

The START study

Salivary dysfunction After Radioiodine Treatment

Results at the 6-month follow-up

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CONTEXT

- **10 000** incident cases of thyroid cancer per year (*SpF 2019*)
- **Therapy** for differentiated thyroid cancer (in 80-85% of the cases) :
➔ **Thyroidectomy + complementary radioiodine capsule (^{131}I)**



Salivary glands: ability to concentrate radioiodine

➔ Possible **inflammation in glands (salivary and lacrimal)**

>> **Changes in glands production >> Impacts** quality of life and nutrition...

- But**
- ➔ **inaccurate incidence** of salivary/lacrimal disorders,
 - ➔ **no dose-response relationship,**
 - ➔ **no calculation of the dose** actually received by the salivary glands in ^{131}I using dosimeter measurements (\neq to administered activity)
 - ➔ **no identified clinical or genetic factors** to define at-risk patients



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OBJECTIVES

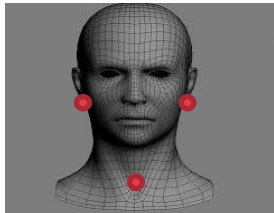
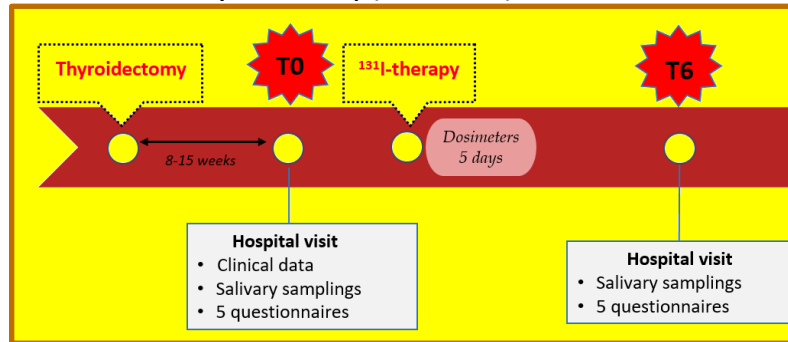


- To **estimate salivary/lacrimal dysfunctions incidence** after ^{131}I therapy
- To **characterize patients at risk** of developing post-treatment dysfunctions using clinical, biomolecular and biochemical factors
- To **estimate a dose-response relationship** between exposure of salivary glands to ^{131}I and salivary/lacrimal dysfunctions
- To **validate a dosimetric method** to calculate the dose actually received at the salivary gland level

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METHODS (1/2)

- Population** : 136 patients, candidates for a ^{131}I -therapy for differentiated thyroid cancer (at Pitié-Salpêtrière hospital, Paris)
 - 2 groups : 44 patients treated by 1.1 GBq (30 mCi)
 - 92 patients treated by 3.7 GBq (100 mCi)



Dosimetry

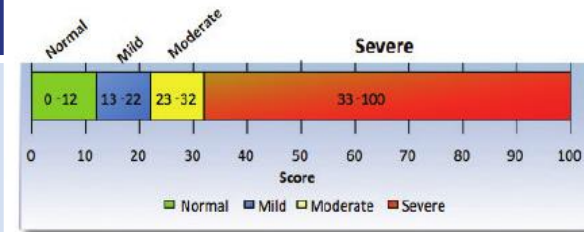
- ✓ 3 external thermoluminescent dosimeters positioned at T0 (immediately before ^{131}I intake), removed 5 days later
- ✓ Dosimetric reconstruction → calculation of the dose precisely received by the salivary glands

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METHODS (2/2)

• Outcomes: lacrimal & salivary dysfunctions

	Salivary dysfunctions	lacrimal dysfunctions
Continuous outcomes	<ul style="list-style-type: none"> • Unstimulated saliva flow (mL/min) • Stimulated saliva flow (mL/min) • Salivary biochemical concentrations in sodium, potassium, chloride, calcium (mmol/L) and amylase (kU/L) 	<ul style="list-style-type: none"> • OSDI© score between 0 and 100
Binary outcomes (yes/no)	<ul style="list-style-type: none"> • Unstimulated hyposalivation: “yes” when the saliva flow of unstimulated saliva was ≤ 0.25 mL/min • Stimulated hyposalivation: “yes” when the saliva flow of stimulated saliva was ≤ 1.00 mL/min • Dry mouth sensation (xerostomia): having answered “yes” to the question “do you feel that your mouth has been or is dry?” • Pain in the parotid gland: having answered “yes” to the question “did you experience pain in the parotid gland?” 	<ul style="list-style-type: none"> • Dry eyes: “yes” when the OSDI© score was >12



- **Gland disorders:** “yes” when at least one of the five following outcomes was recorded as “yes”:
 - ✓ unstimulated hyposalivation,
 - ✓ stimulated hyposalivation,
 - ✓ dry mouth sensation,
 - ✓ pain in the parotid gland,
 - ✓ dry eyes

• Other factors of interest

- ✓ Quality of life (MOS SF-36)
- ✓ Nutrition (EVA of ingesta)
- ✓ Anxiety and depression symptoms (HAD scale)
- ✓ Genetic variants

• Statistical analyses

- ➔ Descriptions
- ➔ Random effect multivariate models (linear and logistic) adjusted for for age at the time of interview, anxiety and depression score (HAD scale), history of systemic diseases, menopause status, and painkillers intake in the last 3 months

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RESULTS (1/4)

- Characteristics of the study population

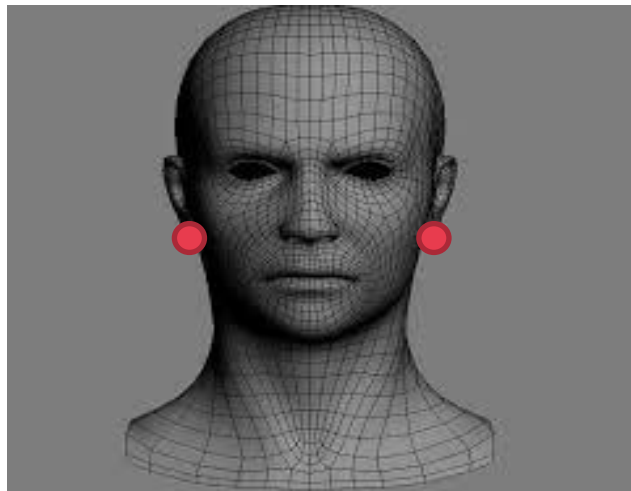


Variables	N(%)
Gender	
women	99 (71.22)
men	40 (28.78)
Age (years \pmsd)	47.07 (14.1)
BMI	27.06 (6.04)
Histology	
Follicular	20 (14.39)
Follicular & papillary	4 (2.88)
Papillary	115 (82.73)
TNM tumor stage	
Tx-T2	101 (73.19)
T3	33 (23.91)
T4	2 (1.45)
Nx-N0	77 (55.40)
N1	61 (43.88)
TSH elevation protocol	
L-thyroxin replacement stop	49 (35.25)
rTSH	90 (64.75)
Family history of thyroid cancer	
No	117 (84.17)
Yes	22 (15.83)
Salivary disorders history	
No	132 (94.96)
Yes	7 (5.04)
Systemic disease comorbidity	
Type 2 diabetes	5 (3.60)
Dyslipidemia	6 (4.32)
Diagnosed hypertension	28 (20.14)

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RESULTS (2/4)

- Characteristics of exposure



Variables	Administred activity		p*
	1.1 GBq group	3.7 GBq group	
Dr (Gy)	0.7 (0.2)	2.2 (0.7)	<.01
DI (Gy)	0.7 (0.2)	2.4 (1.0)	<.01

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RESULTS (3/4)

Salivary outcomes	T0	T6	p-value
Unstimulated saliva flow (mL/min)	0.8 (0.5)	0.7 (0.4)	0.23*
Unstimulated hyposalivation N			
Yes	14 (10.4)	14 (10.4)	1.00 α
No	122 (89.6)	121 (89.6)	
Incidence (%)	-	5.9	
Stimulated saliva flow (mL/min)	2.1 (0.9)	1.9 (0.8)	<.01*
Stimulated hyposalivation N (%)			
Yes	14 (10.4)	14 (10.4)	1.00 α
No	122 (89.6)	121 (89.6)	
Incidence (%)	-	3.7	

Lachrymal outcomes	T0	T6	p-value
OSDI score	6.7 (10.4)	9.4 (14.5)	0.01*
Dry eyes N (%)			
Yes	26 (19.1)	38 (28.2)	0.02 α
No	110 (80.9)	97 (71.9)	
Incidence (%)	-	17.0	

Composite criterion	T0	T6	p-value
Gland disorders N (%)			
Yes	66 (48.5)	73 (54.5)	0.21
No	70 (51.5)	61 (45.5)	
Incidence (%)	-	44.8	



*mean(sd) with paired T-test; α N(%) with McNemar test

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RESULTS (4/4)

Random effect univariate regressions

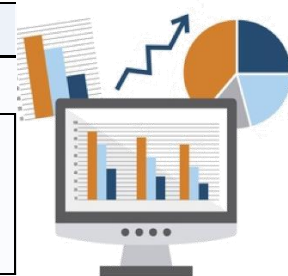
→ **Risk factors:** age at the time of interview, anxiety and depression score (HAD scale), history of systemic diseases, menopause status, and painkillers intake in the last 3 months

Random effect multivariate models

¹³¹ I exposure Categories	N	Unstimulated hyposalivation		Stimulated hyposalivation		Dry mouth sensation		Pain in the parotid gland		Dry eyes		Gland disorders		
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	
MD (Gy)	129	0.69	(0.41-1.18)	1.05	(0.56-1.97)	1.43	(1.01-2.04)	1.40	(0.90-2.18)	n/a		n/a		
Administred activity	Before treatment	136	1	ref	1	ref	1	ref	1	ref	1	ref	1	ref
	1.1 GBq	91	0.63	(0.11-3.52)	0.81	(0.09-7.02)	2.99	(1.07-8.39)	0.48	(0.09-2.53)	3.58	(1.19-10.81)	1.28	(0.54-3.05)
	3.7 GBq	41	0.57	(0.15-2.14)	0.52	(0.08-3.48)	2.37	(1.01-5.58)	1.97	(0.7-5.58)	2.12	(0.85-5.28)	1.49	(0.73-3.02)

¹³¹ I exposure Categories	N	Unstimulated saliva flow (mL/min)		Stimulated saliva flow (mL/min)		Chloride concentration (mmol/L)		Potassium concentration (mmol/L)		OSDI score		
		β	95%CI	β	95%CI	β	95%CI	β	95%CI	β	95%CI	
MD (Gy)	129	0.00	(-0.03;0.03)	-0.08	(-0.12;-0.02)	0.59	(-0.04;1.21)	1.07	(0.42;1.71)	n/a		
Administred activity	Before treatment	136	1	ref	1	ref	1	ref	1	ref	1	ref
	1.1 GBq	91	-0.01	(-0.10;0.08)	-0.26	(-0.44;-0.08)	-0.75	(-2.78;1.27)	-0.05	(-2.08;1.98)	4.07	(0.42;7.73)
	3.7 GBq	41	-0.01	(-0.07;0.07)	-0.15	(-0.29;-0.02)	2.06	(0.53;3.59)	3.10	(1.56;4.64)	1.57	(-1.24;4.37)

Adjusted for the previous risk factors



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CONCLUSIONS

➤ Results at the 6-month follow-up...

- **Low incidences** of salivary and lacrimal disorders based on objective and subjective measures,
- **No statistical difference** in incidences between the two groups of 1.1 GBq and 3.7 GBq,
- Towards a **decrease in glands activity after ¹³¹I-therapy**,
- Several **risk factors** identified,
- **Significant dose-response relationships** for dry mouth sensation, stimulated flow, salivary concentration in potassium, and dry eyes



- Study design
- Objective and subjective outcomes
- Estimations of the dose at the salivary glands
- Adjusted dose-response calculations



- Small study population
- No standardized indicators for hyposalivation
- Need for quality of life impact assessment

➤ Perspectives:

- To work on **genetic factors**
- To repeat analyses for the **follow-up at 18 months**
- To assess the consequences of salivary and lacrimal gland dysfunctions on **quality of life and nutritional status in the long term.**

Thanks!



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