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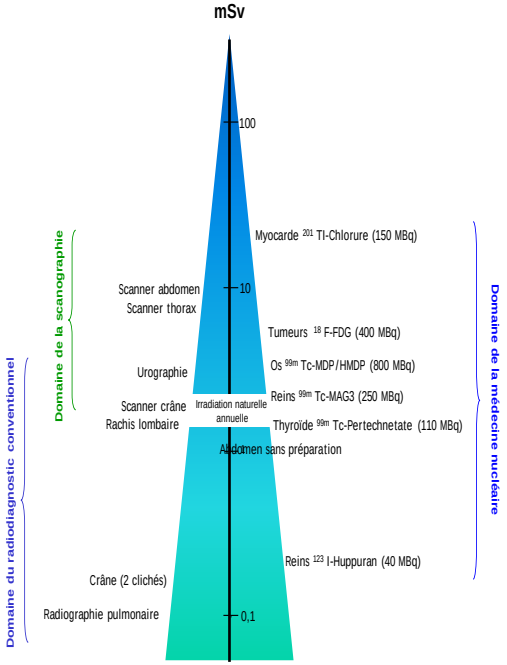
Potential cancer risk associated with CT scan: state of the art of epidemiological studies

CONTEXT

- Medical exposure to Ionizing Radiation (IR)
  - represents the main artificial IR exposure
  - has dramatically increased over time
- CT scan dose
  - 40-70% of the collective dose/ 5-10% of al imaging
- Increased use of CT scan
  - In the USA , 2 million CT scans per year ir 1980 as compared to 69 million in 2007
  - In France, 7 million CT scans reported in 2007



Niveau des expositions médicales à des fins diagnostiques

CONTEXT

- Deterministic effects
  - Severity depends on the dose
  - High doses (> 1 Gy)
  - Short-term and specific effects
  - Model with threshold

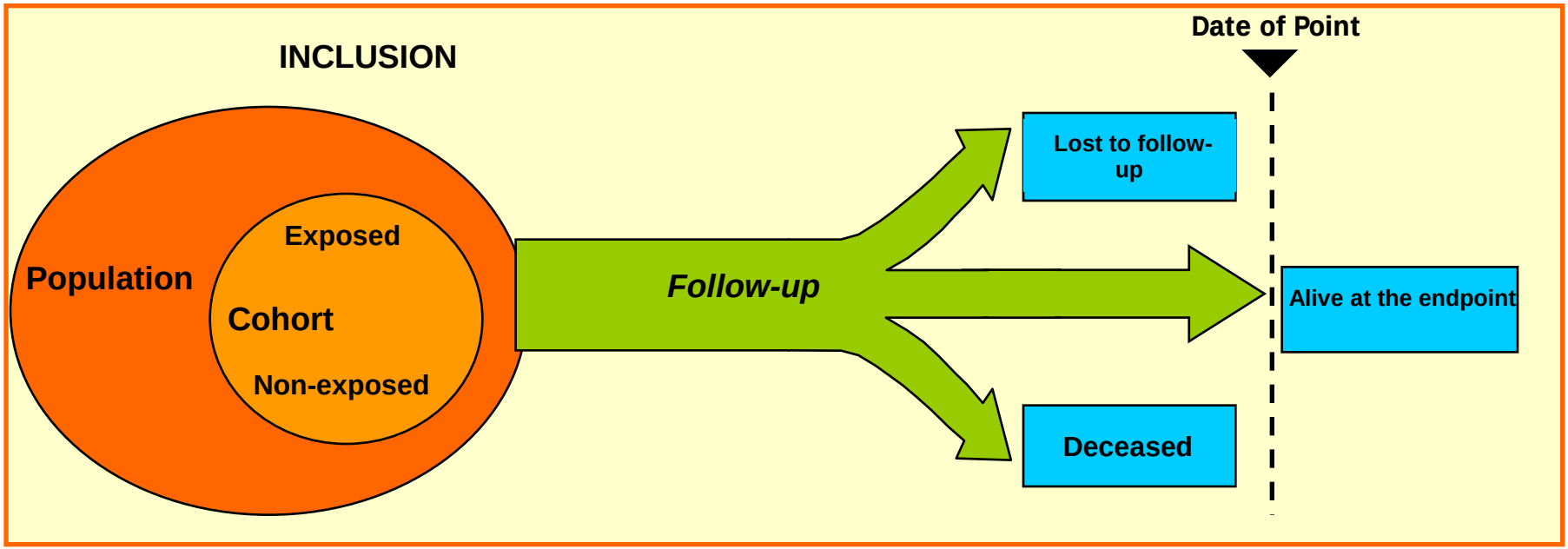
→ **Emergency treatment**

- Stochastic effects
  - Frequency linked to the dose
  - Low doses
  - Long-term and non-specific effects

→ **Epidemiology**

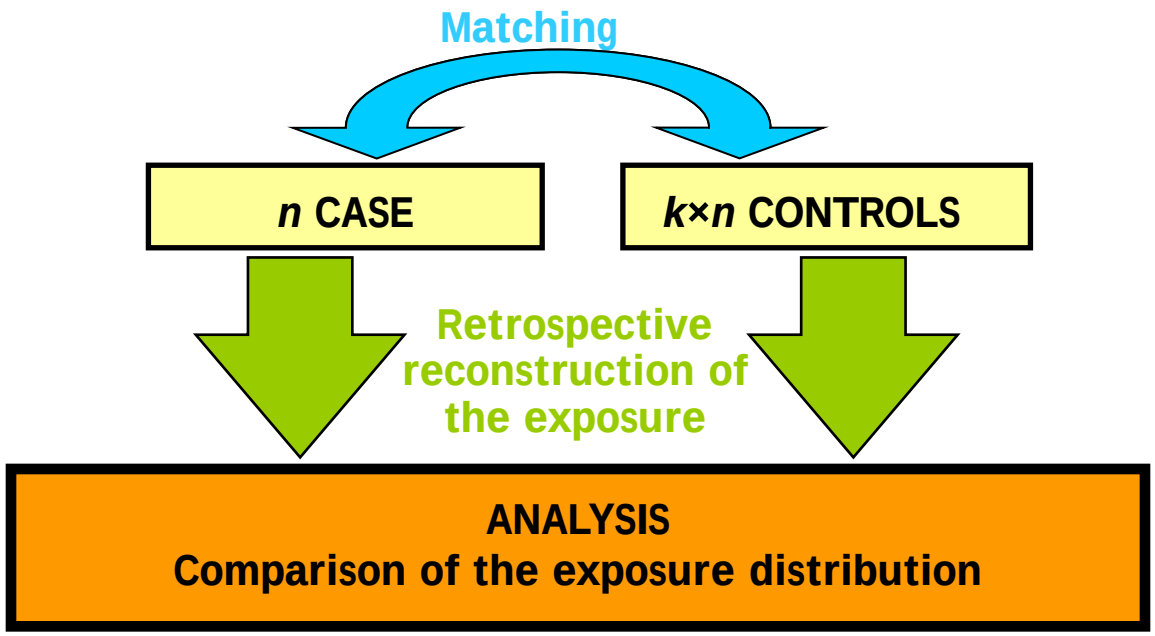
EPIDEMIOLOGICAL STUDY DESIGN

- Cohort studies



EPIDEMIOLOGICAL STUDY DESIGN

- Case control studies



CONTEXT

1950 Radiologists (1900-30)

1950 Painters of luminus (glow in the dark) dial(1910-30)

1950 Medical irradiations for non-cancer or for diagnostic purposes (1920-40)

1950 Hiroshima-Nagasaki survivors (1945)

1960 Miners (uranium) (1940-90)

1970 Populations exposed to atomic bombing experiments (1950-60)

1970 Nuclear workers(1950 to date)

1980 Populations exposed to environmental IR (indoor radon)

1990 Populations exposed to the Tchernobyl accident (1986)

RELATION BETWEEN CANCER AND MEDICAL EXPOSURE

- Exposure during pregnancy
  - Increased risk in case of more than 10 mSv (Wakeford et al).
  - No link any more according to the current dose levels
- Exposures before 1990
  - Excess of breast cancer observed : follow-up of tuberculosis with fluoroscopy (Boice, 1991); Follow-up of scoliosis (Doody, 2000)
  - Cumulated doses > 100 mGy, in the range of 1 Gy
- Exposures after 1990
  - Several reviews of literature (**Baysson, 2012; Schutz, 2010)**
  - No consistent proof of an association between diagnostic medical exposure and cancer risk after paediatric exposure

CT SCANS STUDIES

- Adult CT exposure:
  - 1 study on the risk of cancer following cardiac examinations including CT scan **(Hung, 2013)**

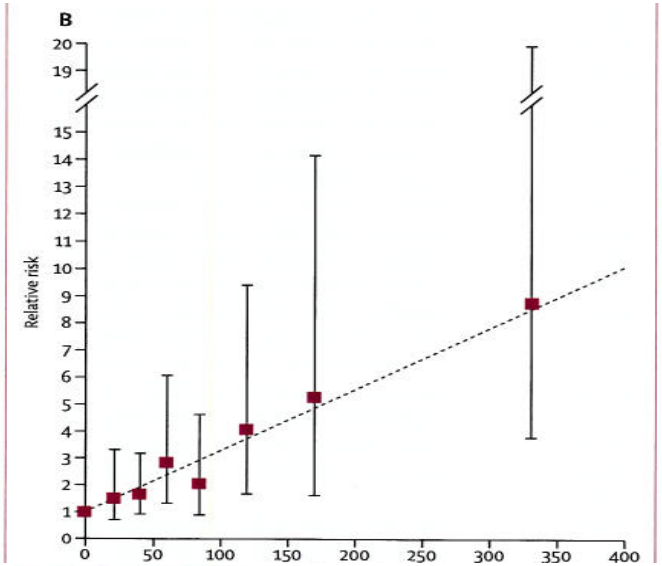
- Paediatric CT exposure: 2 studies
  - Population at risk
  - Long life expectancy
  - Overexposure in case of lack of optimization

PIERCE ET AL, LANCET, 2012

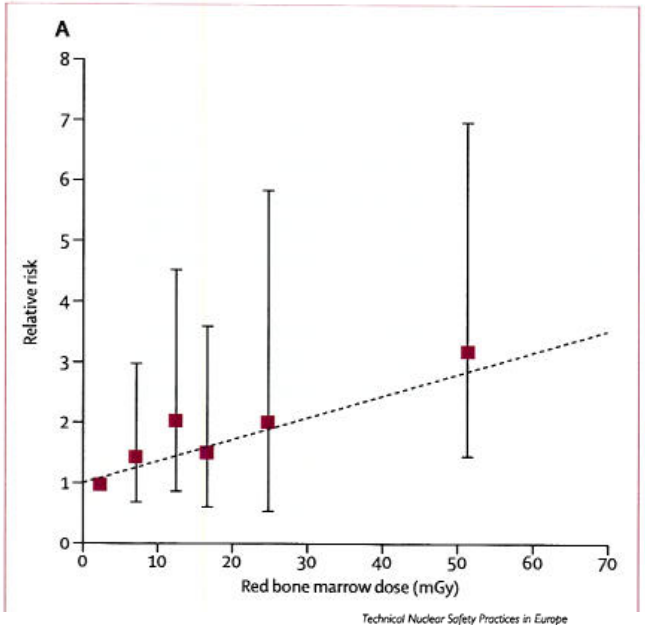
- Cohort study
  - 176,000 children exposed between 1985 and 2000
  - Aged 0 to 22 years at first exposure
  - Over 283,000 CT scans performed
  - Head: 64%, abdomen and/or pelvis: 9%, chest: 7%
  - Median follow-up: less than 10 years
  - 74 incident leukemia
  - 135 incident brain tumors
- Leukemia risk x 3/red bone marrow dose ~50 mGy (5-10 head CTs)
- Brain tumor risk x 3/brain dose ~60 mGy (2-3 head CTs)

PIERCE ET AL, LANCET, 2012

- Dose reconstruction
  - Phantom of several ages
- Mean brain dose: 28-44 mGy
- Mean red bone marrow dose: 29 mGy



- ERR estimated for brain tumors and leukemia



MATHEWS ET AL, BMJ, 2013

- *Cohort study*
  - 11 million people included in the Australian Medicare Insurance database
  - 680,000 children exposed to CT scan between 1985 and 2005
  - Aged 0-19 years at first exposure
  - 857,000 CT scans
  - Head: 59%, Facial bones: 13%, Extremities: 9,5%, Spine: 9%
  - Mean follow-up: 9,5 years
  - 3150 cases of cancer in the exposed group: 283 brain tumors, 643 cases of leukemia; 608 cases of cancer in excess
- Risk of all cancer increased by 20%

LIMITS OF THESE STUDIES

- Dose reconstruction: large uncertainties
  - Technical parameters retrieved from national surveys
  - Lack of individual data
- Absence of clinical information on the indication of the CT

For the Australian study:

- Groups non-comparable due to clinical conditions
- Potential bias of classification
  - people subjected to CT scan before 1985
  - CT performed outside the field of the Medicare system

COMPARISONS OF THESE STUDIES

- Very similar coefficients for the leukemia risk

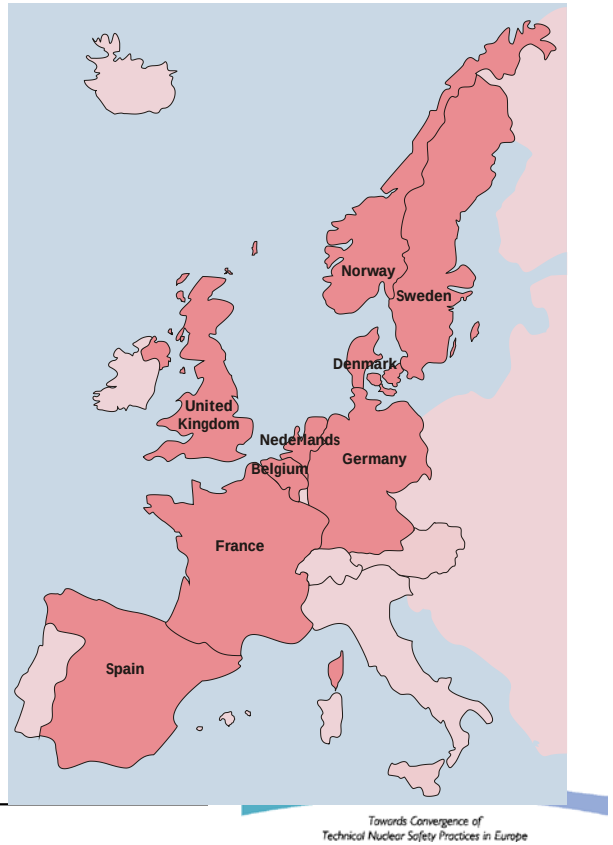
- Larger coefficient for brain tumors compared to the LSS

Tumeurs système nerveux central		
Mathews 2013	ERR/mGy = 0.021	(0.014-0.029)
Pearce 2012	ERR/mGy = 0.023	(0.010-0.049)
LSS, Preston 2007	ERR/mGy = 0.006	(0.000-0.064)
Leucémies + syndromes myélodysplasiques		
Mathews 2013	ERR/mGy = 0.039	(0.014-0.070)
Pearce 2012	ERR/mGy = 0.036	(0.005-0.120)
LSS, Preston 1994*	ERR/mGy = 0.045	(0.016-0.188)
*exclus syndromes myélodysplasiques. Source : Mathews et al BMJ, 2013		

Source: Mathews, 2013

INTERNATIONAL INTEREST ON THIS TOPIC

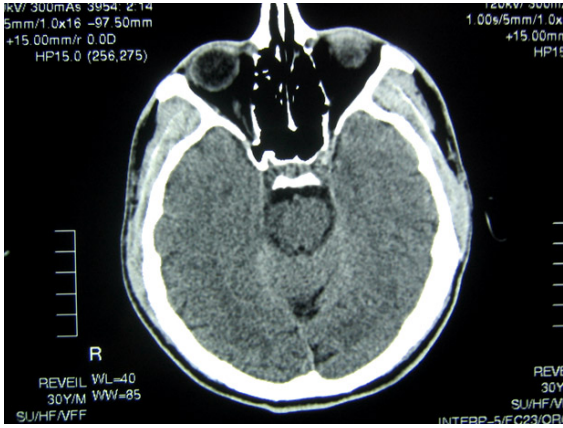
- **European EPI-CT project**
  - 15 partners
  - 9 national cohorts (Belgium, Denmark, **France**, Germany, Netherlands, Norway, Spain, Sweden and the United Kingdom)
  - 1 million children expected to be included
  - Pooled analysis results in 2015



SEVENTH FRAMEWORK PROGRAMME

EU FP7 Euratom grant agreement n°269912

IRSN
INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE



Cohort « Enfant Scanner »
A French cohort of children submitted to CT scan in early infancy

SFIP

SEVENTH FRAMEWORK PROGRAMME

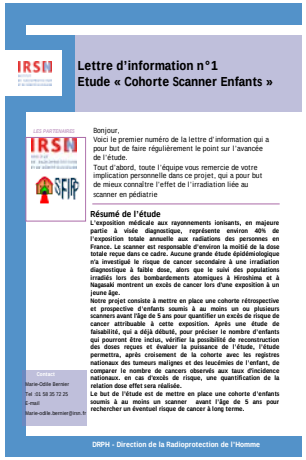
CONTRE LE CANCER
LA LIGUE 101 comités
pour la vie

INSTITUT NATIONAL DU CANCER

COHORT « ENFANT SCANNER »

Aim of the study :

- Estimation of the incidence of leukaemia or cancer following CT scan exposure in the childhood
- Quantification of the dose response relation


IRSN

Lettre d'information n°1
Etude « Cohorte Scanner Enfants »

LES PARTENAIRES

IRSN

SFIP

Bonjour,

Voici le premier numéro de la lettre d'information qui a pour but de faire régulièrement le point sur l'avancée de l'étude.

Tout d'abord, toute l'équipe vous remercie de votre implication personnelle dans ce projet, qui a pour but de mieux connaître l'effet de l'irradiation liée au scanner en pédiatrie

Résumé de l'étude

L'exposition médicale aux rayonnements ionisants, en majeure partie à visée diagnostique, représente environ 40% de l'exposition totale annuelle aux radiations des personnes en France. Le scanner est responsable d'environ la moitié de la dose totale reçue dans ce cadre. Aucune grande étude épidémiologique n'a investigué le risque de cancer secondaire à une irradiation diagnostique à faible dose, alors que le suivi des populations irradiés lors des bombardements atomiques à Hiroshima et à Nagasaki montrent un excès de cancer lors d'une exposition à un jeune âge.

Notre projet consiste à mettre en place une cohorte rétrospective et prospective d'enfants soumis à au moins un ou plusieurs scanners avant l'âge de 5 ans pour quantifier un excès de risque de cancer attribuable à cette exposition. Après une étude de faisabilité, qui a déjà débuté, pour préciser le nombre d'enfants qui pourront être inclus, vérifier la possibilité de reconstruction des doses reçues et évaluer la puissance de l'étude, l'étude permettra, après croisement de la cohorte avec les registres nationaux des tumeurs malignes et des leucémies de l'enfant, de comparer le nombre de cancers observés aux taux d'incidence nationaux, en cas d'excès de risque, une quantification de la relation dose effet sera réalisée.

Le but de l'étude est de mettre en place une cohorte d'enfants soumis à au moins un scanner avant l'âge de 5 ans pour rechercher un éventuel risque de cancer à long terme.

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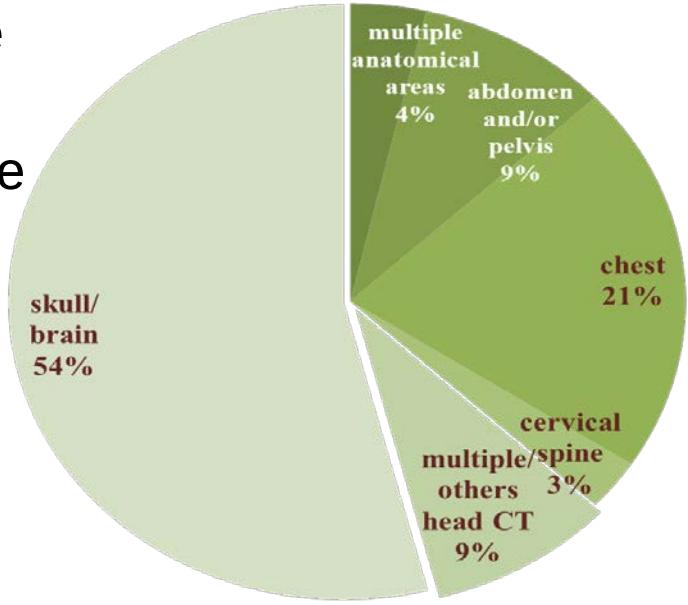
DRPH - Direction de la Radioprotection de l'Homme

- National multicentric cohort study
- Launched in 2009
- 21 large hospitals included

PRELIMINARY RESULTS

- 136,000 children subjected to CT scan between the year 2000 and 2011
- Aged 0-10 years at the first CT scan and born after 1995
  - 30% less than 1 year old at first exposure
  - 69% less than 5 years old at first exposure
- 200,000 CTs
- Clinical information about 73% of the cohort

is available



DOSE RECONSTRUCTION

- Radiological protocols collected for each CT machine
- First reconstitution with the software CT EXPO

Table 3. Median organ dose values per examination, according to the age at exposure and type of CT machine

Explored anatomical area	Median organ doses in mGy (min–max) by age at exposure			
	< 1 year		1–5 years	
	SDCT	MDCT	SDCT	MDCT
Head				
Brain	14 (6–28)	23 (8–55)	14 (6–40)	26 (11–47)
Eye Lenses	21 (0.4–32)	23 (1–73)	24 (0.6–50)	37 (1–60)
Bone marrow	4 (1–7)	6 (3–15)	2 (1–6)	4 (2–7)
Middle ear				
Brain	13 (3–21)	17 (2–55)	5 (2–14)	6 (1–37)
Eye Lenses	49 (17–96)	55 (9–206)	45 (18–127)	43 (8–195)
Bone marrow	6 (2–10)	9 (1–33)	2 (1–5)	2 (0.4–10)
Chest				
Thyroid	10 (1–31)	7 (3–18)	8 (1–25)	5 (2–15)
Oesophagus	9 (1–27)	6 (2–15)	6 (1–21)	4 (2–12)
Lungs	10 (1–30)	6 (3–16)	7 (1–22)	5 (2–13)
Breast	10 (1–30)	6 (3–16)	8 (1–25)	5 (2–15)
Thymus	10 (1–30)	6 (3–17)	7 (1–22)	5 (2 –13)
Bone marrow	2 (0.3–7)	2 (1–4)	1 (0.1–3)	1 (0.3–2)
Abdomen and pelvis				
Liver	15 (6–29)	7 (3–13)	13 (5–25)	9 (2–25)
Stomach	15 (7–30)	7 (3–13)	16 (6–31)	10 (3–27)
Colon	14 (6–28)	7 (3–13)	16 (6–32)	10 (3–27)
Small bowel	16 (7–31)	8 (4–13)	17 (6–33)	11 (3–28)
Testicles	7 (4–16)	7 (3–13)	12 (4–23)	10 (3–28)
Ovaries	16 (7–31)	8 (4–14)	15 (6–30)	9 (3–25)

MDCT, multidetector CT; SDCT, single-detector CT.

CONCLUSION AND PERSPECTIVES (FRENCH COHORT)

- **This cohort permits to better characterize organ doses associated with CT scan exposure in childhood**
  - Quite elevated doses have been observed for radiosensitive organs (lenses, ovaries, breast, etc…) with a large variability according to the protocol used
  - Optimization of the protocols should be reinforced
  - Consideration of alternatives to CT (such as ultrasound or MRI)

- **Follow-up of the cohort will assess cancer risk linked to CT scan exposure, especially for very young children**

CONCLUSIONS AND PERSPECTIVES

- **2 studies in favor of an excess risk of cancer after exposure to CT during childhood**
- **Further studies needed to confirm this excess by:**
  - Focusing on better exposure assessment
  - Including medical information on the exposed population

- **Ongoing international project EPI-CT**
  - Focus on estimation and reduction of uncertainties for the dosimetry
  - Large number of included children will increase the statistical power of the national studies