	8.43	5.85	4.14	+++
4	62	F	0.42	114	165	Y	6.83	NA	3.63	6.71	NA	3.82	+++
5	48	F	0.56	10	228	N	7.63	6.12	4.86	8.71	6.39	5.08	+++
6	72	F	1.01	17	299	N	5.1	4.23	3.94	5.37	4.23	3.97	++
7	52	F	0.8	12	314	N	5.43	4.28	3.31	5.75	4.23	3.14	+++
8	66	M	1.88	65	19	N	3.18	NA	1.93	2.98	NA	1.99	+
9	35	F	1.16	10	123	N	5.65	4.3	3.34	6.51	4.33	3.24	++
10	50	F	8.25	237	233	N	9.47	7.29	4.06	11.45	7.33	4.88	+++
11	61	F	3.22	224	84	N	8.47	6.75	5.45	8.81	6.84	5.82	+++
12	49	F	5.48	130	124	N	8.22	6.64	5.71	7.18	6.49	5.1	+++
13	69	F	3.81	90	<10	N	6.9	5.2	4.21	7.5	7.04	4.07	+++
14	37	F	2.56	153	500	Y	7.68	5.42	3.86	8.28	5.32	3.71	+++
15	39	F	1.5	389	138	N	10.06	6.68	4.65	10.69	6.55	4.28	+++
16	56	M	1.87	110	13	N	5.59	3.84	2.74	5.67	3.86	2.81	++
17	34	F	1.46	231	571	N	6.55	4.43	3.29	6.49	3.97	2.79	+++
18	81	F	3.87	171	395	Y	6.41	4.64	3.56	5.87	4.48	3.31	+++
19	61	F	2.5	307	833	N	3.95	3.16	2.6	3.01	2.34	1.82	++

^{18}FCH, ^{18}fluorocholine; LT4, levothyroxine replacement therapy; N, no; NA, not available; TSH, thyrotropin; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies; Y, yes; thyroiditis: mild, +; moderate, ++; intense, +++.

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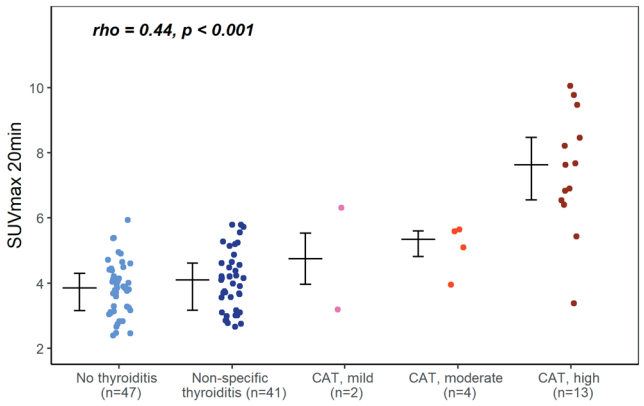

Figure 4
Relationship between SUVmax and thyroiditis on pathology at 20 min in the 107 patients (median with 25–75% quartiles). Parameter rho (ρ) is Spearman's correlation coefficient, associated with *P* - values.

Discussion

^{18}FCH PET/CT studies are increasingly performed in the imaging workup of PHPT because of their high performance for parathyroid adenoma detection (1, 2). ^{18}FCH PET/CT can also be used to reliably exclude malignancy in ^{18}FCH-negative thyroid nodules (3). As CAT, parathyroid disorders, and thyroid nodules predominantly affect women, there is a need to describe the pattern of thyroid ^{18}FCH uptake in a population where female patients are highly represented. The prospective Chocolate trial we previously conducted in 107 patients harboring a thyroid nodule with indeterminate cytology was an opportunity to assess thyroid ^{18}FCH uptake in a mixed series of patients with 73% of women and 18% of CAT. Our results confirm that thyroid uptake is diffusely increased in 68% of patients with CAT. Such a high and diffuse thyroid uptake was not observed in patients without CAT. We also showed that thyroid uptake (i.e. SUVmax) was significantly associated with the intensity of thyroiditis and TPOAb titers. On ^{18}FDG PET studies, Edo *et al.* also found a correlation between SUVmax and TPOAb titers, whereas Karantanis *et al.* did not (6, 8). Of note, unlike previous ^{18}FDG PET studies, our study benefited from histologic data, enabling the correlation between SUVmax and the intensity of thyroiditis and the correlation between SUVmax and the degree of fibrosis to be explored.

Although the mechanisms remain unknown, the degree of lymphocytic infiltration may account for the increased ^{18}FDG uptake in the thyroid gland (6, 7, 8). Because choline is an essential component of phospholipids, ^{18}FCH targets cell membrane incorporation and its uptake reflects the phospholipid synthesis in cell membranes. Lymph nodes are a common site of non-specific ^{18}FCH accumulation, particularly in the neck, the mediastinum, and the inguinal areas. ^{18}FCH may accumulate in inflammatory sites, as previously shown in an aseptic inflammation model (12) and in the vessel walls of the abdominal aorta and aneurysms (13, 14). Karantanis *et al.* suggested that fibrosis might also play a role in ^{18}FDG uptake (6). Our results also show that a high level of fibrosis in CAT is associated with high ^{18}FCH thyroid uptake. However, the mechanisms involved in ^{18}FCH accumulation in CAT are still unclear.

This uptake pattern observed in CAT may lead to misinterpretation in some patients. In the Chocolate trial, we reported one patient with CAT in whom tracer uptake

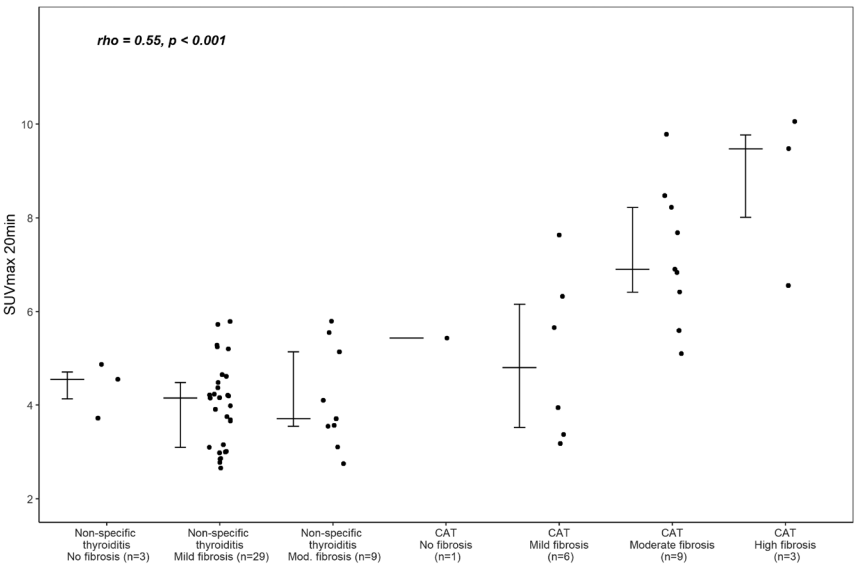

Figure 5
Relationship between SUVmax and fibrosis at 20 min in patients with non-specific thyroiditis and chronic autoimmune thyroiditis (CAT) (median with 25–75% quartiles). Parameter rho (ρ) is Spearman's correlation coefficient, associated with *P* - values.

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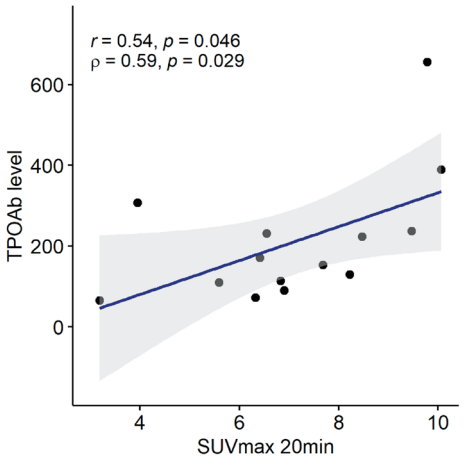

Figure 6
Relationship between SUVmax and TPOAb titers at 20 min in the 14 patients with positive TPOAb. Parameters r and rho (ρ) are Pearson and Spearman's correlation coefficients, respectively, associated with *P* - values.

was higher in the thyroid gland than in the malignant nodule (3). Likewise, intrathyroidal parathyroid adenomas might be masked by such high thyroid uptake, although these ectopic localizations are rare and the association with CAT uncommon.

Our results confirm the need to measure thyroid Ab and TSH levels when facing diffusely increased thyroid uptake in order to search for subclinical hypothyroidism when CAT is not previously known. We reported SUVmax and $SUVmax_{EARL}$ at both acquisition times (i.e. 20 and 60 min). Indeed, both early and delayed acquisition times have been proposed for parathyroid (15) and thyroid (3) imaging with ^{18}FCH PET/CT.

The two major strengths of the present study are histopathologic confrontation and prospective data. The main limitation is the limited cohort of patients with CAT ($n = 19$). However, the sample sizes of patients with CAT with biological data studied in previous ^{18}FDG PET reports were also limited ($n = 18–36$) (6, 7, 8).

Conclusion

More than two-thirds of the patients with CAT present high and diffuse thyroid ^{18}FCH uptake. This uptake pattern is highly specific to CAT. When faced with such an uptake pattern, TSH and thyroid Ab measurements are warranted if CAT is unknown.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding
The Chocolate trial was supported by a grant from the Groupement d'Intérêt Public Cancéropôle Nord-Ouest in partnership with the Groupement Interrégional pour la Recherche Clinique et l'Innovation – Inter-regional group for Clinical Research and Innovation from the Northwest area of France. The funding agencies were not involved in the design and conduct of the study, nor in the collection, management, analysis, and interpretation of the data. They were not involved in the writing of the article.

Ethics approval
This study received ethical approval from the Local Ethics Committee and was approved by the Institution Review Board of Baclesse Cancer Centre in November 2015. It was approved by the North-West III Ethics Committee in April 2016 (Reference 2015-37, N°EudraCT: 2015-005017-71) and by the National Agency for the Safety of Medicines and Health Products (Reference: 151468A-12) in March 2016. This study was performed in line with the principles of the Declaration of Helsinki and its later amendments.

Consent to participate and consent to publish
Informed consent was obtained from all individual participants included in the study.

Author contribution statement
R C conceived the study and drafted the manuscript. S B helped to draft the manuscript and revised it. R C, V S R, M D and C L performed or contributed to data acquisition. R C and S B analysed data. J L and S L A performed the statistical analysis. J L and B C revised the manuscript.

Acknowledgement
The authors thank Guillaume Desmartin and Louis-Bastien Weiswald (INSERM 1086 ANTICIPE).

References

1 Treglia G, Piccardo A, Imperiale A, Strobel K, Kaufmann PA, Prior JO & Giovanella L. Diagnostic performance of choline PET for detection of hyperfunctioning parathyroid glands in hyperparathyroidism: a systematic review and meta-analysis. *European Journal of Nuclear Medicine and Molecular Imaging* 2019 **46** 751–765. (https://doi.org/10.1007/s00259-018-4123-z)
2 Petranović Ovčariček P, Giovanella L, Carrió Gasset I, Hindié E, Huellner MW, Luster M, Piccardo A, Weber T, Talbot JN & Verburg FA. The EANM practice guidelines for parathyroid imaging. *European Journal of Nuclear Medicine and Molecular Imaging* 2021 **48** 2801–2822. (https://doi.org/10.1007/s00259-021-05334-y)
3 Ciappuccini R, Licaj I, Lasne-Cardon A, Babin E, de Raucourt D, Blanchard D, Bastit V, Saguet-Rysanek V, Lequesne J, Peyronnet D, *et al.* 18F-fluorocholine positron emission tomography/computed tomography is a highly sensitive but poorly specific tool for identifying malignancy in thyroid nodules with indeterminate cytology: the chocolate study. *Thyroid* 2021 **31** 800–809. (https://doi.org/10.1089/thy.2020.0555)
4 Calabria F, Chiaravalloti A & Schillaci O. 18F-choline PET/CT pitfalls in image interpretation: an update on 300 examined patients with

prostate cancer. *Clinical Nuclear Medicine* 2014 **39** 122–130. (https://doi.org/10.1097/RLU.0000000000000303)
5 Roland A, Drouet C, Boulahdour H, Cochet A & De Bari B. Unusual uptakes on 18F-fluorocholine positron emission tomography/computed tomography (PET/CT): a retrospective study of 368 prostate cancer patients referred for a biochemical recurrence or an initial staging. *Quantitative Imaging in Medicine and Surgery* 2021 **11** 172–182. (https://doi.org/10.21037/qims-19-981)
6 Karantanis D, Bogsrud TV, Wiseman GA, Mullan BP, Subramaniam RM, Nathan MA, Peller PJ, Bahn RS & Lowe VJ. Clinical significance of diffusely increased 18F-FDG uptake in the thyroid gland. *Journal of Nuclear Medicine* 2007 **48** 896–901. (https://doi.org/10.2967/jnumed.106.039024)
7 Yasuda S, Shohtsu A, Ide M, Takagi S, Takahashi W, Suzuki Y & Horiuchi M. Chronic thyroiditis: diffuse uptake of FDG at PET. *Radiology* 1998 **207** 775–778. (https://doi.org/10.1148/radiology.207.3.9609903)
8 Edo N, Morita K, Sakamoto M, Kaminaga T, Edo H, Okamura E, Ogawa M, Tsukamoto K, Okinaga H & Ishikawa T. Correlation between anti-thyroid peroxidase antibody levels and diffuse thyroid uptake of 18F-fluorodeoxyglucose in Hashimoto's thyroiditis: a retrospective study. *Thyroid Research* 2018 **11** 14. (https://doi.org/10.1186/s13044-018-0058-5)
9 Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, Verzijlbergen FJ, Barrington SF, Pike LC, Weber WA, *et al*. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *European Journal of Nuclear Medicine and Molecular Imaging* 2015 **42** 328–354. (https://doi.org/10.1007/s00259-014-2961-x)
10 Dayan CM & Daniels GH. Chronic autoimmune thyroiditis. *New England Journal of Medicine* 1996 **9** 99–107. (https://doi.org/10.1056/NEJM199607113350206).
11 Berger N & Borda A. Thyroïdites. In *Pathologie Thyroïdienne, Parathyroïdienne et Surrénalienne*, pp. 54–63. Montpellier, France: Sauramps Medical, 2010.
12 Kubota K, Furumoto S, Iwata R, Fukuda H, Kawamura K & Ishiwata K. Comparison of 18F-fluoromethylcholine and 2-deoxy-D-glucose in the distribution of tumor and inflammation. *Annals of Nuclear Medicine* 2006 **20** 527–533. (https://doi.org/10.1007/BF03026816)
13 Bucerius J, Schmaljohann J, Böhm I, Palmedo H, Guhlke S, Tiemann K, Heinz Schild HH, Biersack HJ & Manka C. Feasibility of 18F-fluoromethylcholine PET/CT for imaging of vessel wall alterations in humans – first results. *European Journal of Nuclear Medicine and Molecular Imaging* 2008 **35** 815–820. (https://doi.org/10.1007/s00259-007-0685-x)
14 Sarda-Mantel L, Alsac JM, Boisgard R, Hervatin F, Montravers F, Tavitian B, Michel JB & Le Guludec D. Comparison of 18F-fluoro-deoxy-glucose, 18F-fluoro-methyl-choline, and 18F-DPA714 for positron-emission tomography imaging of leukocyte accumulation in the aortic wall of experimental abdominal aneurysms. *Journal of Vascular Surgery* 2012 **56** 765–773. (https://doi.org/10.1016/j.jvs.2012.01.069)
15 Broos WAM, Wondergem M, van der Zant FM & Knol RJJ. Dual-time-point 18F-fluorocholine PET/CT in parathyroid imaging. *Journal of Nuclear Medicine* 2019 **60** 1605–1610. (https://doi.org/10.2967/jnumed.118.225599)

Received in final form 12 May 2022
Accepted 18 May 2022
Accepted Manuscript published online 18 May 2022