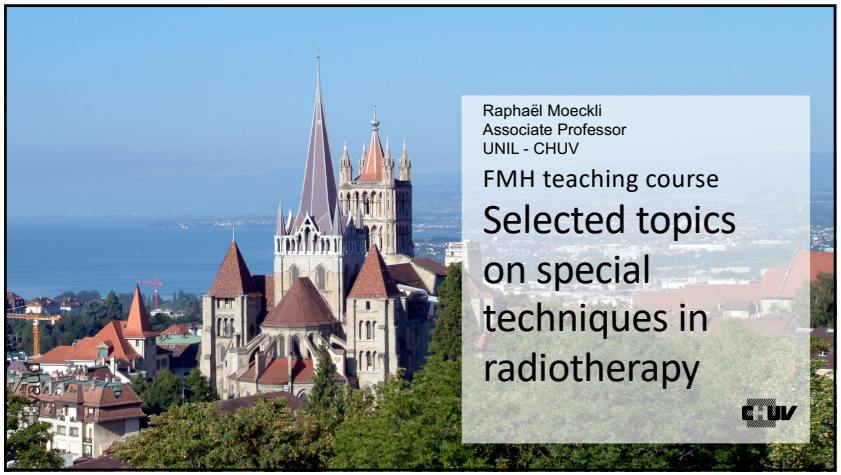


Conflicts of interest

Grant from Accuray

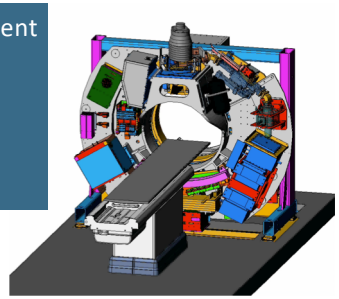
Collaborations with
RaySearch
IntraOp
PMB Alcen
CERN

Tomotherapy
CyberKnife
Flash Therapy

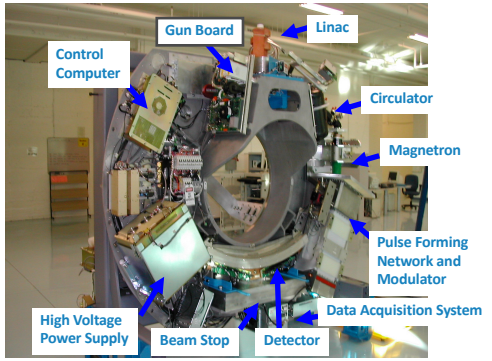
TOMOTHERAPY

Tomotherapy

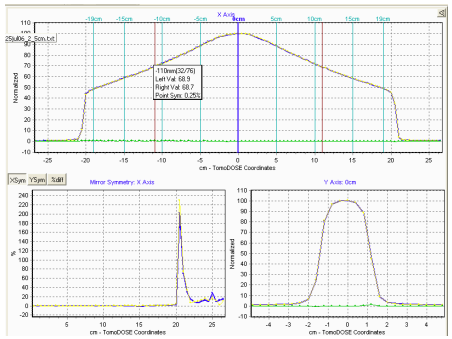
Principle: rotate a linac around the patient
« Mix » between a CT and a linac
Patient table moving during irradiation
Leaves moving during irradiation
Native IMRT and IGRT



Tomotherapy

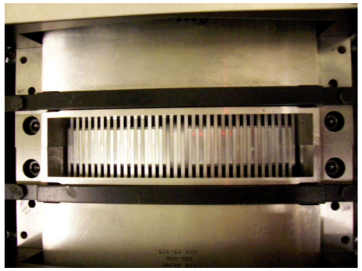


Characteristics



MLC

64 leaves
1 leaf (isocentre)
Width : 6.25 mm
Thickness : 10 cm
Open - close : 20 ms
Leaf transmission: 0.5 %
“Field sizes”: 1, 2.5 and 5 cm



Treatment table

Same as CT, but flat

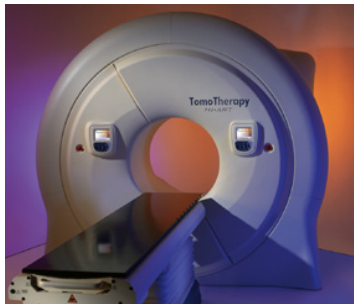
Max. treatment length: 160 cm

Pitch: between 0.1 and 1.5

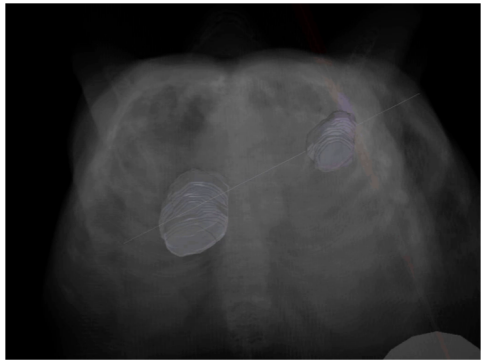
- Usually: 0.35 to 0.5
- 2 - 3 times same "gantry" position
- 2 - 3 times diff. leaves config.

→ Helical irradiation

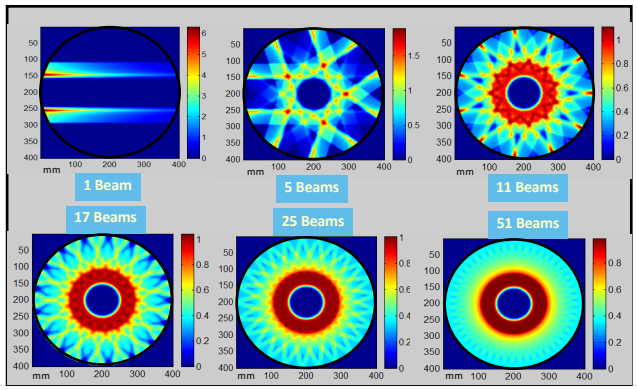
→ IMRT !



Irradiation

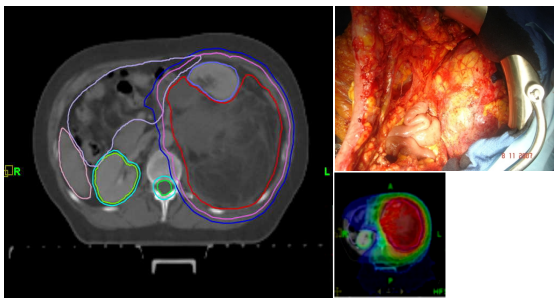


IMRT



IMRT

Retroperitoneal sarcoma

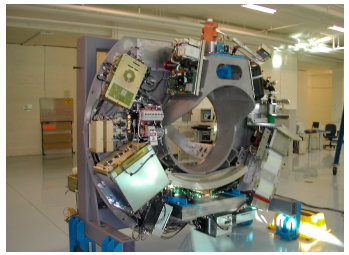


Courtesy: G. Kantor, Bordeaux

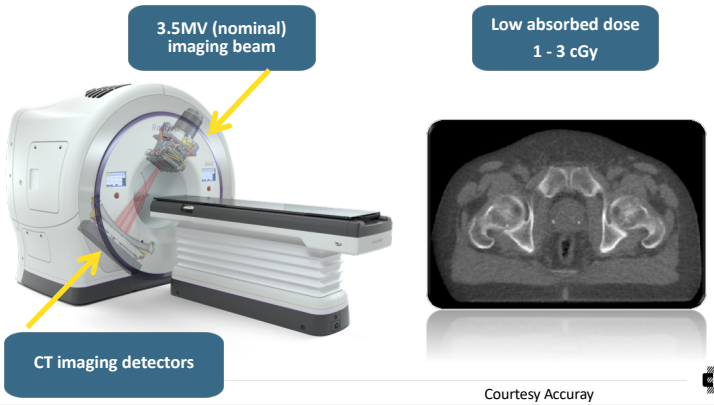
IGRT – MVCT

MV detector

- High energy CT imaging system
- 738 Xe ionisation chambers
- Fan beam geometry
- Volumetric imaging of the patient
- Online acquisition of beam data during the treatment



MVCT imaging



Courtesy Accuray

MVCT image acquisition

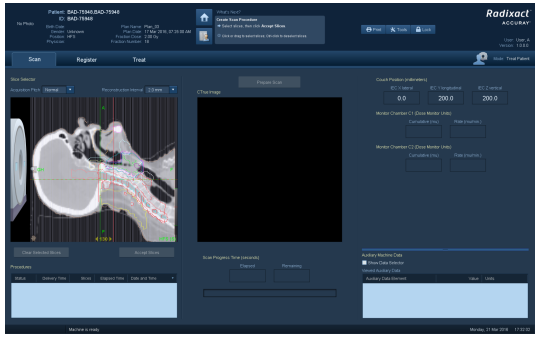
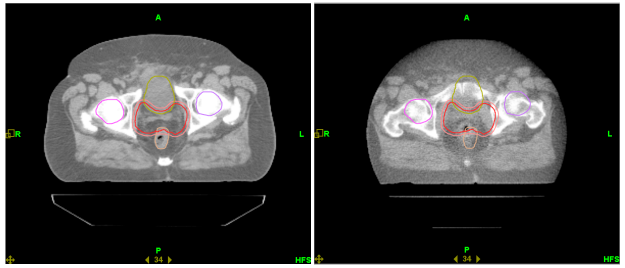


Image registration with planning CT

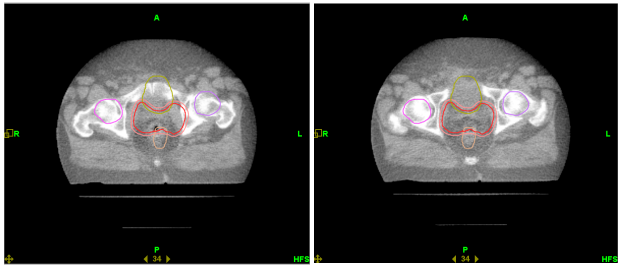
Add dose distribution and contours

Prostate case



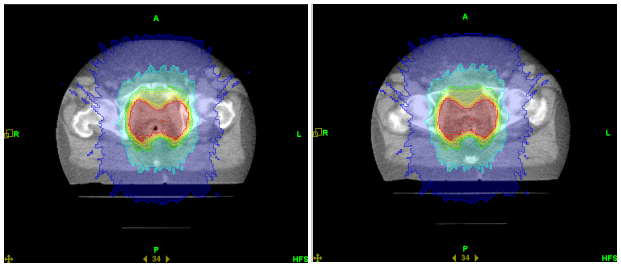
Dedicated CT MVCT tomotherapy

Prostate case



Before After

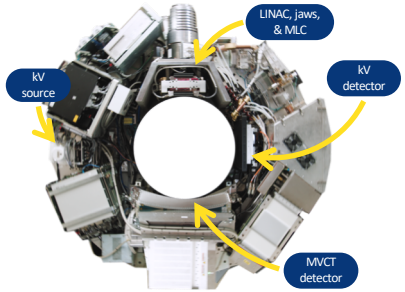
Prostate case

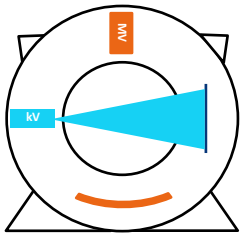


Before After

IGRT – KVCT

kVCT





Courtesy Accuray

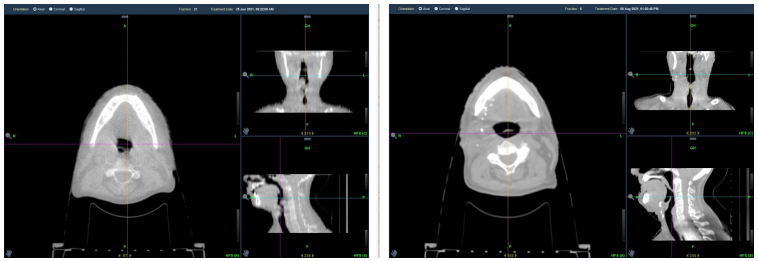
Characteristics

X-ray tube
40 – 150 kV
5 – 800 mA
Focal spot size: 0.6 or 1.2 mm^2
SAD: 104 cm
Bowtie filter and filtration

Detector
aSi
28.8 cm^2 at isocenter
Pixel size: 150 μm^2
DQE: 76% (0 mm^{-1})
MTF: 66% (1 mm^{-1})

Results
Improved image quality
Reduced acquisition time

Comparison MV - kV



QA

Some QA are described in SSRMP recommendations 11

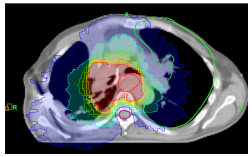
Some QA have disappeared

- Virtual wedges, light fields, MLC precision, electron's check, collimator, table rotation, …

New QA appeared

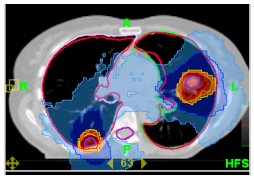
- Dynamic
- Synchronisation between gantry, table and MLC

Examples



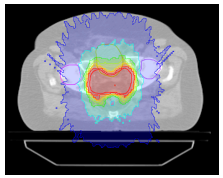
Paraspinal lesion

H&N

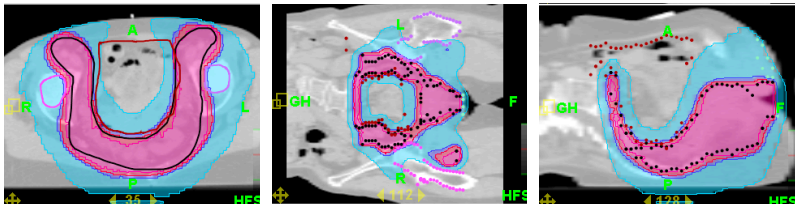


Lung

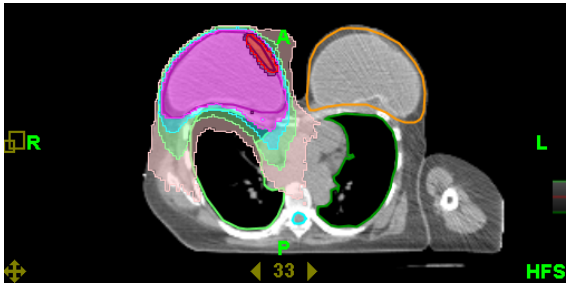
Prostate



Anal canal

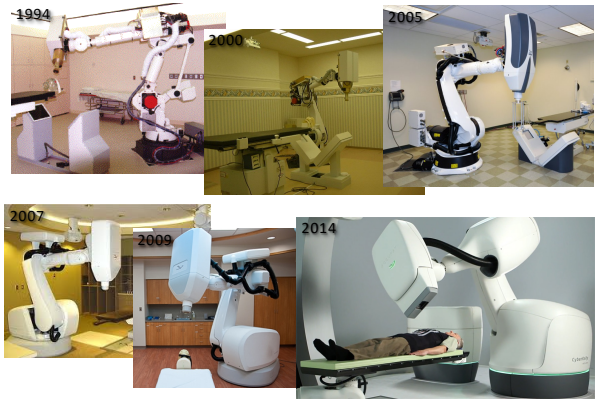


Breast

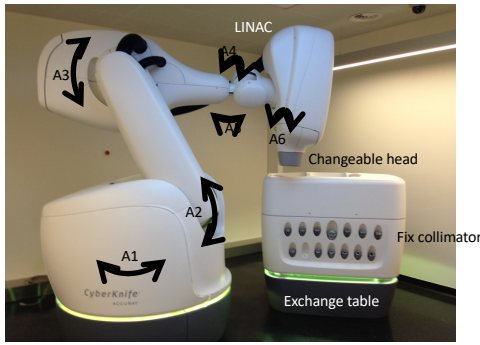


CYBERKNIFE

Cyberknife



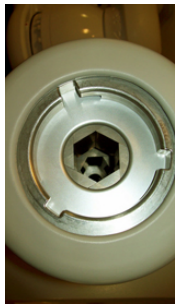
Treatment robot



Collimators

12 fix collimators
- 5 mm
- 7.5 mm
- 10 mm
- 12.5 mm
- 15 mm
- 20 mm
- 25 mm
- 30 mm
- 35 mm
- 40 mm
- 50 mm
- 60 mm

IRIS (dodecagon)
- 5 mm
- 7.5 mm
- 10 mm
- 12.5 mm
- 15 mm
- 20 mm
- 25 mm
- 30 mm
- 35 mm
- 40 mm
- 50 mm
- 60 mm



Collimators

MLC
- 2 banks of 26 leaves
- Leave size: 3.85 mm
- 11.5 x 10 cm^2
- Full digitation
- Overtravel

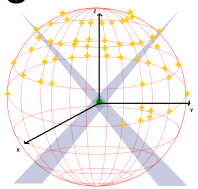
Treatment planning

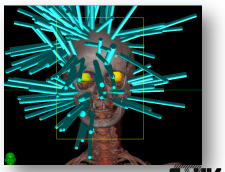
3D with many beams

Each beam starts from a node

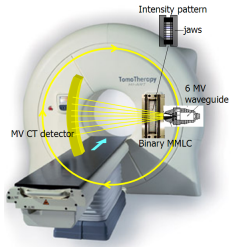
The available nodes depend on the chosen path during optimization

Each beam incidence is corrected according to patient position



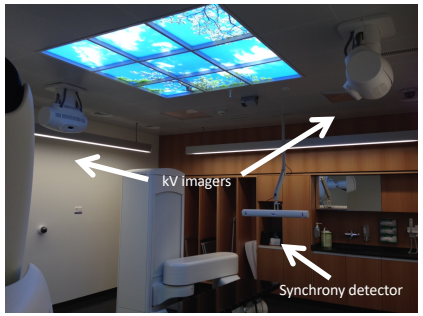


Patient positioning



Only before the irradiation

Patient positioning



Online correction ⇒ tracking

Moving target – Synchrony

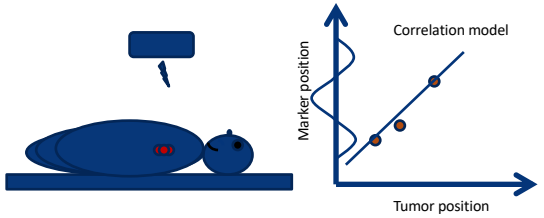
Correlation between external markers and target movement

↓

Synchronization of the beam movement with target movement

Synchrony – Correlation model

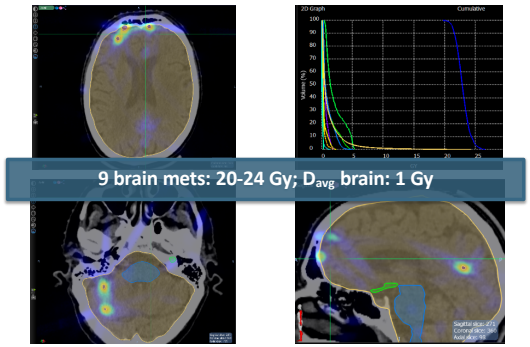
Patient on table
Creation of correlation model



Model update during treatment

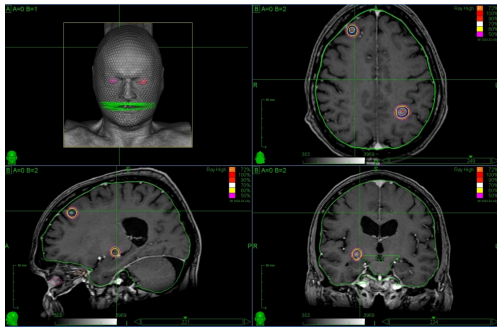
Synchrony – Correlation model

Clinical example

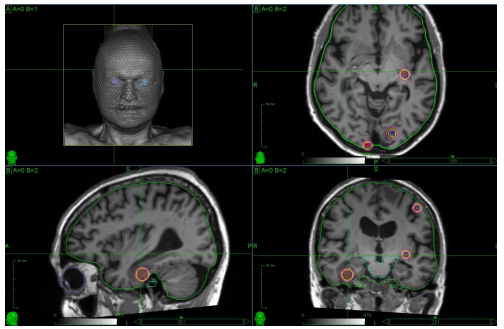


9 brain mets: 20-24 Gy; D_{avg} brain: 1 Gy

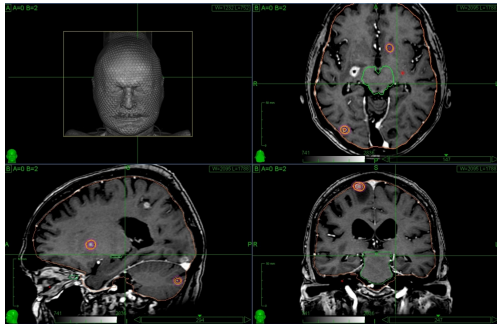
Melanoma – 8/2015 4 mets



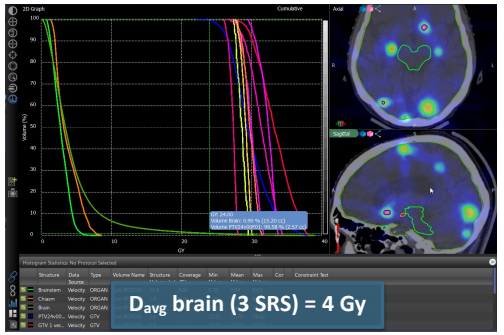
Melanoma – 10/2015 5 mets



Melanoma – 12/2015 9 mets



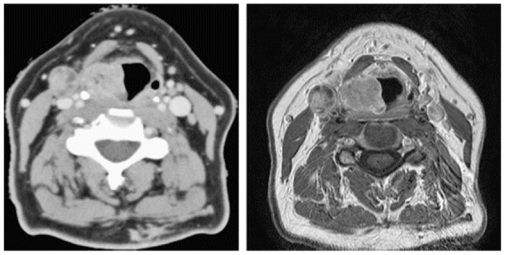
Composite dose of 3 SRS



MR LINAC

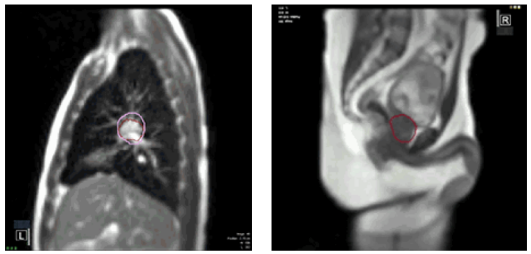
Online MR imaging

Courtesy Elekta & ViewRay



Verduijn, IJROBP, 2009

Motion management with MRI



Courtesy ViewRay

SWOT analysis

Strengths
- Improved image quality
  - Cross-sectional images
  - On-board functional imaging
  - No dose

Weaknesses
- Money
- Fraction time
- Magnetic field
- Bore size

Opportunities
- New workflow
  - On-line adaptive RT
- Motion monitoring during irradiation

Threats
- Workflow and software
- Intra-fraction motion
- Patient selection
- Staffing
- Evidence of clinical benefit

Van Herk, 2018

FLASH RT

What is FLASH RT ?

Ultra high dose rate (UHDR) beam to trigger FLASH effect

Biological effect

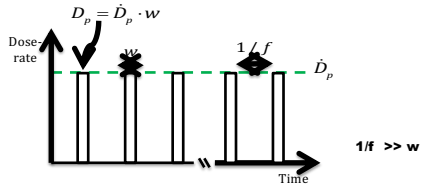
No biology, no FLASH (only UHDR)

Increase in **differential response** between normal tissue and tumors

Short treatment time (<1s)

Motion management, i.e. remove intra-fraction motion

Beam structure



w	pulse width	$[0.5 - 2.2]\ \mu s$
f	pulse repetition frequency	$[10 - 200]\ Hz$
$\dot{D}_p$	dose-rate in pulse	$[10^3 - 5 \cdot 10^6]\ Gy/s$
$D_p = \dot{D}_p \cdot w$	dose per pulse	$[10^{-3} - 5]\ Gy$
$\dot{D}_m = \dot{D}_p \cdot w \cdot f$	mean dose-rate	$[10^{-2} - 1000]\ Gy/s$

FLASH RT

	CONV	FLASH
Dose rate	~10^{-1} Gy/s	>100 Gy/s
Dose per pulse	~10^{-4} Gy	~10 Gy
Time for dose delivery	~ 10^{2} s	<10^{-1} s

Reference dosimetry

Five different dosimeters

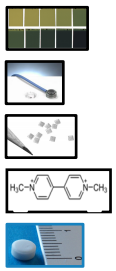
Films

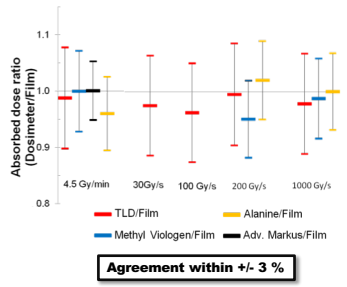
Ionization chamber

TLD

Methyl viologen

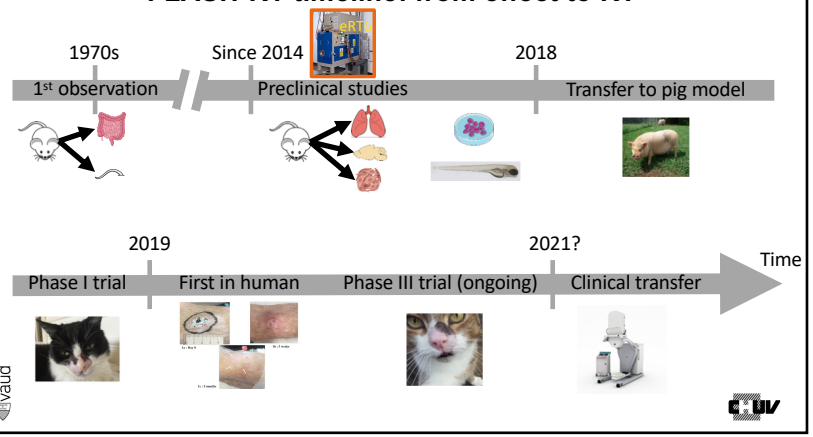
Alanine





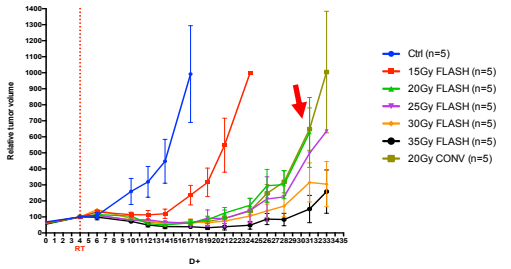
Jaccard, 2017, Petersson, 2017; Gondré, 2020

FLASH-RT timeline: from effect to RT



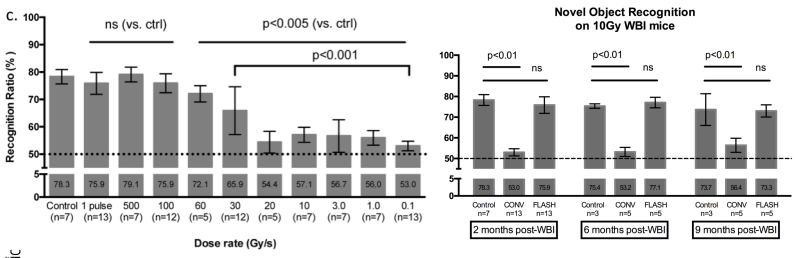
Tumor growth

10 Mio cells engrafted in mice



Healthy tissue tolerance

Memory testing in mice

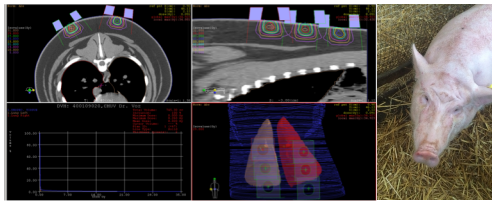


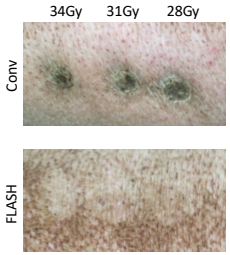
Montay-Gruel, 2017

Healthy tissue tolerance

Vozenin, Clin. Can. Res., 2018

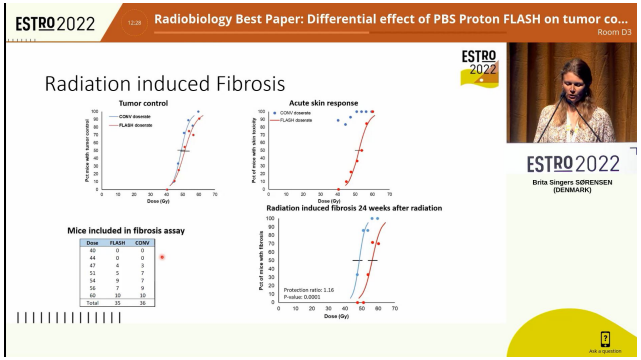
Pig irradiation





Vozenin, Clin. Can. Res., 2018

TCP / NTCP differential



Singers Sørensen, 2022

First patient

Cutaneous lymphoma, 15 Gy single dose
10 pulses, 1 µs, 90 ms

Bourhis, 2018

Clinical trial

FLASH with protons

- First clinical trial completed
- 10 patients
- Primary endpoint: workflow feasibility
- To date, no serious adverse event

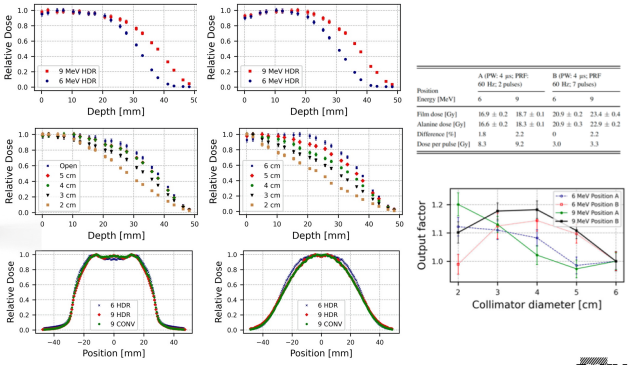
Clinical trial

IntraOp Announces First Patients Enrolled in FLASH Clinical Trial

July 08, 2021

IntraOp Medical Corporation announced today that Lausanne University Hospital (CHUV, Switzerland) enrolled the first patients in the **Impulse Trial: A phase I dose-escalation study of high dose rate radiotherapy with electrons in patients with skin metastases from melanoma**. The trial is a key milestone for the groundbreaking research collaboration agreement between IntraOp and the CHUV, executed in 2020. The Impulse Trial is the first in the world to evaluate the potential of leveraging the biological phenomenon known as the "FLASH Effect" to provide radiotherapy with curative intent to radio-resistant cancers.

Beam commissioning



Moeckli, 2021

Beam commissioning

Test and frequency	Method	Tolerance
Daily		
Output constancy	Daily check setup	3%
Energy constancy	Daily check with 2 cm additional water slabs	2 mm shift in depth dose
Door interlock	Run an irradiation in CONV mode and open the door	Functional
Mechanical motion	Manual and visual check	Functional
Docking system	Manual and visual check	Functional
Monthly		
Output constancy	Daily check setup, ten measurements per mode	2%
Energy constancy	Daily check with 2 cm additional water slab, ten measurement per mode	2 mm shift in depth dose
Flatness and symmetry constancy	Profile at maximum depth comparison	3%
Annually		
Beam output: Definitive calibration	Reference dosimetry with alanine and films	2%
Depth dose curve for all collimators	Same setup as for commissioning	2%/2 mm
Dose profiles: Extensive checks	Same setup as for commissioning	3%
Output factors	Same setup as for commissioning	2–3%
Linearity of the dosimetry system	Same setup as for acceptance	1%

Moeckli, 2021

Beam commissioning

How to do the measurements ?
Limitation comes from radiation protection

Just to fix ideas
CHUV: ~ 1’200 patient / year
How long is the beam on time in UHDR ?

About 5 minutes !

A phase I dose finding study of high dose rate radiotherapy in patients with skin metastases from melanoma

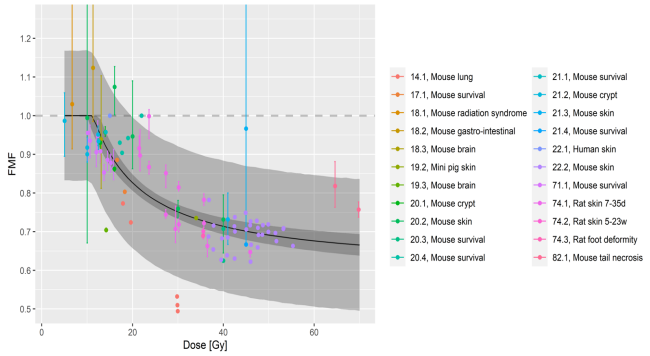
Current level

Dose level	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6	Level 7
Dose	22 Gy	24 Gy	26 Gy	28 Gy	30 Gy	32 Gy	34 Gy

2,2 Gy / pulse → 3.4 Gy / pulse

10 pulses, 100 ms

A final comment on FLASH



Boehlen, 2022