
Harmonic
Health effects of cardiac fluoroscopy and modern radiotherapy in paediatrics
ISGlobal
Barcelona Institute for Global Health
Isabelle THIERRY-CHEF, PhD
Head of the Medical Radiation Group
ISGlobal
Barcelona Institute for Global Health
CLÍNIC BARCELONA Hospital Universitari
Parc de Salut MAR
UNIVERSITAT DE BARCELONA
upf. Universitat Pompeu Fabra Barcelona
Generalitat de Catalunya
"la Caixa"
Institució CERCA Centres de Recerca de Catalunya

Harmonic

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In therapeutic use of ionising radiation, benefits to the patient largely outweigh the risk

However, late effects of exposure are important to understand in children with increased survival

June 2019- Mai 2024

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
- Radiation doses to specific organs
- Possible biological mechanisms
- Recommendations to optimise techniques and reduce radiation doses

Work Packages

Coordination WP1 — ISGlobal

Radiotherapy
WP2

- Quality of Life
- Endocrine
- Cardiovascular
- Neurovascular
- Secondary Cancer

Cardiac catheterization
WP3

- Solid cancer
- Leukaemia
- Lymphoma
- Non-cancer
- Risk analyses

Dosimetry
WP4

Organ dose reconstruction

Biology
WP5

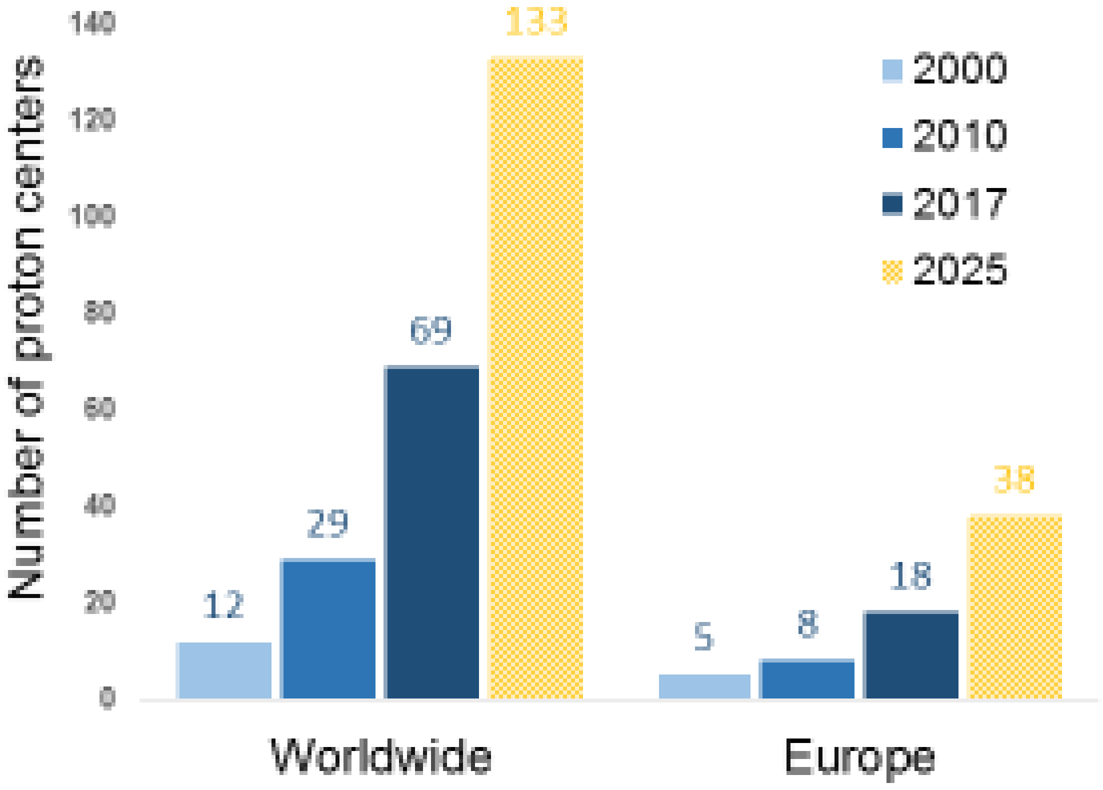
Vascular damage, Biomarkers Cancer
Oxidative stress and inflamatory response

Comunication and Dissemination
WP6

- RP platforms
- Stakeholders
- Medical Associations

WP2 Radiotherapy

Protontherapy centres worldwide and in Europe

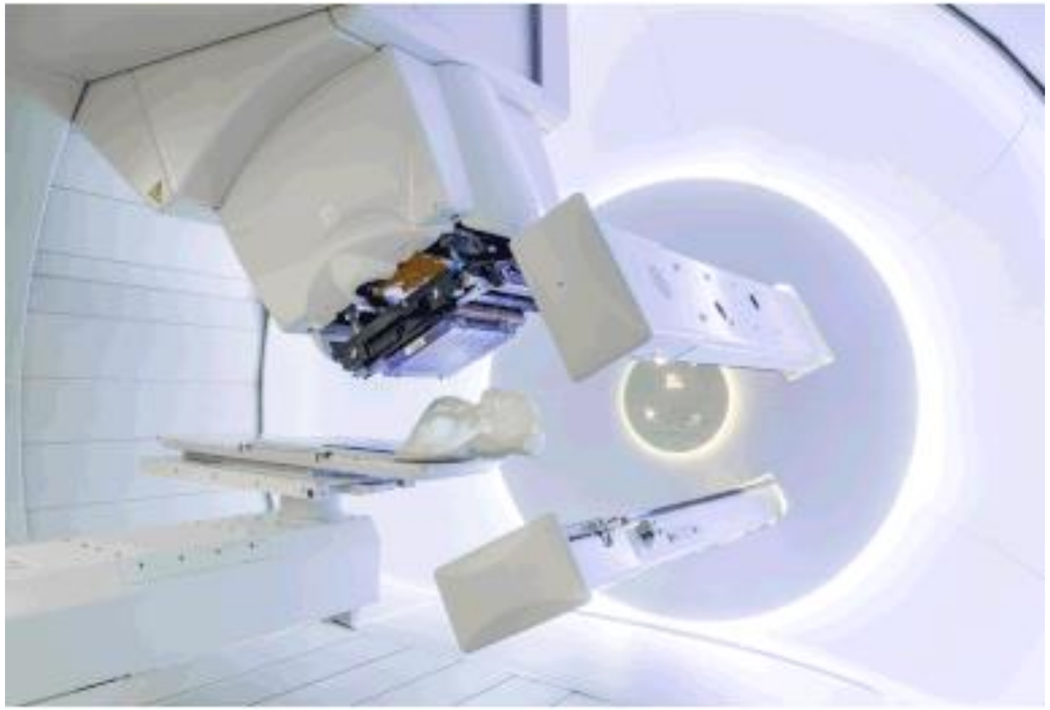


(source: PTCOG website, https://www.ptcog.ch/ accessed on May 4th 2017)

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



Expected number of participants by may 2023

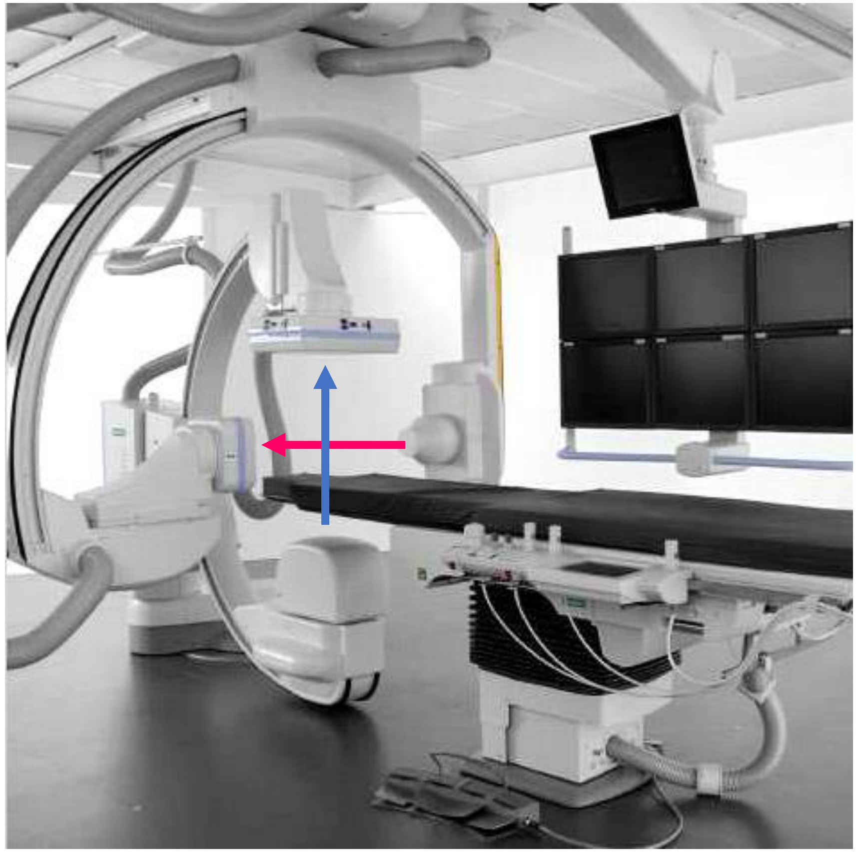
Center	Average number of paediatric patients treated per year	Retrospective inclusion		Prospective inclusion		Total
		Time period	No. patients	Time period	No. patients	
KUL	90	2008-2020	200	2020-2023	230	430
AUH	35	n/a	0	2020-2023	90	90
CRFB	35	n/a	0	2020-2023	90	90
GR	70	2013-2020	380	2020-2023	180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

In blue: Patients are treated with photons

WP3 Cardiology

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 catheterisation				Accrual and follow-up		
	Age (yrs)	Start of cohort accrual and follow-up	Source of CC information: Hospitals	Source of CC information: Type of records	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
Germany	0-18	2004	1-2	Manual until 1990. Electronic after; RIS from 2000; PACS after 2010	2020	2020	4,000
	0-18	2004	health Care data base	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
UK	0-22	1991	13	Paper for early records, electronic for more recent	2020	2020	30,000
Expected total							**~100,000**

WP4 Dosimetry

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

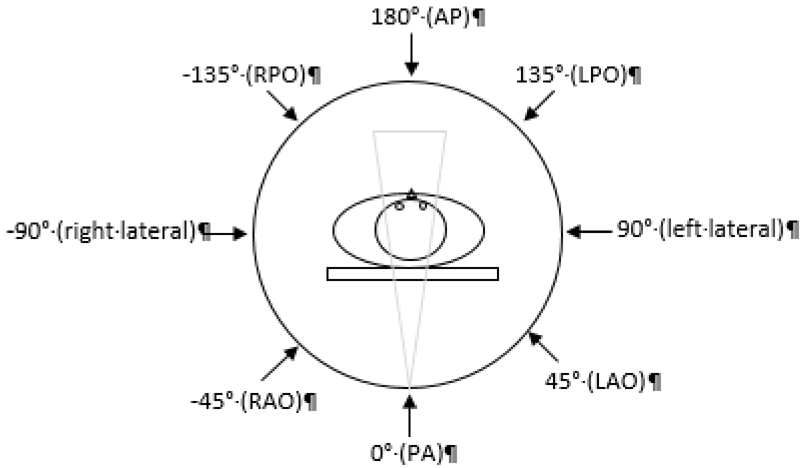
- Use our data and tools to support optimisation of procedures

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

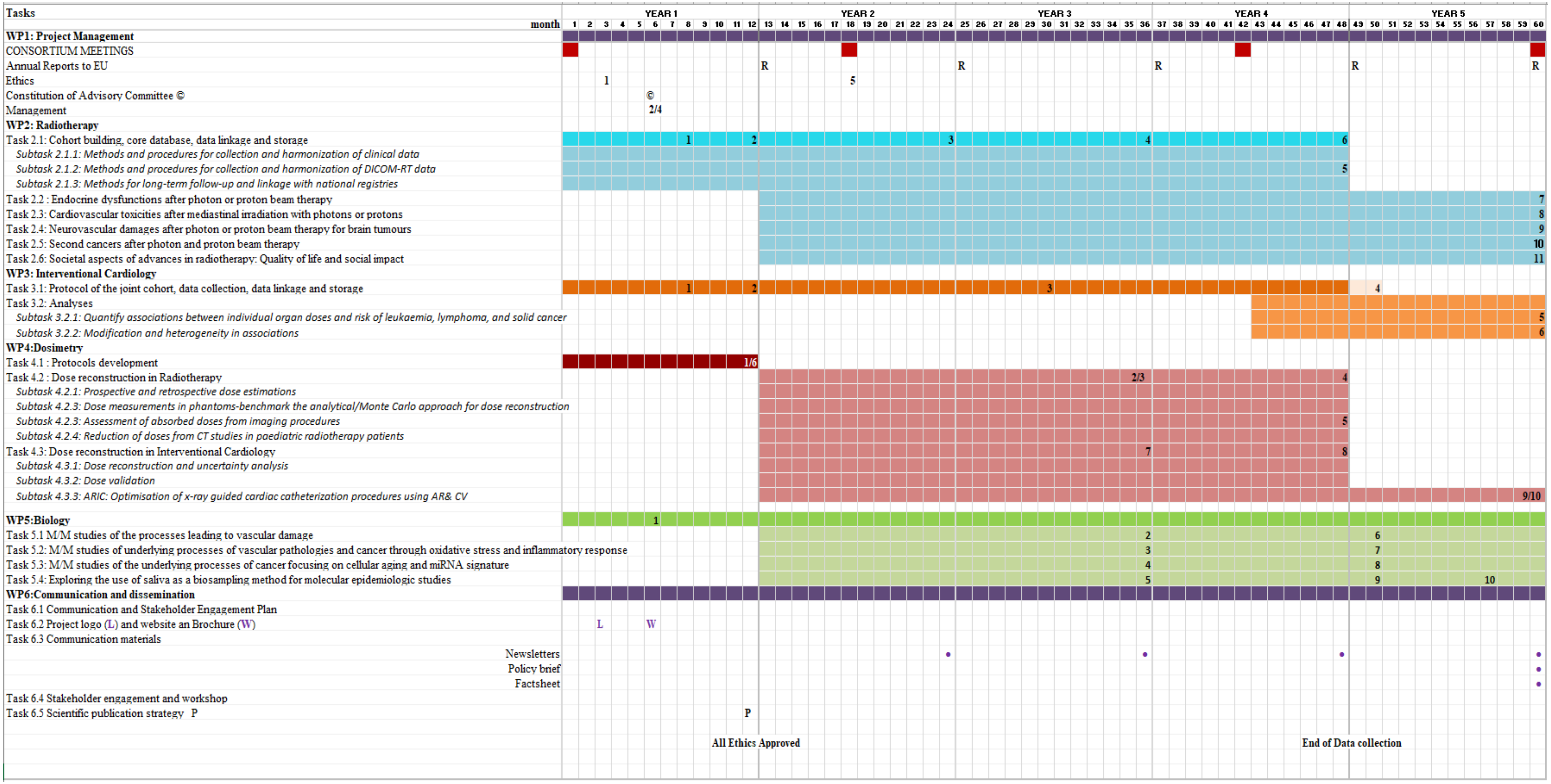
WP5 - Objectives

- 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

- 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.

WP2 - Where are we?



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”

Partners

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Harmonic

pediatrics · radiotherapy · cardiac fluoroscopy

Thank you!

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