RAPTOR – the science case

Dr. Kristjan Anderle

RAPTOR project has received funding from the European Union's Horizon 2020 Marie Skłodowska-Curie Actions under Grant Agreement No. 955956

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Bridging the gap

- How to get from fundamental research to medical product?
- Different requirements at different levels:
  - Research institution
  - Clinical studies
  - Medical product (CE/FDA clearance)
- All are important

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RAPTOR beneficiaries

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RAPTOR beneficiaries

PAUL SCHERRER INSTITUT PSI

UNIVERSITY OF AMSTERDAM

LMU

OncoRay

medPhoton

GSI

POLITECNICO MILANO 1863

DEPARTMENT OF RADIATION ONCOLOGY
MEDICAL UNIVERSITY OF VIENNA
University Hospital Vienna

umcg

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RaySearch Laboratories

Univerza v Ljubljani Fakulteta za matematiko in fiziko

AARHUS UNIVERSITY

Research → Clinic → Industry

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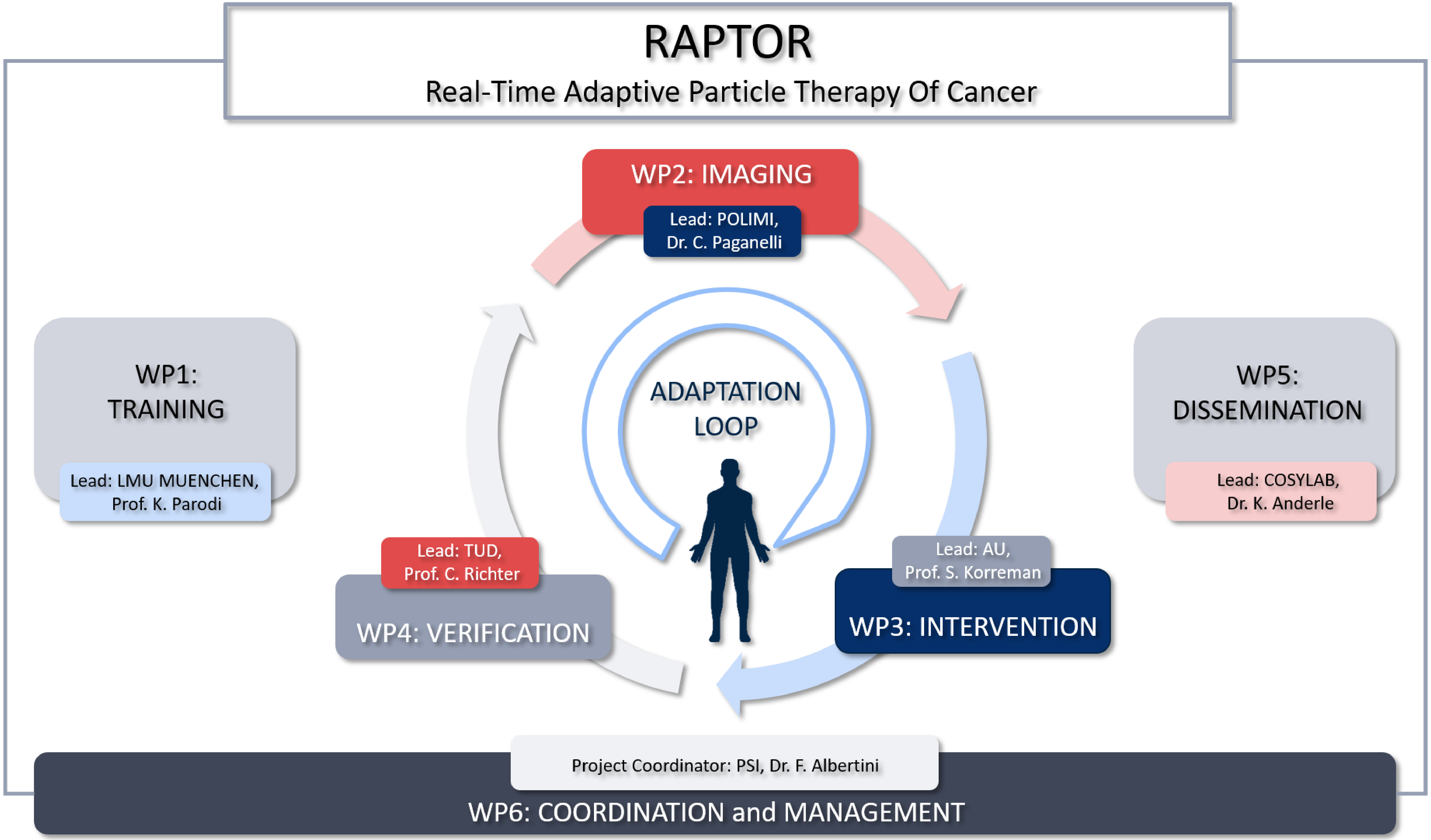

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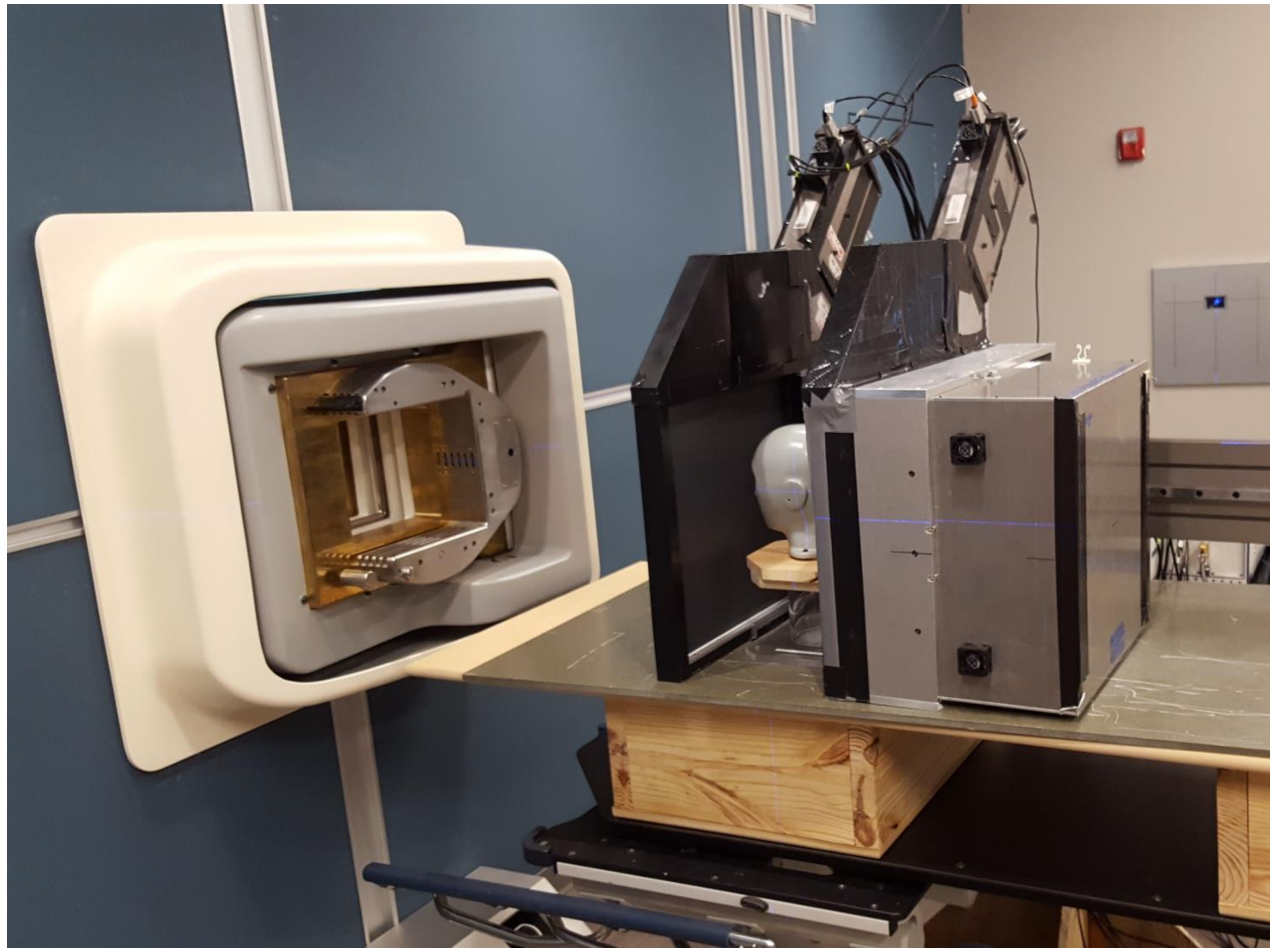
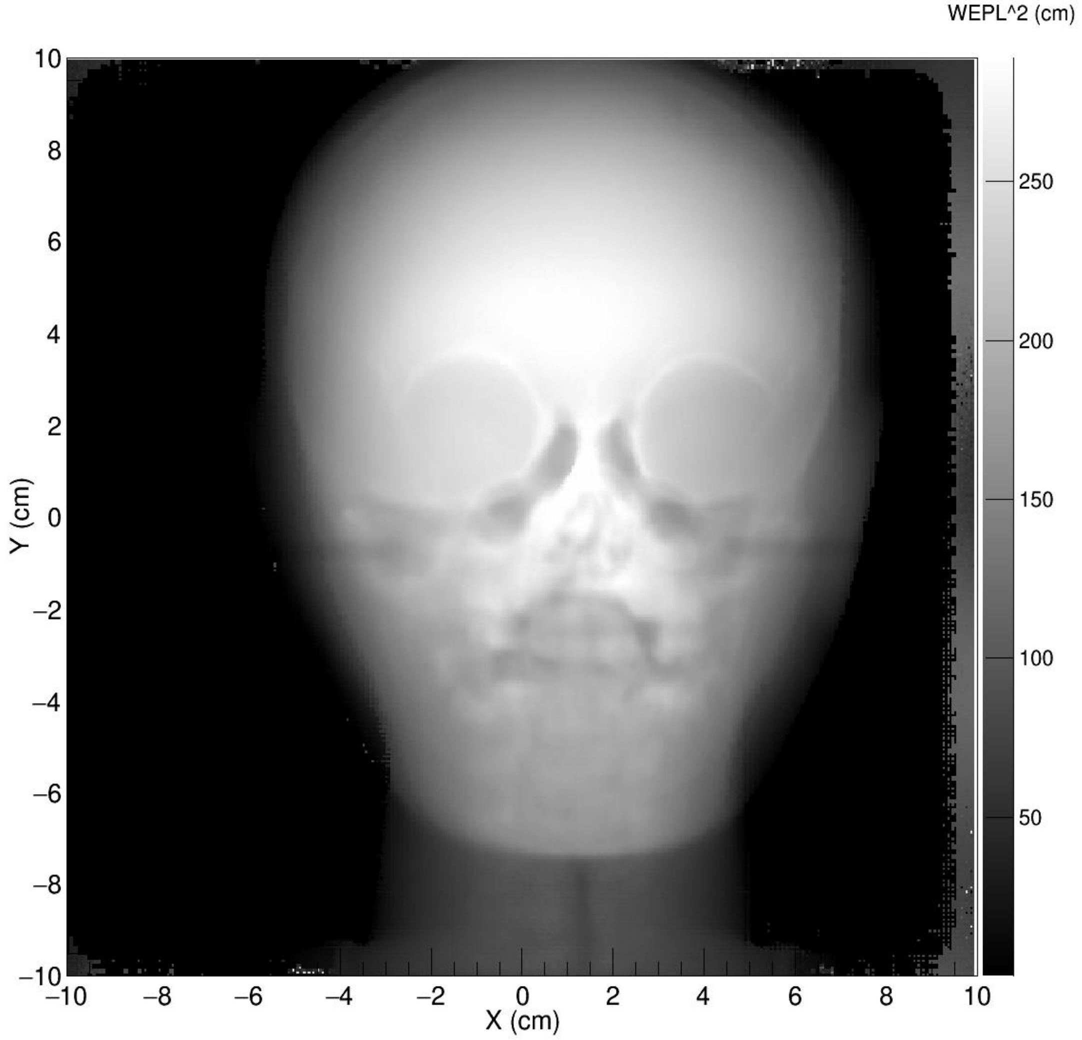
Proton Imaging

ProtonVDA

Transforming Proton Therapy





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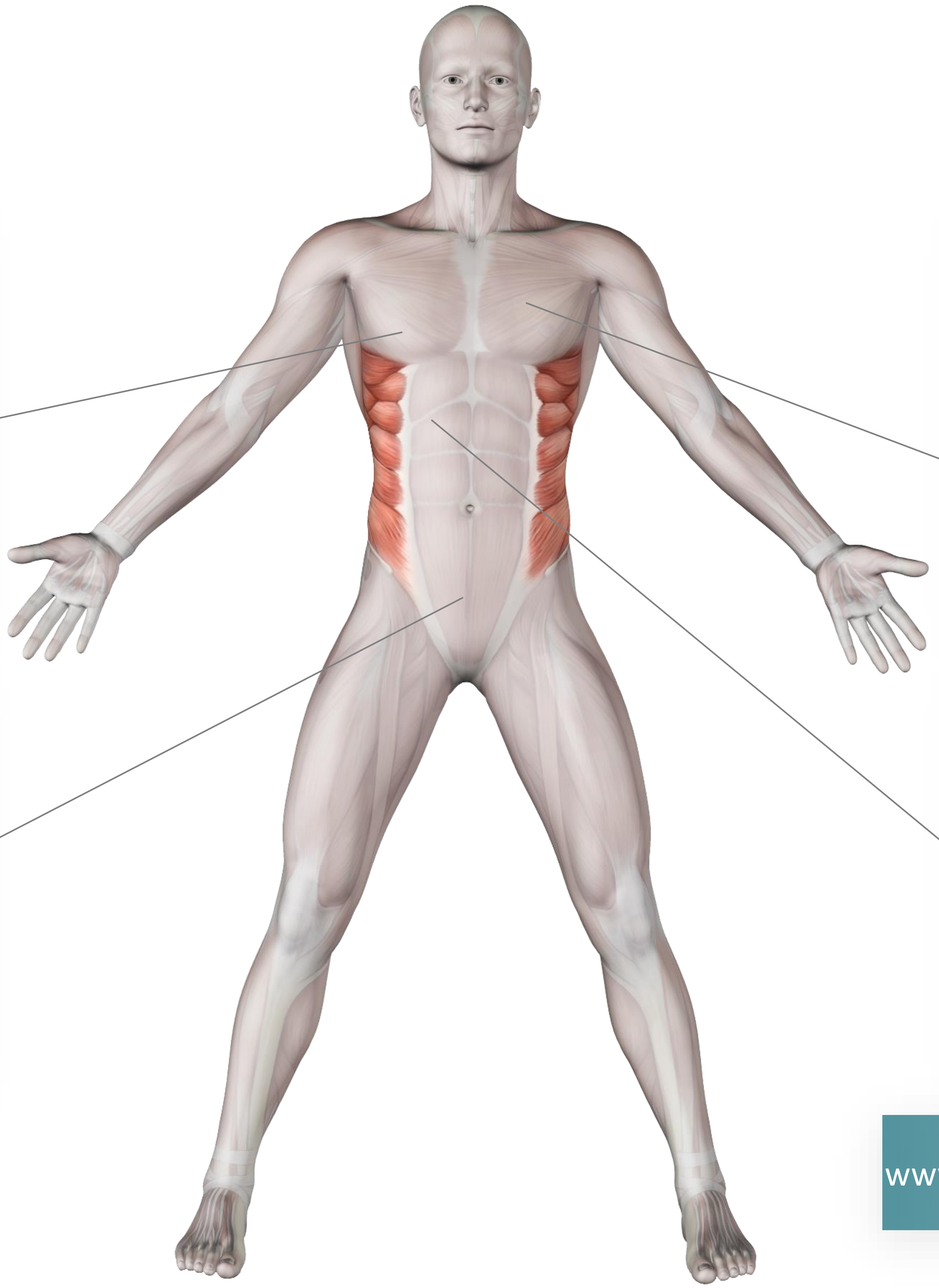
Upright positioning

LEO Cancer Care



Lung

22% of Cancer Cases

Northwestern Medicine®

Breast

22% of Cancer Cases

The University of Texas MD Anderson Cancer Center Making Cancer History®

Prostate

13% of Cancer Cases

LEO Cancer Care

Liver

9% of Cancer Cases

Paul Scherrer Institut PSI

www.who.int/news-room/fact-sheets/detail/cancer

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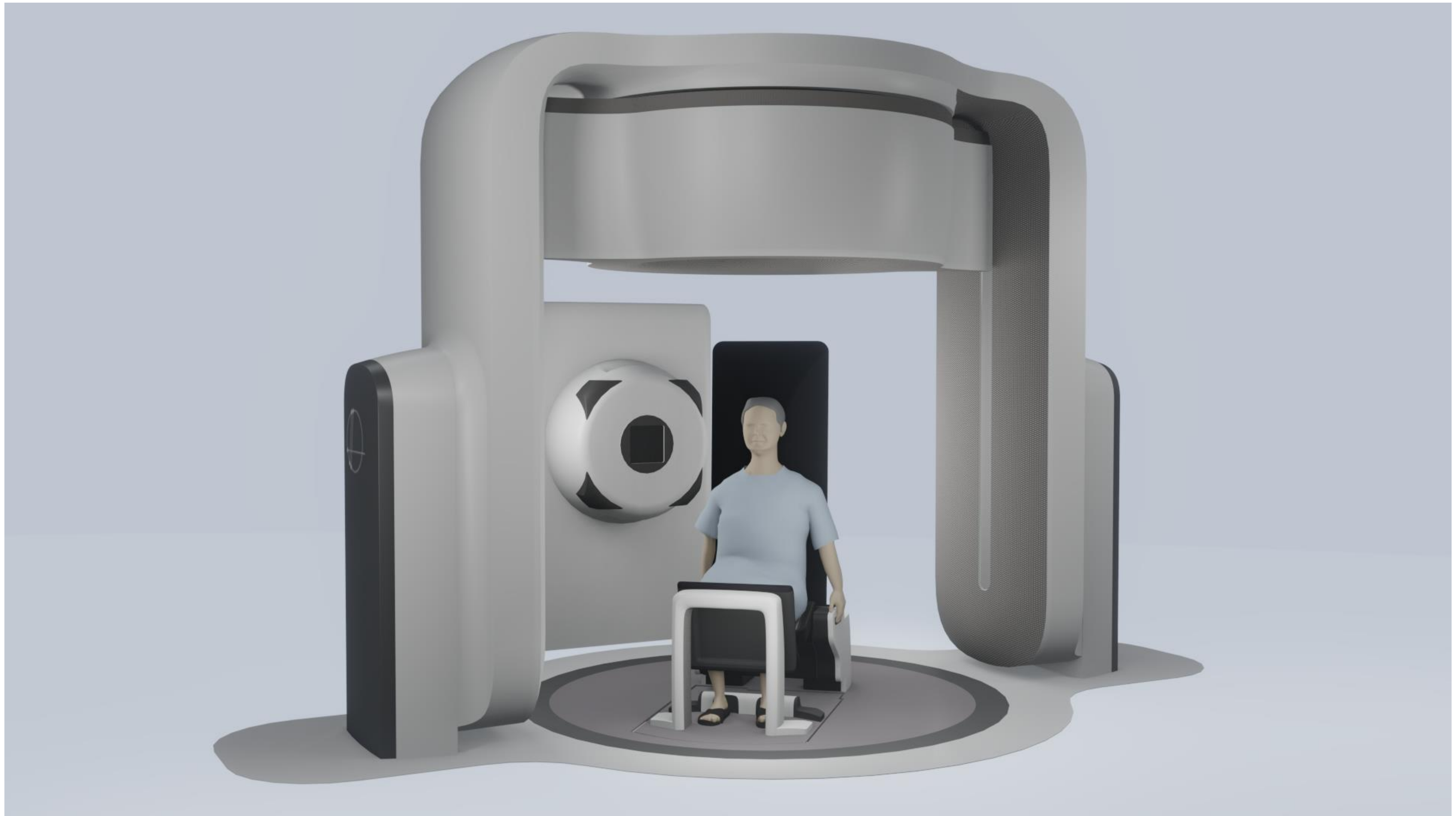
Upright positioning



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LIGHT Patient Positioning System (L-PPS) Modelling, Installation, and Testing

December 2021

Democratising Proton Therapy

The following presentation of the AVO's LIGHT® Proton Therapy Solution is part of our Development roadmap and is subject to conformity assessment(s) by AVO's Notified Body as well as 510(k) clearance by the USA-FDA

FORM-01180-B

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Flash radiotherapy

System	Author	Year	Irradiation		Modality ofradiation	models		Endpoint(s)	Main findings*	
			FLASH-RT	CONV-RT		Tumor	Normal tissue		Tumor	Normal tissue
Brain	Montay-Gruel P (26)	2020	12.5×103 -5.6×106 Gy/s	0.1Gy/s	electron	mice (glioblastoma)	–	tumor growth;cognitive function	similar antitumor effect	protective effect
	Montay-Gruel P (23)	2019	>100 Gy/s	0.07-0.1 Gy/s	electron	–	mice	cognitive function;ROS, neuronal structure, synaptic protein, neuroinflammation	–	fully preserved
	Simmons DA (24)	2019	200, 300Gy/s	0.13 Gy/s	electron	–	mice	cognitive function, neurodegeneration, neuroinflammation	–	protective effect
	Montay-Gruel P (21)	2018	37 Gy/s	0.05 Gy/s	X-ray	–	mice	cognitive function, Cell proliferation, GFAP	–	protective effect
	Montay-Gruel P (20)	2016	0.1,1, 3, 10, 30, 100,500 Gy/s, 5.6 MGy/s		electron	–	mice	cognitive function	–	protective effect above 30 Gy/s, fully preserved above 100 Gy/s
Intestine	Venkatesulu BP (28)	2019	35Gy/s	0.1 Gy/s	electron	–	mice	toxicity, survival	–	No protection effect
	Billy W. Loo (9)	2017	210 Gy/s	0.05 Gy/s	electron	–	mice	survival	–	protective effect
Lung	Fouillade C (29)	2020	40–60GY/S	?	electron	–	mice	cell proliferation, DNA damage, inflammatory genes		protective effect
	Buonanno M (22)	2018	0.025 Gy/s - 1500 Gy/s		proton	–	human lung fibroblasts	cell survival, b-gal, TGFb		protective effect
	Favaudona V (30)	2015	>40 Gy/s,	< 0.03Gy/s	electron	mice(lung tumor)	mice	tumor growth, apoptosis, lung fibrosis	similar antitumor effect	protective effect
	Favaudon V (19)	2014	≥40 Gy/s	< 0.03Gy/s	electron	mice(lung tumor)	mice	tumor growth, early and late complications	similar antitumor effect	protective effect
Skin	Bourhis J (10)	2019	166.7Gy/s	–	electron	patient (lymphoma)	–	tumor response; Soft tissue toxicity	complete response	grade 1 epithelitis, grade 1 oedema
	Vozenin MC (27)	2018	300 Gy/s	0.083 Gy/s	electron	cat (squamous carcinoma	pig	skin toxicity, PFS	PFS at 16 months was 84%	protective effect
Blood	Chabi S (25)	2020	200Gy/S	<0.072 Gy/S	electron	mice (leukemia)	mice	tumor growth, normal hematopoiesis	similar antitumor effect	protective effect
Other	Adrian G (31)	2020	600 Gy/s	0.233 Gy/s	electron	prostate cancer cells	–	survival	flash effect depends on oxygen concentration	
	Beyreuther E (32)	2019	100 Gy/s	0.083 Gy/s	proton	–	zebrafish embryo	survival	–	Similar toxicity except for pericardial edema at one dose point(23Gy)

*FLASH-RT, FLASH radiotherapy; CONV-RT, conventional dose-rate radiotherapy; *Effects of FLASH-RT compared with CONV-RT.*

Source:
L. Binwei et al., 2021

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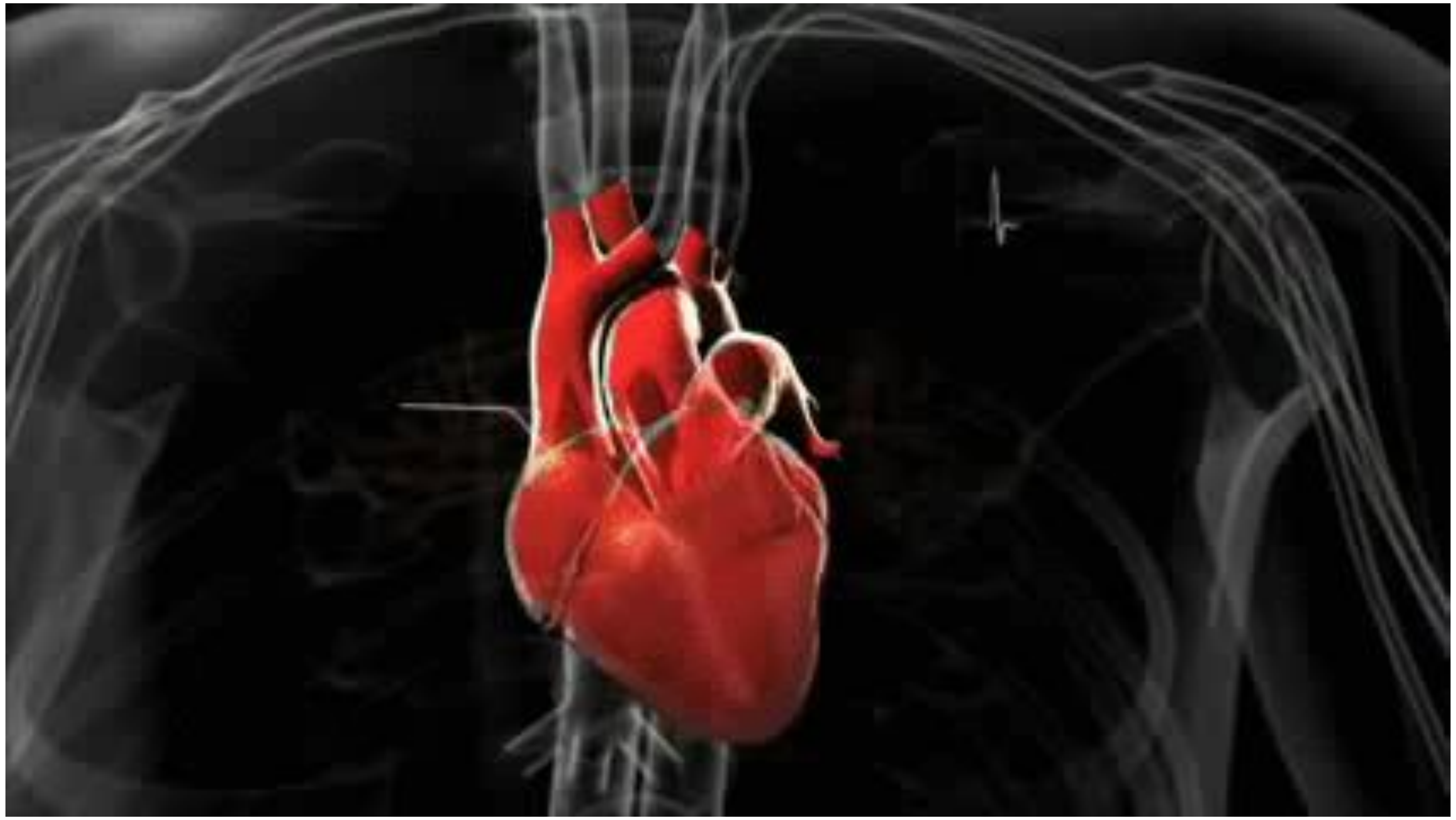
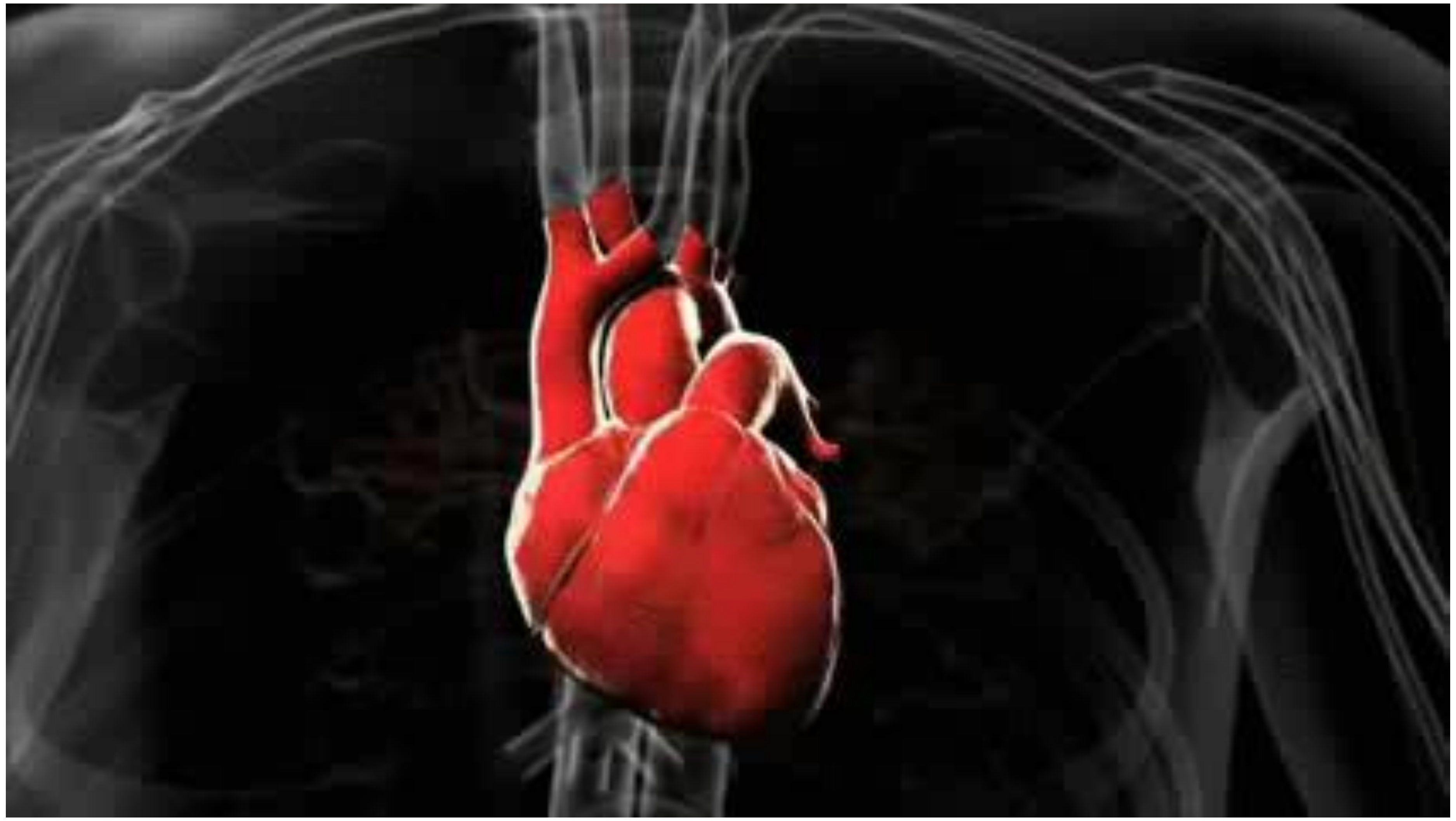
Regular heartbeat



Atrial fibrillation



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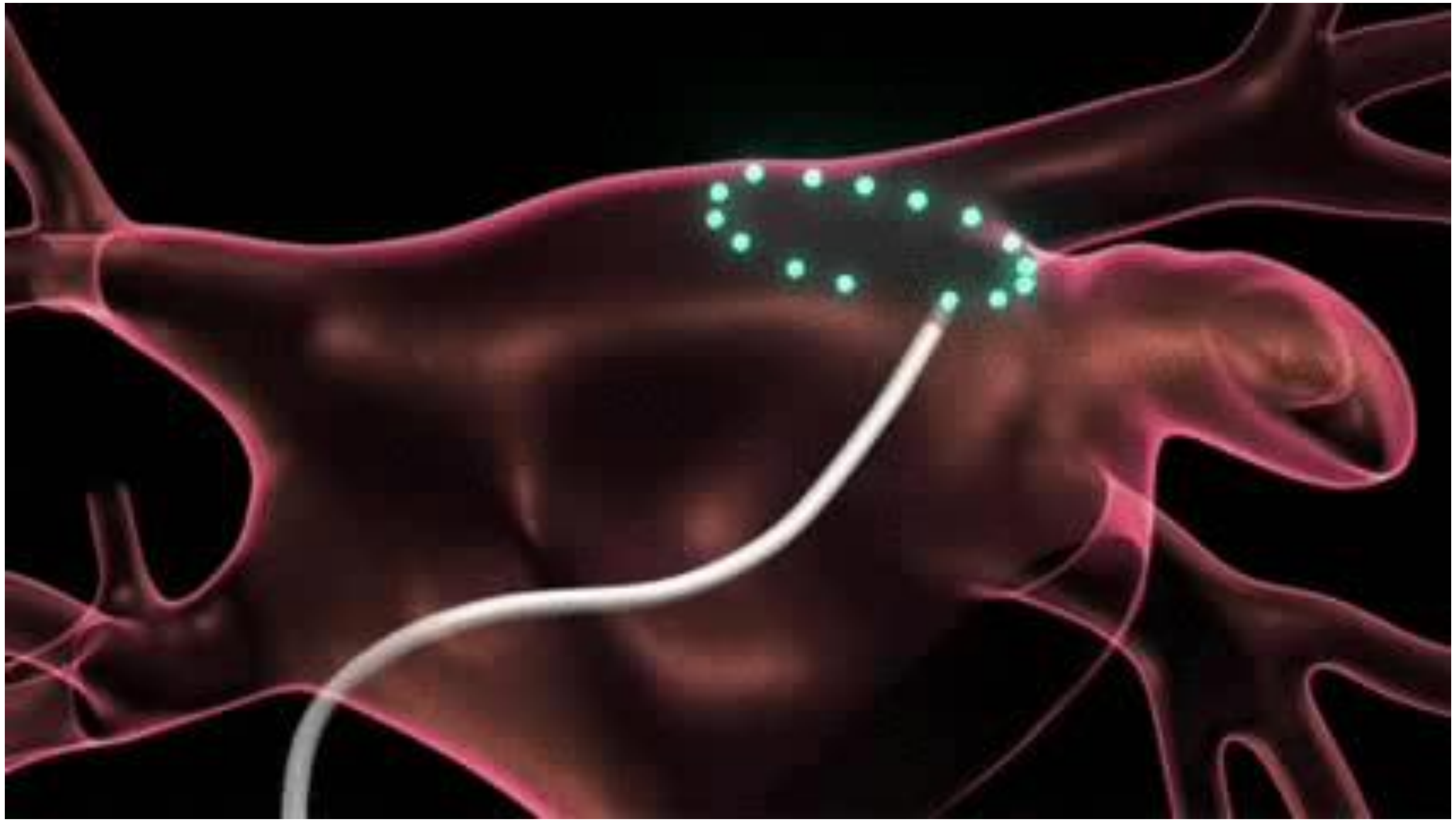

Video: Catheter Ablation for Atrial Fibrillation, Cleveland Clinic, 2011

Cappato R et al., Circulation 111(9), 2005 und Cappato R et al., Circ. Arrhythm. Electrophysiol 3(1), 2010; Jongbloed MR et al., Radiology, 234(3), 2005

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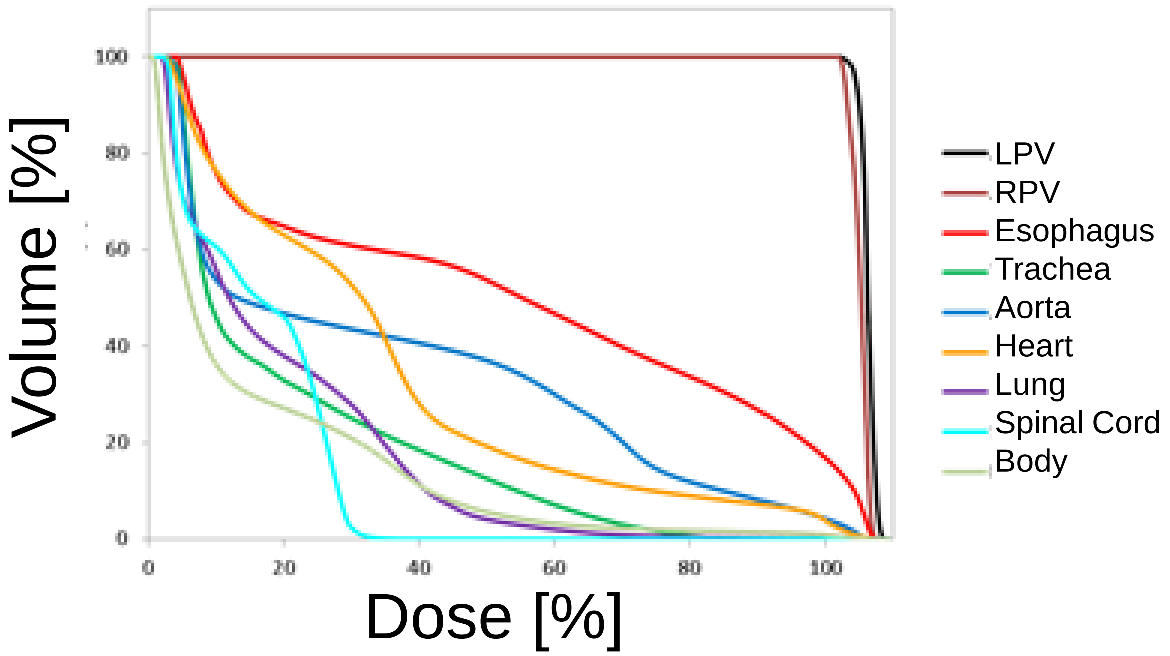
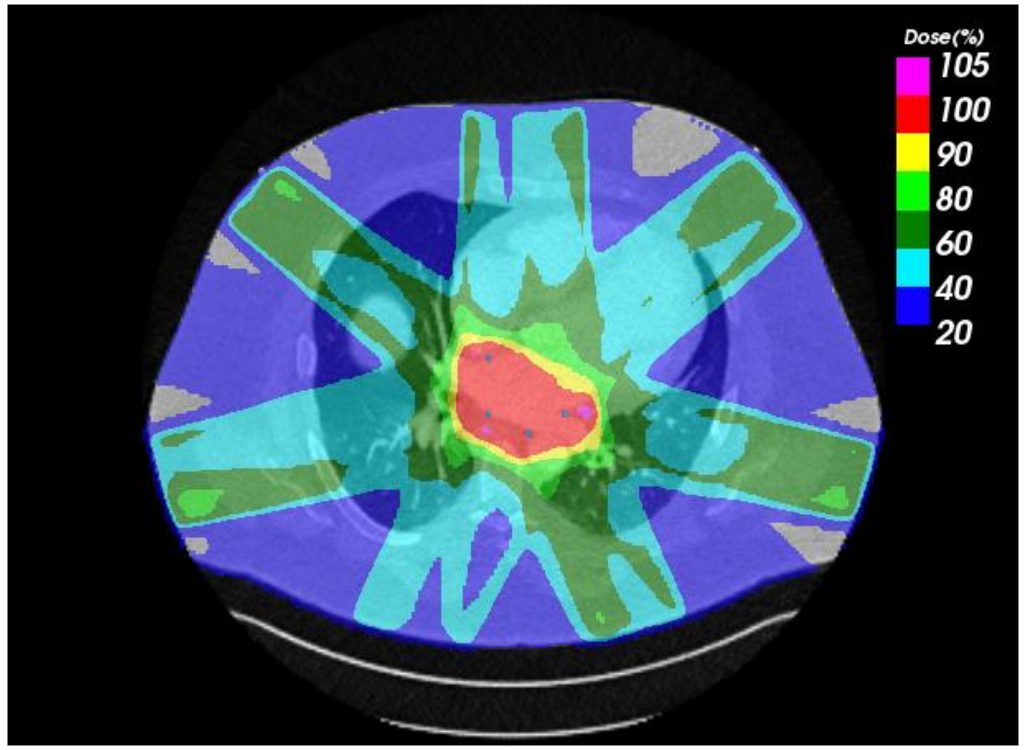
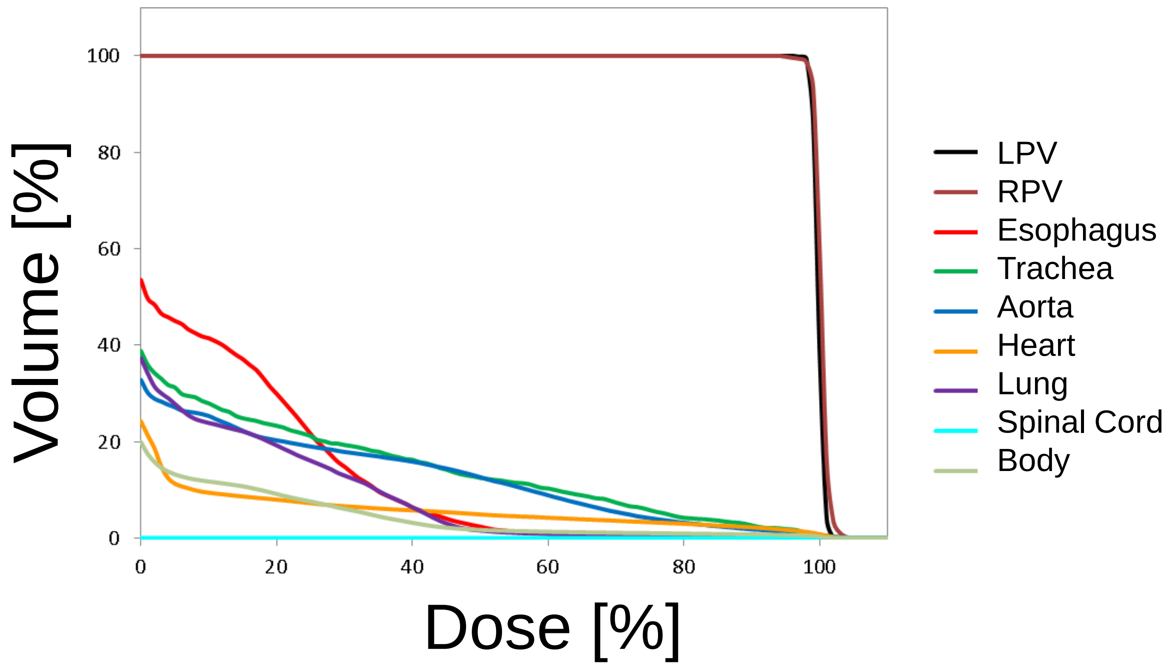
Radiotherapy for treatment?

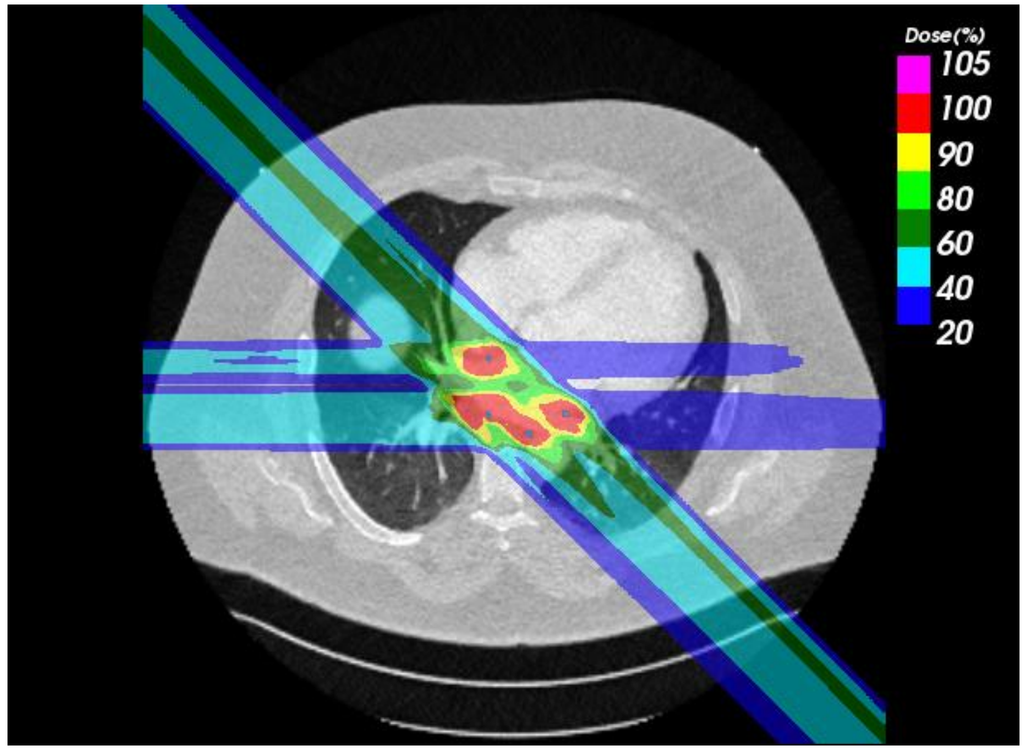
Photons (IMRT)





Carbon (IMPT)





Photonplan is courtesy of Dr. Amanda Deisher (Mayo Clinic).
Carbon-ion plan is courtesy of Dr. Anna Connstantinescu (GSI)

RAP
Actions under Grant Agreement No. 955956

Challanges

- Clinical impact
  - Patient outcome
  - Patient throughput
- Funding
  - Grants
  - Collaboration with industry
- Medical certification
  - CE & FDA & CFDA
- Time

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Ion beam therapy: An historical perspective

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Fundamental Research → Clinical Research → Clinical Application

1946 Ion therapy proposal for deep seeted tumors

1954 Lawrence Berkeley National Laboratory starts proton therapy in USA

1957 Uppsala starts proton treatment in Europe (Sweden)

1961 Proton treatment starts at Harvard Cyclotron

1975 Lawrence Berkeley National Laboratory starts therapy using heavy charged particles

1990 Opening of the Proton Therapy Center in Loma Linda

1993 Start of Carbon Ion Therapy in Chiba (Japan)

1996 Proton therapy with spot scanning starts at PSI in Villingen (Switzerland)

1997 Carbon ion therapy with raster scanning starts at GSI in Darmstadt (Germany)

Since 2000: Various clinical centers

Source: Lawrence Berkeley Lab/science photo library, Loma Linda University Medical Center, Courtesy S. Combs

Source: Katia Parodi‘s talk.

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Adaptive RT – How close are we?

- Time frame:
  - At the beginning of the treatment
  - Between fractions
  - Between positioning and delivery
  - During delivery
- Modality:
  - LINAC / MR-LINAC
  - PT
- Scope:
  - New plan
  - Adapted plan

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The best way to predict your future is to create it.

Abraham Lincoln

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Thank you!

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