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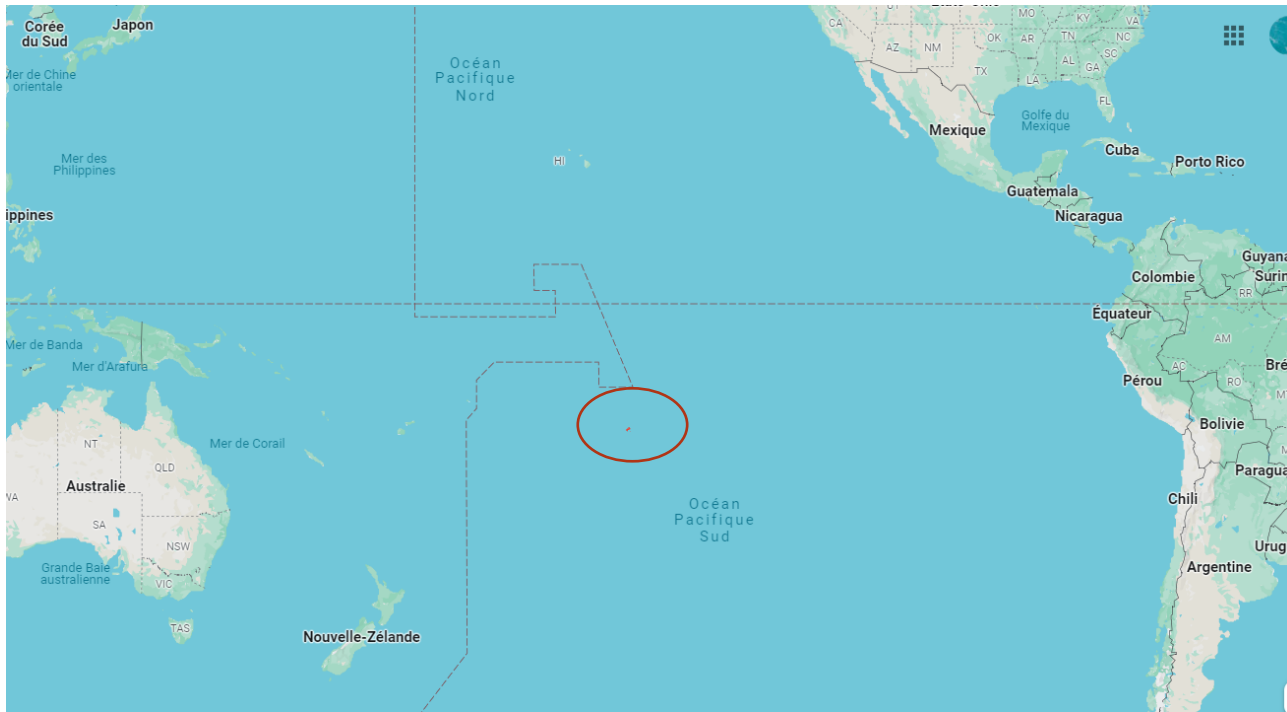
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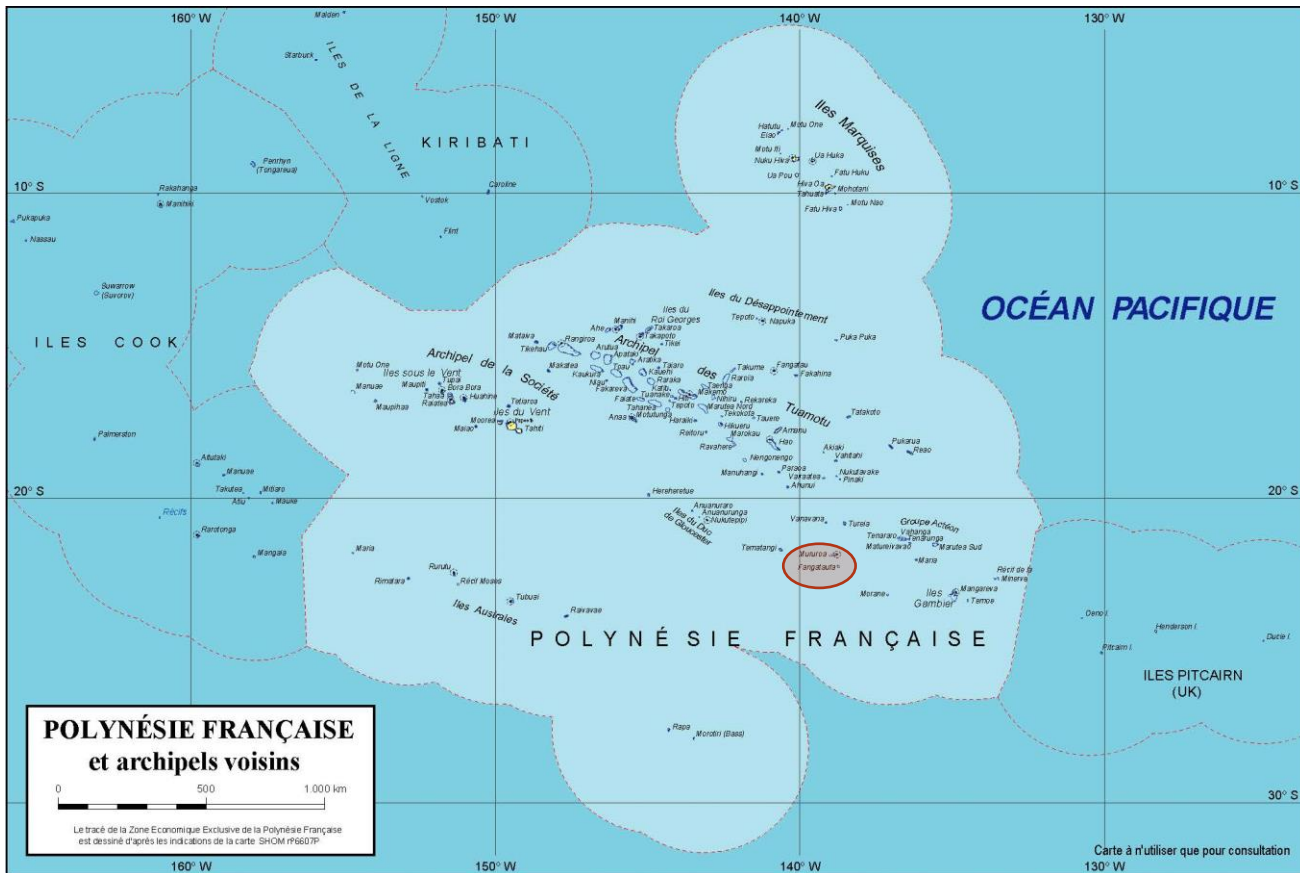


Differentiated thyroid cancers in French Polynesia. Role of nuclear tests

Florent de Vathaire, Monia Zidane, U1018 INSERM / Gustaver Roussy, Paris Saclay University
Vladimir Drozdovitch, André Bouville, REB, DCEG, NCI, NIH, Bethesda, USA.

Presenting author : **Médéa Locquet**





Name	Date	Time (UT ²)	Type	Height (m)	Yield (kt) ³			Partitioned fission yield (kt)		
					Fission	Fusion	Total	Local and regional	Tropo-sphere	Strato-sphere
Aldébaran	02/07/1966	15h34	Barge	0	28 ⁴	0	28	14	14	-
Tamouré	19/07/1966	15h05	Air drop	1000	50 ⁴	0	50	-	49	1
Bételgeuse	11/09/1966	17h00	Balloon	470	110 ⁴	0	110	-	-	110
Rigel ⁵	24/09/1966	17h00	Barge	3	125 ⁴	0	125	62.5	59.5	3
Sirius	04/10/1966	21h00	Barge	10	205 ⁴	0	205	102.5	92.1	10.4
Altair	05/06/1967	19h00	Balloon	295	15 ⁴	0	15	-	15	-
Antarés	27/06/1967	18h30	Balloon	340	120 ⁴	0	120	-	-	120
Arcturus	02/07/1967	17h30	Barge	0	22 ⁴	0	22	11	11	-
Capella	07/07/1968	22h00	Balloon	463	115 ⁴	0	115	-	-	115
Castor	15/07/1968	19h00	Balloon	650	450 ⁴	0	450	-	-	450
Pollux	03/08/1968	21h00	Balloon	490	150 ⁴	0	150	-	-	150
Canopus ⁵	24/08/1968	18h30	Balloon	520	1300	1300	2600	-	-	1300
Procyon	08/09/1968	19h00	Balloon	700	640	640	1280	-	-	640
Androméde	15/05/1970	18h00	Balloon	220	13 ⁴	0	13	-	13	-
Cassiopeé	22/05/1970	18h30	Balloon	500	150	74	224	-	-	150
Dragon ⁵	30/05/1970	18h00	Balloon	500	472.5	472.5	945	-	-	472.5
Eridan	24/06/1970	18h30	Balloon	220	12 ⁴	0	12	-	12	-
Licorne	03/07/1970	18h30	Balloon	500	457	457	914	-	-	457
Pégas	27/07/1970	19h00	Balloon	220	0.05 ⁴	0	0.05	-	0.05	-
Orion ⁵	02/08/1970	19h00	Balloon	400	72 ⁴	0	72	-	70	2
Foucan	06/08/1970	19h00	Balloon	500	297	297	594	-	-	297
Dioné	05/06/1971	19h15	Balloon	275	34 ⁴	0	34	-	34	-
Enclade	12/06/1971	19h15	Balloon	450	290	150	440	-	-	290
Iapet	04/07/1971	21h30	Balloon	230	9 ⁴	0	9	-	9	-
Phoebé	08/08/1971	18h30	Balloon	230	4 ⁴	0	4	-	4	--
Rhéa	14/08/1971	19h00	Balloon	480	478	477	955	-	-	478
Umbriel	25/06/1972	19h00	Balloon	230	0.5 ⁴	0	0.5	-	0.5	-
Titania	30/06/1972	18h30	Balloon	220	4 ⁴	0	4	-	4	-
Obéron	27/07/1972	18h40	Balloon	220	6 ⁴	0	6	-	6	-
Euterpe	21/07/1973	18h00	Balloon	220	11 ⁴	0	11	-	11	-
Melpoméne	28/07/1973	23h00	Balloon	270	0.05 ⁴	0	0.05	-	0.05	-
Pallas	18/08/1973	18h15	Balloon	270	4 ⁴	0	4	-	4	-
Parthénope	24/08/1973	18h00	Balloon	220	0.2 ⁴	0	0.2	-	0.2	-
Tamara	28/08/1973	18h30	Air drop	-	6 ⁴	0	6	-	6	-
Capricorne	16/06/1974	17h30	Balloon	220	4	0	4	-	4	--
Gémeaux	07/07/1974	23h15	Balloon	312	100	50	150	-	-	100
Centaure	17/07/1974	17h00	Balloon	270	4	0	4	-	4	-
Maquis	25/07/1974	17h30	Air drop	250	8	0	8	-	8	-
Scorpion	15/08/1974	00h30	Balloon	312	96	0	96	-	93	3
Faureau	24/08/1974	23h45	Balloon	270	14	0	14	-	14	-
Verseau	14/10/1974	23h30	Balloon	433	221	111	332	-	-	221

² Universal time. Universal time coordinated (local time) in Tahiti: UTC = UT - 10h

³ Estimated fission and fusion yields unless otherwise indicated; reported total yields.

⁴ Reported fission or fusion yield.

⁵ This test was conducted on Fangataufa Atoll, others - on Mururoa Atoll.

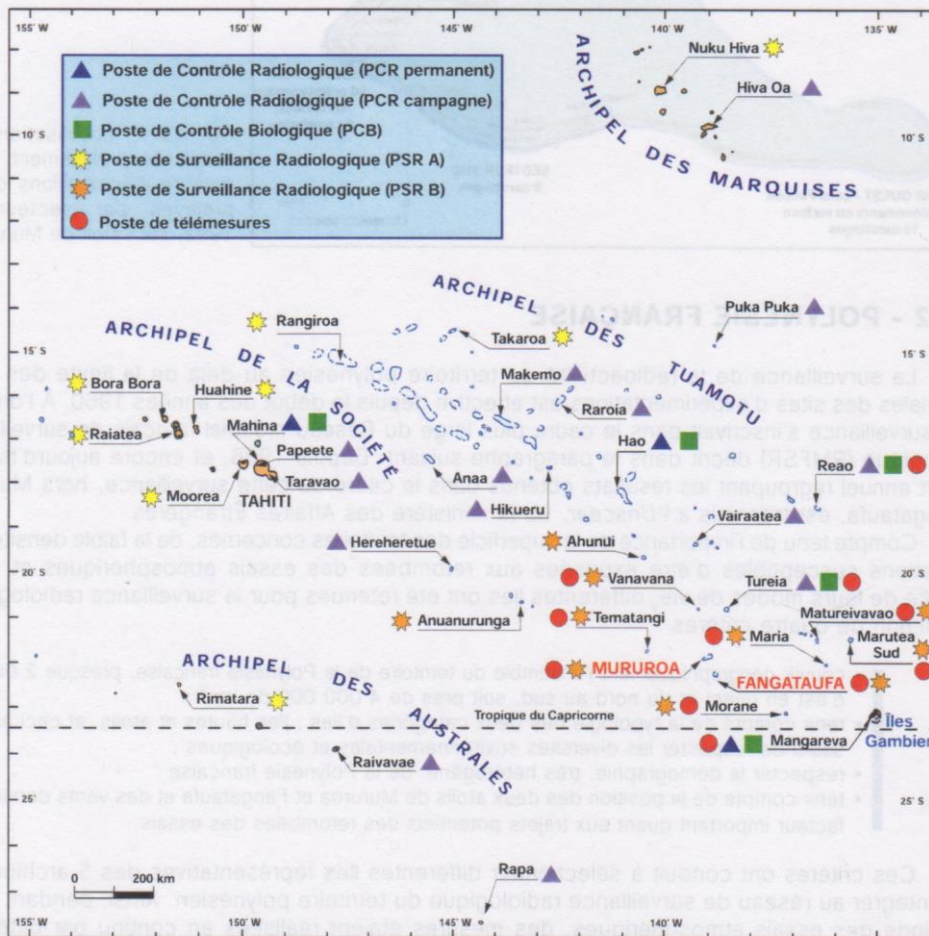


Fig. 50. - Localisation des postes de contrôle et de surveillance radiologique et biologique, en Polynésie française, lors de la période des essais atmosphériques.

+ 13 meteo stations

+ Measurements on buoys, ships, and aircrafts

+ anthropo-gammametry measurements among the population of the islands close to the nuclear test (non usable ?)

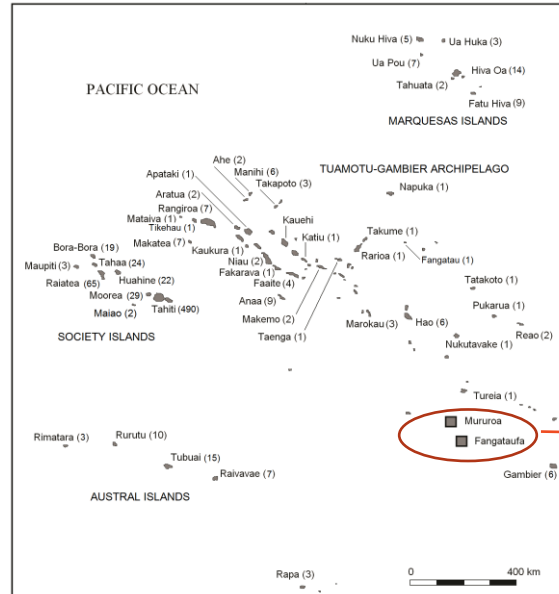
French Polynesia at time of atmospheric tests

Almost no permanent inhabitants in Mururoa and Fangataufa.

Fewer than 500 inhabitants in a circle of 500 km around the test sites

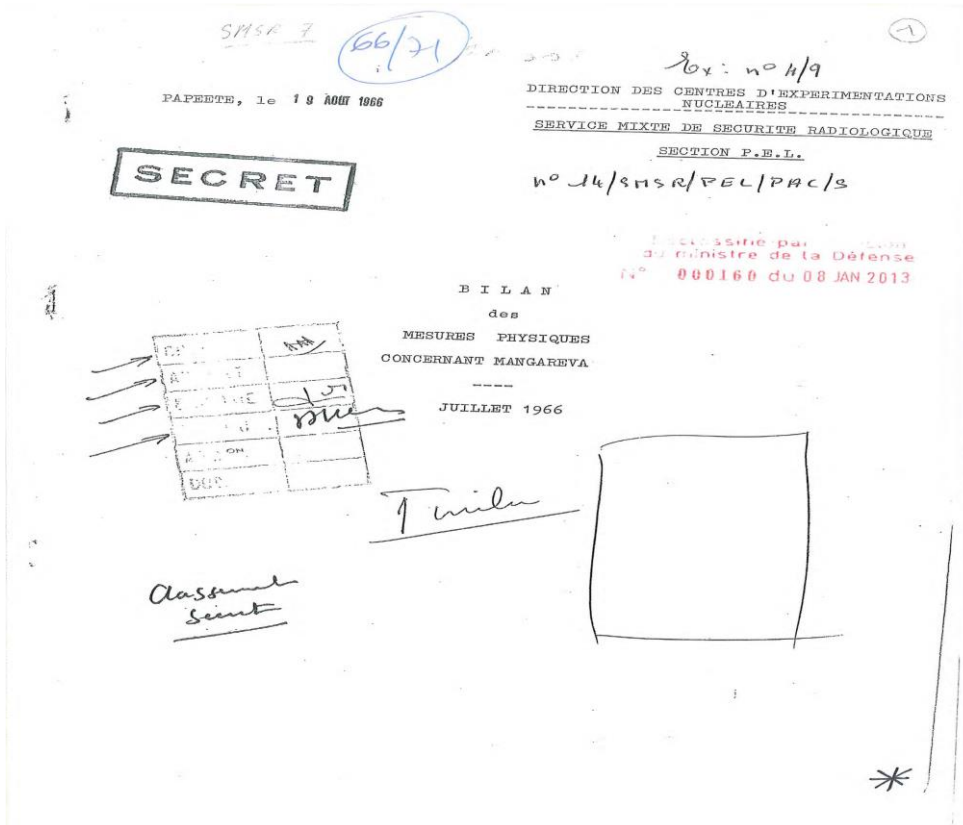
Only 3 airports in FP : Tahiti, Hao (main logistic base during the tests) and Moruroa

Except in Tahiti, Hao, and Mururoa, almost all of the food was produced locally in each island and atoll.



Nuclear test sites

2013 : French army declassified all the original reports of the radiation protection services (SMSR and SMCB)



Case-control studies (2003-2008) and (2015-2018)

Methodology

- All the living inhabitants born in FP with diagnostic of thyroid cancer from 1984 to 2016
- Initial goal : 2 controls for each case of thyroid cancer, matched on date of birth, and sex, randomly chosen in the population registry
- 395 cases and 555 controls
- Face to face interview by trained interviewer,
 - ◆ Place of birth, of residence, and of school.
 - ◆ Occupational exposure / Medical and familial history / Origin of drinking water
 - ◆ Diet – recently and during childhood
 - ◆ Menstrual and reproductive history
- ◆ Trimming of nails (in order to measure mercury, lead, iodine, selenium)
- ◆ Saliva sampling -> Constitutional DNA in order to investigate genetic susceptibility
- ◆ Thanks to IRSN and to ANSES, set up of a nutritional composition table (Measure of iodine, lead, selenium..... in diet from all archipelagos of French Polynesia)

Dosimetry



DOI:10.31557/APJCP.2019.20.12.3667
Behavior and Consumption in French Polynesia

RESEARCH ARTICLE

Editorial Process: Submission:07/11/2019 Acceptance:11/30/2019

Behavior and Food Consumption Pattern of the French Polynesian Population in the 1960s –1970s

Vladimir Drozdovitch^{1*}, André Bouville², Tetuaura Tetuanui³, Marc Taquet³, Jacques Gardon⁴, Constance Xhaard^{5,6,7,8}, Yan Ren^{5,6,7}, Françoise Doyon^{5,6,7}, Florent de Vathaire^{5,6,7}

Self questionnaire data:

- Age
- Place of residence,
- Type of habitation (open or not),
- Diet at age 15 y, including cow's milk and vegetables
- Source of drinking water

Reports sent by France to UNSCEAR during nuclear test period:

- Total beta-activity in air
- ¹³¹I in cow's milk
- Beta- and gamma-activity in some food
- Ground deposition density (total activity)

Meteorological data:

- For each nuclear test, measurements each day, from 21 days before to 7 days after each test.
- Data from 13 meteorological stations -> specific model of fallout dispersion for each test.
- Reports from the CEA/French Army Radioprotection Services, declassified in 2013
- Focus groups study conducted in all FP archipelagos, including key informant interviews

Risk projection

- Thyroid cancer incidence in French Population : Cancer Incidence in 5 continents volume VII for the period before 1995 and volume IX afterward
- Estimation of population in each island, by gender, age and calendar year, from 1971 to 2022 and projection up to 2071.
- Average dose per age class, gender, and archipelago during the tests.
- Risk model : BEIR VII
 - $RR = \text{Incidence} * (1 + \text{ERR/Gy} * \text{dose})$.
 - Thyroid ERR/Gy does not depend on the time elapsed since irradiation or on the dose rate, but only on the gender and on the age at irradiation :
 - ERR/Gy=1.5 (95%CI:0.28-3.90) for women if > age 30y or more at irradiation
 - ERR/Gy=0.53 (95%CI:0.14-2.0) for men if > age 30y or more at irradiationthese values being multiplied by $\exp(-0.83 * ((\text{age at irradiation} - 30) / 10))$, if the age is less than 30 years at irradiation (19).

Results

Characteristics of cases and controls			
Characteristic	Thyroid cancer cases (395)	Controls (555)	P-value*
Women (n, %)	336 (85.1%)	473 (85.2%)	-**
Mean age at end of follow-up (years)	43.6	42.3	-**
Parents Ethnic origin (n,%)			
Both polynesian	219 (55.6%)	283 (51.0%)	0.09
Polynesian- Asian	57 (14.5%)	76 (13.7%)	
Polynesian-European	71 (18.0%)	103 (18.6%)	
Polynesian-Asian-European	34 (8.6%)	47 (8.5%)	
Other	14 (3.5%)	76 (13.7%)	
Familial history of thyroid cancer (n, %)	20 (5.1%)	9 (1.6%)	0.006
Familial history of thyroid pathology (n, %)	155 (39.2%)	96 (17.3%)	<0.0001
Personal history of radiation therapy (n, %)	34 (8.6%)	5 (0.9%)	<0.0001
Archipelago of birth (n,%)			
Tahiti & Moorea	223 (56.5%)	328 (59.1%)	0.8
Other Société islands	80 (20.2%)	102 (18.4%)	
Australes	25 (6.3%)	30 (5.4%)	
Marquises	18 (4.6%)	18 (4.9%)	
Tuamotu-Gambier	49 (12.4%)	49 (12.3%)	

* Univariate conditional logistic regression

** Matching criteria

Results

Characteristics of cases and controls			
Characteristic	Thyroid cancer cases (395)	Controls (555)	P-value*
Average height in m (std)			
Women	1.65 (0.06)	1.64 (0.06)	0.001
Men	1.76 (0.07)	1.74 (0.07)	
Mean weight at end follow-up in kg (std)			
Women	84 (21)	75 (19)	<0.0001
Men	103 (23)	91 (19)	
Mean BMI at end follow-up (std)			
Women	30.7 (7.3)	27.9 (6.9)	<0.0001
Men	33.3 (6.9)	30.0 (5.9)	
Diploma (n, %)			
No	161 (40.8%)	197 (35.5%)	0.03
Yes	234 (59.2%)	358 (64.5%)	
Insufficient dietary intake (n, %)			
No	282 (39.8%)	427 (60.2%)	0.05
Yes	113 (46.9%)	128 (53.1%)	
Number of pregnancies (n, %)			
0	40 (11.9%)	67 (14.2%)	0.002
1-4	162 (48.2%)	264 (55.8%)	
5-16	134 (39.9%)	142 (30.0%)	

* Univariate conditional logistic regression

** Matching criteria

New Dosimetry: Estimation of thyroid doses

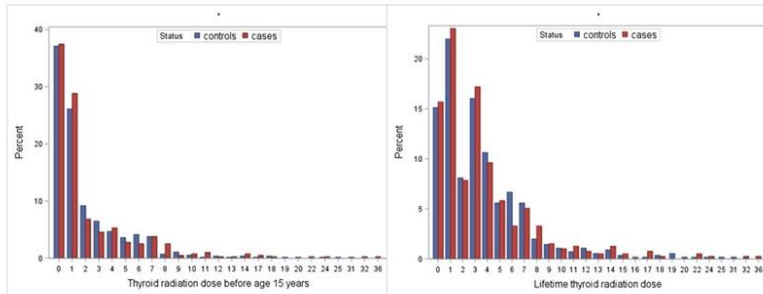
Exposure pathways to the thyroid gland:

- (i) intake of ^{131}I and of short-lived radioiodine isotopes (^{132}I , ^{133}I , ^{135}I) and ^{132}Te via inhalation and ingestion with cow's milk (Tahiti only), leafy vegetables and drinking water
- (ii) external irradiation from gamma-emitting radionuclides deposited on the ground, and
- (iii) ingestion of long-lived ^{137}Cs with foodstuffs

Paper

Thyroid Doses to French Polynesians Resulting from Atmospheric Nuclear Weapons Tests: Estimates Based on Radiation Measurements and Population Lifestyle Data

Vladimir Drozdovitch,¹ André Bouville,² Marc Taguet,³ Jacques Gardon,⁴ Constance Xhaard,^{5,6,7,8} Yan Ren,^{5,6,7} Françoise Doyon,^{3,6,7} and Florent de Vathaire^{5,6,7}



New Dosimetry: Origin of thyroid doses

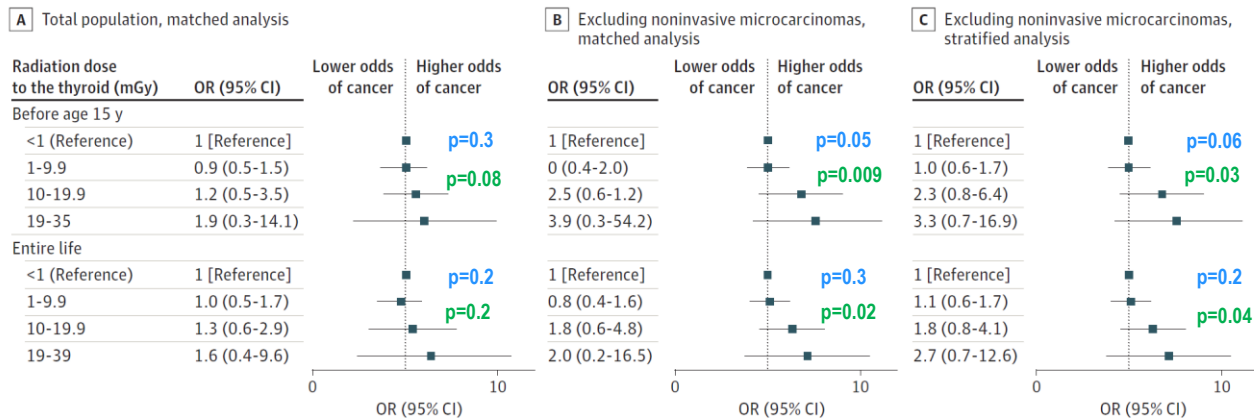
Table 3 – Characteristics of the thyroid dose due to atmospheric nuclear tests: subjects born in or before 1974, and who were present in French Polynesia at the time of the tests

Dose in mGy mean, median (min-max)	Thyroid cancer cases	Controls
<i>Lifetime dose</i>		
Whole sample	4.71; 3.47 (<0.01-36.25)	4.60; 3.65 (<0.01-31.19)
Gender		
Male	4.32; 3.28 (<0.01-17.89)	4.29; 3.27 (<0.01-22.15)
Female	4.77; 3.54 (<0.01-36.25)	4.65; 3.66 (<0.01-31.19)
Source		
Leafy vegetables	3.28; 2.59 (<0.01-23.01)	3.30; 2.55 (<0.01-29.63)
Fresh cow's milk*	0.58; 0.02 (<0.01-17.65)	0.56; 0.09 (<0.01-8.92)
Inhalation	0.22; 0.16 (<0.01-4.64)	0.19; 0.16 (<0.01-1.63)
Cistern drinking water	0.16; <0.01 (<0.01-6.52)	0.11; <0.01 (<0.01-5.64)
Other foodstuffs	0.04; 0.02 (<0.01-0.35)	0.05; 0.02 (<0.01-0.94)
External irradiation	0.43; 0.43 (<0.01-5.81)	0.39; 0.44 (<0.01-3.5)
<i>Dose received before the age of 15</i>		
Whole sample	2.93; 1.30 (<0.01-36.15)	2.71; 1.50 (<0.01-31.19)
Gender		
Male	2.61; 1.16 (<0.01-17.89)	2.15; 1.03 (<0.01-11.87)
Female	2.99; 1.32 (<0.01-36.15)	2.81; 1.56 (<0.01-31.19)
Source		
Leafy vegetables	1.95; 0.92 (<0.01-23.01)	1.84; 0.87 (<0.01-29.63)
Fresh cow's milk*	0.43; <0.01 (<0.01-17.65)	0.42; 0 (<0.01-8.92)
Inhalation	0.16; 0.06 (<0.01-4.64)	0.13; 0.07 (<0.01-0.75)
Cistern drinking water	0.13; <0.01 (<0.01-6.52)	0.09; <0.01 (<0.01-5.64)
Other foodstuffs	0.02; <0.01 (<0.01-0.24)	0.02; <0.01 (<0.01-0.29)
External irradiation	0.25; 0.09 (<0.01-5.8)	0.22; 0.10 (<0.01-2.25)

* Only in Tahiti

Results of the case-control study : Role of thyroid dose

Figure 2. Thyroid Cancer Risk by Thyroid Dose Before Age 15 y and Lifetime



Conditional (left and center) or unconditional (right) logistic regressions, adjusted by ethnic group, level of education, obesity, family history of thyroid cancer, personal history of radiotherapy, occupation at nuclear test site, dietary iodine intake, and number of pregnancies for women, are presented. OR indicates odds ratio.

P : p-values for an association between OR and thyroid radiation dose in a [linear model](#)

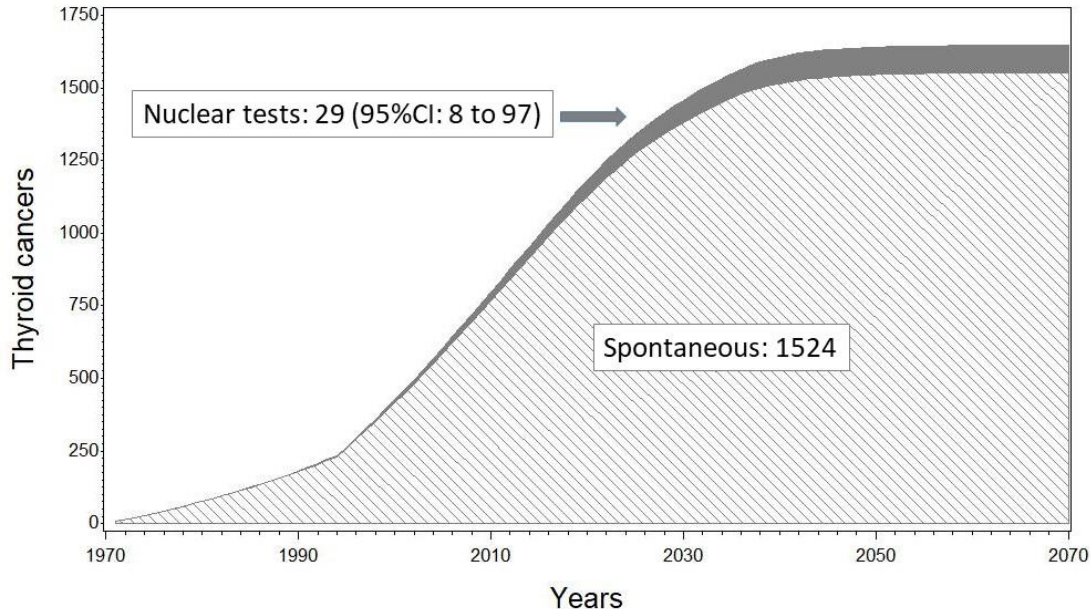
P : p-values for an association between OR and thyroid radiation dose in a [exponential model](#)

Risk projection : Results

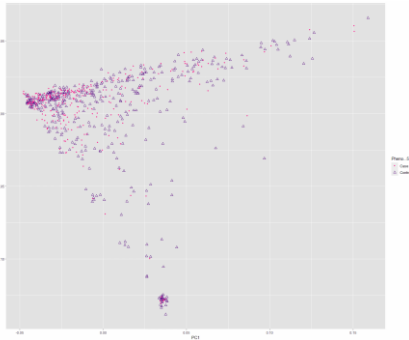
Lifetime attributable risk predicted in the whole native population present in FP during atmospheric nuclear tests: **29 DTC (95%CI: 8.0- 97)**, i.e., **2.3% (95%CI: 0.6-7.7) of the 1524 spontaneous DTC expected from 1971 to 2070 in this population.**

Among these 29 DTC in excess,

- 17 DTC (95%CI: 5-58) before 2022, in addition to the 1141 "natural" DTC predicted for this period.
- 27 (95%CI: 7-88) were expected to have occurred in women and 2 (95%CI: 1-7) in men.



Results of the case-control study : Role of genetic factors



French Polynesian : very specific genetic structure



Precision Clinical Medicine, 2023, 6: pbad015
DOI: 10.1093/pcmedi/pbad015
Research Article

Genetic factors for differentiated thyroid cancer in French Polynesia: new candidate loci

Monia Zidane¹, Marc Haber^{2,3}, Thérèse Truong⁴, Frédérique Rachédi⁵, Catherine Ory⁶, Sylvie Chevillard⁶, Héliane Blanché⁷, Robert Olasso⁸, Anne Boland⁹, Éric Conte⁹, Mojgan Karimi⁴, Yan Ren¹, Constance Xhaard¹⁰, Vincent Souchard¹, Jacques Gardon¹¹, Marc Taquet¹², André Bouville¹³, Jean-François Deleuze^{7,8}, Vladimir Drozdovitch¹⁴, Florent de Vathaire^{1,5} and Jean-Baptiste Cazier^{2,3}

Epithyr Oncoarray chips, set up specifically for this projects, by adding 13 759 markers (thyroid hormones and DNA repairs pathways) to the OncoArray-500K BeadChip

3 loci significant associated with thyroid cancer risk in 6q24.3, 10p12.2 et 17q21.32.

- Previously associated with cancer, but not with differentiated thyroid cancer
- P-values for main SNPs in these loci : $1,66 \cdot 10^{-7}$, $2,39 \cdot 10^{-7}$ et $7,19 \cdot 10^{-7}$
- Low ORs : 2,02, 1,89 et 2,37.

No significant interaction with radiation dose, but not the power to investigate this power.

BUT, DNA chips built using results from European ancestry populations.
Need for Whole Genome Sequencing

On-going investigations and perspectives

On going

- All cancers risk prediction (coll V Drozdovitch, NCI)
- Investigations on genetic susceptibility to radiation induced thyroid cancer
- miRNA : Catherine Ory (IRSN).

Classical epidemiological investigations on other pathologies

- Very difficult to perform and very low power due to low doses

Perspectives

- WGS on the case-control study (partially funded)
- Transgenerational effects project (project submitted)
 - Such effects not seen in a recent NCI study on children from population exposed in Chernobyl
 - But specificities of the French Polynesian population?

**THANK YOU FOR YOUR
ATTENTION**



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