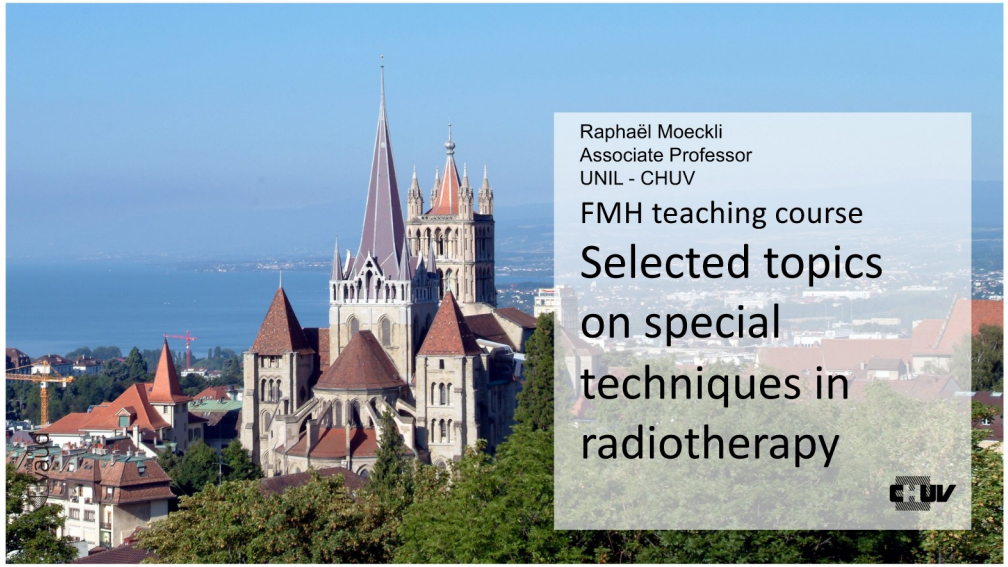


Conflicts of interest

Grant from Accuray

Collaborations with
RaySearch
IntraOp
PMB Alcen
CERN

Tomotherapy
CyberKnife
Flash Therapy

TOMOTHERAPY

Tomotherapy

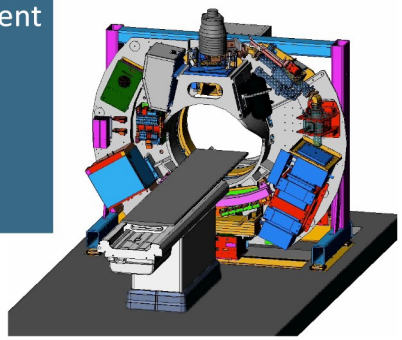
Principle: rotate a linac around the patient

« Mix » between a CT and a linac

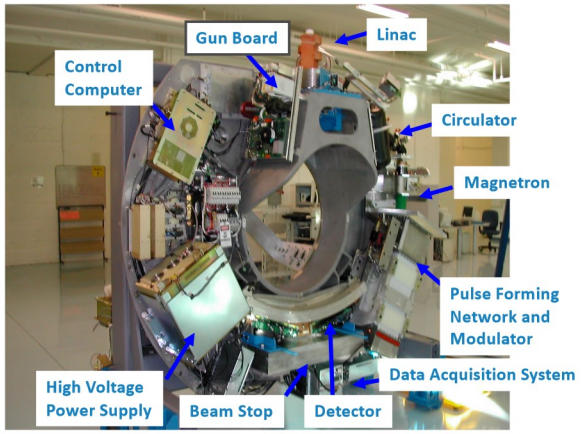
Patient table moving during irradiation

Leaves moving during irradiation

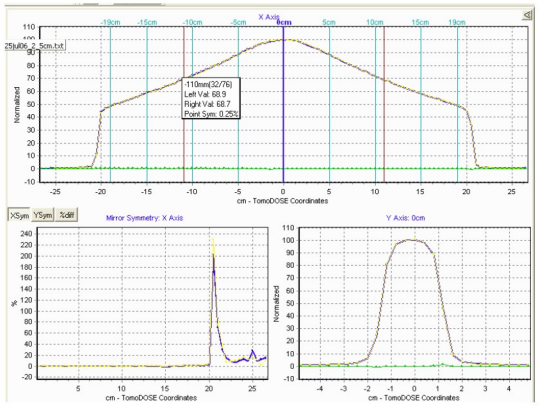
Native IMRT and IGRT



Tomotherapy



Characteristics



MLC

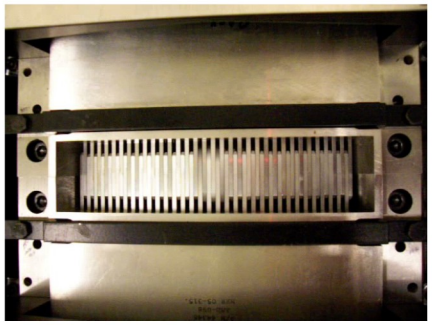
64 leaves

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

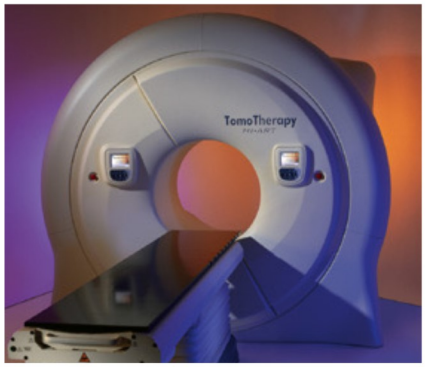
Max. treatment length: 160 cm

Pitch: between 0.1 and 1.5

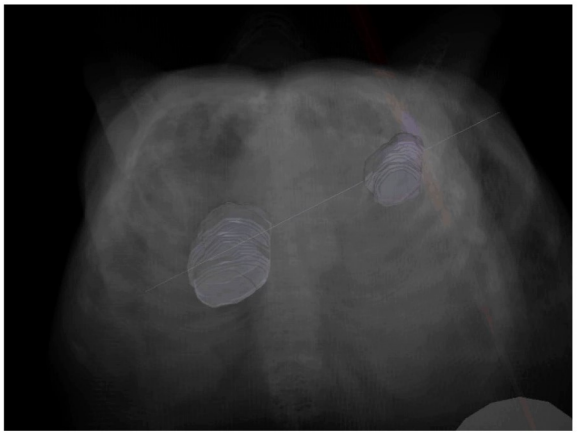
- Usually: 0.35 to 0.5
- 2 - 3 times same “gantry” position
- 2 - 3 times diff. leaves config.

➜ Helical irradiation

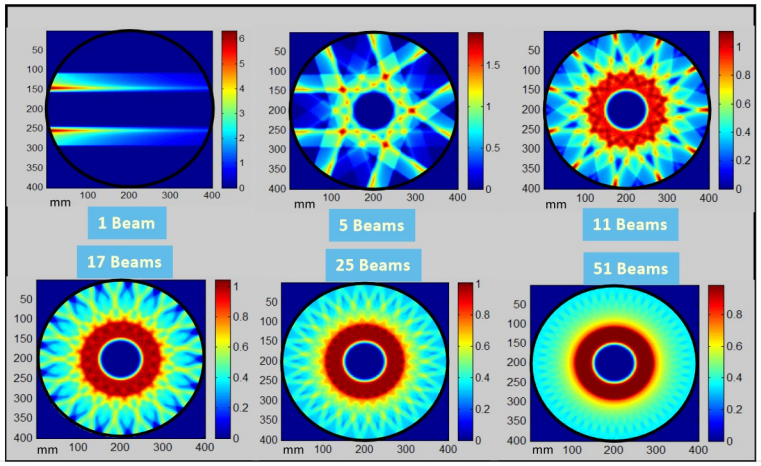
➜ IMRT !



Irradiation

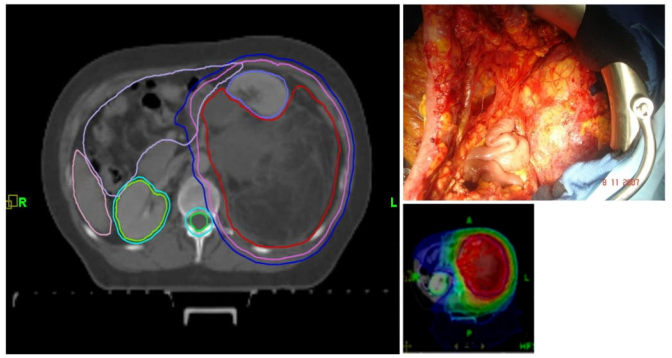


IMRT



IMRT

Retroperitoneal sarcoma

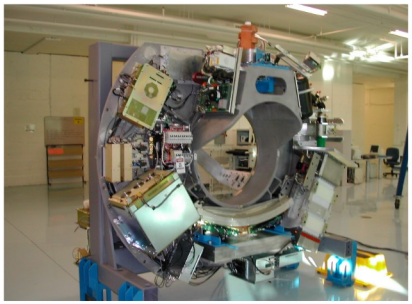


Courtesy: G. Kantor, Bordeaux

IGRT – MVCT

MV detector

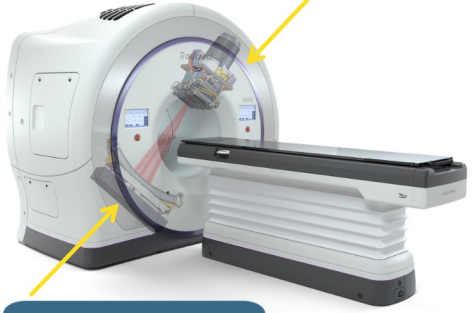
- High energy CT imaging system
- 738 Xe ionisation chambers
- Fan beam geometry
- Volumetric imaging of the patient
- Online acquisition of beam data during the treatment



MVCT imaging

3.5MV (nominal) imaging beam

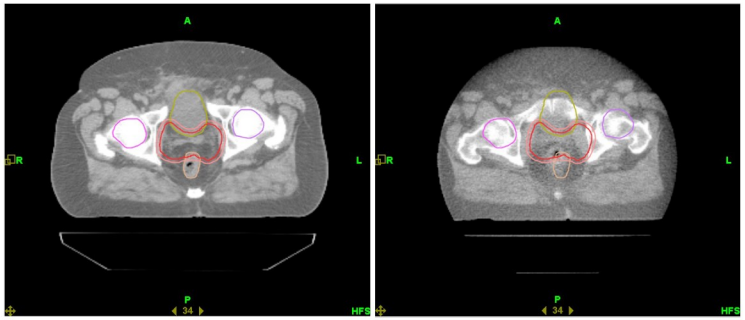
Low absorbed dose 1 - 3 cGy



CT imaging detectors

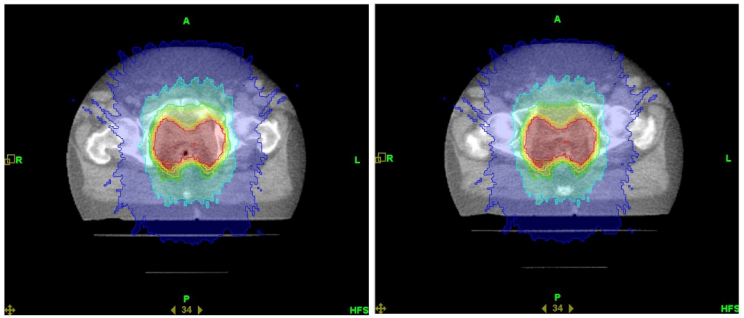
Courtesy Accuray

Prostate case



Planning CT MVCT tomotherapy

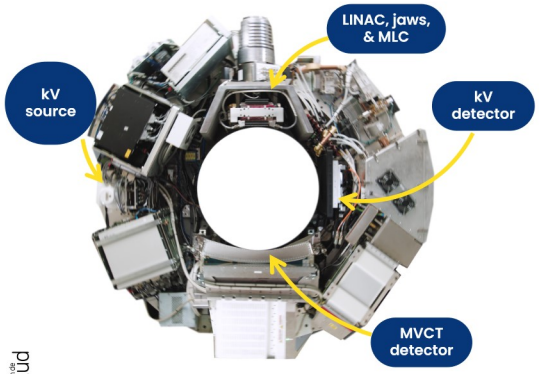
Prostate case

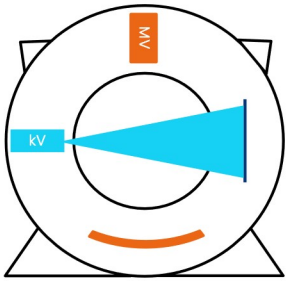


Before After

IGRT – kVCT

kVCT





Courtesy Accuray

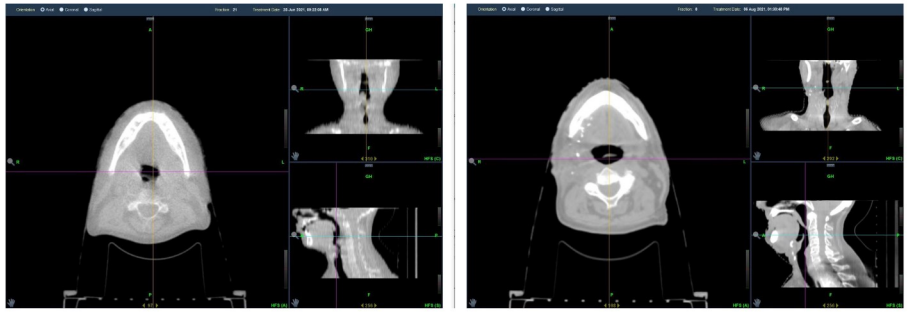
Characteristics

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

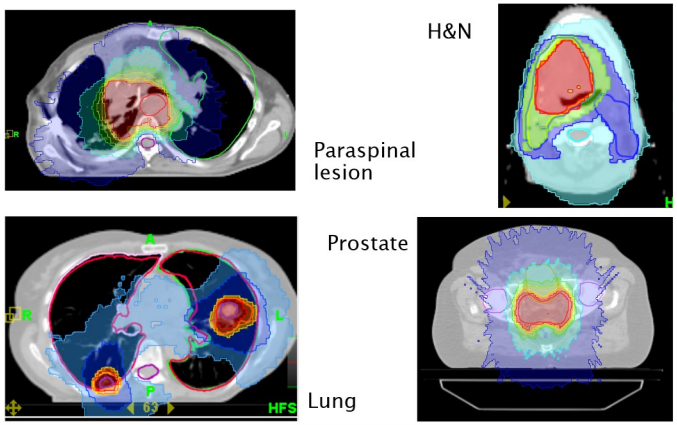
Some QA have disappeared

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

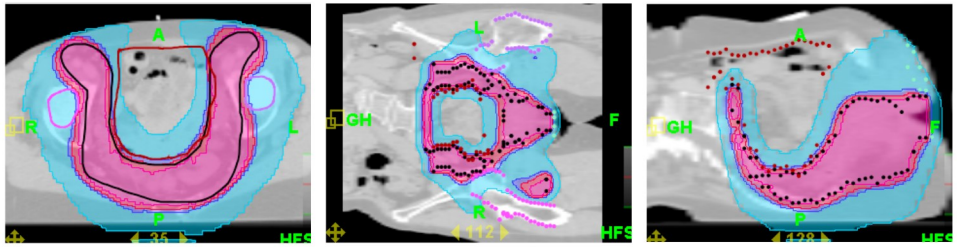
New QA appeared

- Dynamic
- Synchronisation between gantry, table and MLC

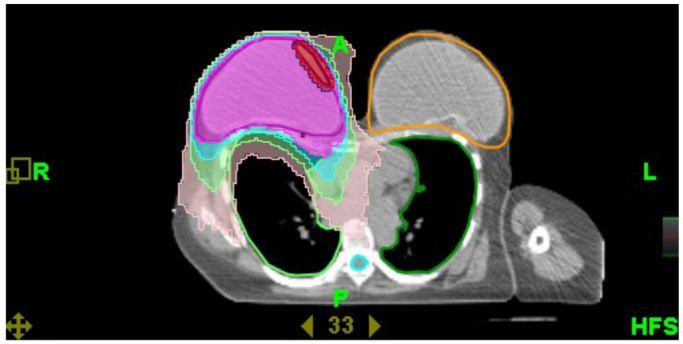
Examples



Anal canal

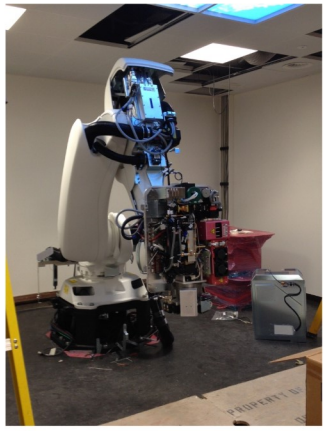


Breast

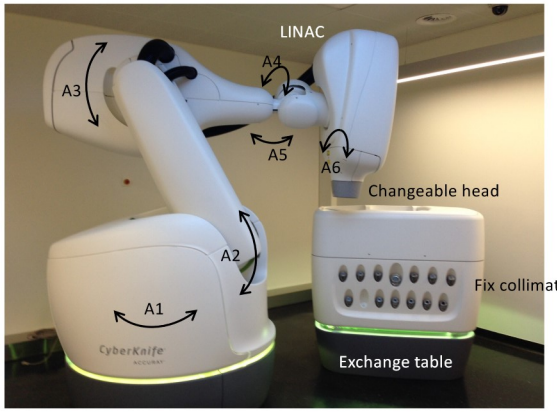


CYBERKNIFE

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

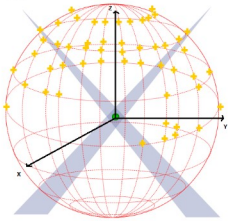
Treatment planning

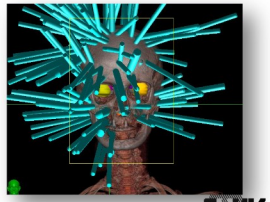
3D with many beams

Each beam starts from a node

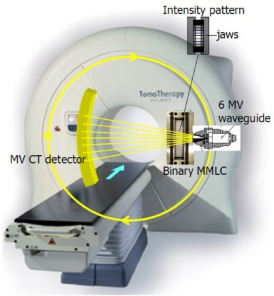
The available nodes depend on the chosen path during optimization

Each beam incidence is corrected according to patient position



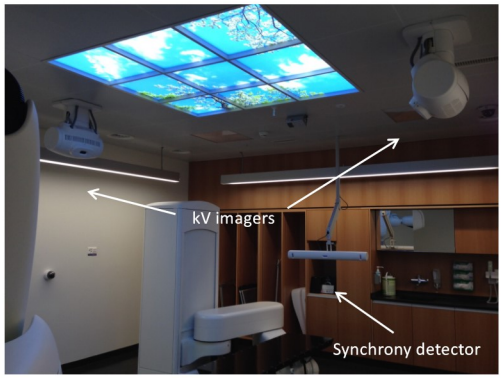


Patient positioning



Only before the irradiation

Patient positioning



Online correction ⇒ tracking

Moving target – Synchrony

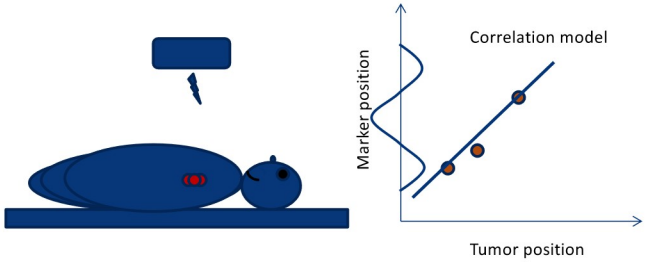
Correlation between external markers and target movement

↓

Synchronization of the beam movement with target movement

Synchrony – Correlation model

Patient on table
Creation of correlation model

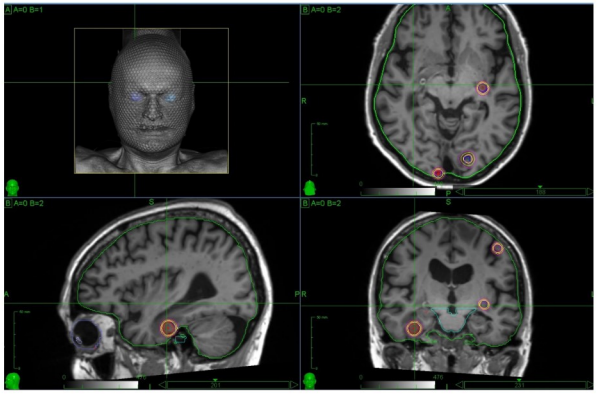


Model update during treatment

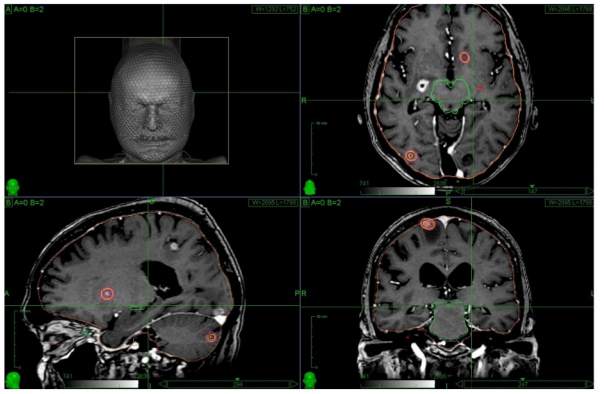
Synchrony – Correlation model

Melanoma – 8/2015 4 mets

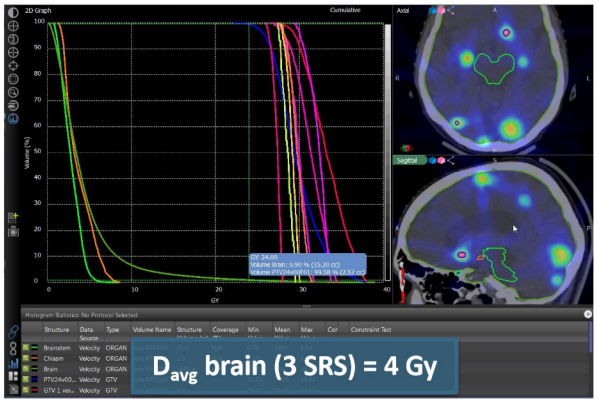
Melanoma – 10/2015 5 mets



Melanoma – 12/2015 9 mets



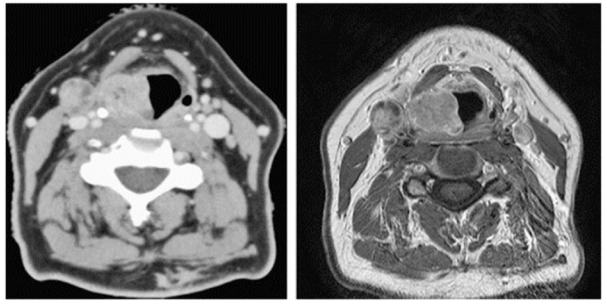
Composite dose of 3 SRS



MR LINAC

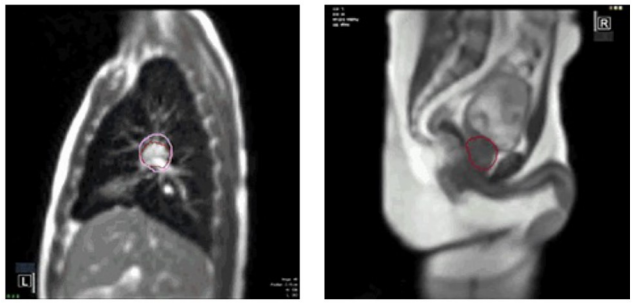
Online MR imaging

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

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

Van Herk, 2018

FLASH RT

What is FLASH RT ?

U**ltra high dose rate** (UHDR) beam to trigger FLASH effect

Biological effect

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

Short treatment time (<1s)

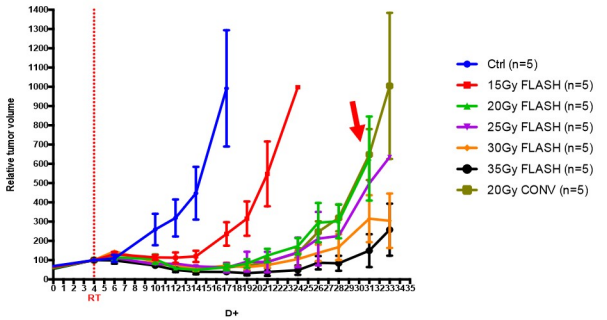
Motion management, i.e. remove intra-fraction motion

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

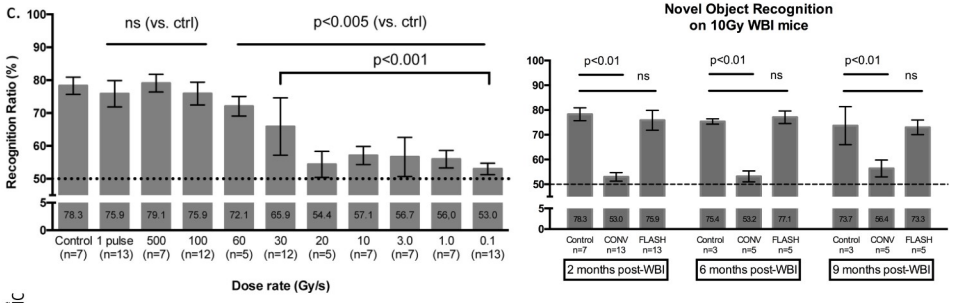
Tumor growth

10 Mio cells engrafted in mice



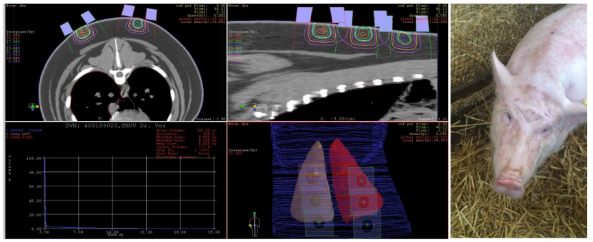
Healthy tissue tolerance

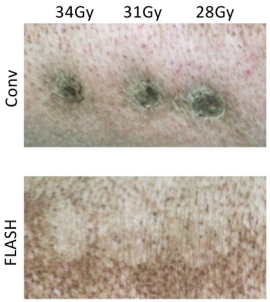
Memory testing in mice



Montay-Gruel, 2017

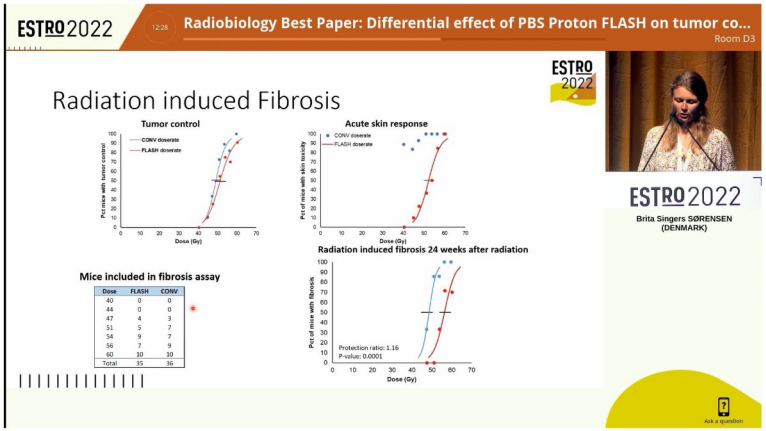
Pig irradiation





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

IMPulse 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.

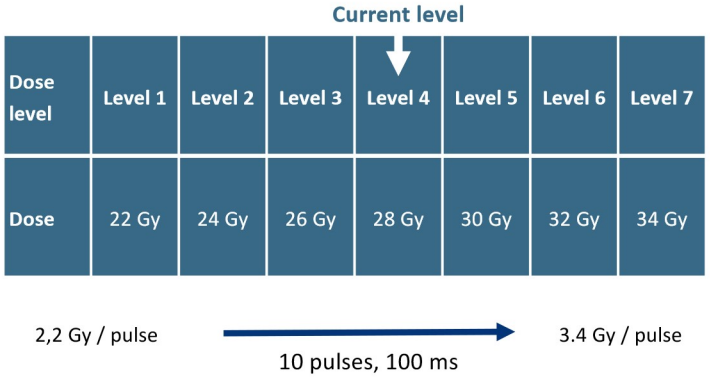
IMPulse clinical trial

Phase I dose escalation for melanoma skin metastases

Same parameters associated with FLASH in pig skin
Dose escalation 22 Gy to 34 Gy
Primary endpoint DLT (acute)
Small (< 30 cc) and large tumors (30-100 cc)
Recruiting in both cohorts (14 lesions; 8 patients yet)

https://clinicaltrials.gov

IMPulse clinical trial



Dosimetric evaluation IMPulse

Redundent dosimetry before and after the irradiation
Alanine and TLD in treatment conditions
In vivo dosimetry when possible
Expected max variation ± 5%

Lesion #	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Prescr. [Gy]	22	22	22	22	24	24	24	24	24	26	26	26	28	28
Measure [Gy]	22.2	21.6	22.1	22.6	24.8	24.8	24.3	24.3	24.8	26.2	26.2	26.2	27.8	27.7
Diff. [%]	0.9	-1.9	0.4	2.7	3.3	3.3	1.3	1.3	3.3	0.7	0.7	0.7	-0.9	-1.1

Global: 1.0% ± 1.7%

Jorge, in preparation

Lance clinical trial

Phase II FLASH vs CDR RT for cutaneous SCC or BCC

T1: 22 Gy single dose
T2: 5 x 6 Gy fractionated
Primary endpoints
- Safety by > grade 3 after 6 weeks
- Efficacy by local control

Kinj, 2024

Lance clinical trial

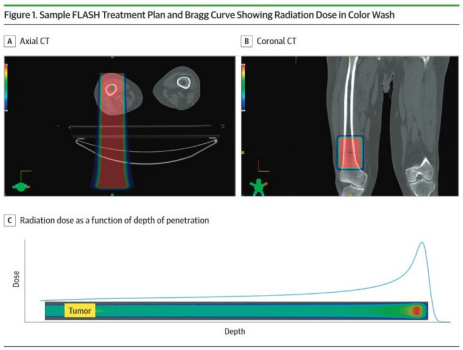
So far

T1: 22 Gy single dose
- 2 lesions in CDR and 4 lesions in UHDR

T2: 5 x 6 Gy fractionated
- 5 lesions in CDR and 1 lesion in UHDR

Kinj 2024

FAST-01 trial: Extremity bone metastases



FLASH-enabled Varian ProBeam
250 MeV transmission protons
8 Gy single fraction, 51-62 Gy/s
10 pts, palliative setting
Nov 2020 – Oct 2021

Follow up: FAST-02 trial
(Bone metastases in the thorax)
Started Feb 2023

Feasibility, efficacy, safety

VHEE

The DEFT project

First objective of FLASH therapy : contribute to increase cancer cure rate

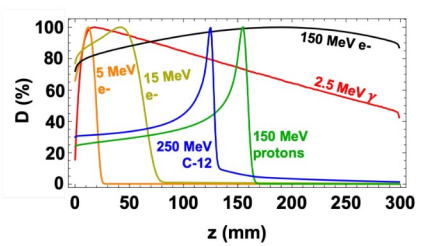
Non curable disease first

Dose escalation for glioblastoma and large-volume brain metastases

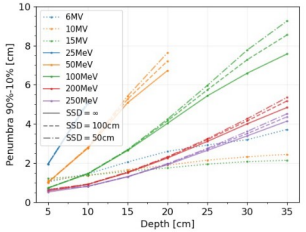
Switch from palliative 12 x 3 Gy to curative 12 x 4 Gy

All types of unresectable locally-advanced cancers

The DEFT project



PDD to reach deep-seated tumors.

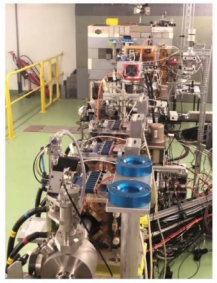


Sharp lateral penumbra for highly conformal treatments

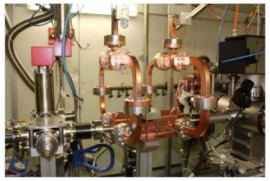
Very High Energy Electrons – 100 to 250 MeV
Shoot-through less sensitive to heterogeneities

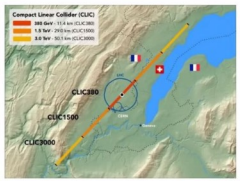
The DEFT project

CLIC - Compact Linear Collider



The CLEAR user facility at CERN, beam energies up to 220 MeV.

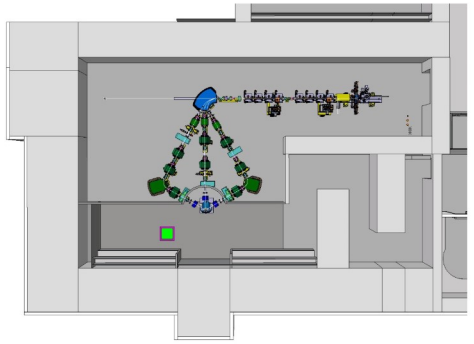


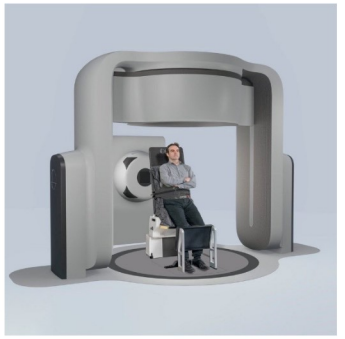


100 MeV/m accelerating gradient prototype developed for a TeV high-energy physics facility.

The DEFT project

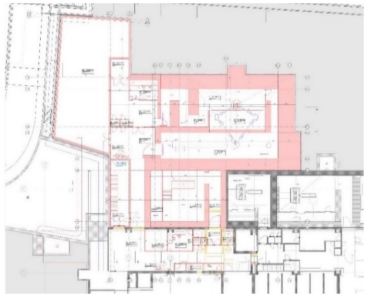
Treatment from multiple directions in less than 0.1s



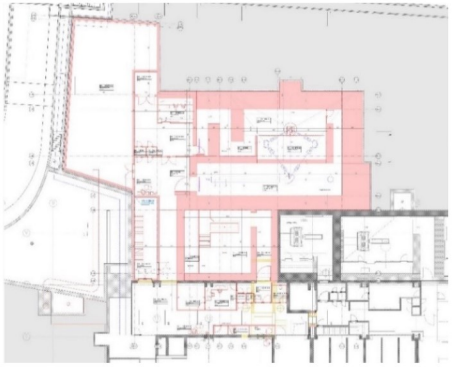


THERYQ

The DEFT project

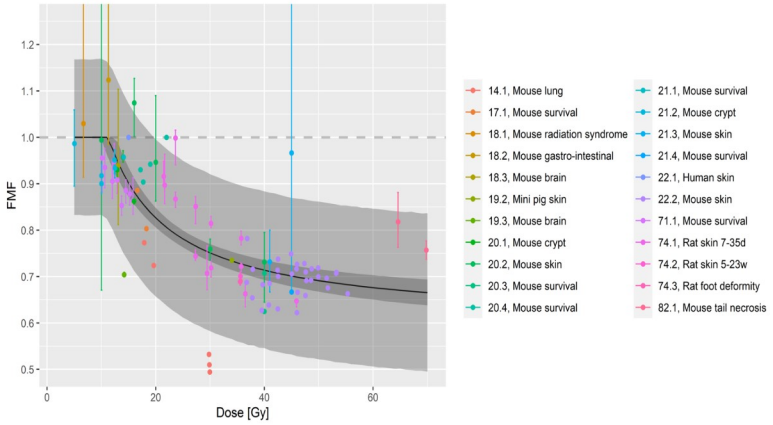


The DEFT project



THERYQ

Post scriptum



Boehlen, 2022