SCK•CEN
STUDIECENTRUM VOOR KERNENERGIE
CENTRE D'ETUDE DE L'ENERGIE NUCLEAIRE

SCK•CEN ACADEMY
FOR NUCLEAR SCIENCE AND TECHNOLOGY

Emerging issues with regard to organ/tissue doses

The thyroid: a radiosensitive organ

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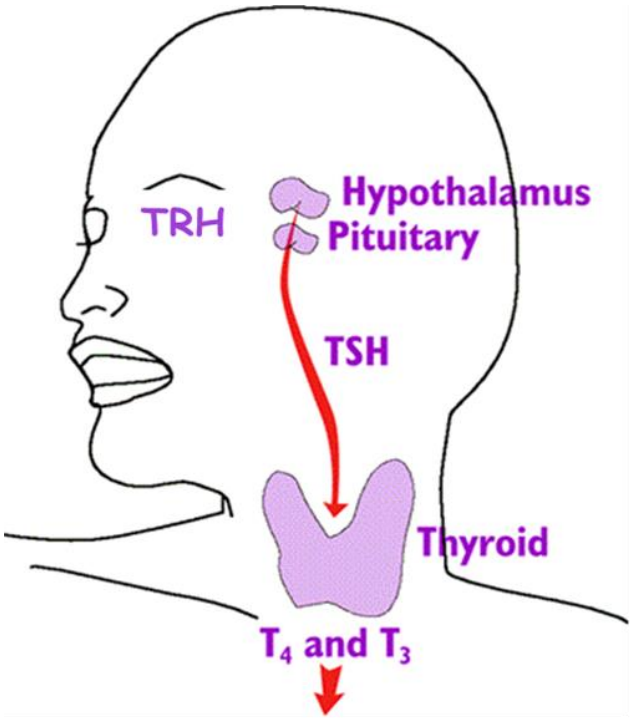
Belgian Society for Radiation Protection 09-12-2016

Thyroid: gland and hormones



\+ **Iodine** } T3 and T4

Control of metabolism rate

- Lipid metabolism
- Carbohydrate metabolism
- Body temperature
- Growth
- Brain development (fetal/neonatal)
- Cardiovascular system
- Reproductive system

- Disturbed TH production: thyroid disorders

Thyroid disorders and cancers

- Thyroid disorders :
  - Hyperthyroidism : *Metabolism is accelerated*
  - Hypothyroidism: *Metabolism slowdown*
  - Goiter: *Enlarged thyroid: linked to iodine deficiency*

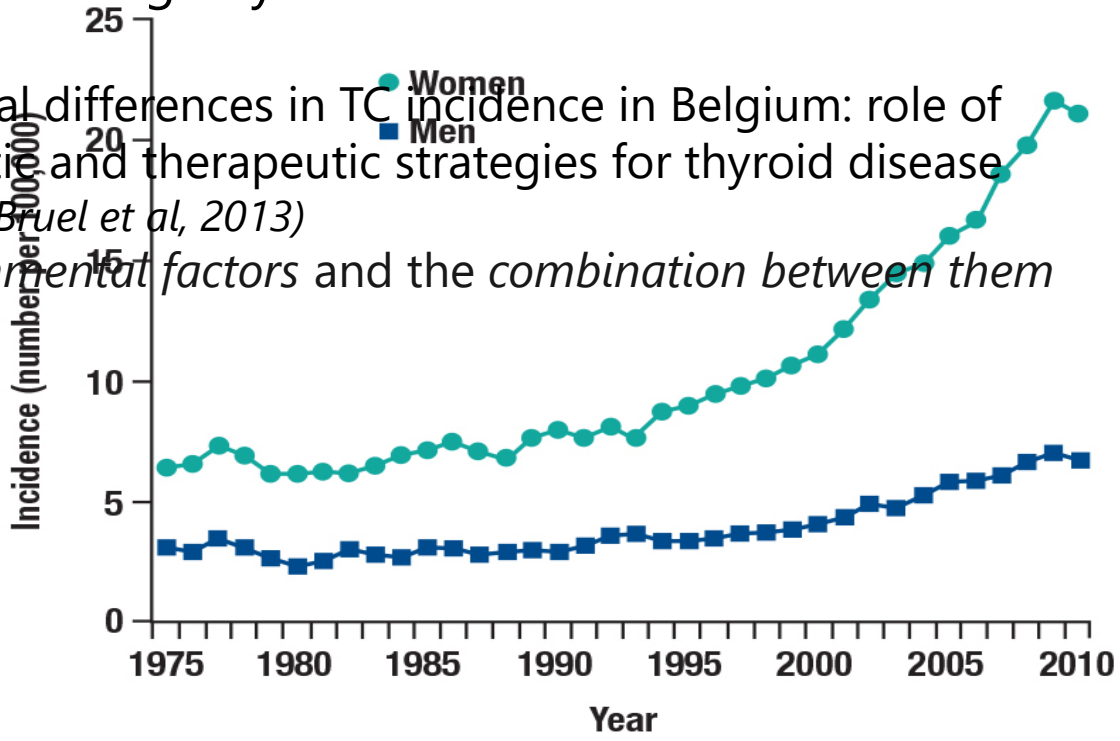
- Thyroid cancers :
  - 4 types: Papillary, Follicular, Medullary, Anaplastic
  - Annual incidence : ~ 6/100,000
  - Thyroid cancer is most common endocrine cancer
  - Gender ratio is 3:1 (Female:Male)
  - Peak after 30, aggressiveness increases with old age

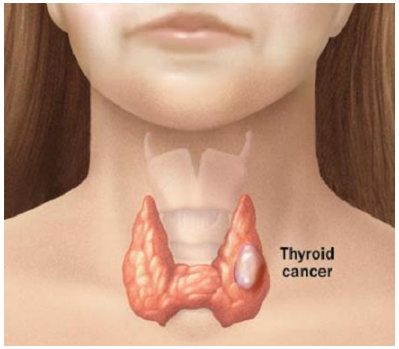
Thyroid Cancer

- Thyroid cancer incidence is rapidly increasing worldwide.

Belgian Cancer Registry Foundation:

- Regional differences in TC incidence in Belgium: role of diagnostic and therapeutic strategies for thyroid disease *(Van den Bruel et al, 2013)*
- E*nvironmental factors* and the *combination between them*





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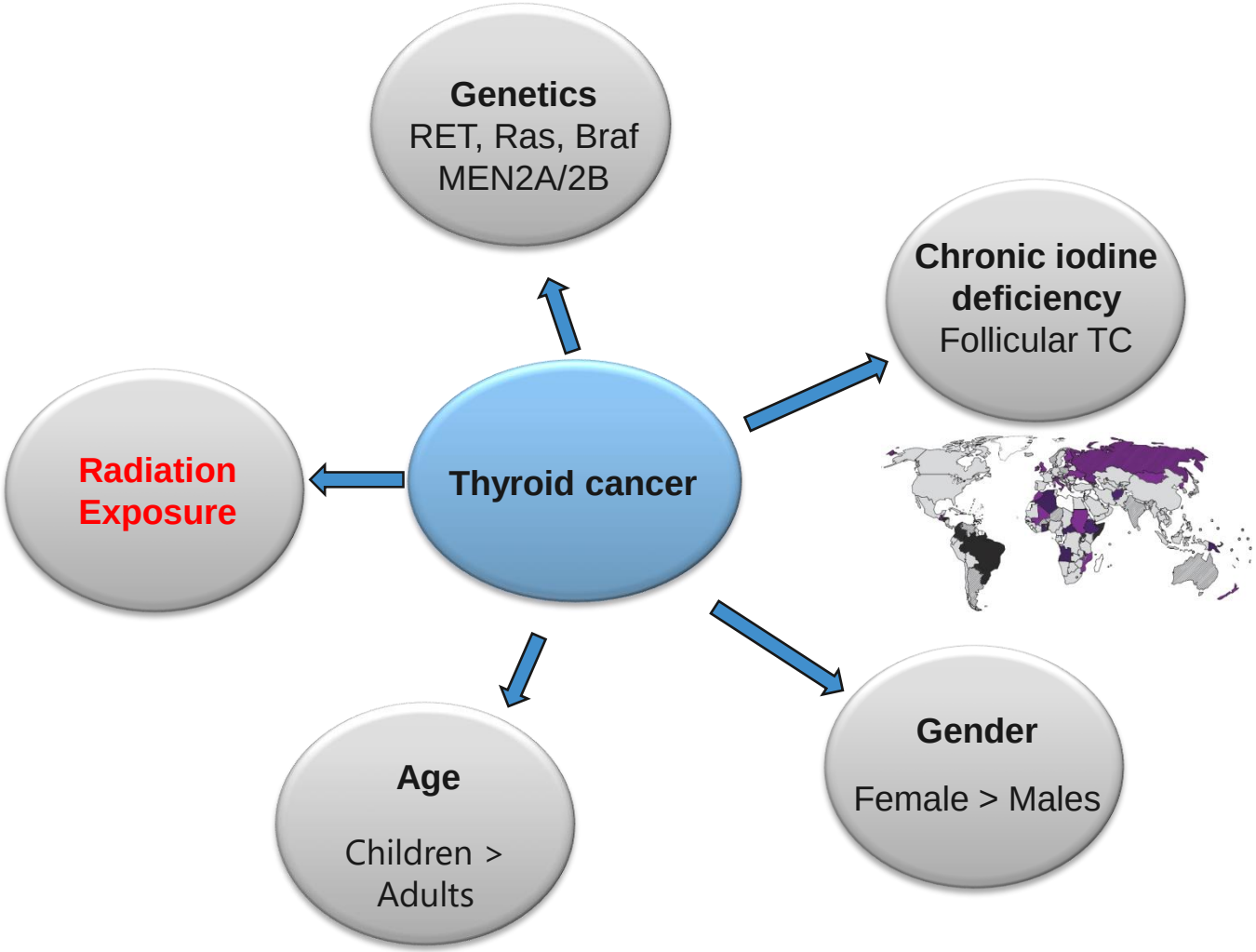
SEER Cancer Statistics

Causes and risk factors of thyroid cancer



Induction of thyroid cancer by ionising radiation

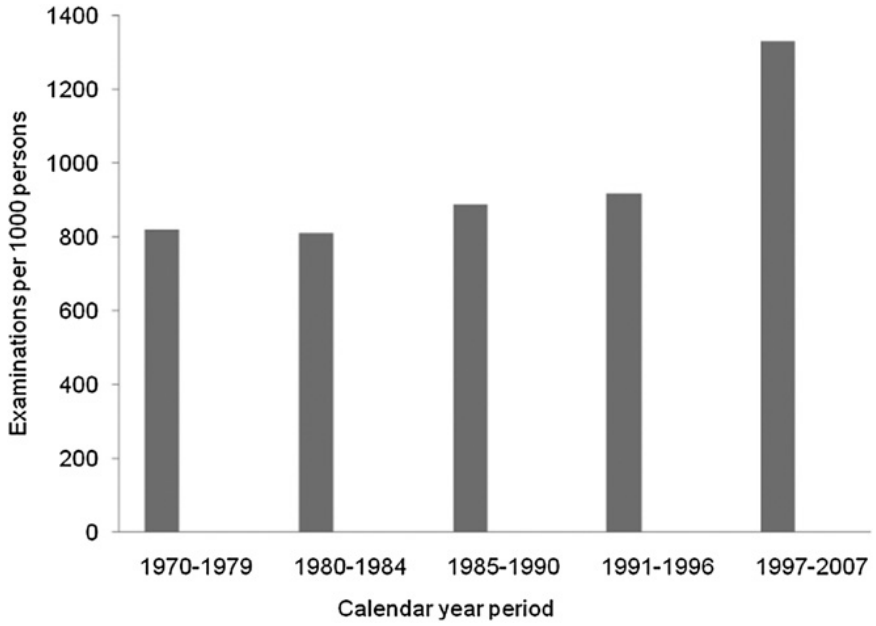
Human experience after exposure to radiation

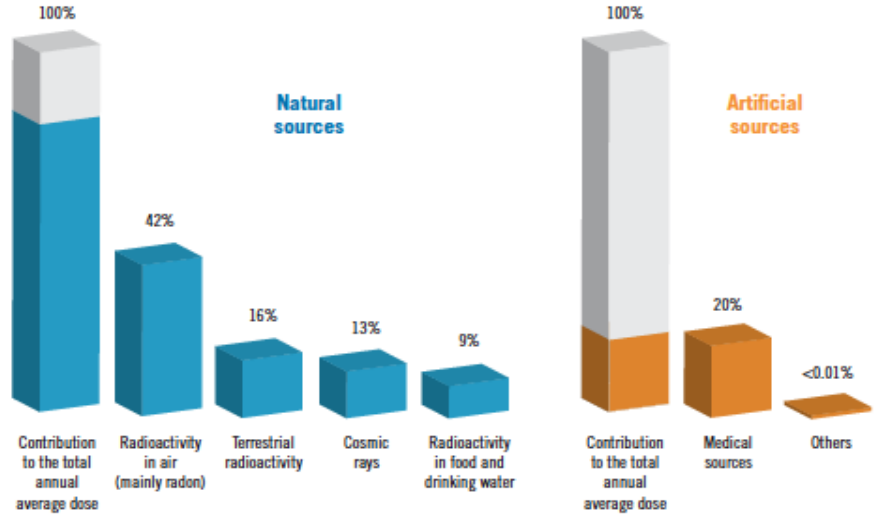
- Medical exposure
- Non- medical exposure
  - » Exposure to radioactive fallouts from experimental explosions
  - » Exposure following nuclear power plant accidents

Medical exposure and thyroid cancer

Medical radiation exposures increased dramatically in level I healthcare countries

- Increase in the number of diagnostic medical radiological examinations per 1000 people for countries with at least one physician for every 1000 people (UNSCEAR, 2008)
- USA = $3X10^6$ in 1980 to $62\ X10^6$ in 2006 (7-11% in children < 15y)
- UK: $1.7X10^6$ in 1995-1996 to $3.8X10^6$ in 2006-2007





http://whqlibdoc.who.int/publications/2012/9789241503662_eng.pdf

Historical medical exposures: *therapeutic applications*

Type of therapy/disease	Exposure period	Statistical significant increase
^{224}Radium • Bone tuberculosis • Bechterew's disease*	± 1950 - '60	bone cancer leukaemia
X-rays • Bechterew's disease*	± 1935 - '55	leukaemia
X-rays • Hypertrophy of thymus • Hypertrophy of tonsils	± 1926 - '57	thyroid cancer breast cancer
X-rays • *Tinea capitis***	± 1949 - '60	thyroid cancer, skin cancer, cancer of CNS

**Chronic inflammatory disease from the spine*
*** superficial fungal infection of the scalp*

External radiation exposure and TC

- **Ron et al, 1995 :** Pooled analysis of 7 cohorts
  - Atomic bomb (japan); Thymus (Rochester); Tinea Capitis (Israel); Tonsils (Chicago, Boston); cervical cancer (international) and :Childhood cancer survivors (international)
  - **Childhood exposure:** statistically significant excess relative risk per Gy **(ERR/Gy) of 7,7**
  - Pooled study provided evidence for an **increased risk of TC even at relatively low doses (0,09-1,36 Gy)**
  - ERR/Gy is linear untill ~ 20Gy and then it decreases = cell killing effect at high doses
  - ERR starts to decline after 30 years after exposure but was still elevated after 40 years
  - **Factors that modifies the risk**
    - Age at exposure
    - Time since exposure

Thyroid cancer after radiotherapy

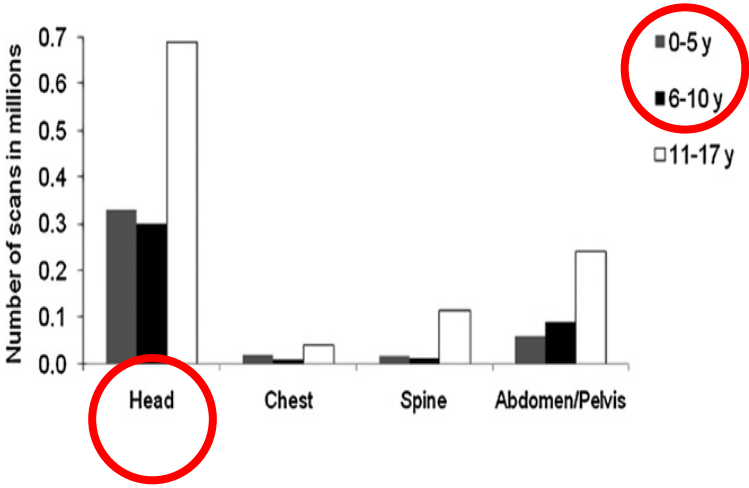
- Radiotherapy for certain cancers, including head and neck, lung, lymphoma/leukaemia, breast and brain, can expose the thyroid to 0.25 Gy.
- In the Childhood Cancer Survivor Study (Bhatti et al, 2010), the highest thyroid doses were observed :
  - Hodgkin lymphoma (mean dose = 35 Gy)
  - Central nervous system (mean dose= 11.1 Gy)
  - Neuroblastoma (mean dose = 5.2 Gy)
- Thyroid cancer is one of the most common second cancers after radiotherapy for Hodgkin lymphoma during childhood
- Confirmation of downturn of TC risk at 20Gy due to cell killing
- Significant increased risks of thyroid cancer have been observed from 5 to more than 40 years after childhood radiotherapy

Diagnostic Computed Tomography (CT-Scan)

- 1/3 of all CT scans are performed in the head and neck region (61 % overlap of radiation field with the thyroid gland)
- A CT of abdomen and chest (15s) =10mSV = 100 X higher than a conventional chest X-ray (0.1mSv)
- CTs contributes largely (47%) to the radiation diagnostic dose
- Increasing concern regarding radiation exposure to the thyroid from pediatric CT scans

Diagnostic Computed Tomography (CT-Scan)

- The doses to the thyroid depend on the scanner and the protocol used :
  - CT torso protocol in children : 10-21 mGy (0-10years)
- Mazonakis et al, 2006 : in children, thyroid scattered dose
  - Head CT : 0.6 mGy to 8.7 mGy
  - Neck Ct : 15 (age 0)-52mGy (age 15)
- Berrington de Gonzalez , 2011:
  - Site distribution : age related variability for anatomical site of CT and thus implications of the thyroid.
  - 75 % of scans among children < 5 years included Ct in the head region



Diagnostic Computed Tomography (CT-Scan)

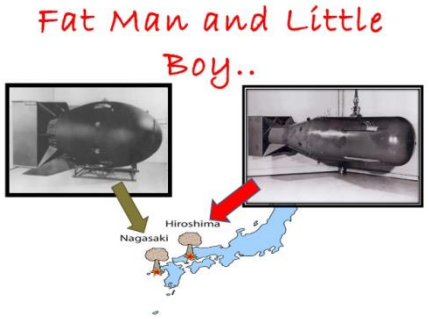
- Studies are currently underway to assess the incidence of cancer in large cohorts of children who received computed tomography scans.
- Risk projections can be used to estimate the potential cancer burden from computed tomography given the age at scan and the type of scan.
- For the highest dose procedure, chest CT:
  - risk estimates ranged from 11 thyroid cancers per 10,000 scans at age 10 years to 35 thyroid cancers per 10,000 scans at age 0 among females.

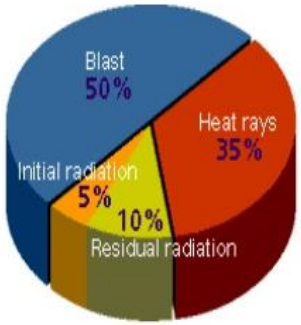
- **The primary public health issue is the increasingly large pediatric population exposed**
- **Use of Ct should be based on on a proper understanding of its risks and benefits .**

Non-medical exposure and thyroid cancer

Thyroid cancer after Hiroshima & Nagasaki

- Thyroid cancer: **1st solid tumor reported** to be increased in frequency among atomic bomb survivors (PTC).
- Latent period of thyroid cancer in children ~5 yrs.
- *Imaizumi et al, 2007-2011 :* Thyroid nodules and thyroid cancer in World War II atomic bombs survivors 60 years later:
- 2,668 Hiroshima and Nagasaki atomic bomb survivors who were younger than 10 years of age during radiation exposure.
- The youngest **children** were those most likely to have a thyroid nodule and **thyroid cancer**
- The risk decreased sharply with increasing age-at-exposure and there was little evidence of increased thyroid cancer rates for those exposed after age 20
- 17% were found to have significant thyroid nodules when imaged by ultrasound
- 1% of all people were found to have a thyroid cancer after thyroid biopsy





The health risks of radiation can be long-lasting

Nuclear experimental explosions

- **Marshal islands: (BRAVO thermonuclear test, Bikini atoll, 1st March 1954)**
  - The largest US nuclear test record : 1,6 Hiroshima bombs each day /12 years
  - Major exposition = iodine radio-isotopes
  - Increased cases of hypothyroidisms, thyroid nodules
  - **Increased cases of thyroid cancers among women and children** between 1964 and 1979

- **Nevada atmospheric nuclear tests (1952-53-55-57)**
  - Institut of cancer : Fallout of these tests marked **increase in cancers in the neighbouring cities** (St-George, Utah), such as leukemia, lymphoma, **thyroid cancer**, breast cancer, melanoma, bone cancer, brain tumors, and gastrointestinal tract cancers (50s-80s)

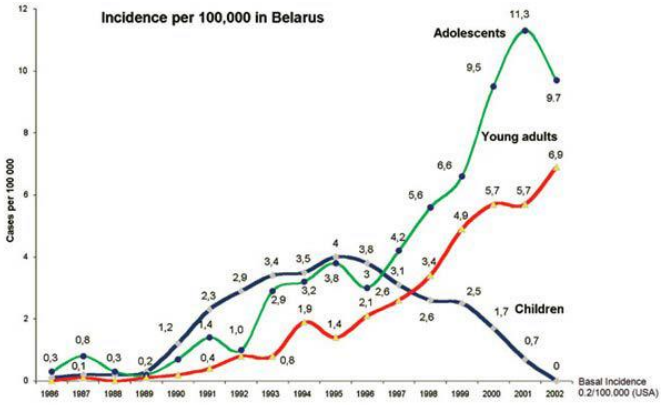
Nuclear power plant accidents

Chernobyl accident (26 April, 1986)

- Exposure to radioactive iodine during childhood or adolescence : **increased thyroid cancer**, particularly papillary carcinoma (Belarus, Ukraine and western part of Russia)

- Equivalent dose to the thyroid in childern:
  - 17000 children received more than 1 SV, 6000 more than 2SV and 500 more than 10SV.

- Belarus study (Demidchick EP, 1999):
  - relative cancer incidence : 0,1-0,3 between 1986-1989 , increased to 4 in 1995.
  - in the region of Gomel which was most heavily contaminated, the relative incidence increased to 13,5 in 1995.



Accident Fukushima 11 mars 2011

- Release of Cs from Fukushima about 1/5th of release from Chernobyl. Overall release about 10% www.unscear.org/docs/reports/2008/11-80076_Report_2008_Annex_D.pdf
- Thyroid doses (from radioiodine) less than 1/100th those of Chernobyl (4.2mSv vs 500 mSv)

Population at large

- 150,000 people evacuated, sample of 1700 showed 98% <5mSv, only 10 >10mSv
- Mean thyroid dose 4.2mSv in children (3.5 mSv adults) compared with 500mSv in Chernobyl evacuees

Thyroid cancer after Fukushima

- Toshihide Tsuda , Epidemiology 2016;27: 316–322
  (University Okayama, Japan)
  - An excess of thyroid cancer (110 cases) has been detected by ultrasound among children and adolescents (less then 18) in Fukushima Prefecture within 4 years of the release (2011-2014)

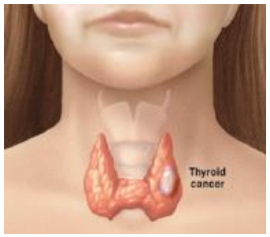
- Critisisms :
  - Methodology used: 54 cases were presented with metastases (not early stage cancers)
  - Study based on national statistics covering all age groups
  - no numbers of TC in this prefecture before the accident.
- Too early to conclude

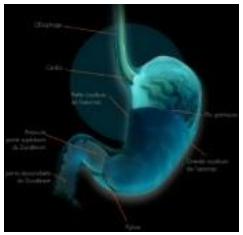
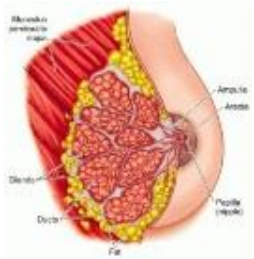
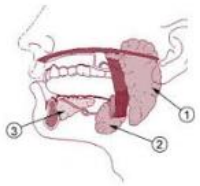
Conclusions

- **Childhood exposure (radiotherapy) :**
- The health risks of radiation can be long-lasting
- Factors influencing TC : age, gender, ID

Thyroid research @ Radiobiology

- **ThyrRes:** ***Synergetic effect of iodine deficiency and radiation on the development of thyroid and breast carcinomas***



Conclusions:

1- **ID induces microvascular changes**, VEGF increase which was HIF1-a and ROS dependent in normal thyrocytes but ROS independent in thyroid cancer cells

2- Like the thyroid, Nis expressing cells respond to ID by microvascular changes probably to optimize iodide bioavailability at regional or systemic level

1- *Gerard AC,* ***Derradji H****, et al. Thyroid. 2012 Jul;22(7):699-708.*

2- *Vanderstraeten J,* ***Derradji H****, et al. Histol Histopathol. 2016 Feb 3:11727*

Thyroid research @ Radiobiology

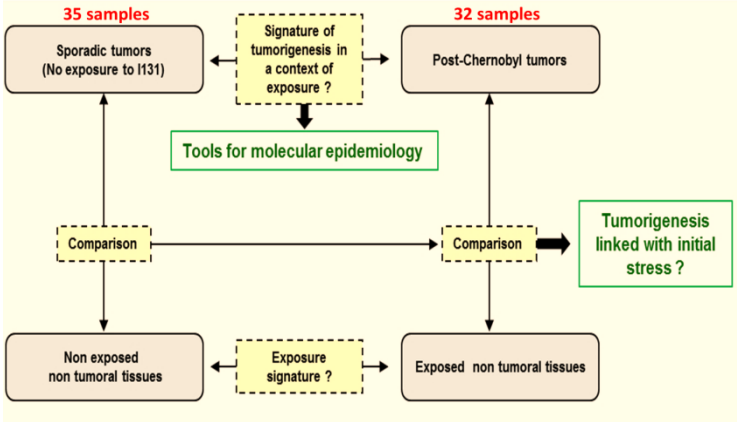
- ***Genetic/epigenetic signatures of radiation-induced thyroid cancer in post-Chernobyl samples***

Objectives:

Find a molecular **signature discriminating sporadic from radiation-induced thyroid tumors**

=> Tools for molecular epidemiology : *Transcriptomic and epigenetic signatures*

Characterize the **link between the initial radiation exposure** and the **development of a radiation-induced tumour**



Samples provided by the Chernobyl Tissue Bank

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