

Health effects of cardiac fluoroscopy and modern radiotherapy in paediatrics



Institute for Global Health

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CLÍNIC BARCELONA

X "la Caixa"





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In therapeutic use of ionising radiation, benefits to the patient largely <u>outweigh the risk</u>

However, <u>late effects</u> of exposure are important to understand in children with <u>increased survival</u>



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This project has received funding from the Euratom research and training programme 2014-2018 under grant agreement No 847707

### Goal

#### Better understand the long-term health effects of medical exposure to ionising radiation in children:

- Cancer patients treated with modern radiotherapy modalities
- Cardiac patients treated with X-ray guided imaging procedures





#### How

## Build European cohorts and registries of paediatric patients to investigate / establish:



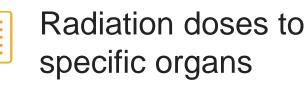
Late health effects of ionising radiation in children



Cancer and non-cancer outcomes



Tools for long-term follow-up of children exposed



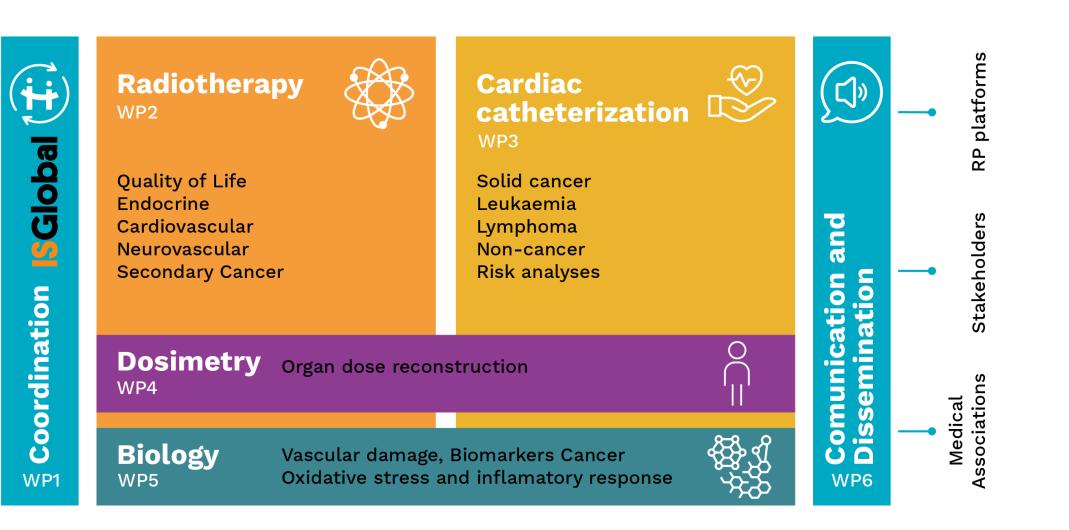


Possible biological mechanisms



Recommendations to optimise techniques and reduce radiation doses

## **Work Packages**





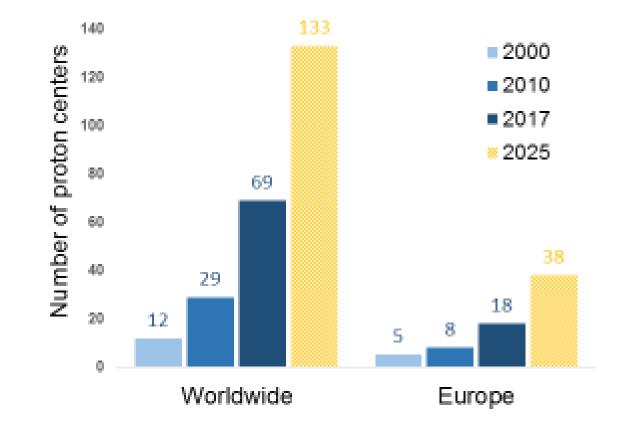








## Protontherapy centres worldwide and in Europe



(source: PTCOG website, https://www.ptcog.ch/ accessed on May 4th 2017)





## WP2 - Objectives

 To implement the infrastructure of a long-time registry of paediatric patients treated with modern radiotherapy techniques

- To assess incidence and severity of health and social outcomes
  - Endocrine dysfuntions
  - Cardiovascular toxicities
  - Neurovascular damages
  - Second primary cancers
  - Quality of Life, Educational and Social Outcomes





Center	Average number	Retrospectiv	ve inclusion	Prospective	Total	
	of paediatric patients treated <u>per year</u>	Time period	No. patients	Time period	No. patients	
KUL	90	2008-2020	200	2020-2023	230	430
AUH	35	n/a	0	2020-2023	90	90
CRFB	35	n/a	0	2020-2023	90	90
GR	70	2013-2020	380	2020-2023	180	560
UK Essen	200	2013-2020	1140	2020-2023	360	1500
Overall	430		1720		950	2670



## WP3 Cardiology

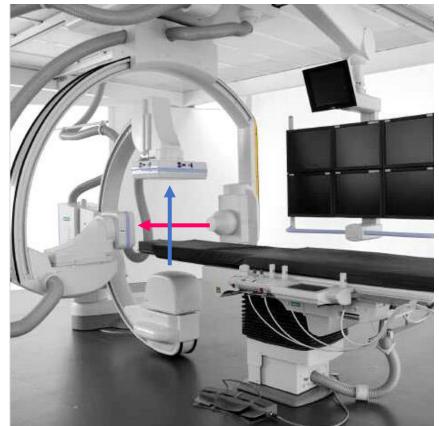


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## **WP3 - Objectives**

- To establish a cohort of approximately 100,000 paediatric patients who underwent cardiac fluoroscopy for long term passive follow-up (existing UK and Coccinelle in France)
- Describe patterns of use of cardiac catheterisation over time
- Evaluate radiation related risk of
  - Childhood leukaemia
  - All childhood cancers
  - other tumours located in, or near to, the chest (breast, oesophagus, lung, thyroid)
- Assess impact of potential confounding factors



Country			Cardiac cath	Accrual and follow-up			
	Age (yrs)	Start of cohort accrual and follow-up	Hospitals	Source of CC information	End of cohort accrual (years)	End of follow- up (years)	Expected cohort size
Belgium	0-18	2004	4	Mostly electronic; possibly PACS for more recent	2020	2020	6,000
France	0-16	2000	15	RIS, PACS, medical records, health care data base depending of the centers and years	2013	2016	19,000
Cormony	0-18	2004	1-2	Manual until 1990. Electronic after; RIS from 2000; PACS after 2010	2020	2020	4,000
Germany	ny health Care		Claims data (no dose data)	2020	2018	30,000	
Italy	0-18	2017	2 to 4	Medical electronic records	2021	2022	1,000
Norway	0-18	1990	1 (Oslo)	Manual until 1990. Electronic after; RIS from 2000; PACS after 2010	2019	2019	5-8,000
Spain	0-21	1995	2	Structured report (~2012-2020) and paper files before	2020	2020	5,000
ик	0-22	1991	13	Paper for early records, electronic for more recent	2020	2020	30,000
Expected to	Expected total						~100,000



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## WP4 Dosimetry

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## WP4 - Objectives

- Develop tools to improve individual-specific estimation of doses to specific organs from diagnostic and therapeutic exposures
  - In radiotherapy
  - In cardiology

#### In both cases

On phantom measurements to validate models



Use our data and tools to support optimisation of procedures



## WP4 - Dosimetry for Radiotherapy

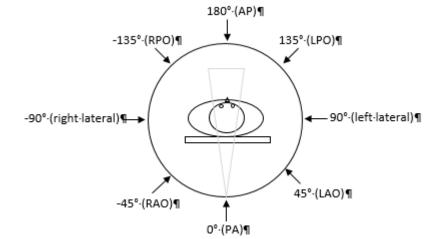
- Measurement and computation of whole-body
  dose and doses delivered to the specific organs
  at risk: in field and out-of-field doses
  - Prospective and retrospective dose estimations
  - Photons, Protons and neutrons
  - Assessment of absorbed doses from imaging procedures (CT)





## WP4 - Dosimetry for Cardiology

- Reconstruction of individualised doses delivered to the specific organs
  - Mainly retrospective dose estimation
  - For early years paper records
  - In recent years Dose Structured Reports
- Monte-Carlo simulations
- Accounting for uncertainties on the dose
- Develop a Mixed-Reality tool for practicioners (for trainaing purposes at least)





## **Optimization activities in Cardiology**

- We will contribute to optimizing doses to cardiac patients by taking advantage of the dosimetric information collected in the framework of the project to assess indication-specific diagnostic reference levels (DRLs).
- The software tool used to estimate the organ dose from examination settings will be make freely available to the medical community.
- Help define recommendations and guidelines on optimization techniques to guide treatments and further reduce patient doses when using ionising radiation in diagnostic and therapeutic X-ray guided imaging.





## WP5 Biology







## **WP5 - Objectives**

- Identification of biomarkers that are characteristic for patients at increased risk of developing acute or late adverse health effects.
- Provide a mechanistic understanding of radiation-induced cellular responses to be used for molecular epidemiological studies of low dose health effects
  - Investigate mechanisms and identify biomarkers in both populations in parallel
  - Focus will be on oncogenic processes and vascular diseases



## WP5 - Protocol

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Biomarkers will be studied in blood and saliva

- 1) before start of treatment,
- 2) immediately after completed exposure or anytime up to 3 months after exposure
- 3) one year after last exposure.
- The biomarkers will be characterized depending on the dose/radiation quality, stability and relevance for mechanistic understanding of radiation induced cellular responses.
- Changes induced by radiation at the level of the transcriptome (miRNA), the proteome (plasma and saliva protein profiling; and RPPA) and the epigenome (gene expression regulation and protein modification) as well as inflammation and oxidative stress levels.



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## WP2 - Where are we?

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Tasks		YEAR 1		YEAR 2		AR 3	YEAR 4	YEAR 5
VP1: Project Management	2 3	4 5 6 7 8 9	10 11 12 13 14 15	16 17 18 19 20 21	22 23 24 25 26 27 28 29 3	0 31 32 33 34 35 36 37 38 39 40 4	1 42 43 44 45 46 47 48 43 50 51 52	53 54 55 56 57 58 59
XONSORTIUM MEETINGS								
Innual Reports to EU			R		R	R	D D	
thics			ĸ	5	<b>K</b>		N N	
	1			2				
Constitution of Advisory Committee ©		©						
Management		2/4						
VP2: Radiotherapy								
ask 2.1: Cohort building, core database, data linkage and storage		1	2		3	4	6	
Subtask 2.1.1: Methods and procedures for collection and harmonization of clinical data								
Subtask 2.1.2: Methods and procedures for collection and harmonization of DICOM-RT data							5	
Subtask 2.1.3: Methods for long-term follow-up and linkage with national registries								
Task 2.2 : Endocrine dysfunctions after photon or proton beam therapy								
Fask 2.3: Cardiovascular toxicities after mediastinal irradiation with photons or protons								
Fask 2.4: Neurovascular damages after photon or proton beam therapy for brain tumours								
Fask 2.5: Second cancers after photon and proton beam therapy								
Fask 2.6: Societal aspects of advances in radiotherapy: Quality of life and social impact								
VP3: Interventional Cardiology								
ask 3.1: Protocol of the joint cohort, data collection, data linkage and storage		1	2			3	4	
Yask 3.2: Analyses								
Subtask 3.2.1: Quantify associations between individual organ doses and risk of leukaemia, lymphoma, and solid cancer								
Subtask 3.2.2: Modification and heterogeneity in associations								
VP4:Dosimetry								
ask 4.1 : Protocols development			1/6					
ask 4.2 : Dose reconstruction in Radiotherapy						2/3	4	
Subtask 4.2.1: Prospective and retrospective dose estimations								
Subtask 4.2.3: Dose measurements in phantoms-benchmark the analytical/Monte Carlo approach for dose reconstruction								
Subtask 4.2.3: Assessment of absorbed doses from imaging procedures							5	
Subtask 4.2.4: Reduction of doses from CT studies in paediatric radiotherapy patients								
Task 4.3: Dose reconstruction in Interventional Cardiology						7	8	
Subtask 4.3.1: Dose reconstruction and uncertainty analysis								
Subtask 4.3.2: Dose validation								
Subtask 4.3.3: ARIC: Optimisation of x-ray guided cardiac catheterization procedures using AR& CV								0
VP5:Biology		1						
ask 5.1 M/M studies of the processes leading to vascular damage						2	6	
ask 5.2: M/M studies of underlying processes of vascular pathologies and cancer through oxidative stress and inflammator	y respons	e				3	7	
ask 5.3: M/M studies of the underlying processes of cancer focusing on cellular aging and miRNA signature						4	8	
ask 5.4: Exploring the use of saliva as a biosampling method for molecular epidemiologic studies						5	9	10
VP6:Communication and dissemination								
ask 6.1 Communication and Stakeholder Engagement Plan								
ask 6.2 Project logo (L) and website an Brochure (W)	L	W						
ask 6.3 Communication materials								
Newsletters					•	•	•	
Policy brief								
Factsheet								
ask 6.4 Stakeholder engagement and workshop								
ask 6.5 Scientific publication strategy P			Р					
			All Ethics Approved				End of Data collection	



Impact









Provide much-needed **information on the effects** of low to moderate doses of radiation on humans Help **improve radiological protection** in medicine Impact on patient care and quality of life



## "Our ultimate goal is to improve the quality of life of children treated with medical radiation"











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# **Harmonic**

pediatrics · radiotherapy · cardiac fluoroscopy

Thank you!

