Radiation epidemiology for cancer radiotherapy in Europe

Florent de Vathaire

Cancer and Radiation Group

INSERM / Gustave Roussy

European collaborations of radiation epidemiologists on long term risks radiotherapy

Childhood cancer

PanCare Group : PanCareSurFup and PanCareLife projects

Euratom funded projects: Procardio, CerebRad

PanCare Network

PanCare Network : Pan-European, Network for Care of Survivors after Childhood and Adolescent Cancer

Founded in 2008 in Lund : 13 European countries

Aims : to reduce the frequency, severity and impact of late side-effects of the treatment of children and adolescents with cancer.

Two Projects funded by ECC

PanCareSurFup

PanCareLife

PanCareSurFup (2010-2016)

Table 1
Comparative summary of the two EU-funded sister projects arising from the PanCare Network.

	PanCareSurFup: PanCare childhood and adolescent cancer survivor care and follow-up studies
Main focus	Cardiotoxicity, second primary neoplasms, late mortality, guidelines for long-term follow-up and transition and models of care
Participants (countries)	16 Partners from 11 countries (Austria, Belgium, France, Germany, Hungary, Ireland, Italy, Netherlands, Sweden, Switzerland, UK)
Work packages	1: Data collection and harmonisation (D. Grabow, Mainz, Germany) 2: Radiation dosimetry (F. de Vathaire, Paris, France) 3: Cardiac disease: cohort and nested case-control study (L. Kremer, Amsterdam, Netherlands) 4: Subsequent primary neoplasms: cohort and nested case-control studies (M. Hawkins, Birmingham, UK) 5: Late mortality (S. Garwicz, Lund, Sweden) 6: Guidelines, long-term follow-up and transition (R. Skinner, Newcastle, UK) 7: Dissemination and Training (M. Jankovic, Monza, Italy) 8: Management and coordination (L. Hjorth, Lund, Sweden)
Start of 5-year project	February 2011
Coordinator	L. Hjorth (Lund, Sweden)
Project Manager	E. Witthoff/H. Linge (Lund, Sweden)
Ethical (both projects) and scientific (PCSF only) advisory board	J.D. Beck (Erlangen, Germany), G. Bode (Bonn, Germany), P. Inskip (Washington, US), M. Jenney (Cardiff, UK)
Grant	FP7-HEALTH-2010.2.4.1-7 (Grant Agreement Number 257505)

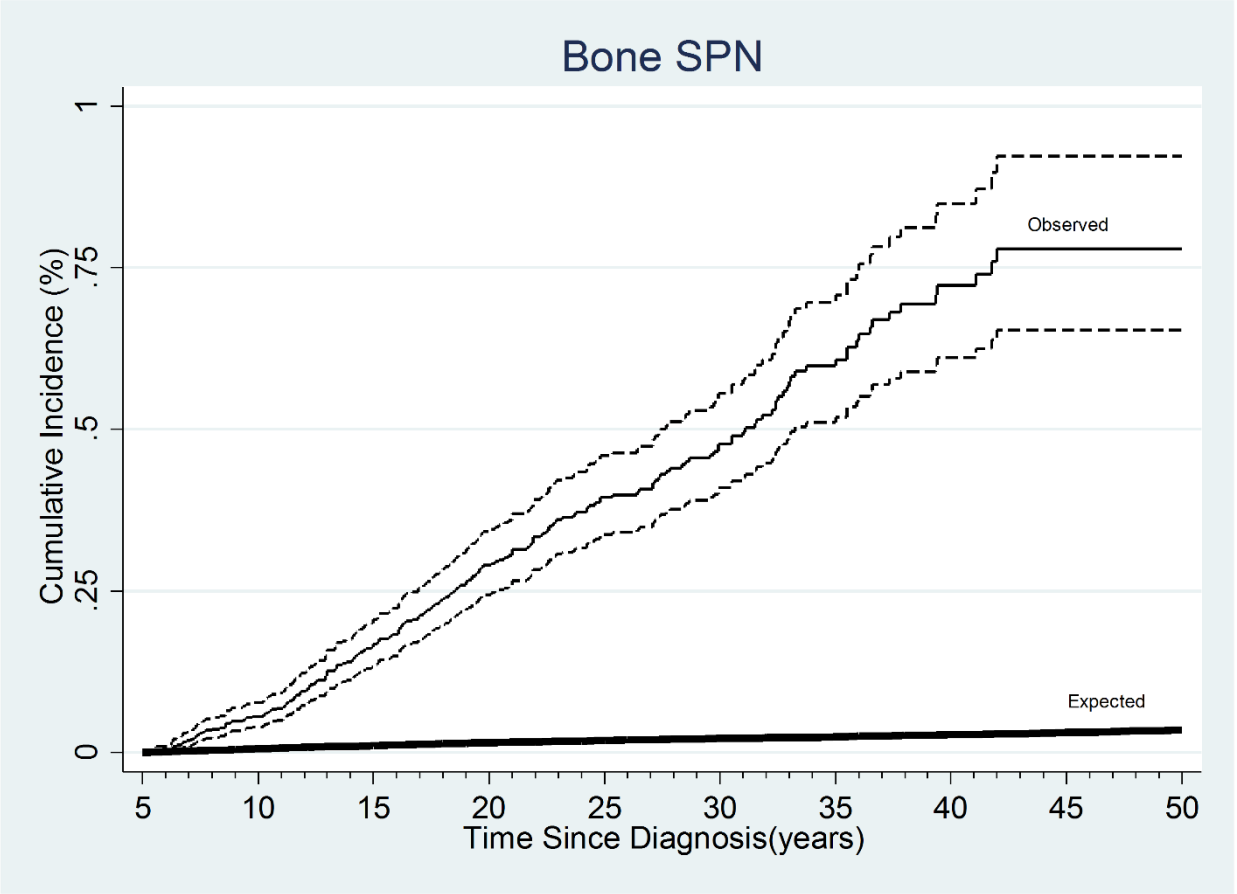
PanCareSurFup

- European Cohort of childhood and adolescent cancer survivors (about 80.000 5-years survivors)
  - Death causes, all second cancers, cardiac diseases
- Second cancer case-control study (1200 cases and 1200 controls)
  - Sarcomas, digestive, pulmonary and genito-urinary second cancers
- Cardiac diseases case-control study (600 cases and 600 controls)
- Dosimetry : Whole body extention of TPS calculation

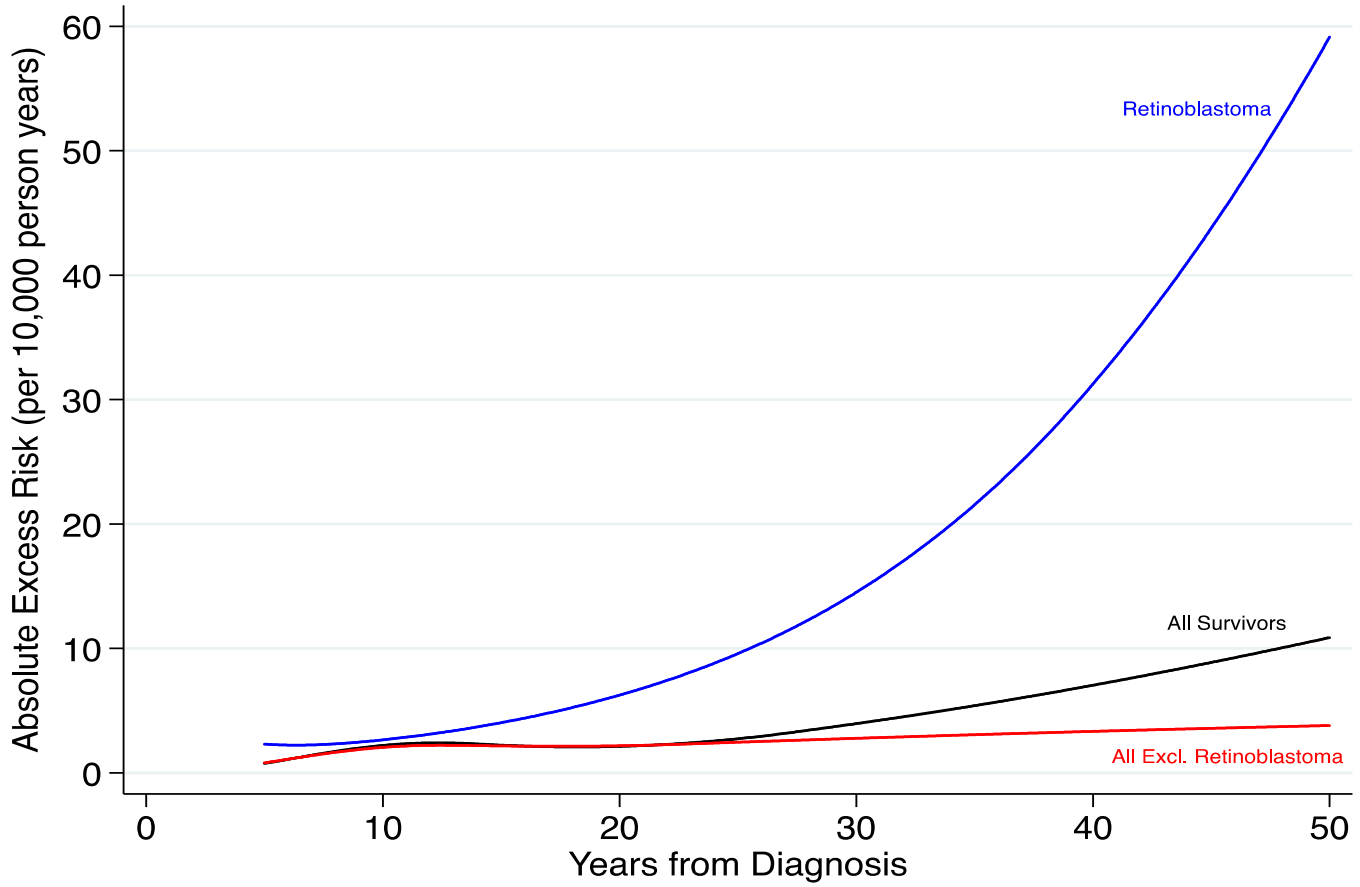
PanCareSurFup cohort : about 80.000 5-years survivors

Country of origin	Number of 5-year Survivors	Period of Childhood Cancer Diagnosis	Childhood Cancer Ascertainment	Age at Childhood Cancer Diagnosis (in years)
France	3,138	1946–1986	Hospital–based	< 19
Hungary	4,885	1971–2008	Population–based	< 20
Italy (Population)	10,781	1964–2005	Population–based	< 20
Italy (Hospital)	9,129	1960–2008	Hospital–based	< 20
Netherlands	6,044	1963–2001	Population–based	< 18
Denmark	4,832	1943–1998	Population–based	< 20
Sweden	7,709	1958–1998	Population–based	< 20
Norway	3,877	1953–1997	Population–based	< 20
Finland	6,229	1953–2006	Population–based	< 20
Iceland	274	1955–1998	Population–based	< 20
Slovenia	1,252	1960–2002	Population–based	< 17
Switzerland	4,373	1964–2005	Population–based	< 20
UK	17,960	1940–1991	Population–based	< 15

PanCareSurFup cohort : 229 second bone cancers (mostly osteosarcmas)



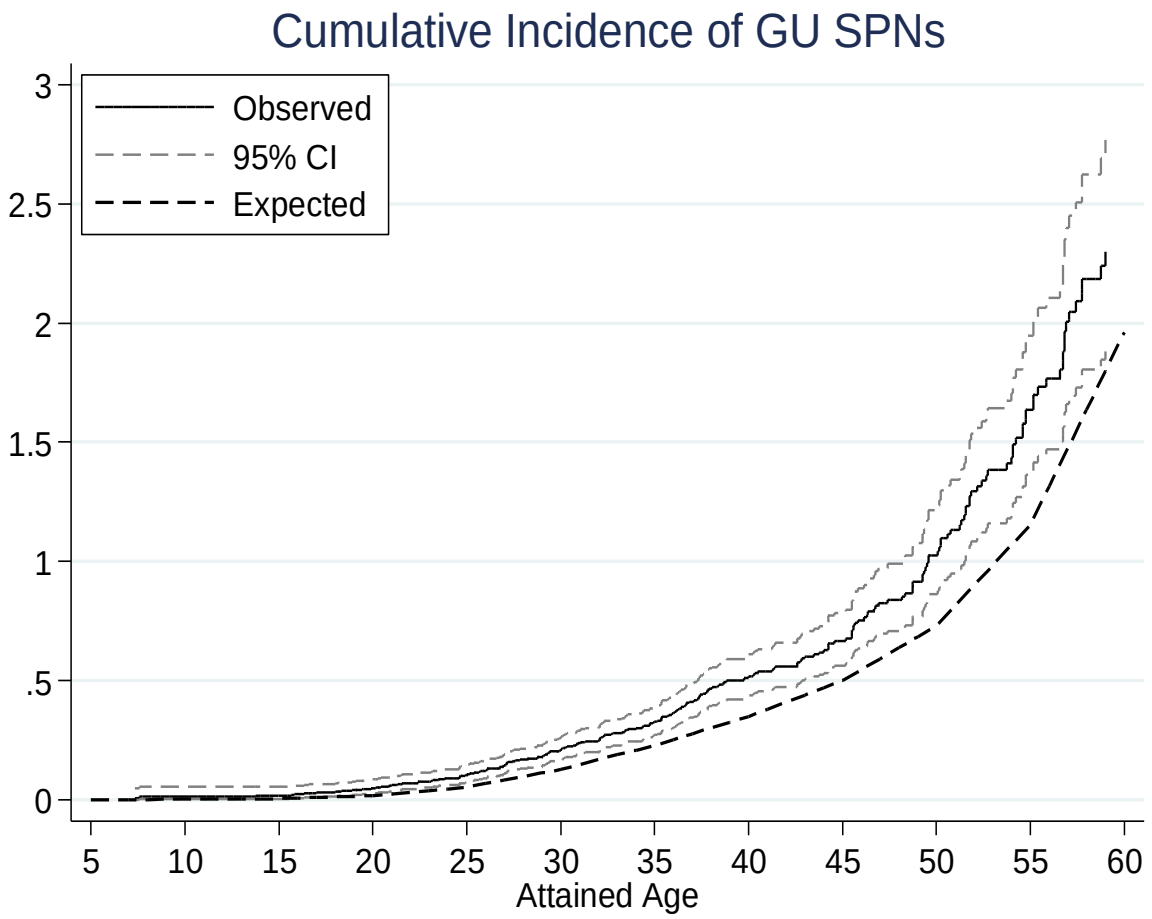
PanCareSurFup cohort : 291 second soft tissue sarcomas



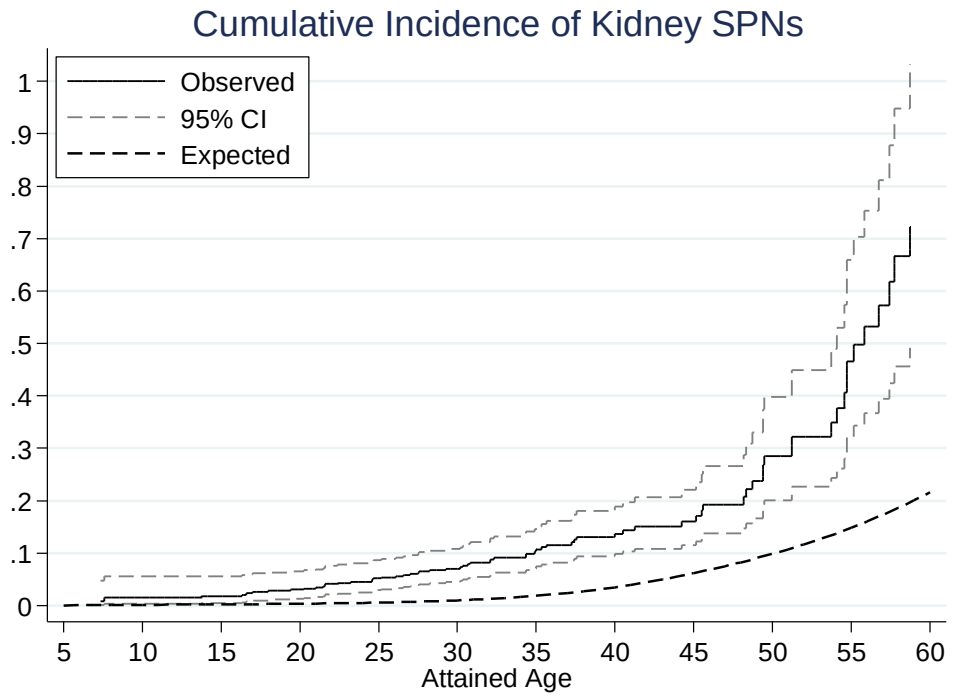
PanCareSurFup cohort : 291 second soft tissue sarcomas

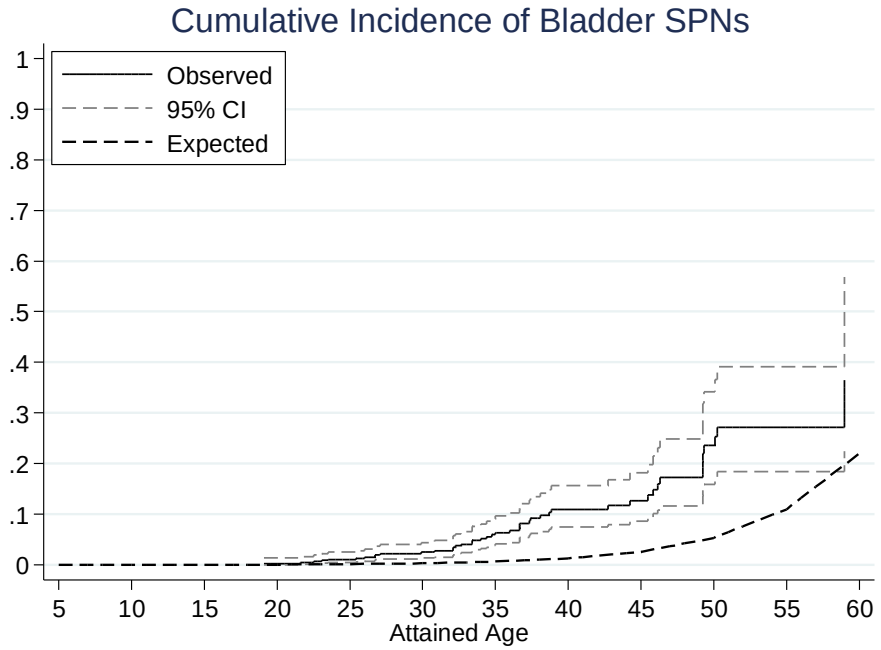
Factor	Level	O/E	SIR (95% CI)	RER (95% CI)*
Overall	All combined	291/17.8	16.3 (14.5,18.3)	
Decade of Diagnosis	<1970	109/6.4	17.0 (14.0,20.5)	1.0 (1.0,1.0)
	1970-1979	82/5.1	16.2 (12.9,20.1)	1.1 (0.7,1.5)
	1980-1989	66/4.4	15.0 (11.6,19.0)	1.0 (0.7,1.5)
	>=1990	34/1.9	17.6 (12.2,24.6)	1.2 (0.7,2.0)
	Ptrend		0.689	0.672
Attained Age	0-19 rs	67/3.0	22.2 (17.2,28.2)	1.0 (1.0,1.0)
	20-29 yrs	92/5.2	17.7 (14.2,21.6)	1.6 (1.1,2.3)
	30-39 yrs	79/4.9	16.2 (12.8,20.2)	2.4 (1.6,3.6)
	40+ yrs	53/4.7	11.3 (8.5,14.8)	2.9 (1.8,4.7)
	Ptrend		<0.001	<0.001
Years from Diagnosis	5-14 yrs	105/5.3	20.0 (16.3,24.2)	1.0 (1.0,1.0)
	15-24 yrs	77/5.4	14.3 (11.3,17.9)	1.1 (0.8,1.6)
	25-34 yrs	56/4.2	13.4 (10.1,17.4)	1.6 (1.1,2.3)
	35-44 yrs	41/2.2	18.6 (13.3,25.2)	3.2 (2.0,4.9)
	45+yrs	12/0.8	15.3 (7.9,26.7)	3.7 (1.9,7.3)
	Ptrend		0.194	<0.001

PanCareSurFup cohort : 297 genito-urinary secondary cancers

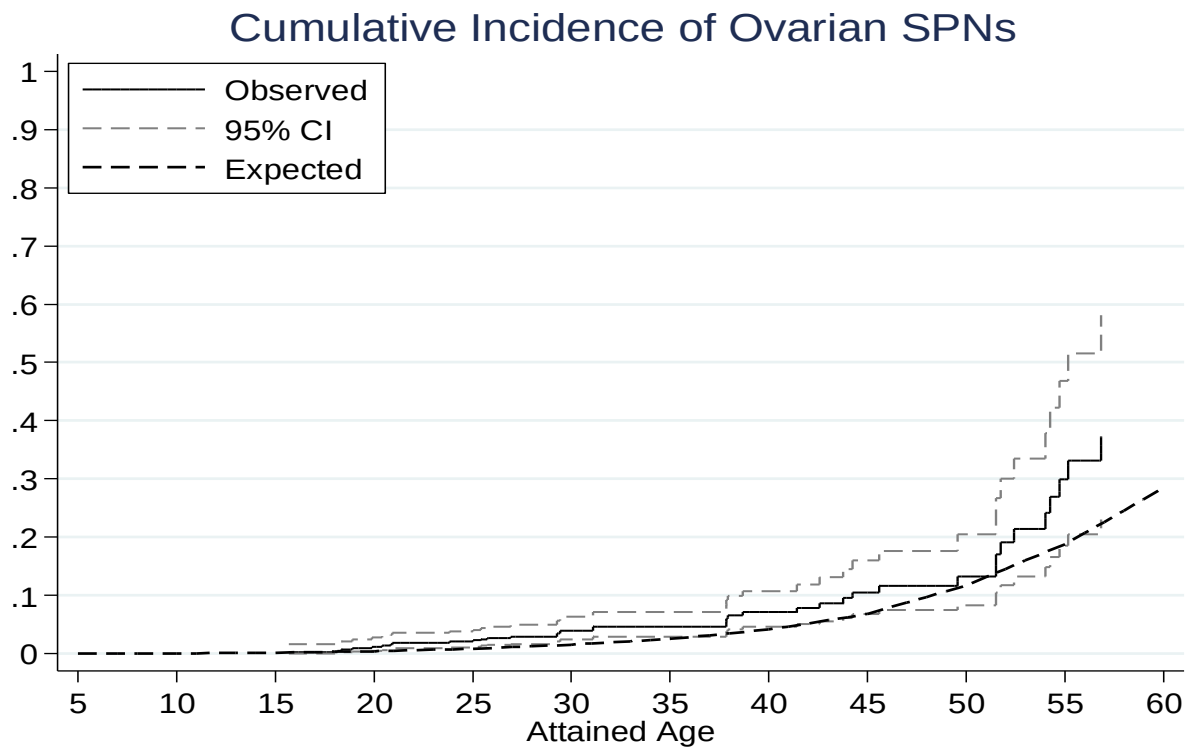


PanCareSurFup cohort : 73 Kidney and 48 bladder secondary cancers

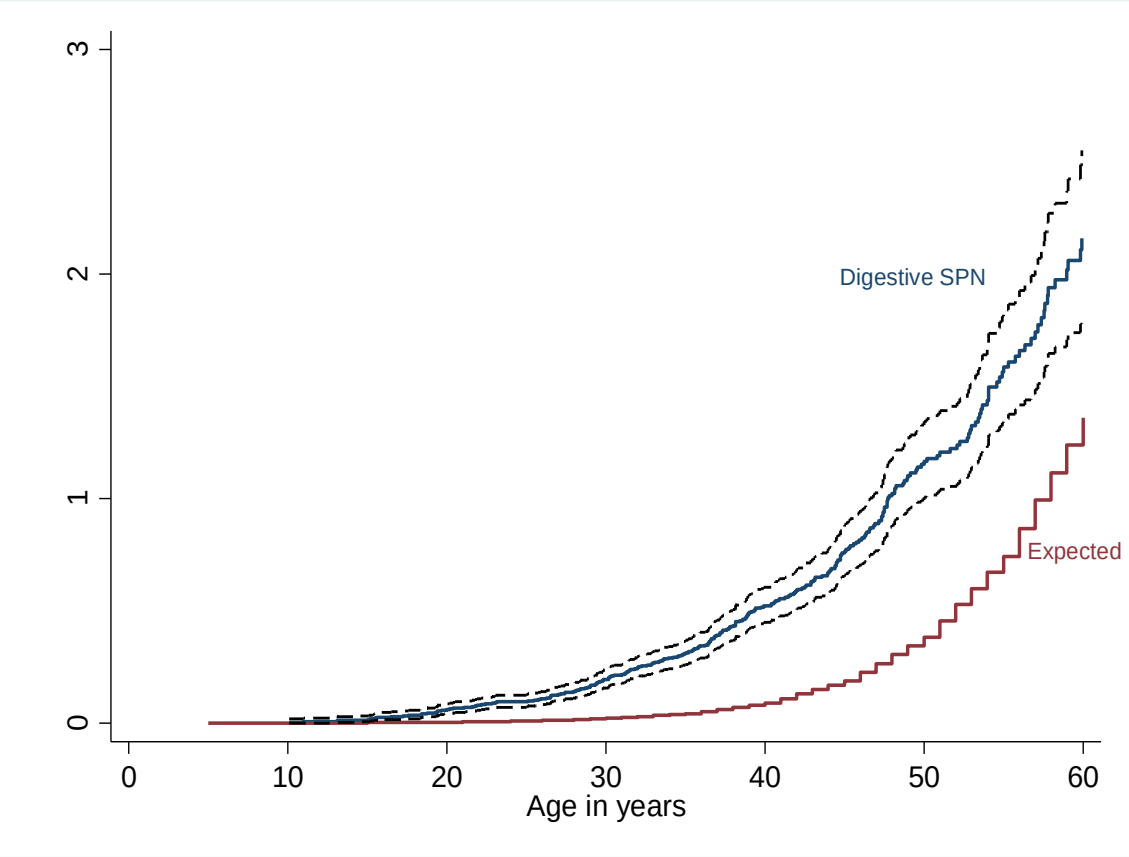




PanCareSurFup cohort : 40 secondary ovary cancers



PanCareSurFup cohort : 323 secondary digestive cancers



PanCareSurFup cohort : 323 second digestive cancers

Factor	level	O/E	SIR (95% CI)	RER (95% CI)
Overall	All combined	323/84.6	3.8 (3.4, 4.3)	NA[1]
Sex	Male	202/47.9	4.2 (3.7, 4.8)	1.0 (REF)
	Female	121/36.7	3.3 (2.8, 3.9)	0.6 (0.4, 0.8)
	$P_{heterogeneity}$			0.001
Age at Diagnosis	0-4 yrs	94/14.70	6.4 (5.2, 7.8)	1.0 (REF)
	5-9 yrs	75/14.17	5.3 (4.2, 6.6)	1.2 (0.8, 1.7)
	10-14 yrs	89/28.23	3.2 (2.6, 3.9)	0.8 (0.5, 1.2)
	15-19yrs	65/27.46	2.4 (1.9, 3.0)	0.8 (0.4, 1.5)
	P_{trend}			0.270
Era of Diagnosis	<1970	136/57.27	2.4 (2.0, 2.8)	1.0 (REF)
	1970-1979	111/16.70	6.6 (5.5, 8.0)	1.3 (0.9, 1.9)
	1980-1989	59/8.14	7.2 (5.6, 9.4)	1.1 (0.7, 1.7)
	1990-1999	14/2.23	6.3 (3.7, 10.6)	0.8 (0.4, 1.8)
	>=2000	3/0.22	13.9 (4.5, 43.2)	1.3 (0.3, 5.6)
	P_{trend}			0.610
Attained Age	0-19 yrs	25/1.69	14.8 (10.0, 21.8)	1.0 (REF)
	20-29 yrs	70/7.12	9.8 (7.8, 12.4)	2.9 (1.7, 5.0)
	30-39 yrs	92/15.37	6.0 (4.9, 7.3)	7.0 (4.1, 12.0)
	40-49 yrs	75/24.26	3.1 (2.5, 3.9)	14.9 (8.1, 27.4)
	50+ yrs	61/36.11	1.7 (1.3, 2.2)	19.1 (8.2, 45.0)
	P_{trend}			< 0.01

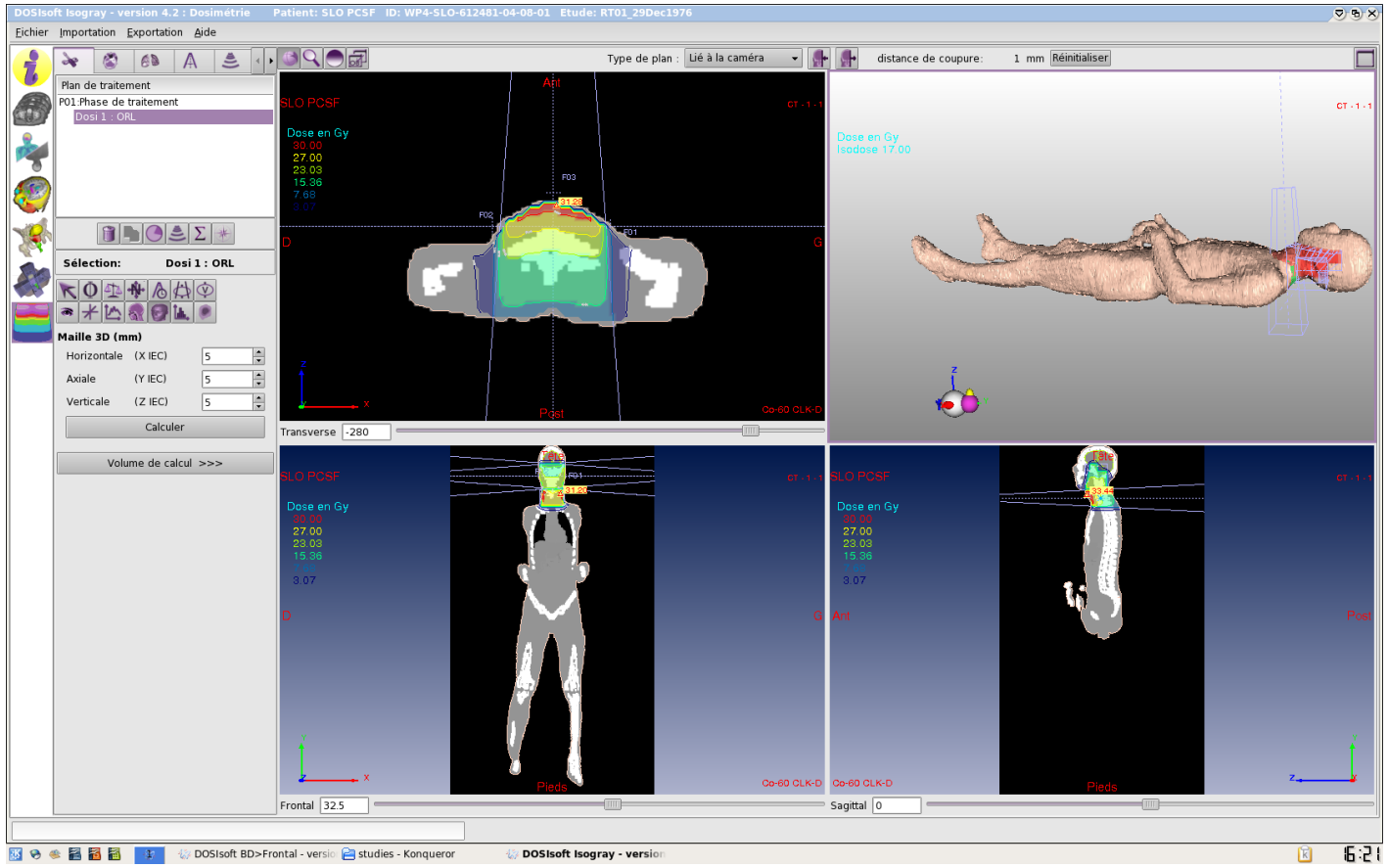
PanCareSurFup cohort : 154 colorectal cancers

Factor	level	O/E	SIR (95% CI)	RER (95% CI)
Overall	All combined	154/48.46	3.2 (2.7, 3.7)	NA[1]
Age at	0-4 yrs	41/8.56	4.8 (3.5, 6.5)	1.0 (REF)
diagnosis	5-9 yrs	43/8.16	5.3 (3.9, 7.1)	0.9 (0.5, 1.8)
	10-14 yrs	42/16.13	2.6 (1.9, 3.5)	0.3 (0.1, 0.7)
	15-19yrs	28/15.61	1.8 (1.2, 2.6)	0.2 (0.0, 0.5)
	P_{trend}			< 0.01
Era of	<1970	68/32.26	2.1 (1.7, 2.7)	1.0 (REF)
diagnosis	1970-1979	52/9.64	5.4 (4.1, 7.1)	5.3 (2.3, 12.0)
	1980-1989	24/4.94	4.9 (3.3, 7.2)	7.0 (2.4, 20.6)
	1990-1999	7/1.46	4.8 (2.3, 10.0)	14.0 (3.1, 64.6)
	>=2000	3/0.15	19.6 (6.3, 60.7)	84.1 (12.5, 564.0)
	P_{trend}			< 0.01
Attained Age	0-19 yrs	4/0.98	4.1 (1.5, 10.8)	1.0 (REF)
	20-29 yrs	27/4.47	6.0 (4.1, 8.8)	7.6 (2.1, 27.2)
	30-39 yrs	37/8.95	4.1 (3.0, 5.7)	19.4 (5.4, 69.3)
	40-49 yrs	39/13.65	2.9 (2.1, 3.9)	64.7 (18.0, 232.7)
	50+ yrs	47/20.41	2.3 (1.7, 3.1)	164.5 (42.4, 638.8)
	P_{trend}			< 0.01

Dosimetry in PCSF

General principles :

- Using medical records
- Extension of TPS calculation
- Analytical calculations
- Voxelized (2mm) phantoms in treatment positions
- Localisation of SMN by medical doctors



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A multi-plane source model for out-of-field head scatter dose calculations in external beam photon therapy

FEATURED ARTICLE

Mohamed Amine Benadjaoud[1,2,3], Jérémi Bezin[1,2,3], Attila Veres[4], Dimitri Lefkopoulos[2], Jean Chavaudra[2], André Bridier[2], Florent de Vathaire[1,2,3] and Ibrahima Diallo[1,2,3]

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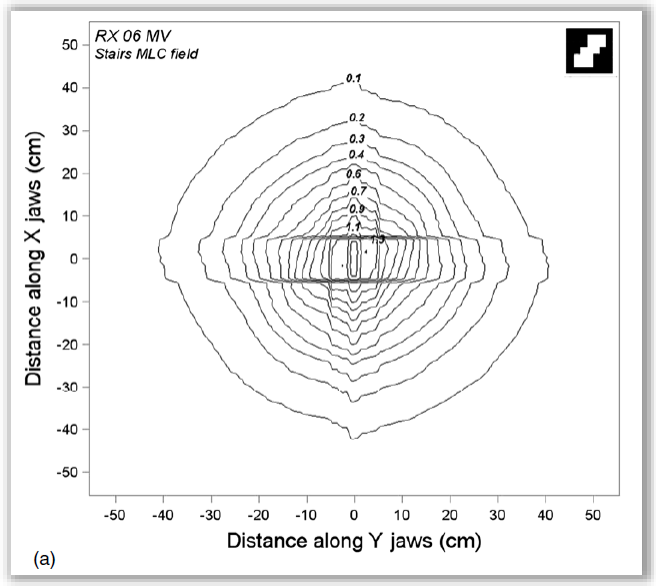

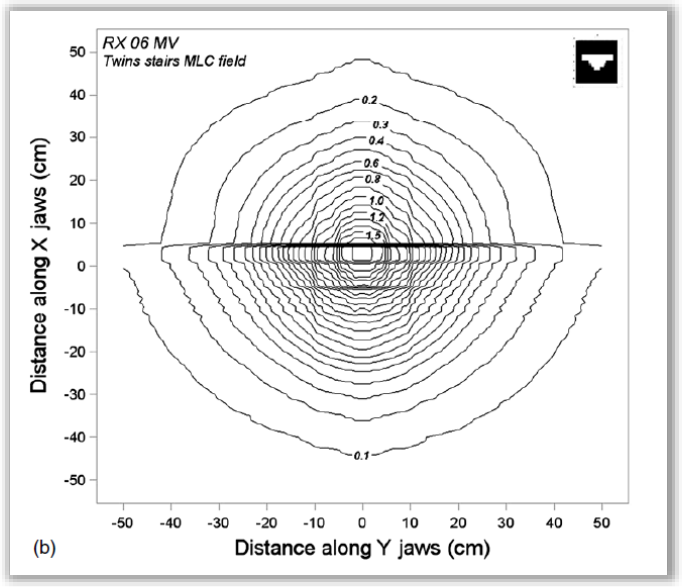

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Phys. Med. Biol. **60** (2015) 2103–2116 doi:10.1088/0031-9155/60/5/2103

Field size dependent mapping of medical linear accelerator radiation leakage

Jérémi Vũ Bezin[1,2,3], Attila Veres[4], Dimitri Lefkopoulos[3], Jean Chavaudra[3], Eric Deutsch[3,5], Florent de Vathaire[1,2,3] and Ibrahima Diallo[1,2,3]

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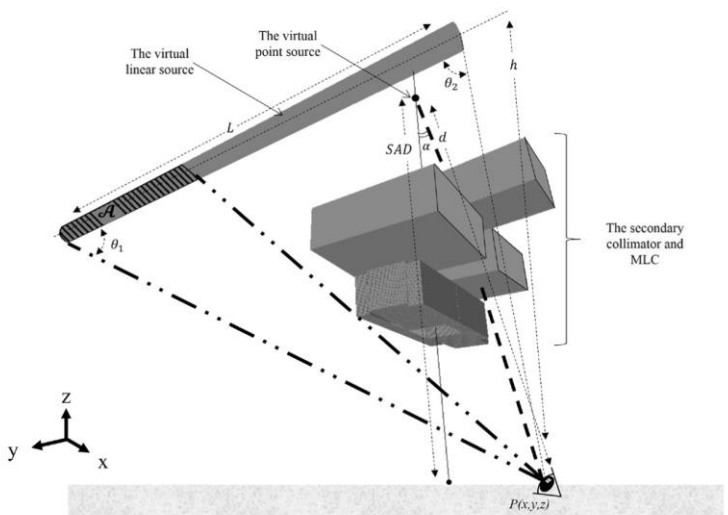
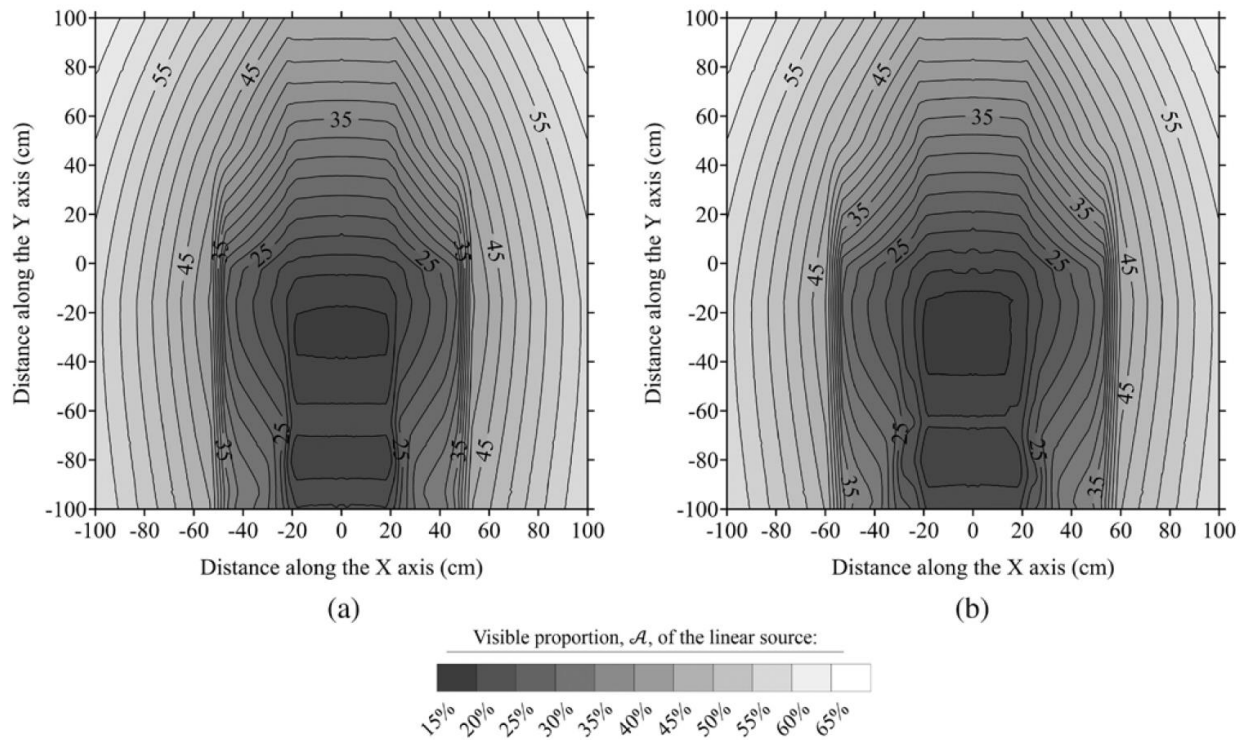


Figure 2. 3D rendering of a four-jaws-plus-MLC linac using the GL OpenGL. The point of calculation $P(x, y, z)$ is located in a plane perpendicular to the beam central axis, at the level of the isocentre and pictured here as a schematic eye.



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Phys. Med. Biol. 55 (2010) N507–N519 doi:10.1088/0031-9155/55/21/N02

NOTE

Thyroid volume measurement in external beam radiotherapy patients using CT imaging: correlation with clinical and anthropometric characteristics

C Veres[1,2,3], J P Garsi[1,2,3], C Rubino[1,2,3], F Pouzoulet[3,4,5], F Bidault[3], J Chavaudra[3], A Bridier[3], M Ricard[3], I Ferreira[3], D Lefkopoulos[3], F de Vathaire[1,2,3] and I Diallo[1,2,3]

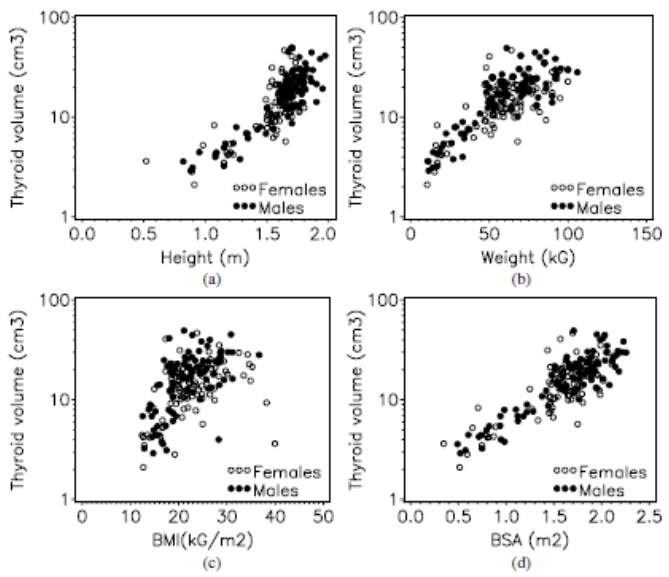

Figure 4. Variation in 'true thyroid volume' according to anthropometric parameters. (a) Height, (b) weight, (c) body mass index and (d) body surface area.

Table 4. Median values for thyroid volume evaluated by equation (6) for children and equation (7) for adults among patients under study.

	Thyroid volume (cm^3)			
	Adults		Children[a]	
BSA(m^2)	Males ($n = 61$)	Females ($n = 71$)	Males ($n = 30$)	Females ($n = 26$)
0.3	–	–	–	2.7
0.5	–	–	3.1	3.3
0.6	–	–	3.4	3.5
0.7	–	–	4.4	4.3
0.8	–	–	4.8	4.6
0.9	–	–	5.3	5.3
1.0	–	–	6.0	–
1.1	–	–	7.2	–
1.2	–	–	8.3	9.1
1.3	–	–	8.7	9.1
1.4	15.3	13.2	10.2	–
1.5	16.5	13.8	11.6	11.7
1.6	18.1	14.8	12.8	13.6
1.7	19.2	16.2	15.5	13.4
1.8	20.5	17.5	16.2	15.8
1.9	22.3	18.8	–	–
2.0	24.6	20.2	19.4	–
2.1	26.7	22.2	–	–
2.2	28.1	–	–	–
2.3	29.9	–	–	–

[a] Patients less than 20 years old.

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Total heart volume as a function of clinical and anthropometric parameters in a population of external beam radiation therapy patients

Audrey Nadège Ilembe Badouna[1,2,3], Cristina Veres[1,2,3], Nadia Haddy[1,2,3], François Bidault[2], Dimitri Lefkopoulos[2], Jean Chavaudra[2], André Bridier[2], Florent de Vathaire[1,2,3] and Ibrahima Diallo[1,2,3]

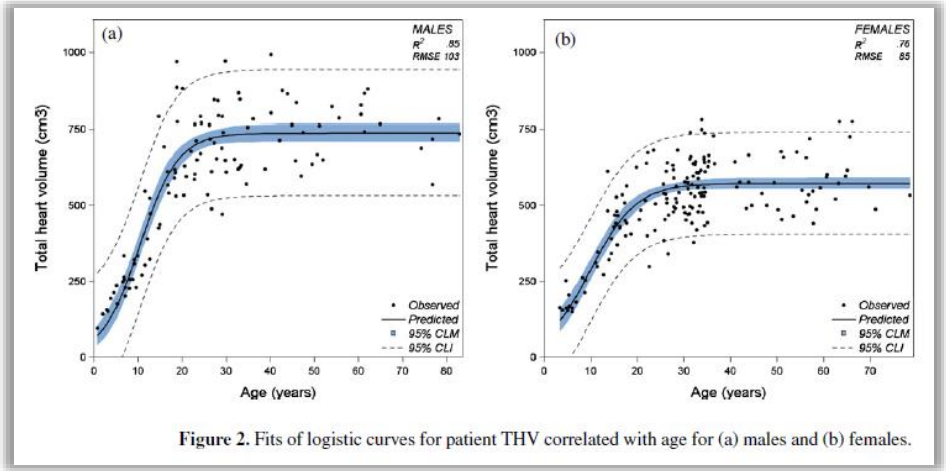

Figure 2. Fits of logistic curves for patient THV correlated with age for (a) males and (b) females.

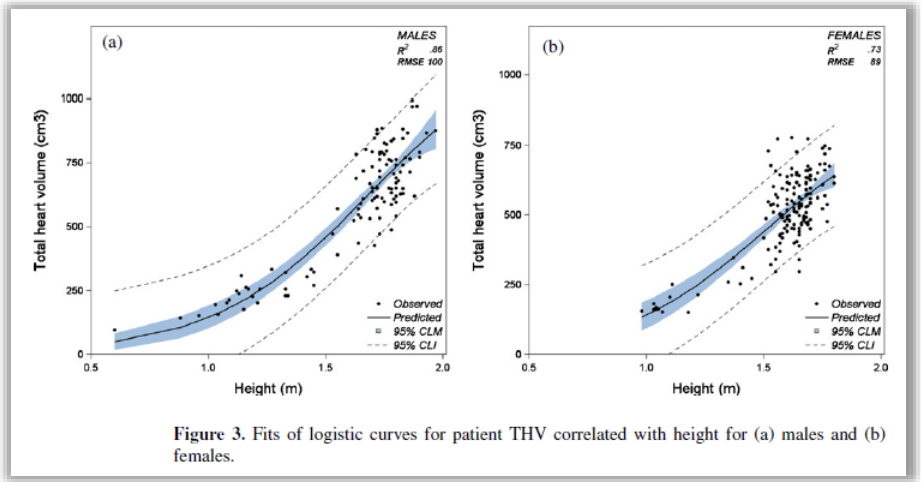

Figure 3. Fits of logistic curves for patient THV correlated with height for (a) males and (b) females.

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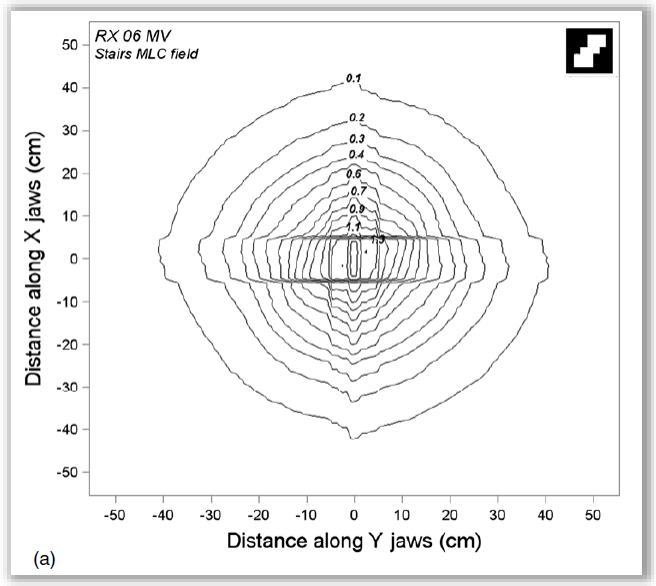
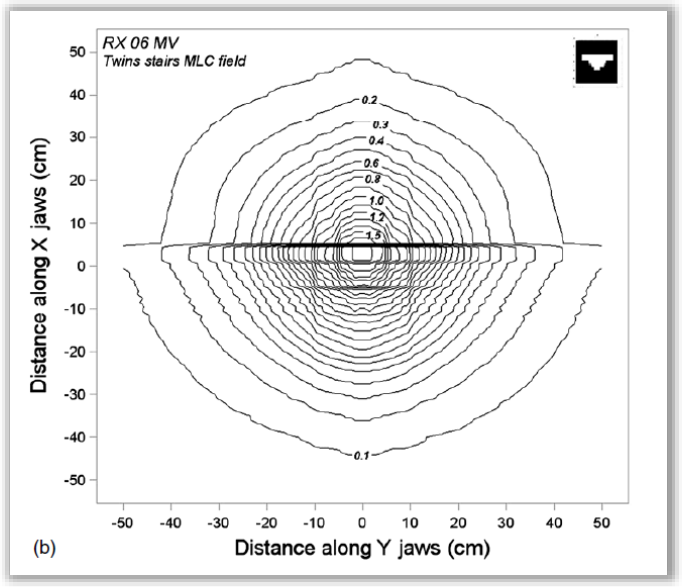
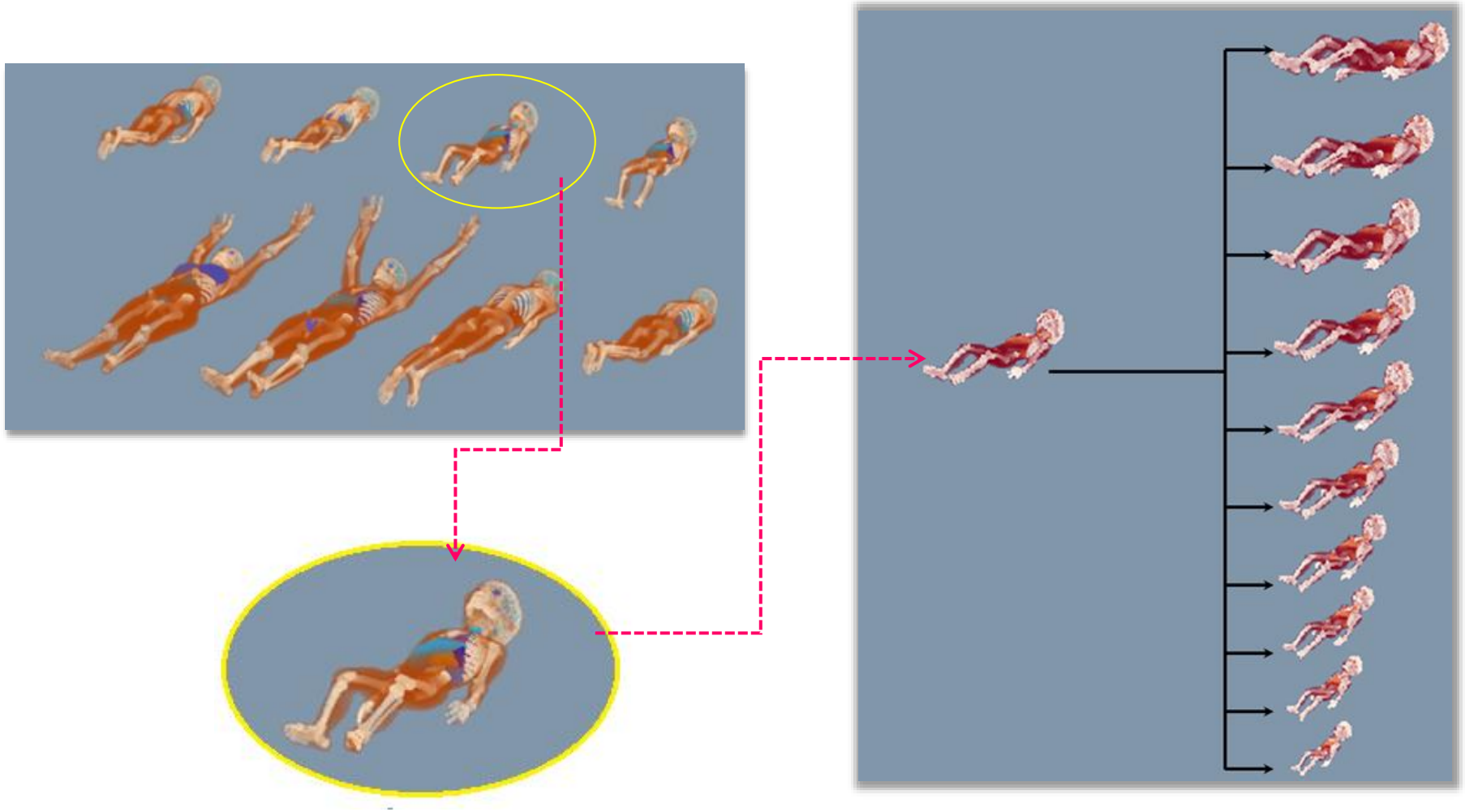


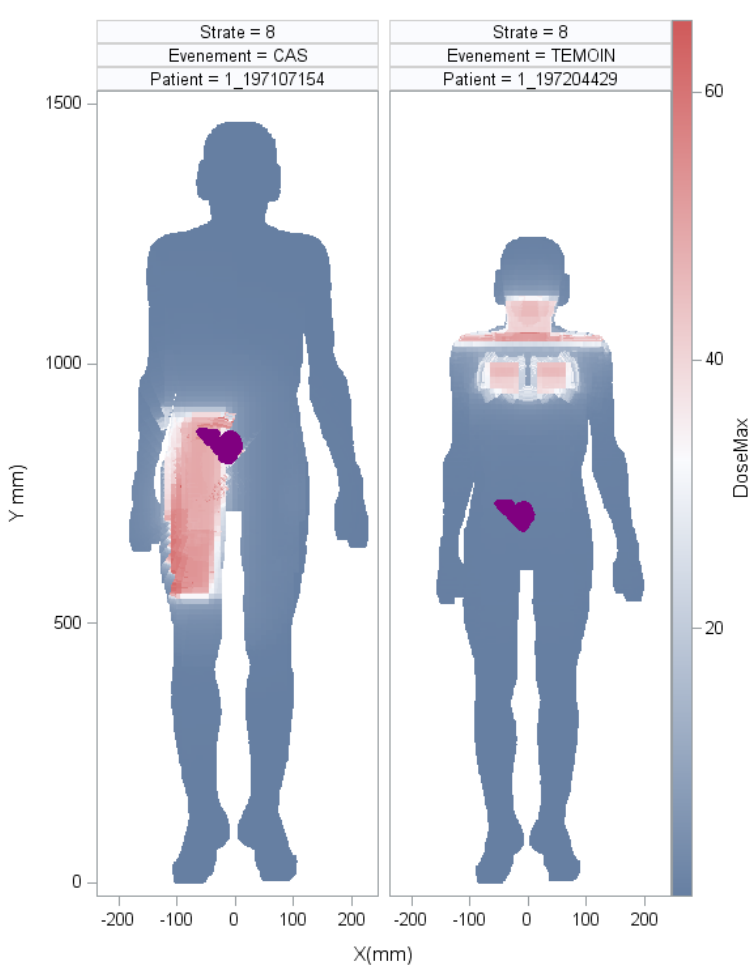


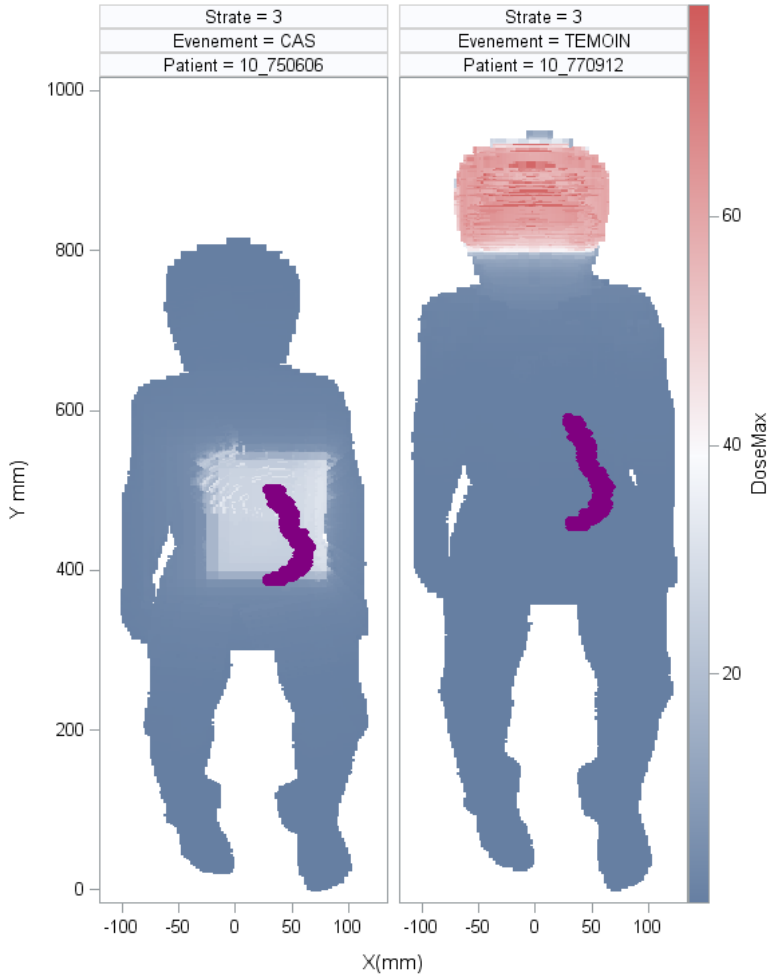
Initial library of childhood and adolescent in cancer position

Derivated phantoms (auxology)



Exemples of dosimetric reconstuction in PCSF : cases (left) and controls (right)





Main issue : dose-volume considerations

Radiation therapists cannot use results and dose-response relationships of epidemiologists based on mean dose. This, also for relatively smal organs.

Epidemiologists have to try to use concepts and parameters which could facilitate discussion with radiation-therapists

Is it possible to use classical dosimetric parameter used by radiation therapists, such as Dx% and VxGy ?

Exemples : Strokes in CerebRad european project

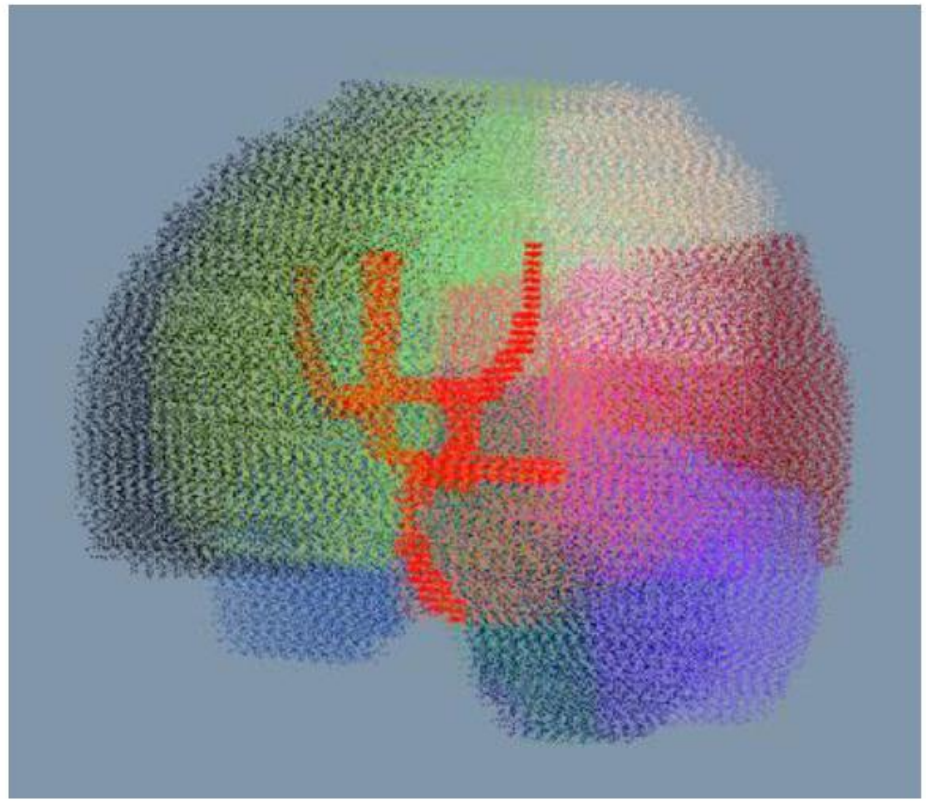
thyroid cancer as a SMN in a French/UK cohort.

CerebRad case-control study : strokes after childhood cancers

Table 1-2– Type of childhood cancer of the cases of stroke included in the CerebRad case-control study.

Childhood cancer type	France (130)	UK (75)	The Netherlands (29)	Whole case-control study (233)
Wilms tumor	4	0	1	5
Neuroblastoma	9	1	0	10
Lymphoma	20	9	7	36
Soft tissue sarcoma	13	1	3	14
Bone sarcoma	4	2	0	6
Central Nervous System tumour	65	49	8	122
Gonadal	3	4	1	8
Leukaemia	1	5	8	14

Figure 1-1 3D representation of the voxels available at brain level for the calculation of the brain sub- structures doses distributions in the case of a 17 years aged male patient



CerebRad : dose-response,when using mean dose to brain arteries

Figure 1-5 - Odds-ratio of ischemic stroke as a function of the average radiation dose received to the cerebral arteries: observed values and linear exponential model

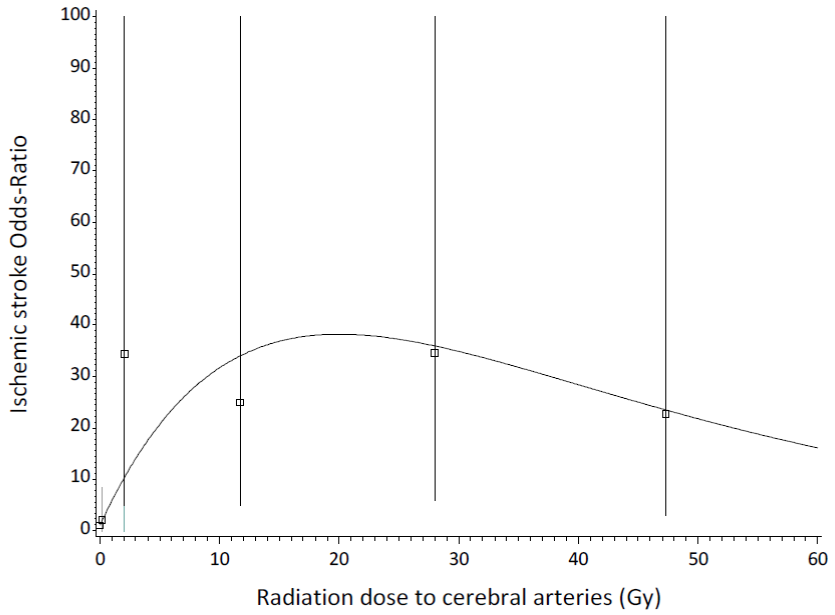
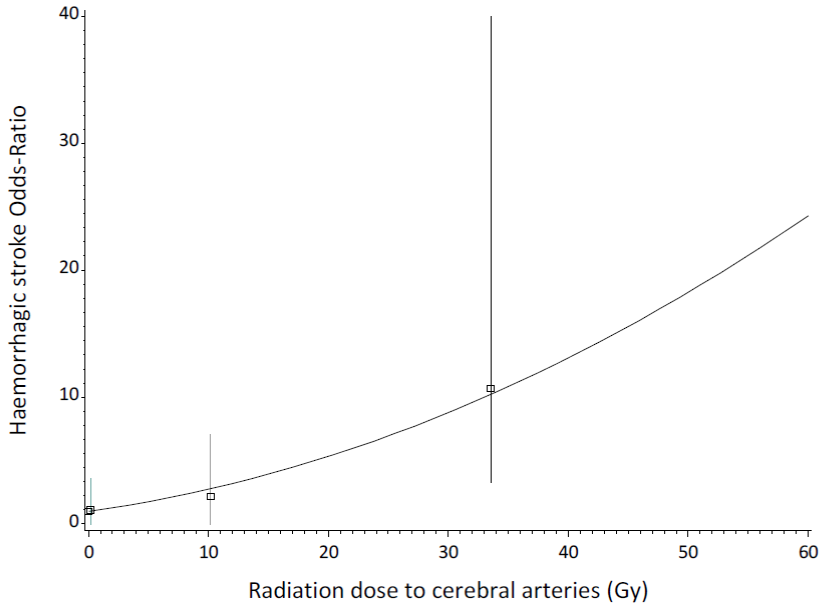


Figure 1-6 - Odds-ratio of haemorrhagic stroke as a function of the average radiation dose received to the cerebral arteries: observed values and linear quadratic model



CerebRad : All strokes, dose distribution in the whole cerebral arteries

	All strokes			
	n/N	OR (95%CI)	p-value	Chi-2
%V of arteries received:				
0 (No RT)		1 (ref)		
>0-2 Gy		2.3 (1.1-4.9)	0.03	0.83
2-5 Gy		27.8 (4.9-129.7)	<.0001	3.3
5-20 Gy		55.2 (11.7-260.4)	<.0001	4.0
20-40 Gy		11.9 (3.9-36.7)	<.0001	2.5
40+ Gy		53.3 (12.6-225.7)	<.0001	4.0
Heart dose : mean, Gy		1.0 (0.99-1.1)	0.08	0.05
Lung dose : mean, Gy		0.92 (0.86-0.99)	0.02	-0.08
Brain tumor as 1st cancer (y/n)	70/228	1.4 (0.74-2.78)	0.28	0.36
Chemotherapy drugs : n		1.1 (0.97-1.2)	0.17	0.07

CerebRad : CerebRad : All strokes, dose distribution in the whole cerebral arteries

	All strokes			
	n/N	OR (95%CI)	p-value	Chi-2
D40% to cerebral arteries (Gy)				
0 (No RT)				
> 0-5	48/571	3.0 (1.4-6.1)	0.003	1.08
5-15	26/86	14.7 (6.0-36.3)	<.0001	2.7
15-25	9/57	7.2 (2.6-20.0)	0.0001	2.0
25-50	39/113	19.3 (7.5-49.3)	<.0001	3.0
+50	5/13	28.0 (6.2-125.6)	<.0001	3.3
Heart dose : mean, Gy		1.1 (1.0-1.1)	0.05	0.05
Lung dose : mean, Gy		0.91 (0.85-0.97)	0.003	-0.1
Brain tumor as 1st cancer (y/n)	70/228	2.91 (1.7-5.0)	0.0001	1.1
Chemotherapy drugs : n		1.1 (0.97-1.2)	0.21	0.06

CerebRad : ischemic strokes, dose distribution in the whole cerebral arteries

	Ischemic strokes			
	n/N	OR (95%CI)	p-value	Chi-2
%V of arteries received:				
0 (No RT)		1 (ref)		
> 0-2 Gy		1.6 (0.39-6.8)	0.50	0.49
2-5 Gy		?	<.0001	7.0
5-20 Gy		62.9 (5.8-678.7)	0.001	4.1
20-40 Gy		42.5 (6.2-292.5)	0.0001	3.7
40+ Gy		110.0 (12.9-936.8)	<.0001	4.7
Heart dose : mean, Gy		1.1 (0.98-1.1)	0.14	0.06
Lung dose : mean, Gy		0.88 (0.80-0.97)	0.01	-0.13
Brain tumor as 1st cancer (y/n)	41/120	2.4 (0.93-6.0)	0.07	0.85
Chemotherapy drugs : n		1.2 (0.98-1.4)	0.08	0.15

CerebRad : ischemic strokes, dose distribution in the whole cerebral arteries

	Ischemic strokes			
	n/N	OR (95%CI)	p-value	Chi-2
D30% to cerebral arteries (Gy)				
0 (No RT)		1 (ref)		
> 0-5	15/292	3.1 (0.81-11.9)	0.10	1.1
5-15	16/44	31.9 (7.2-140.8)	<.0001	3.5
15-25	5/27	20.9 (3.9-113.3)	0.0004	3.0
25-50	27/67	56.9 (12.8-252.8)	<.0001	4.0
+50	8/21	63.7 (10.5-388.0)	<.0001	4.2
Heart dose : mean, Gy		1.01 (0.94-1.1)	0.73	0.01
Lung dose : mean, Gy		0.93 (0.8-1.0)	0.11	-0.07
Brain tumor as 1st cancer (y/n)	41/120	3.18 (1.4-7.	0.006	1.2
Chemotherapy drugs : n		1.14 (1.0-1.3)	0.13	0.13

Strokes in Cerebrad

Very preliminary descriptive results, but it seems that classical parameters used by radiation therapists could be use in epidemiology of second cancers.

- Efficient communication with radiation therapists, and more usefull results
- Not shown : no better prediction when working on the exact artery in which stroke occured (known for about 60% of cases) than when working on whole cerebral arteries
- Individual prediction of SMN risks in TPS ?

Second thyroid cancers : EURO2K French-UK cohort

Table 1. Multivariate analysis of the thyroid carcinoma risk in a cohort of 4338 5-year childhood cancer survivors

	Thyroid carcinomas / patients	Average thyroid radiation dose (Gy)	Standardized incidence ratio* (95%CI)	Absolute excess risk per 1000 people per year (95C%I)	Relative risk (95%CI)**
All cohort	55/4338	3.8	20.0 (15.2–25.8)	0.43 (0.31–0.57)	
Gender					
Female	30/1919	3.4	14.6 (10.0–20.5)	0.49 (0.30–073)	1.5 (0.9–2.5)
Male	25/2429	4.1	35.7 (25.3–51.6)	0.38 (0.25–0.56)	1 (ref)
Nitrosoureas (BCNU or CCNU)					
No	46/4089	3.6	17.5 (13.0–23.1)	0.36 (0.26–0.51)	1 (ref)
Yes	9/249	7.2	67.9 (32.7–122.5)	1.5 (0.70–2.8)	6.6 (2.5–15.7)
Rx dose to pituitary gland > 10 Gy					
No	47/3497	3.1	21.3 (15.8–28.0)	0.45 (0.32–0.62)	1 (ref)
Yes	8/841	6.3	14.5 (6.7–27.2)	0.32 (0.12–0.64)	0.2 (0.1–0.6)
Splenectomy or Rx dose to the spleen > 20 Gy					
No	33/3787	3.1	13.9 (9.7–19.2)	0.28 (0.17–0.41)	1 (ref)
Yes	22/551	8.9	58.2 (37.2–86.1)	1.4 (0.90–2.2)	2.3 (1.3–4.0)
Average thyroid radiation dose (Gy)					
No Rt	6/1646	0	8.6 (3.4–17.5)	0.12 (0.02–0.29)	1* (ref)
>0 to 0.9 Gy	9/1529	0.3	7.2 (3.3–13.5)	0.14 (0.04–0.30)	1.3 (0.5–4.2)
1 to 4.9 Gy	12/471	2.3	32.9 (17.6–55.1)	0.80 (0.39–1.4)	6.9 (2.4–21.4)
5 to 19.9 Gy	16/362	11.7	58.0 (34.2–109.5)	1.6 (0.89–2.5)	8.7 (3.2–26.4)
20 to 39.9 Gy	11/263	28.6	63.9 (33.2–109.5)	1.6 (0.79–2.8)	13.8 (4.5–45.5)
40 Gy or more	1/67	48.8	23.5 (1.3–103.7)	0.59 (?–2.6)	4.9 (0.3–32.0)

* Number of observed thyroid carcinoma divided by the expected number of thyroid carcinoma in the cohort, from the incidence in French and UK populations.

** Relative Risk in a Poisson Regression adjusted for gender, date and age of diagnosis, country of treatment (UK / France), surgical or radiological (>20 Gy to the spleen) splenectomy, radiation dose to the pituitary and thyroid glands, nitrosourea administration, and attained age, as compared to the SIR for nephroblastoma patients.

Dose distribution in the thyroid gland, by category of average radiation dose to thyroid

Average radiation dose to thyroid	N	% of the thyroid volume having received				
		0 to 1 Gy	1 to 5 Gy	5 to 20 Gy	20 to 40 Gy	40 Gy or more
No rx	1787					
0-1 Gy	1091	**96.02**	3.92	0.04	0	0
1-5 Gy	683	13.23	**81.59**	5.11	0.06	0
5-20 Gy	440	1.77	21.49	**64.15**	11.88	0.70
20-40 Gy	264	0.54	1.25	19.07	**64.45**	14.68
40+ Gy	74	0.00	0.05	2.50	18.36	**79.08**
Total patients with RT		***45.0***	***27.4***	***14.5***	***9.3***	***3.9***

Analyse with classical VxGy used by radiation therapists (a seraparate analysis for each parameter)

VxGy	Thyroid cancer relative risk		
	Relative Risk and 95% CI	P-value	AIC
V0.5Gy	4.0 (2.0-7.8)	<0.0001	719.5
V1Gy	4.3 (2.3-8.1)	<0.0001	716.7
V2Gy	4.7 (2.5-8.8)	<0.0001	714.5
V5Gy	4.3 (2.2-8.3)	<0.0001	720.1
V10 Gy	3.6 (1.7-7.7)	0.0008	727.4
V20 Gy	1.5 (0.5-3.9)	0.5	737.2
V40 Gy	3.5 (0.8-15.3)	0.1	735.4

Relative risk of thyroid cancer per category of V5Gy

V5Gy (in % of the thyroid volume)	K thyr / Patients	Thyroid cancer relative risk	
		Relative Risk and 95% CI	P-value
Pas de RT	6/1787	1	
0 – 25	21/1738	1.0 (0.6-2.5)	0.6
25-50	2/108	4.0 (1.1-14.3)	0.03
50-75	6/112	7.4 (2.8-20.6)	<0.0001
75-100	13/243	5.2 (2.4-11.3)	<0.0001

Relative risk of thyroid cancer per category of V15Gy

V15Gy (in % of the thyroid volume)	K thyr / Patients	Thyroid cancer relative risk	
		Relative Risk and 95% CI	P-value
Pas de RT	6/1787	1	
0 – 25	34/2027	2.7 (1.2-6.5)	0.02
25-50	7/123	6.9 (2.3-21.2)	0.0007
50-75	5/106	8.4 (2.6-27.8)	0.0004
75-100	5/155	7.5 (2.3-24.7)	0.0009

Relative risk of thyroid cancer per percent of the thyroid volume

Dose range	Thyroid cancer relative risk per fraction of the thyroid volume		Thyroid cancer relative risk per fraction of the thyroid volume	
	Relative Risk and 95% CI	P-value	Relative Risk and 95% CI	P-value
0 (no RT)	1 (ref)		1 (ref)	
>0-1 Gy	1.4 (0.5-3.9)	0.5	1.4 (0.5-3.9)	0.5
1-5 Gy	3.2 (1.1-9.3)	0.04	3.2 (1.1-9.4)	0.04
5-20 Gy	10.3 (3.7-28.3)	<0.0001	9.8 (3.5-26.9)	<0.0001
20-40 Gy	1.5 (0.3-8.2)	0.6	3.4 (1.0-12.1)	0.05
40 +	11.1 (2.2-56.3)	0.004		

Thanks for your attention