Institute of radiation physics, Switzerland

Dosimetry in Modern Radiation Therapy: FLASH-RT

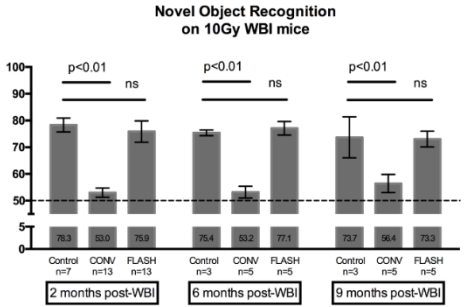
C. Bailat

First, what are we talking about…….

FLASH-RT in very short: Irradiation at ultra high dose-rate increases the differential response between normal and tumour tissue

Flash

Conventional



Context: History of FLASH-RT

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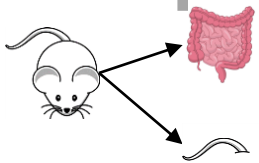
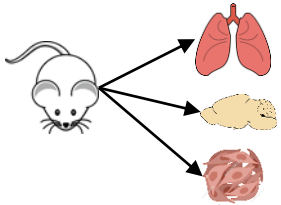
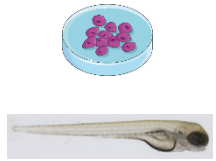
1970s — 1st observation



Since 2014 — Preclinical studies



2018 — Transfer to pig model



2019 — Phase I trial

First in human

Phase III trial (ongoing)

2022… — Clinical transfer

Time

Context: from point A to point B …to H

Point A: Conventional radiotherapy

- Well-crafted code of practice for decades
- Based on well standardized beam qualities and irradiation geometries.

Point B: FLASH-RT

- Ultra high dose rate (UHDR)
- No code of practice
- No standardized beam qualities

Context: Conventional RT

Clinical LINAC delivery is predictable

Output is stabilized

Diagnostic → feedback loops → control of the beam → stability

Beam characteristics are defined according to international recommendations (IEC, ISO, ICRU, IAEA, AAPM,…)

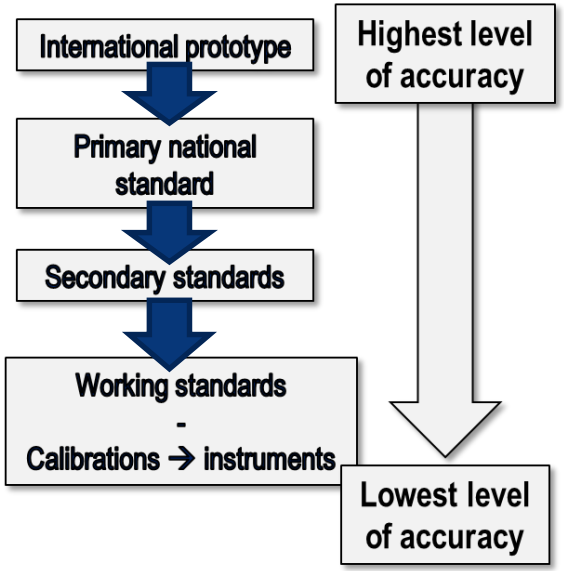
Physical beam indicators are well-defined

→ Dosimeter calibration in a standardized beam quality and correction factors to other beam qualities are provided

→ **Traceability is insured**

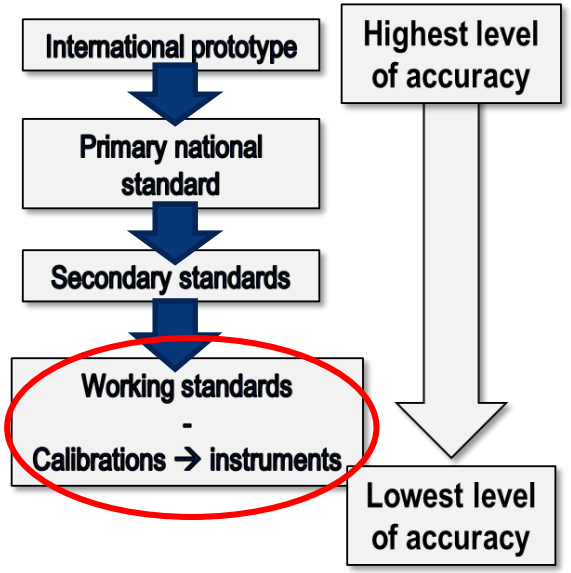
Context: Traceability

Refers to an unbroken chain of comparisons relating an instrument's measurements to a known standard.



Context: Traceability

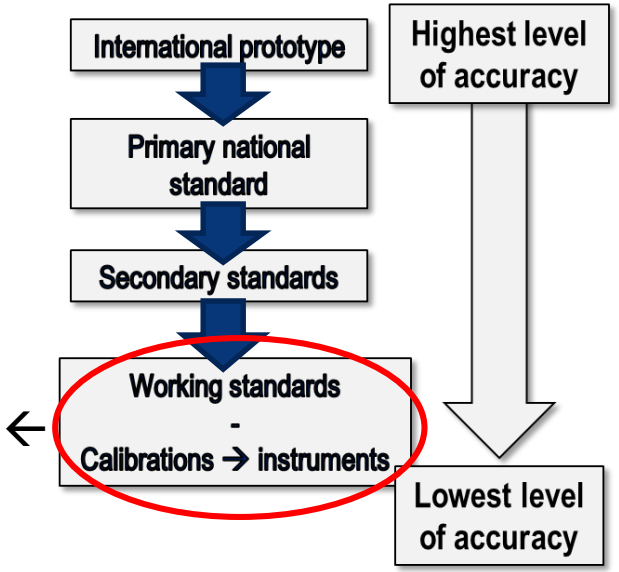
For absorbed dose to water in external beam radiotherapy (EBRT)?



Context: Traceability

For absorbed dose to water in external beam radiotherapy (EBRT)?

For ex: Ionisation chamber and 2 % uncertainty



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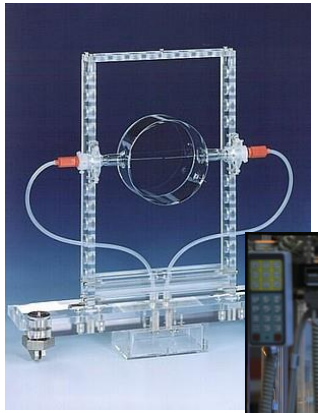
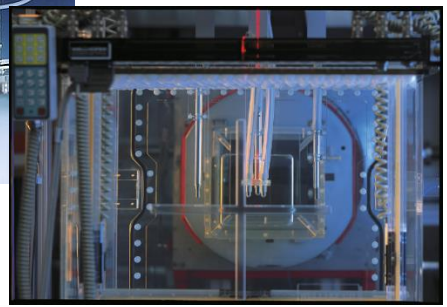
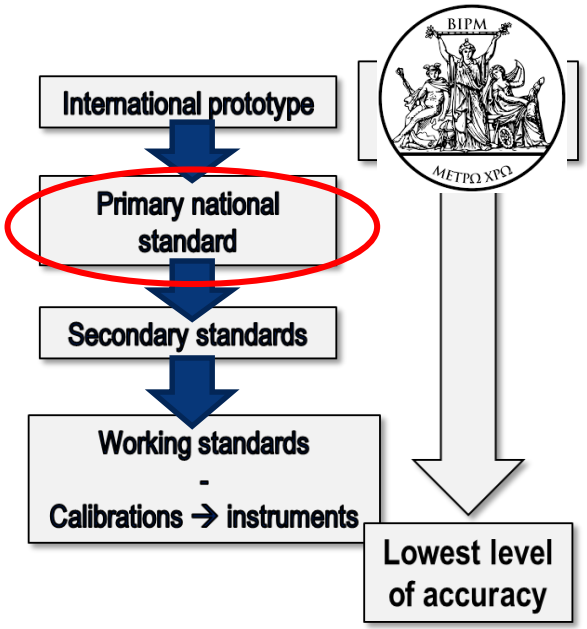


For ex: Water calorimeter ←



→ ΔmK



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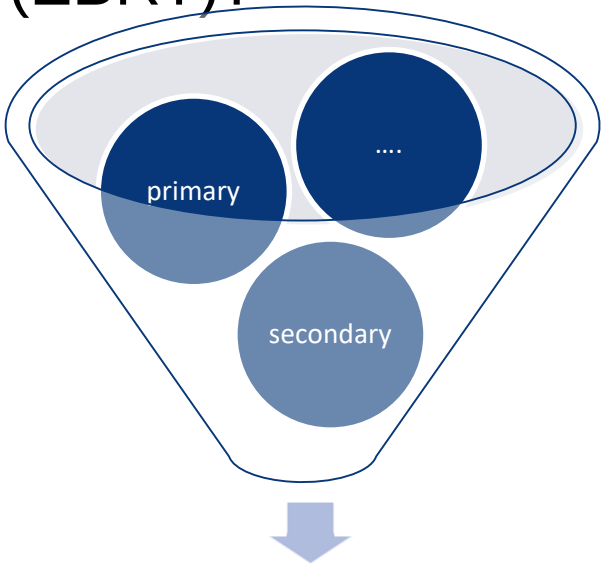
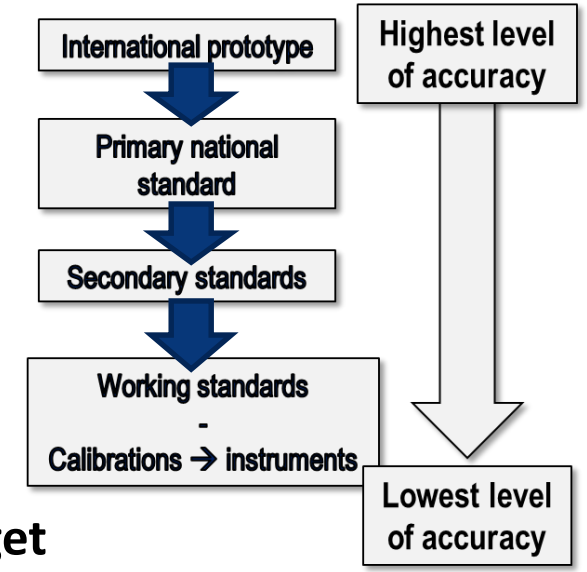
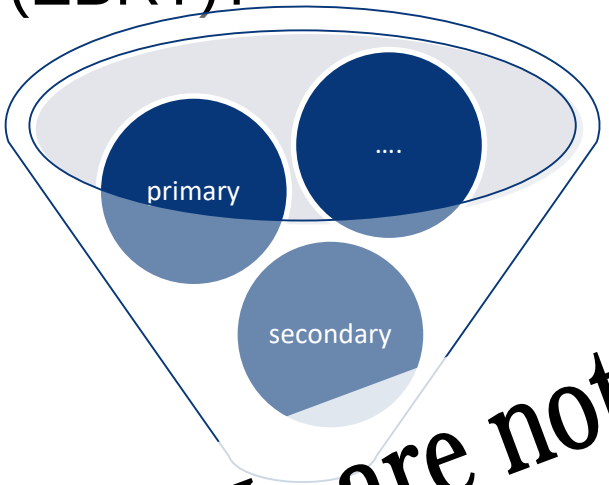




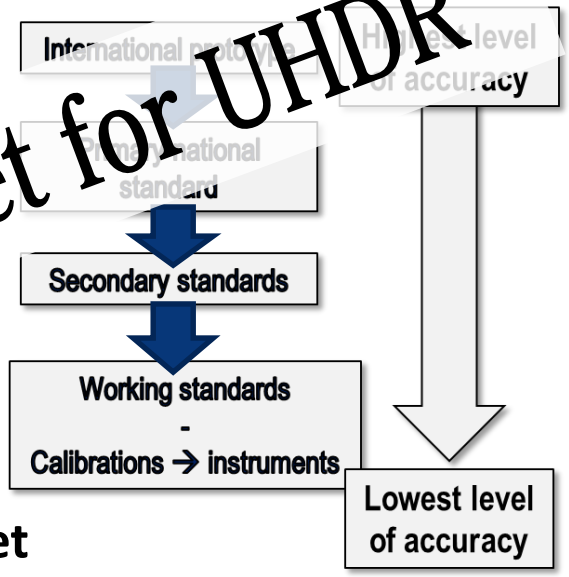
Quadratic sum → **Uncertainty budget**

Context: Traceability

For absorbed dose to water in external beam radiotherapy (EBRT)?



We are not there yet for UHDR

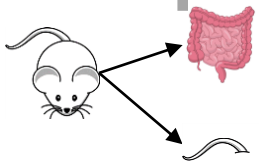


Quadratic sum ➡ **Uncertainty budget**

eRT6 arrival at CHUV

1970s

1st observation



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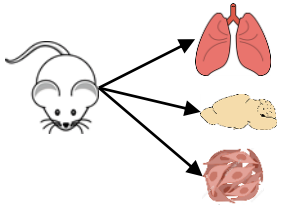

2018

Transfer to pig model

2019

Phase I trial

First in human

2022

Phase III trial (ongoing)

Clinical transfer

Time

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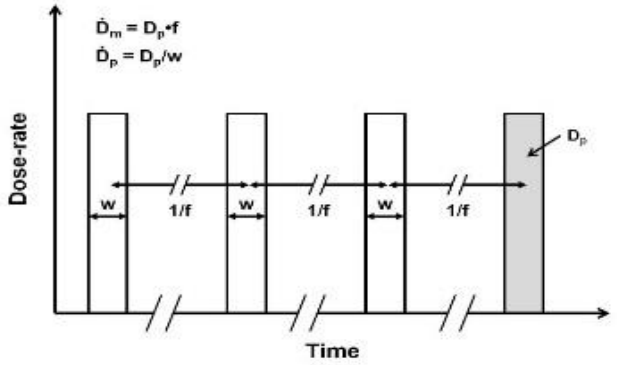
CHUV

Issues AND solutions

At CHUV, we work with an electron beam delivering UHDR pulsed 4-6 MeV electron irradiations.

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	$10^{-3} - 10\ Gy$
$\dot{D}_m = \dot{D}_p \cdot w \cdot f$	mean dose-rate	$10^{-2} - 1000\ Gy / s$

Microseconds pulses
in a millisecond cadence



Flash parameters vs conventional

TABLE I. Parameter definitions and corresponding dose-rates (at a SSD of 1 m and at the depth of dose maximum in water) of the Flash and Conv functioning modes of the eRT6.

	Flash	Conv
GT (V)	300	100
w (μs)	2.2	1.0
f (Hz)	200	10
$\dot{D}_m$ (Gy/s)	200	0.05
$\dot{D}_p$ (Gy/s)	4.5×10^5	4.9×10^3

EFFECT **NO EFFECT**

Time to deliver 20Gy ~200 ms (μs) ~500 sec (8 min)

Flash parameters vs conventional

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EFFECT **NO EFFECT**

WHAT DOES IT MEAN?

Time to deliver 20Gy

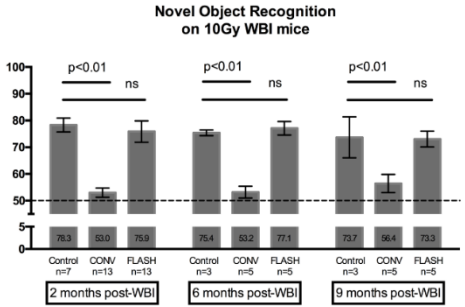
FLASH effect is a biological effect!

We do not have a unique physical beam parameter indicating the effect.

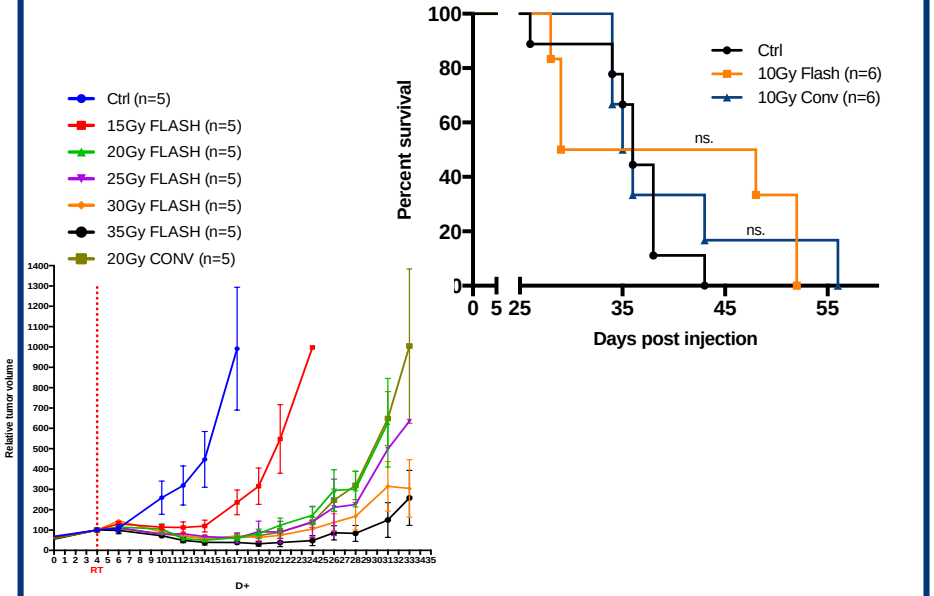
→ Biological validation is necessary

Flash

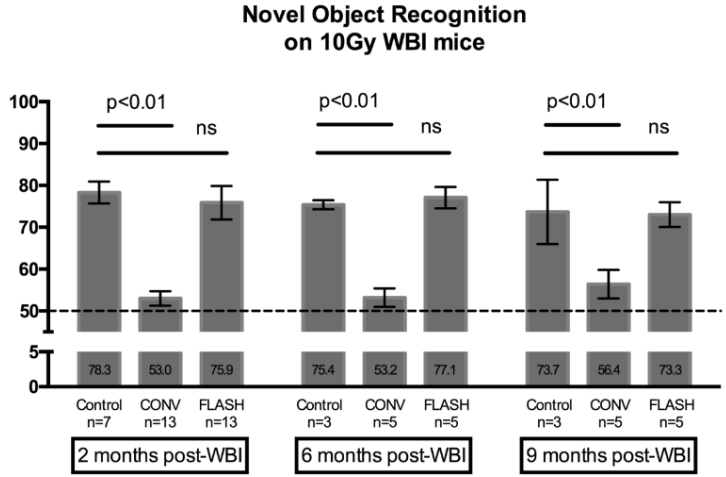
Conventional



No clear difference



Clear difference



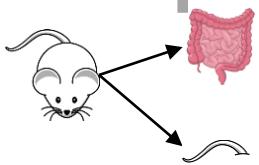
Survival and **tumor growth** are the same using FLASH and CONV -RT

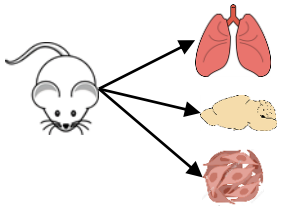
BUT cognitive abilities are preserved.

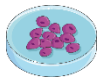
How do you compare 2 experiments in time and space

1970s — Since 2014 — 2018

1st observation | Preclinical studies | Transfer to pig model



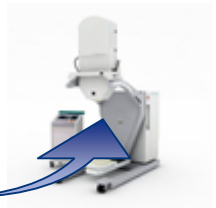




How do you repeat an experiment

2019 — 2021?

Phase I trial | First in human | Phase III trial (ongoing) | Clinical transfer — Time



How do you guarantee prescribed dose

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CHUV

How do you compare 2 experiments in time and space

1970s

Since 2014

2018

1st observation

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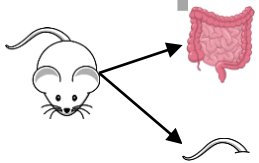
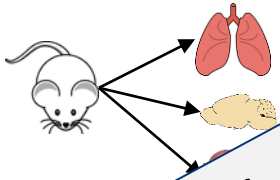
nsfer to pig model





Dosimetry/traceability

How do you repeat an experiment

2019

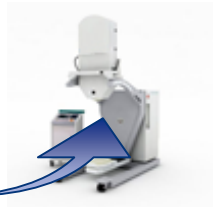
2021?

Time

Phase I trial

Phase III trial (ongoing)

Clinical transfer



How do you guarantee prescribed dose

UHDR beam differs from reference beams

Issues

- Dose-rate
- Time structure (pulsed)
- Field size
- Energy spectrum
- Lateral beam profile
- Distance
- Irradiation in air / solid water / ….
- Electrons are annoying…..

All that needs correction factors → u n c e r t a i n t i e s ☹

RELATIVE DOSIMETRY

ABSOLUTE – REFERENCE DOSIMETRY

TRACEABILITY

STABILITY

RELATIVE DOSIMETRY - QA

STABILITY

Standard strategy for RT dosimetry

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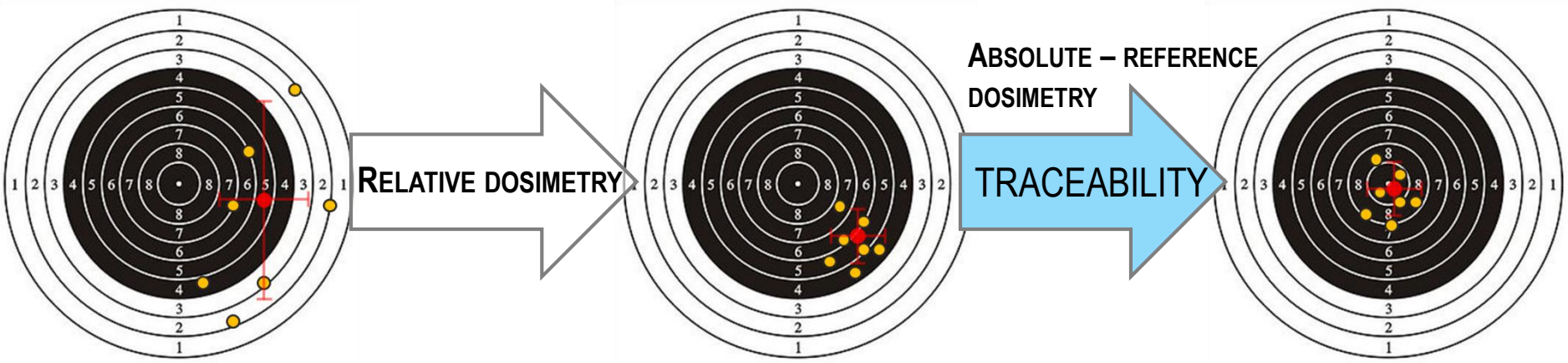
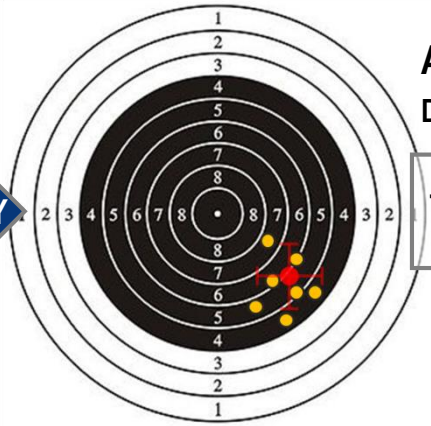


UHDR do not benefit from absolute dosimetry

→ UHDpulse project

UHDpulse

RELATIVE DOSIMETRY

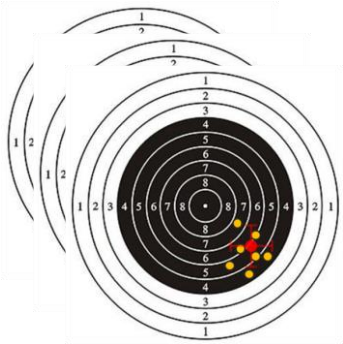


ABSOLUTE – REFERENCE DOSIMETRY

TRACEABILITY

We have to focus 1st on relative dosimetry

STABILITY



RELATIVE DOSIMETRY - QA

STABILITY

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UHDR dosimetry strategy

Plan A

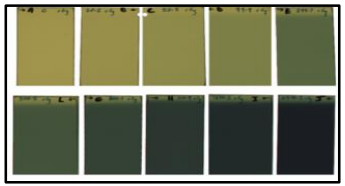
There is no National Metrology Institute (NMI) providing calibration in UHDR beams…… so what……

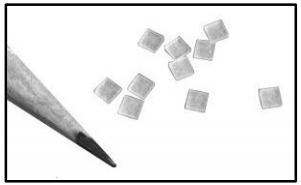
Plan B

Take dosimeters with different detecting principles
→ The dose rate dependency must be different

Start with reference conditions (CONV) and extrapolate to FLASH

UHDR dosimetry





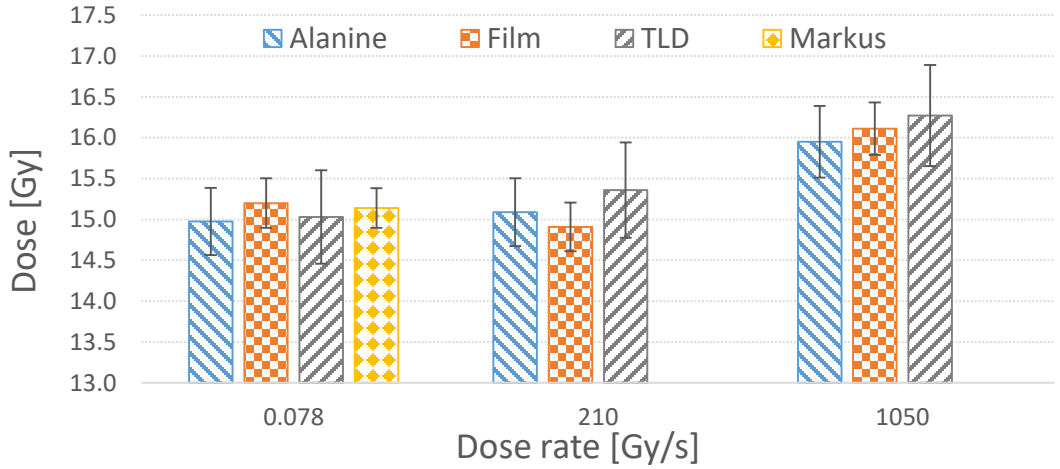

Next best thing

At CHUV, we work currently with 4 types of dosimeters:

- Films
- Ionization chamber
- Thermoluminescent dosimeter (TLD)
- Alanine

UHDR dosimetry

Redundancy of dosimetric measurements ▫▫▫▫⇨ traceability

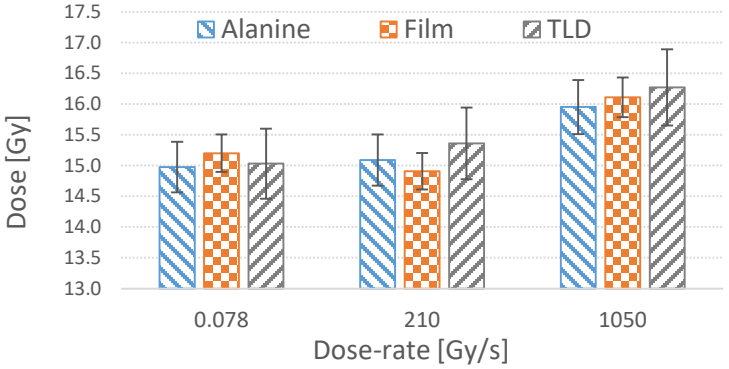


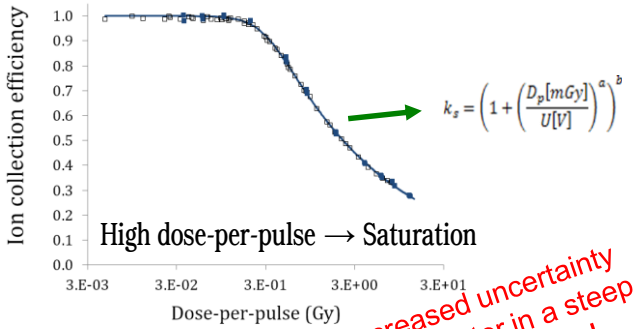
Agreement within 3 % for FLASH and within 2 % for CONV

Dose-rate effect on calibration factors → 2 strategies

“independent of” or “corrected for”

dose-rate





! Increased uncertainty bc corr. factor in a steep part of the curve!

Radiochromic films, TLD, Alanine

Ionization chambers

Warning!!!

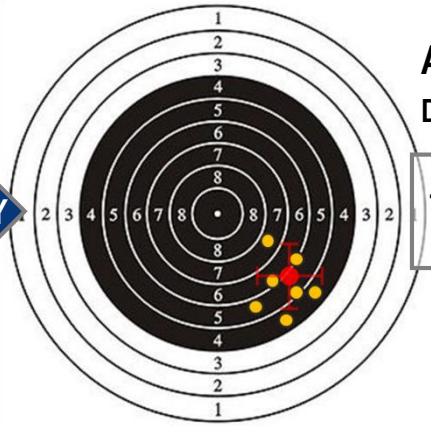
The dosimeters are calibrated in reference fields

→ correcting for eRT6 ‘’beam quality’’ is not always trivial

Pre-irradiation dosimetry must be as close as possible to the irradiation conditions

Minimization of correction factors for: collimators, depth, dose-rate, …

RELATIVE DOSIMETRY



ABSOLUTE – REFERENCE DOSIMETRY

TRACEABILITY

We have established relative dosimetry

STABILITY

RELATIVE DOSIMETRY - QA

STABILITY

Then keep it together for as long as possible

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What about clinical transfer?

Stability: duration, tools, procedures

Safety: delivery + radiation protection

Commissioning: tools, relevance

Treatment planning: clinical transfer

STABILITY - monitoring

Commercial UHDR needs better diagnostic, monitoring and controlling of the beam:

Ionization chambers needs improvement to be used as UHDR monitoring

For preclinical experiments, we need a large dynamic range (CONV to UHDR)

Home-made solution:
Current transformers
(ICT, BCT, ACCT)

Use of diagnostic to stabilize the beam output → SAFETY

SAFETY - delivery

Beam output stabilization

- Real-time control to reach the prescribed dose
  - Integral measurement and amplitude correction of the next pulse at least

For pulsed beams, beam interruption between pulses

- If possible increase the number of pulses to decrease the consequences of a machine errors.

→ Fast diagnostic and beam control needed due to the high dose-rate

SAFETY - Radiation protection

Depends on national regulations however some general consideration translate across continents.

The issue is measurements, because in essence the **prescribed doses** are **not higher**!!!

Need to measure dose rates outside the bunker:

- For electrons: not many dose-rate meter measures pulsed beams
  - IC, dedicated pulsed beam (typically for fluoroscopy)
  - Passive dosimeter necessitate some signal → high load on bunker (we delivered MGy in order to measure using TLDs)

- Support of MC calculations to extend the measurements to the full area.

- At the end, it seems that RP and physics measurements are the one bringing the most doses around the bunker, which is slightly ironic.

Commissioning

Chain of traceability need to be established

Use same dosimetric tools to do a commissioning as close as possible to recommendation

Unluckily, it won’t save much on routine dosimetry prior to irradiation, but rather give an idea of the possibilities (beam stability, field size, dose rate / dose per pulse, etc)

Treatment planning

The current TPS can support the absorbed dose to water planification

- Electron beam can be simulated

The current TPS could predict a FLASH effect if a clear beam parameter indicators of FLASH effect was isolated

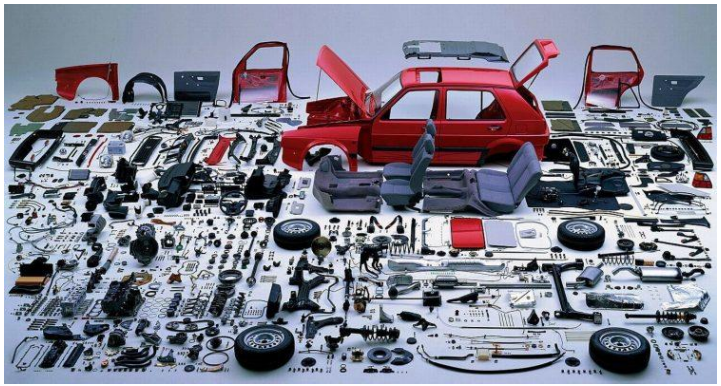
- Ponderation of the beam could reflect / predict FLASH benefits
- Not easy today

In conclusion, beam can be physically simulated, but we still need some work/evidence on the radiobiologic and/or simulation part.

CONCLUSION

UHD dosimetry is a work in progress...

...Ready for clinical test but still need work for clinical routine



We need:

A biophysical dosimeter indicating the FLASH effect…

…maybe we need to replace the abosrbe dose to water by a new quantity (FLASH-effective-dose).

Many acknowledgements

Thanks to my colleagues at IRA:
Bochud, Buchillier, Bühlmann, Cherbuin, Grilj, Jorge, Moeckli, Mora, Moratal, Pitzschke, Santos, Zufferey, …

And all my colleagues at CHUV and everywhere
(but only the one helping…..)

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Institute of radiation physics, Switzerland
Thank you
Any questions?
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