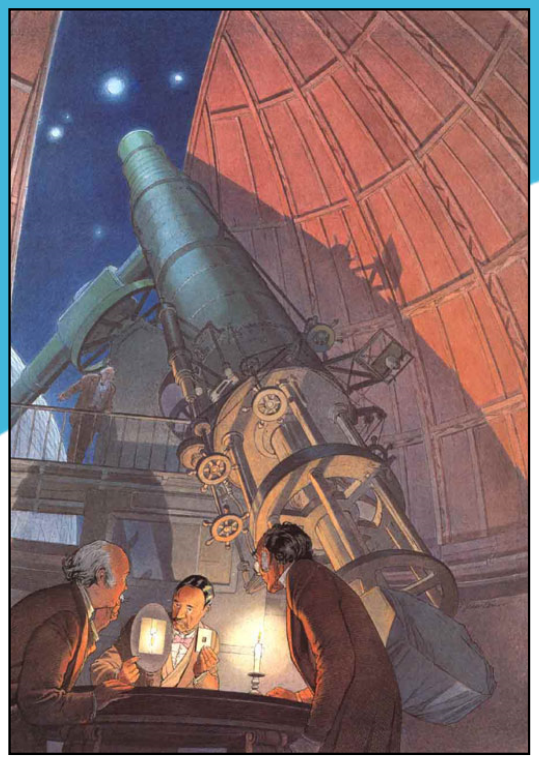
Back to the future, management of innovation: *The Medical Physics Point of View*



L' expérience cruciale, F. Schuiten

Dirk Verellen

Universiteit Antwerpen

iridium netwerk Topzorg in radiotherapie

Disclaimer:
most examples are based on personal experience
(other examples and commercial solutions exist)

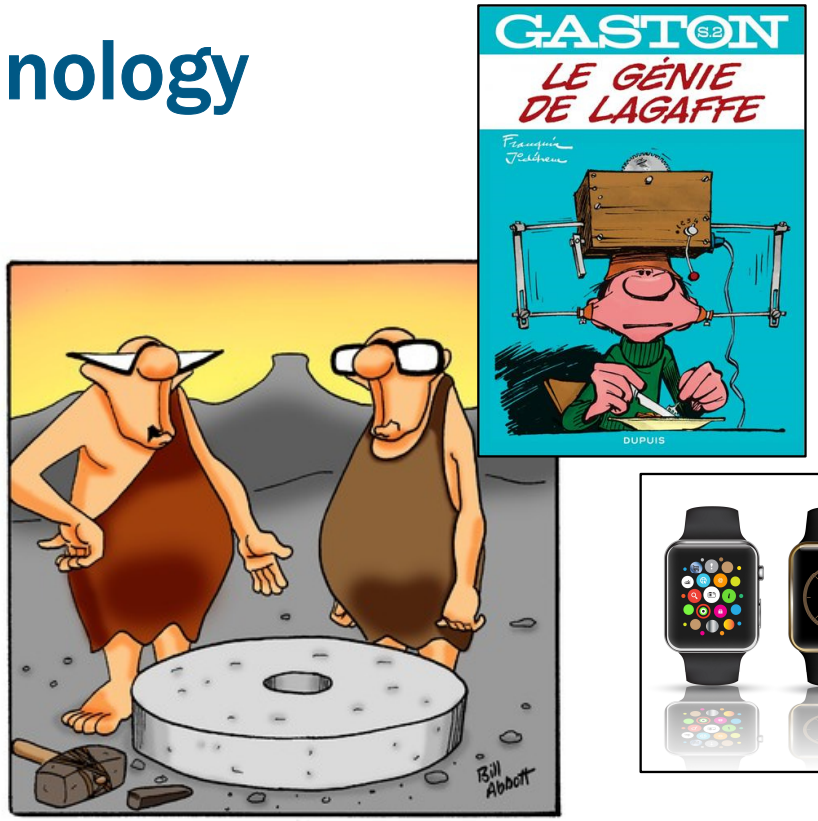
Outline

- Cargo Cult Science
- From early adopters ...
- ... to introducing a new but existing technology/technique
- The process of implementation and regulations

3 phases of introducing technology

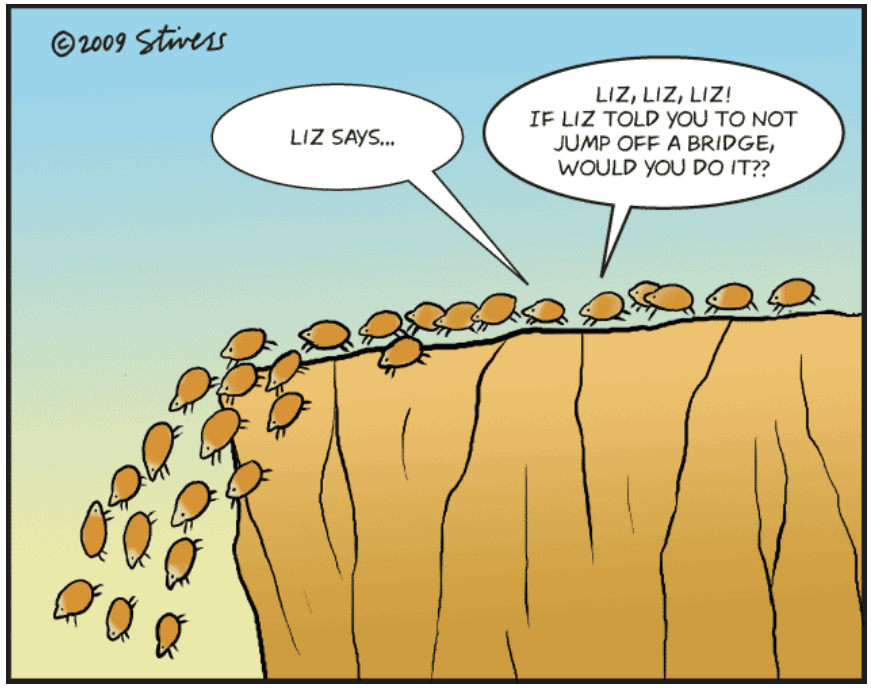
- A tool using culture
- The development of tools and extending their use for wider benefit
- The technology itself becomes the focus of the intellectual effort:

"applications race ahead of any proven utility"



"I thought I was on to something but I can't figure out how to move it."

Technology for the sake of …



- "Developments in RT can best be described as **a blind gallop** towards increasingly more precise means of tumor localization …"

POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Future developments in external beam radiotherapy will be unlikely to significantly improve treatment outcomes over those currently achieved with 3D-conformal and IMRT treatments

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Colin G. Orton, Ph.D., Moderator

… for the sake of technology

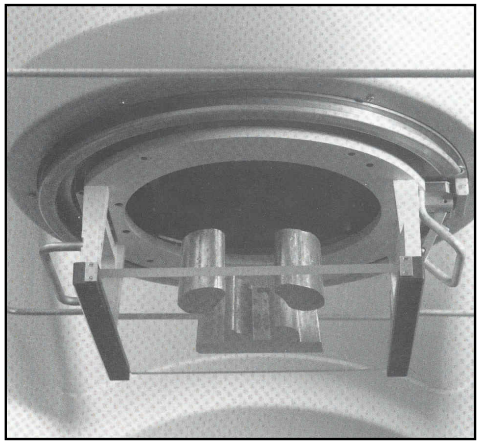
- Technology should adapt to the user, not force the user to adapt to the technology.
- Yet, sometimes, it seems as George Orwell already described:

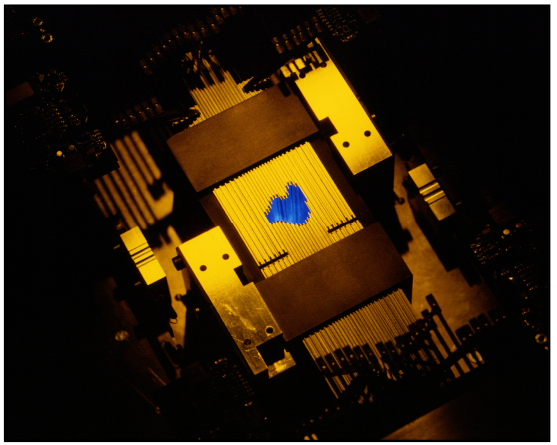
> **“the true genius is to create a problem and then sell the solution.”**

“A fish desperatly looking for a bicycle”

Some examples: MLC

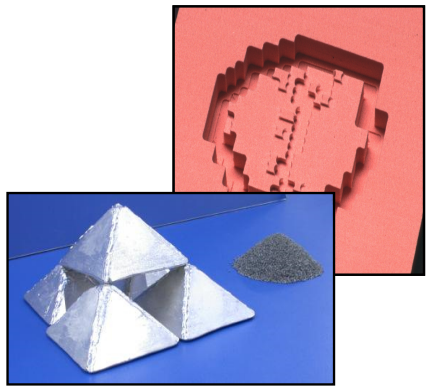
- The MLC was introduced to replace blocks





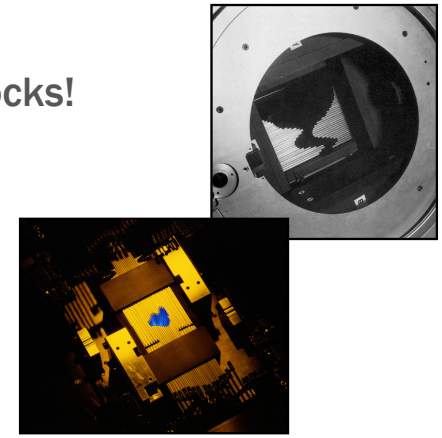
- But the perception was created that "**IMRT required an MLC**"

Is the MLC designed for IMRT?



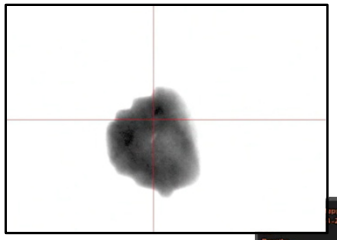
- The "old" block is still better suited for IMRT

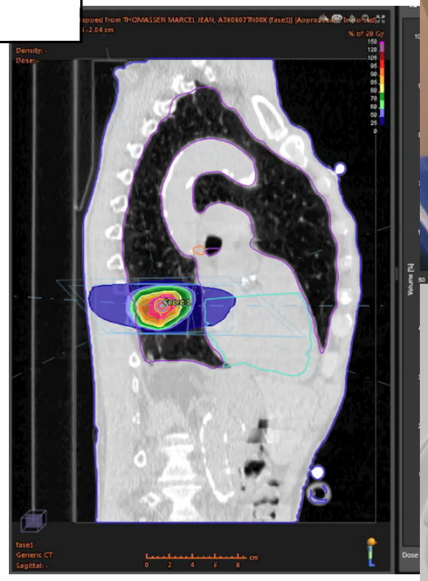
- **Blocks** never fail to absorb photons the same way every time:
  - Superior and isotropic resolution
  - Deals better with tumor mobility
  - If Monte Carlo is to become the standard in TPS, it certainly prefers blocks!

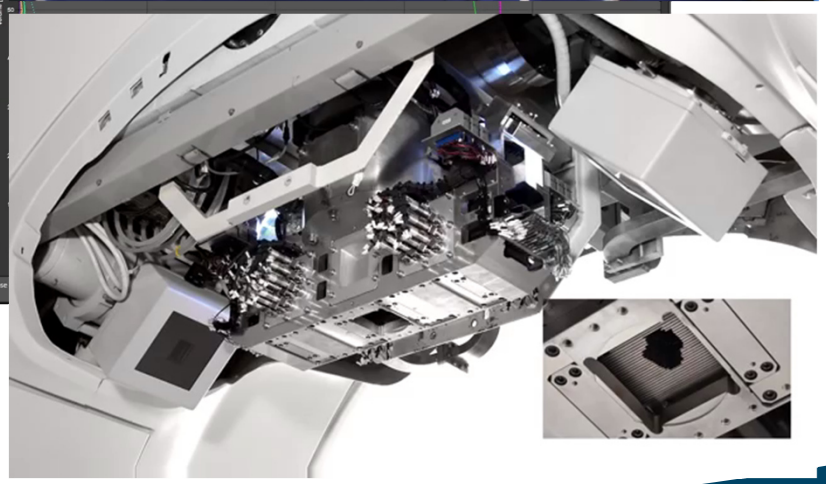


- **MLC's** fail in a variety of interesting ways:
  - Interleaf leakage and transmission
  - Tongue and Groove effects
  - MLC is a complex electromechanical system that *will* fail
  - Calibration of leaves, limitation in velocity and resolution

Some examples: Tumour Tracking

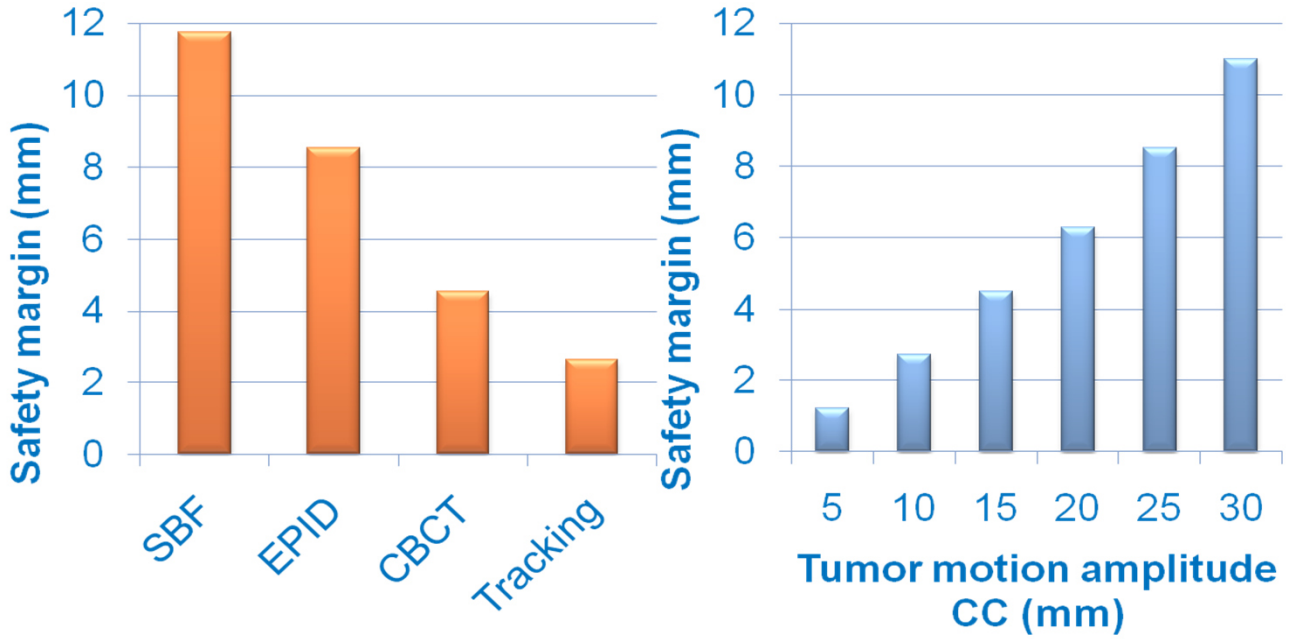






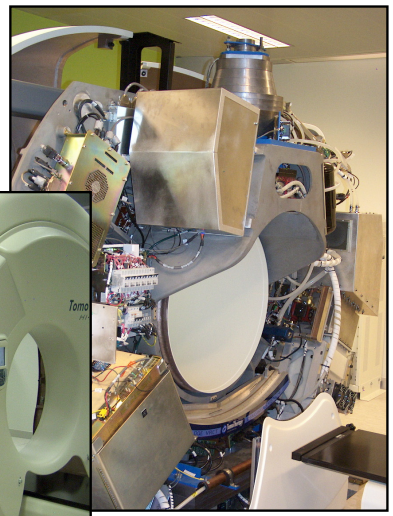
Some examples: Tumour Tracking

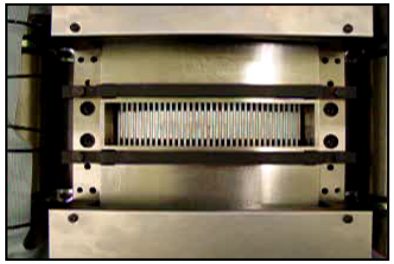
- Does SBRT require RTTT?



Some examples: Speed

- When tomotherapy came into the picture (1992), IMRT suddenly became clinically feasible
- … by the way, the binary MLC was *designed* for IMRT, not *adapted*…

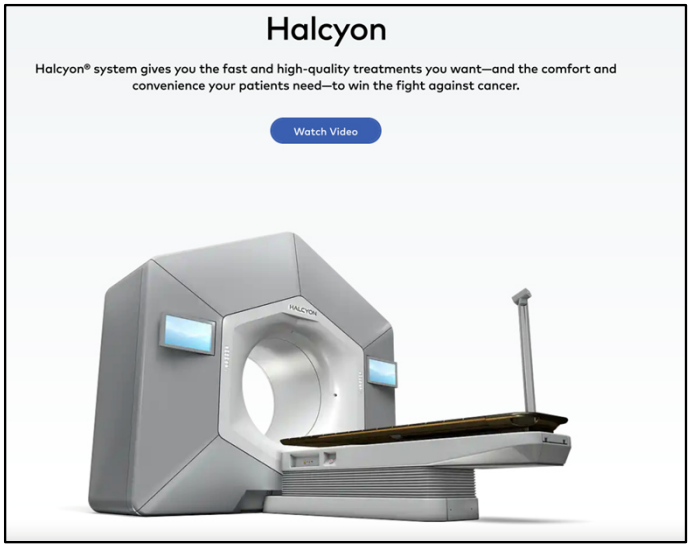




Some examples: Speed

- So, the “problem” **delivery time** was created (prevailing quality and safety?) to sell the “solution” **speed**.

VARIAN ONCOLOGY



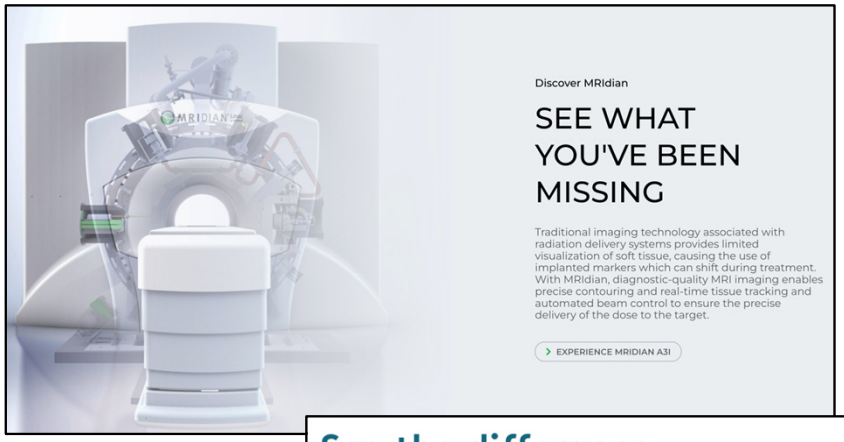
Some examples: FFF

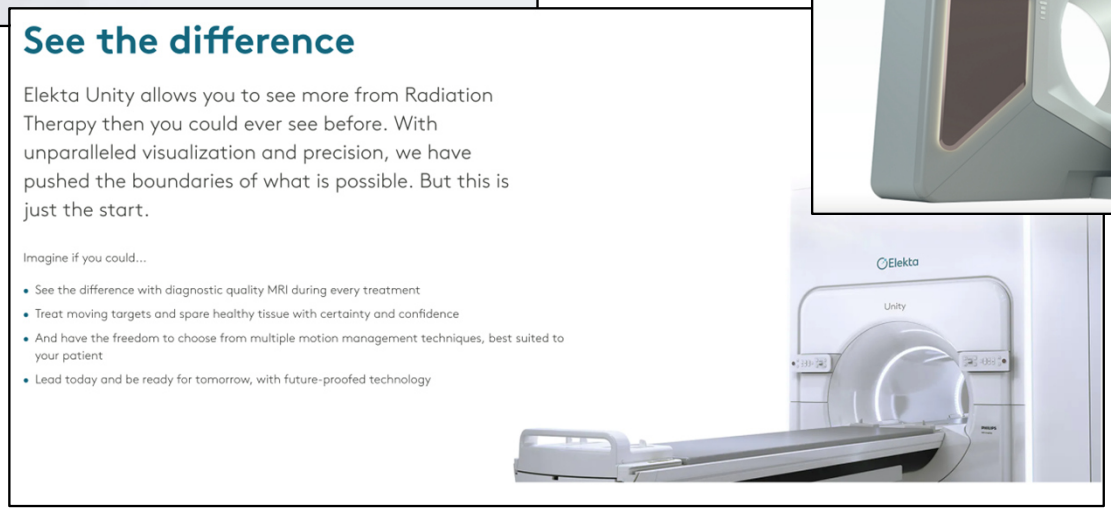
- … and again, using the mantra “faster is better”:

  - Treatment times are reduced from **6’ to a staggering 4’**
  - … maybe not economically/clinically relevant, but
  - … reduced treatment time will influence **intrafractional motion** in favorable way …

  - Alas, Nielsen *et al.* did not observe reduction of intrafractional motion comparing FF with FFF treatments for lung and brain cases.
  - Ong *et al.*: 2 arcs are required to reduce interplay effect.

Some examples: real-time ART





Some examples: real-time ART

- Ask yourself:
- What indications truly require real-time ART?

Back to the future - DIrk Verellen

… and society pays

- The true cost of something, is what you give up to acquire it!
  - If an expensive technology comes at the cost of reducing health care for the average cancer patient, it is expensive.

- Halperin's rule:

  - Most tumours are radioresistant if you miss them …
  - Protons may offer many **new** and **expensive** ways of missing the tumour

ESTRO vision

- There is a risk in that too much focus on sophisticated expensive technology may create a double layer health care system where not all patients have access to best of care.

Corporate funding is not helping …

- Enthusiasm and “gentle” pressure from industry results in publication of favorable results only.

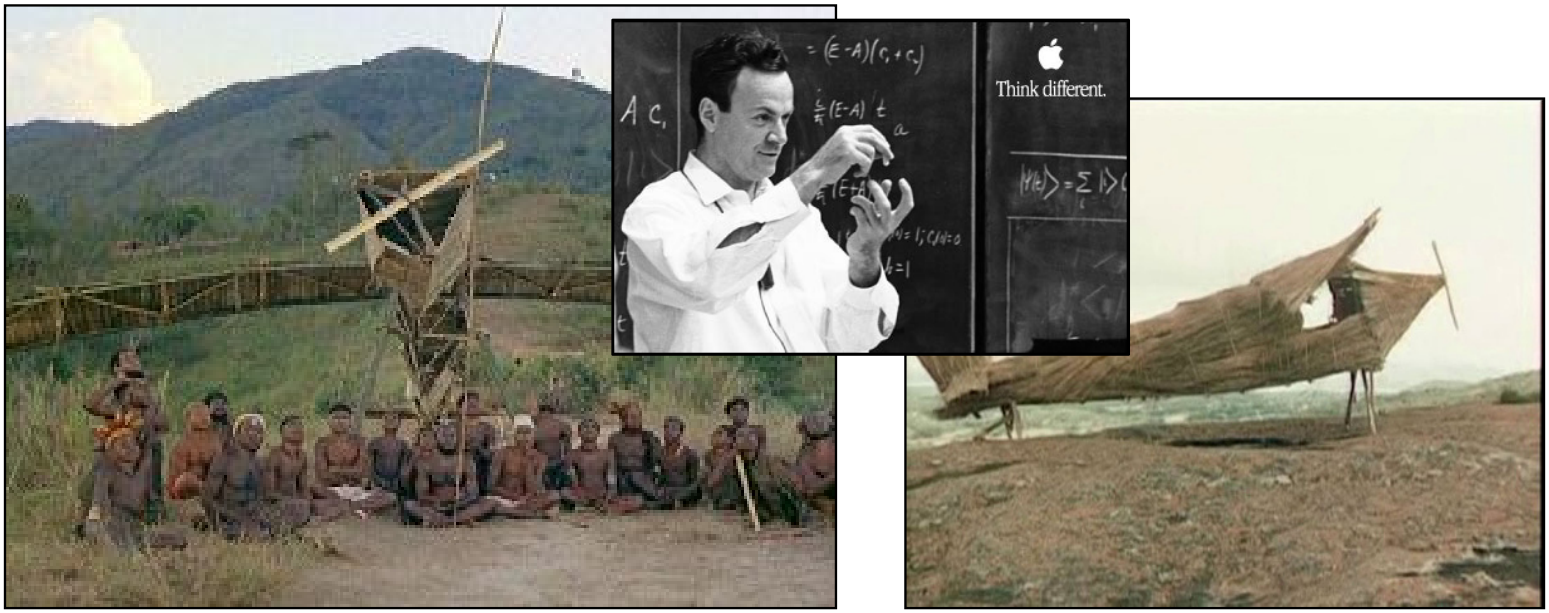
Corporate funding is not helping …

- "Drugs [technologies] are tested by the people who manufacture them, in **poorly designed trials**, on hopelessly **small numbers** of weird, **unrepresentative patients**, and analysed using techniques which are flawed by design, in such a way that they **exaggerate the benefits of treatments**." … "not to mention '**missing data**'."
- "**Unsurprisingly, these trials tend to produce results that favor the manufacturer**."
  - *Ben Goldacre, Bad Pharma, 2012.*

Back to the future - DIrk Verellen

Is RT R&D Cargo Cult Science?

- Just as cargo cultists create mock airports that fail to produce airplanes, cargo cult scientists conduct flawed research that fails to produce useful results
  - R. Feynman, Commencement address at CALTECH, 1974.

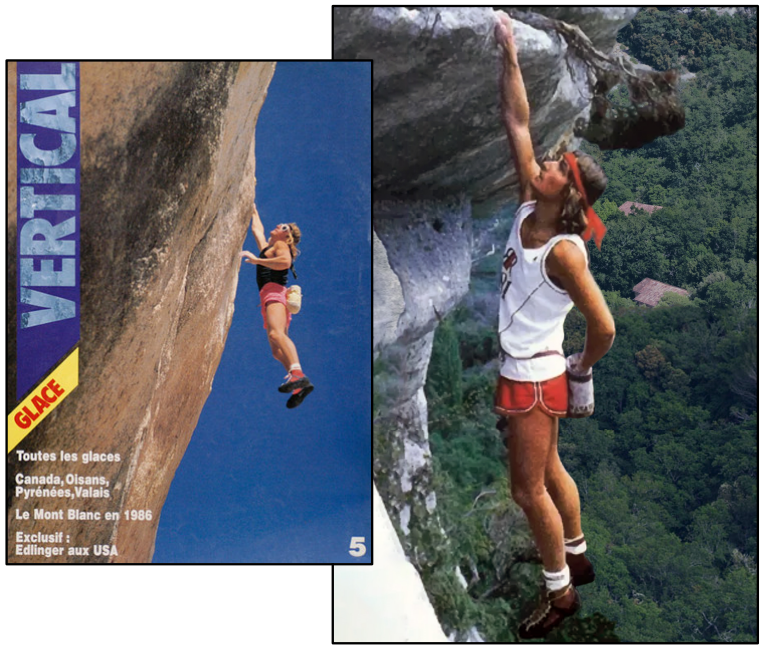


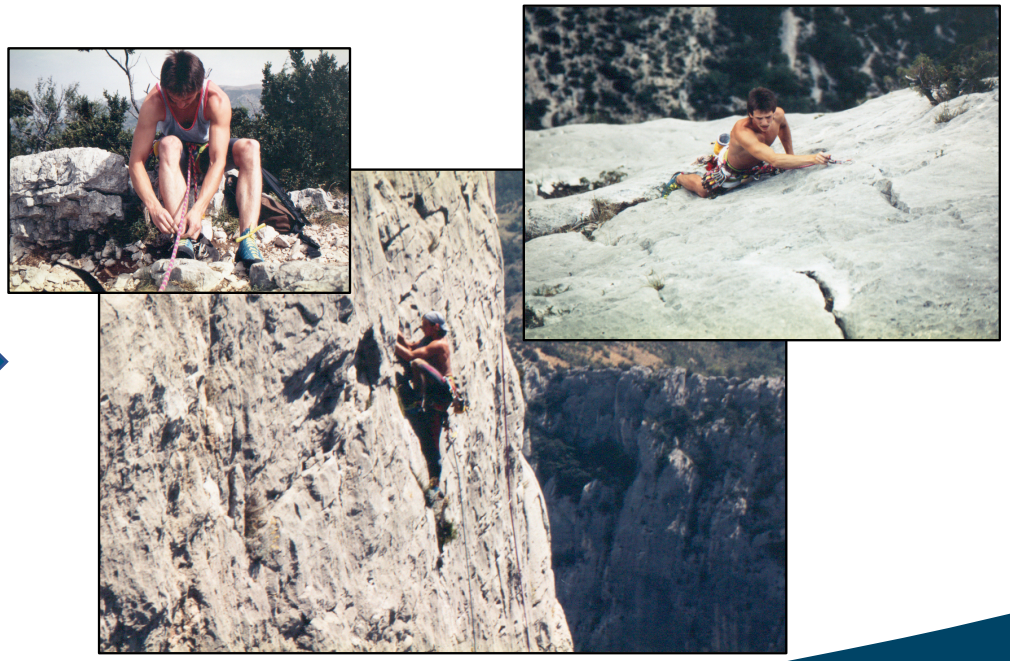
Outline

- Cargo Cult Science
- From early adopters ...
- ... to introducing a new but existing technology/technique
- The process of implementation and regulations

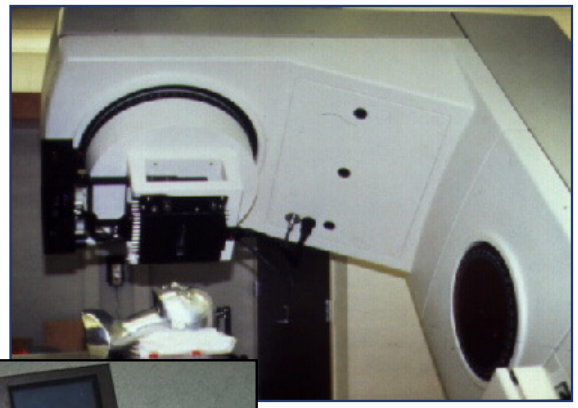
Early adopters

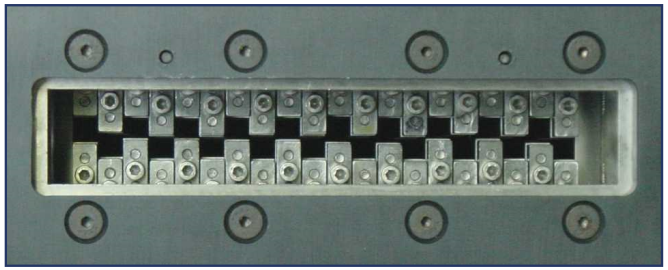
- Guidelines are no longer valid or applicable
- Requires **creative solutions** … ensuring safe implementation
- …. can be pretty uncomfortable

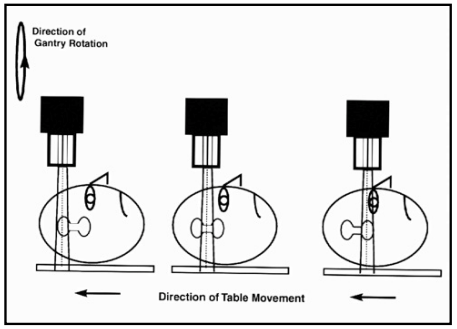


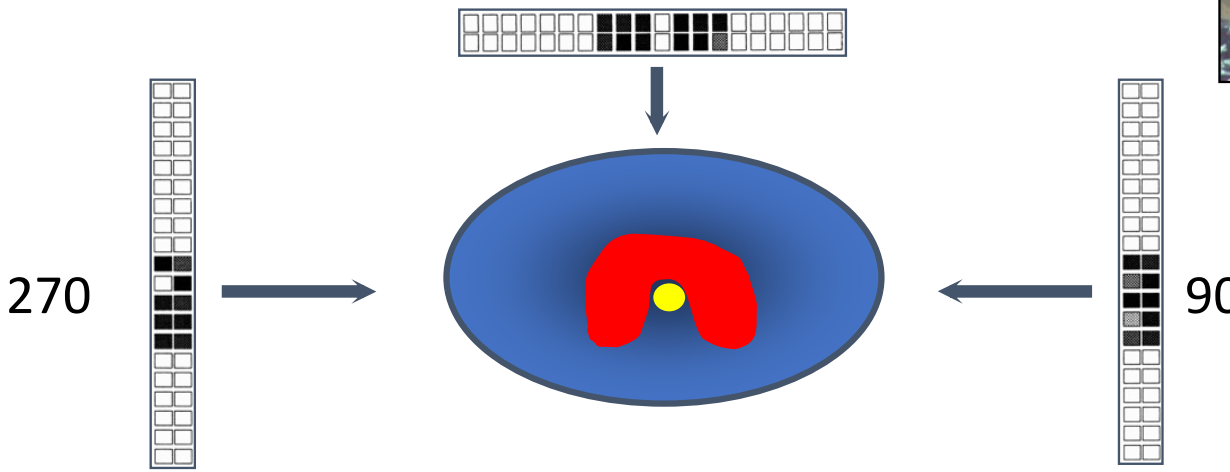


Sequential TomoTherapy





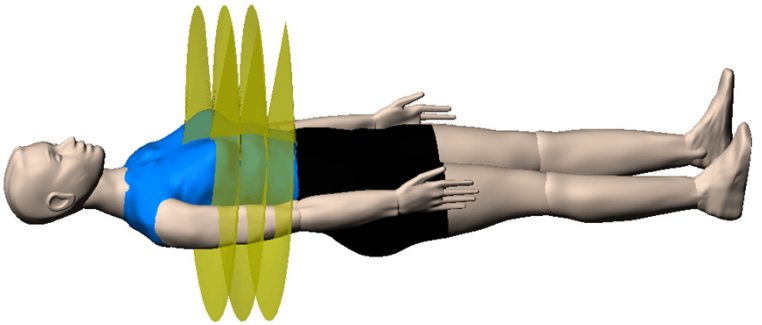


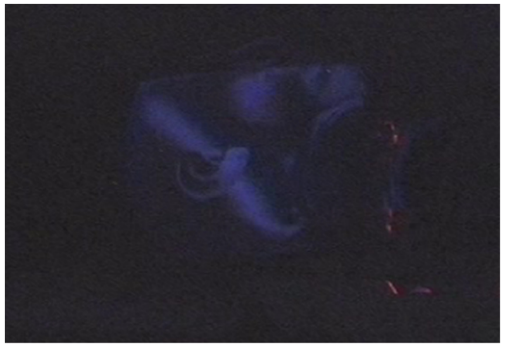


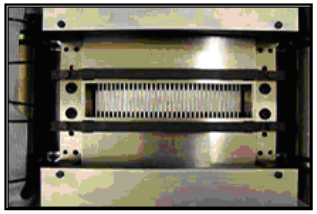
Helical TomoTherapy

Designed for IGRT & IMRT:

! integration - synergy !

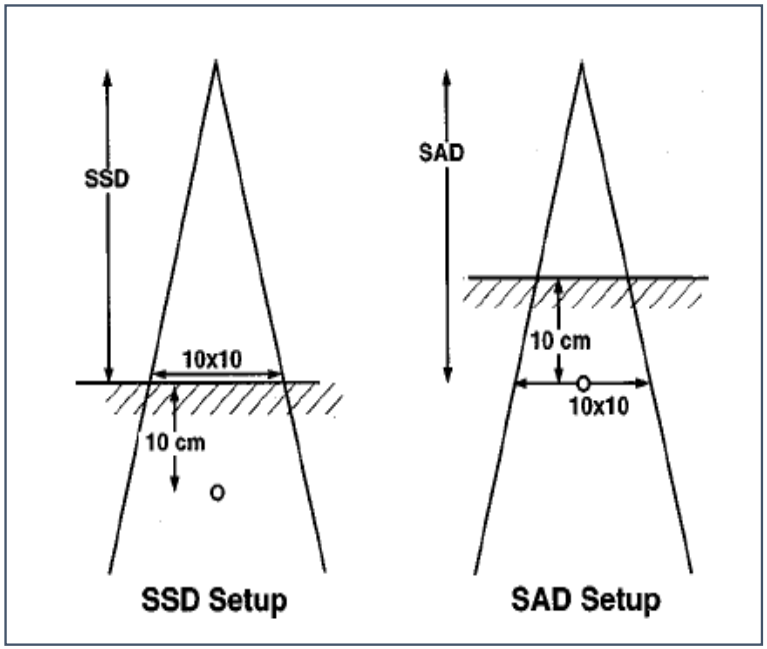


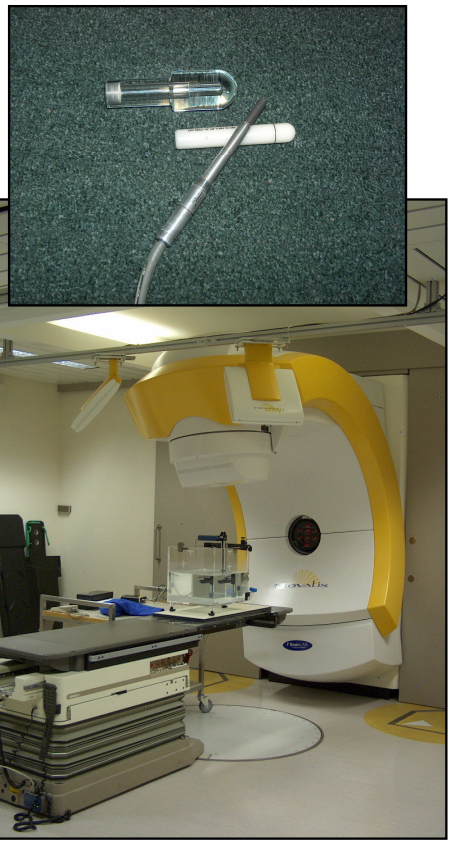


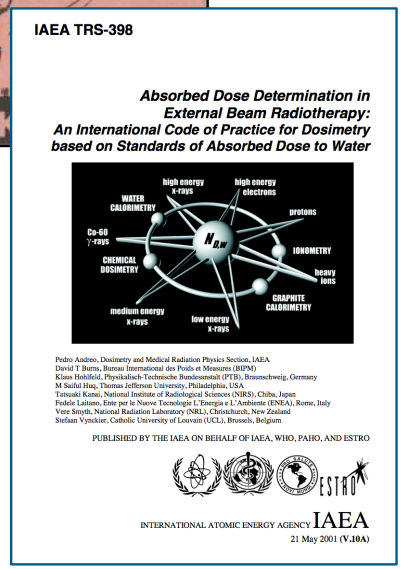


Dose calibration

- ... requires reference conditions







$$D_{w,Q_{msr}} = M_{corr,Q} \cdot N_{D,w,Q_0} \cdot k_{Q,Q_0}$$

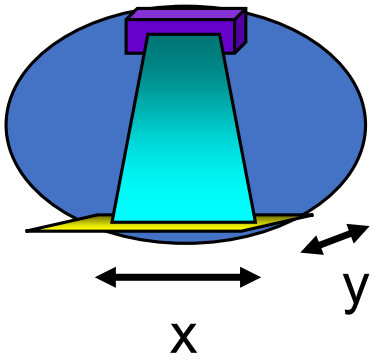
Dose calibration

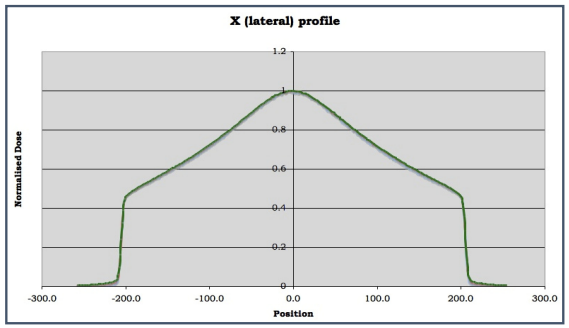
- … requires reference conditions …. the guitare pitch problem

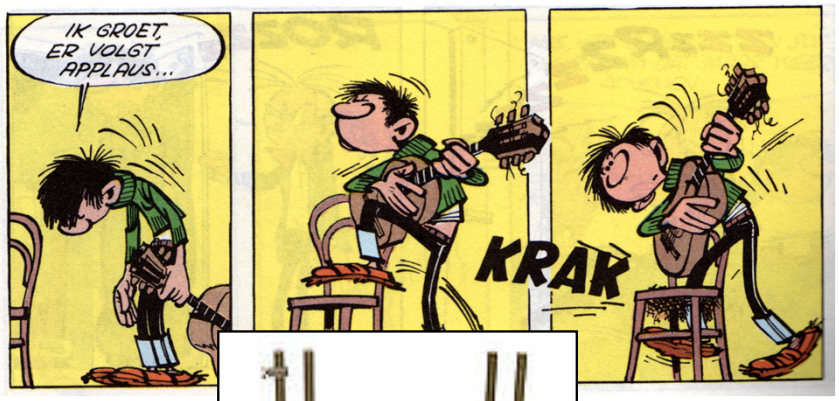
"40cm" x (1.0,2.5,5.0)cm

SSD 85cm

NO FLATTENING FILTER!!!!

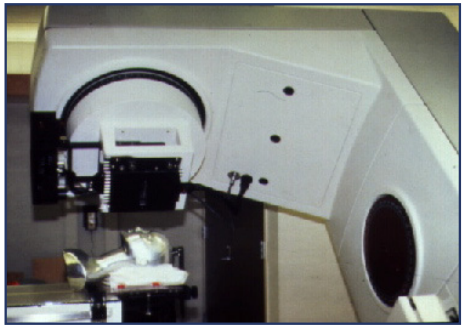


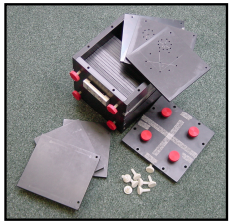
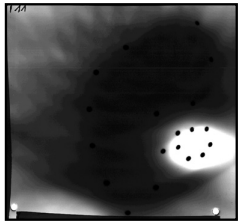
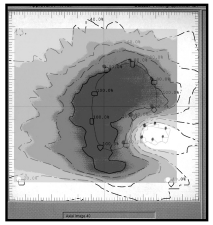
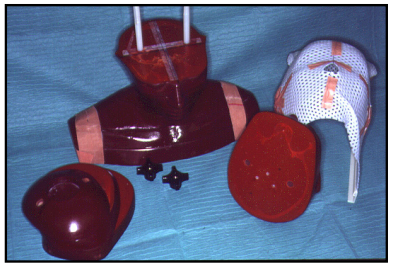
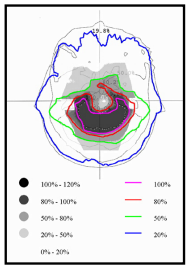


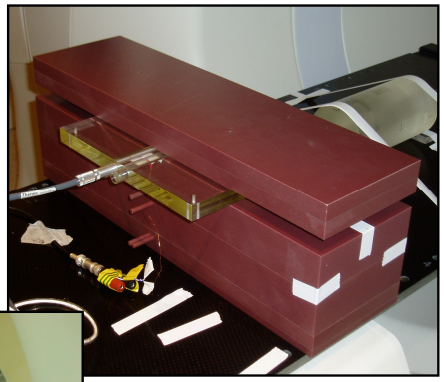


Dose calibration

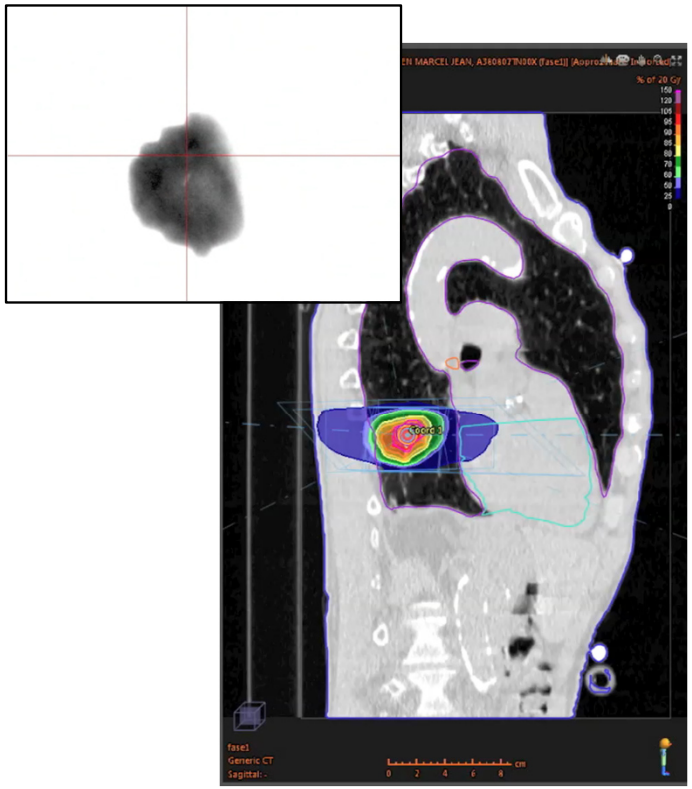
- ... requires traceability

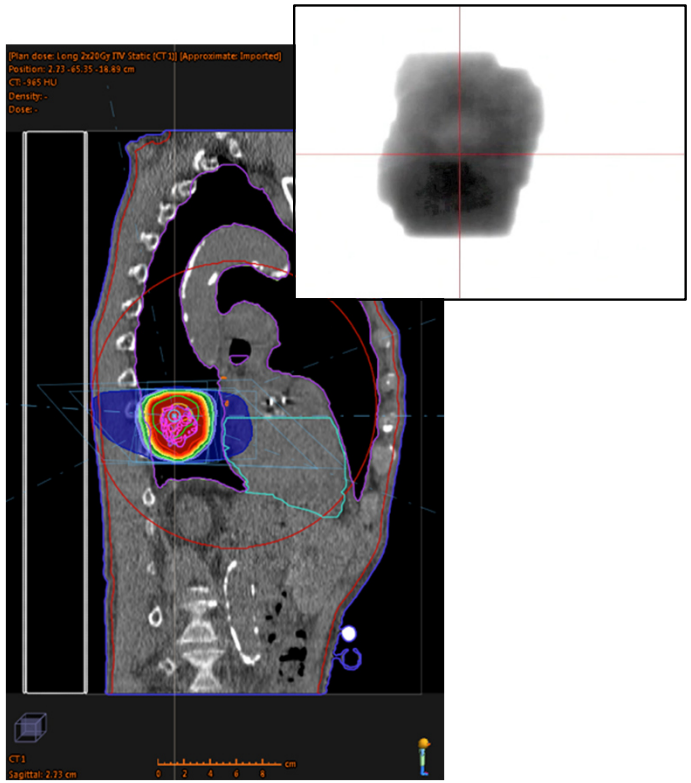


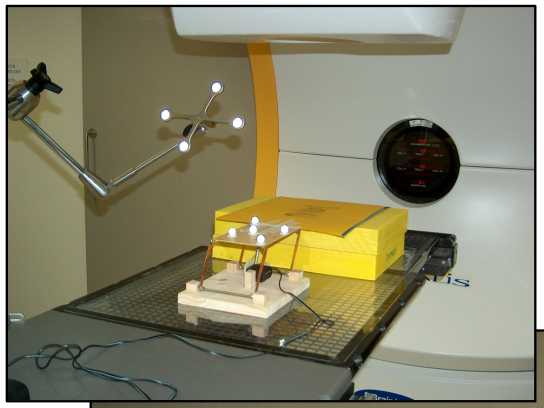
Tumour tracking: “sticky” dose

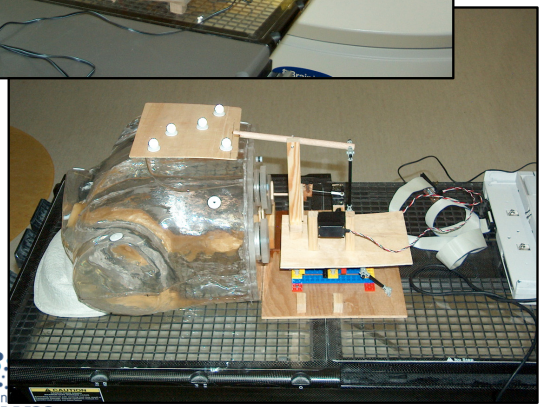


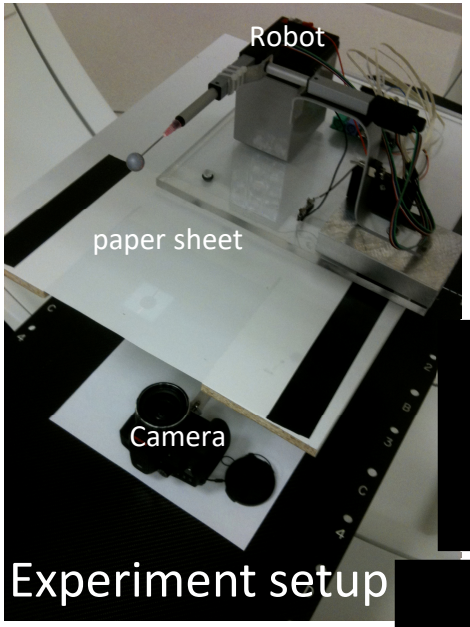


Tumour gating-tracking: Validation

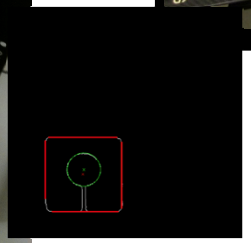
- Requires creative solutions

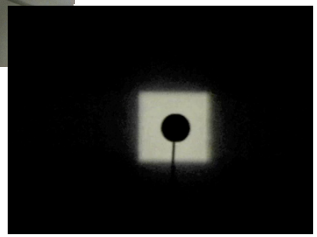


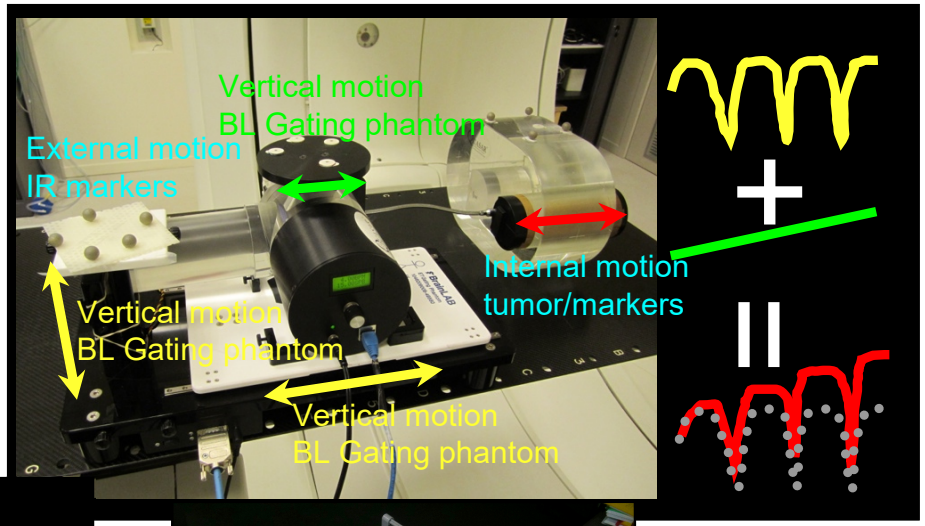


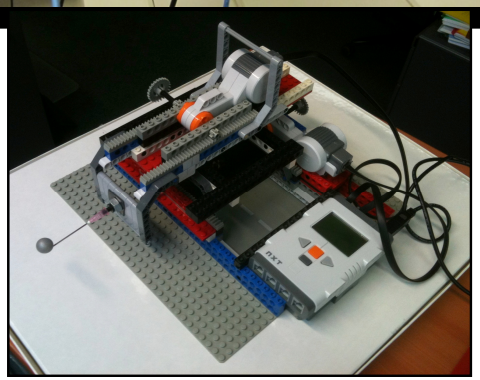


Experiment setup



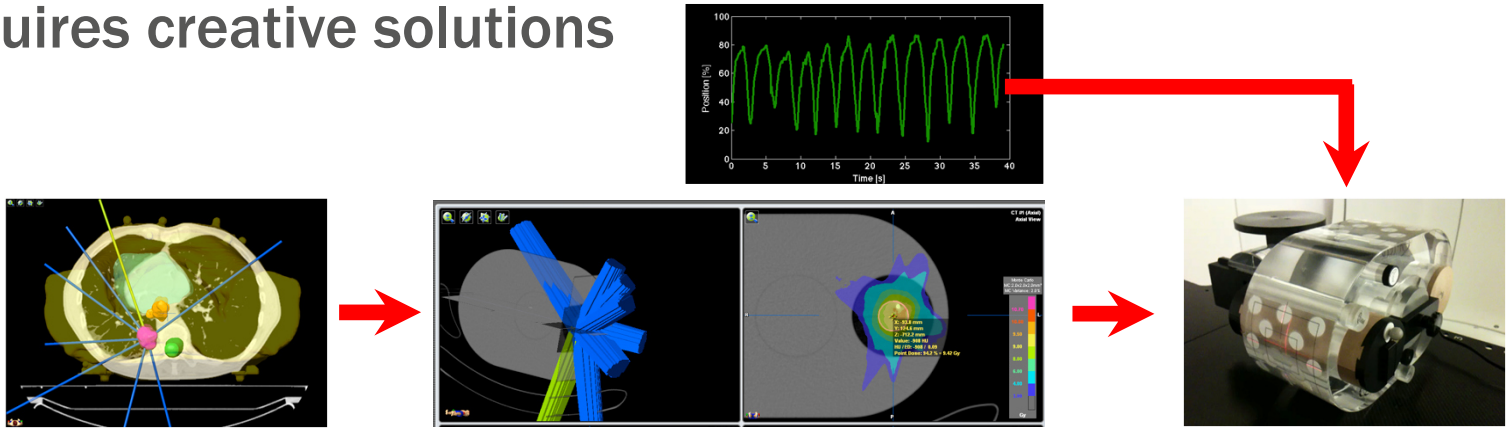


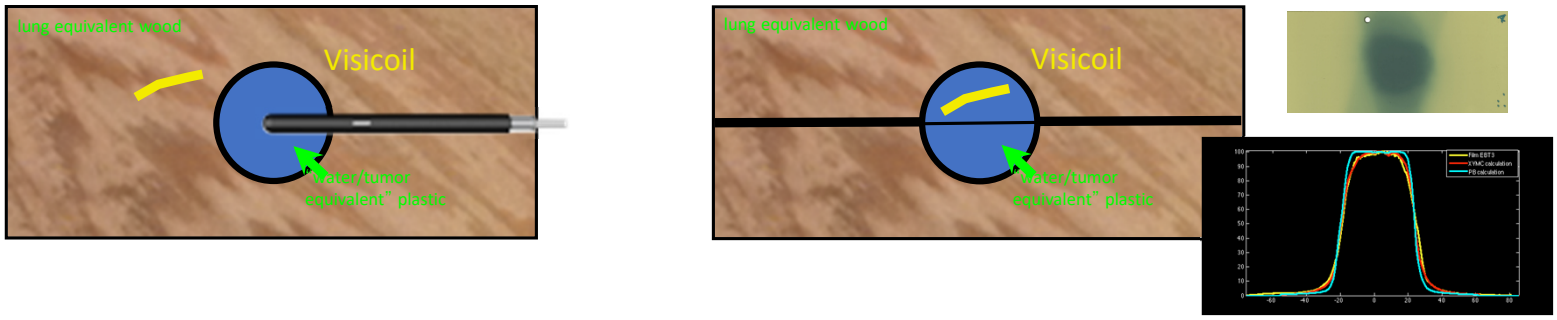




Tumour gating-tracking: Patient specific QA

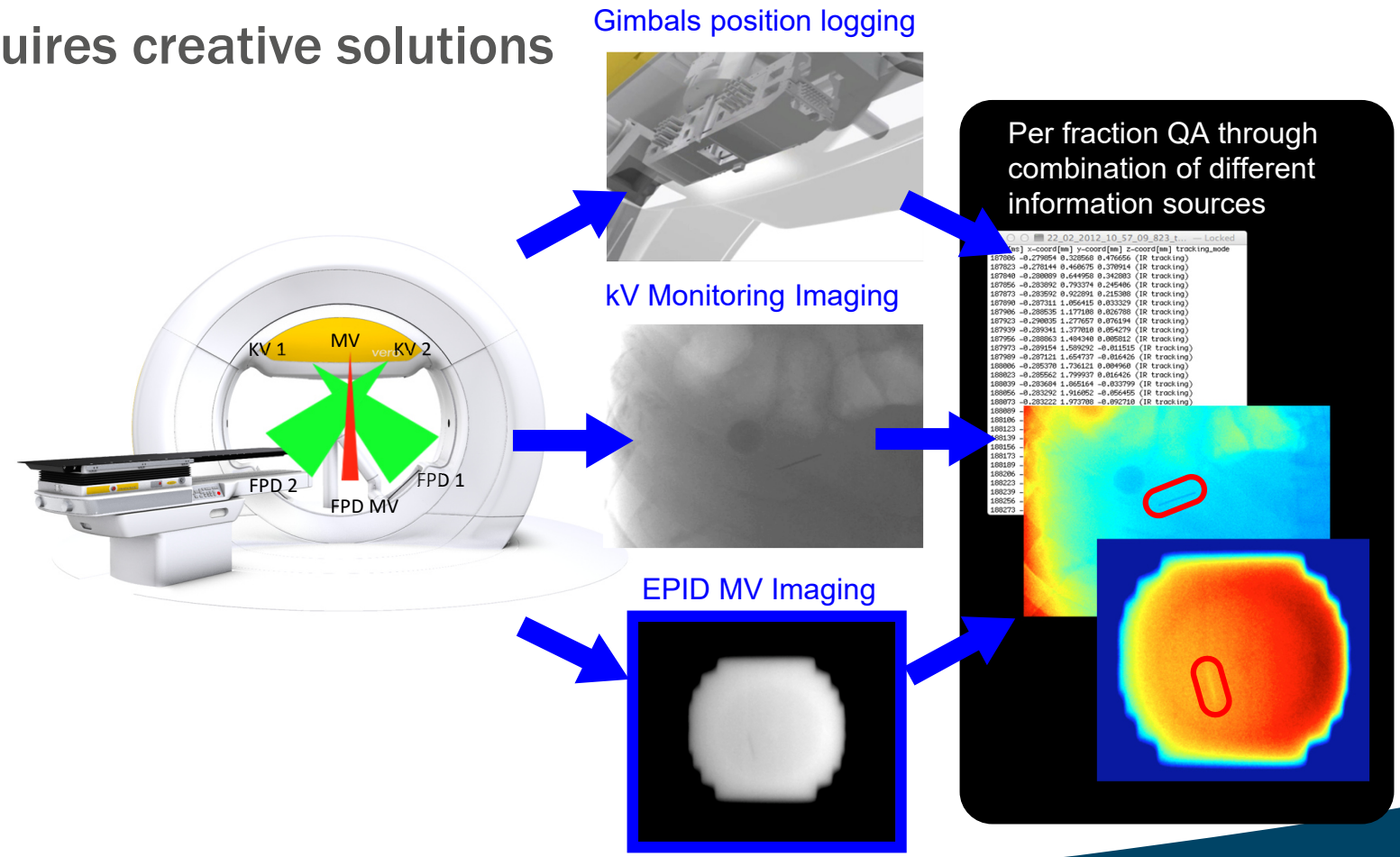
- Requires creative solutions





Tumour gating-tracking: Verification

- Requires creative solutions



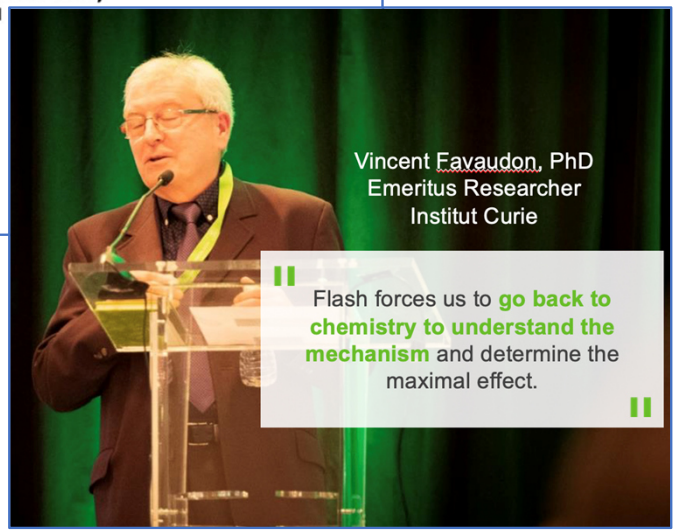
FLASH …

www.ScienceTranslationalMedicine.org 16 July 2014 Vol 6 Issue 245 245ra93

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

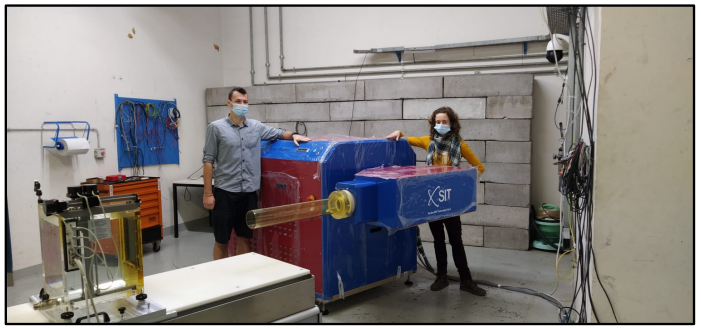
Vincent Favaudon,[1,2]* Laura Caplier,[3†] Virginie Monceau,[4,5‡] Frédéric Pouzoulet,[1,2§] Mano Sayarath,[1,2¶] Charles Fouillade,[1,2] Marie-France Poupon,[1,2‖] Isabel Brito,[6,7] Philippe Hupé,[6,7,8,9] Jean Bourhis,[4,5,10] Janet Hall,[1,2] Jean-Jacques Fontaine,[3] Marie-Catherine Vozenin[4,5,10,11]

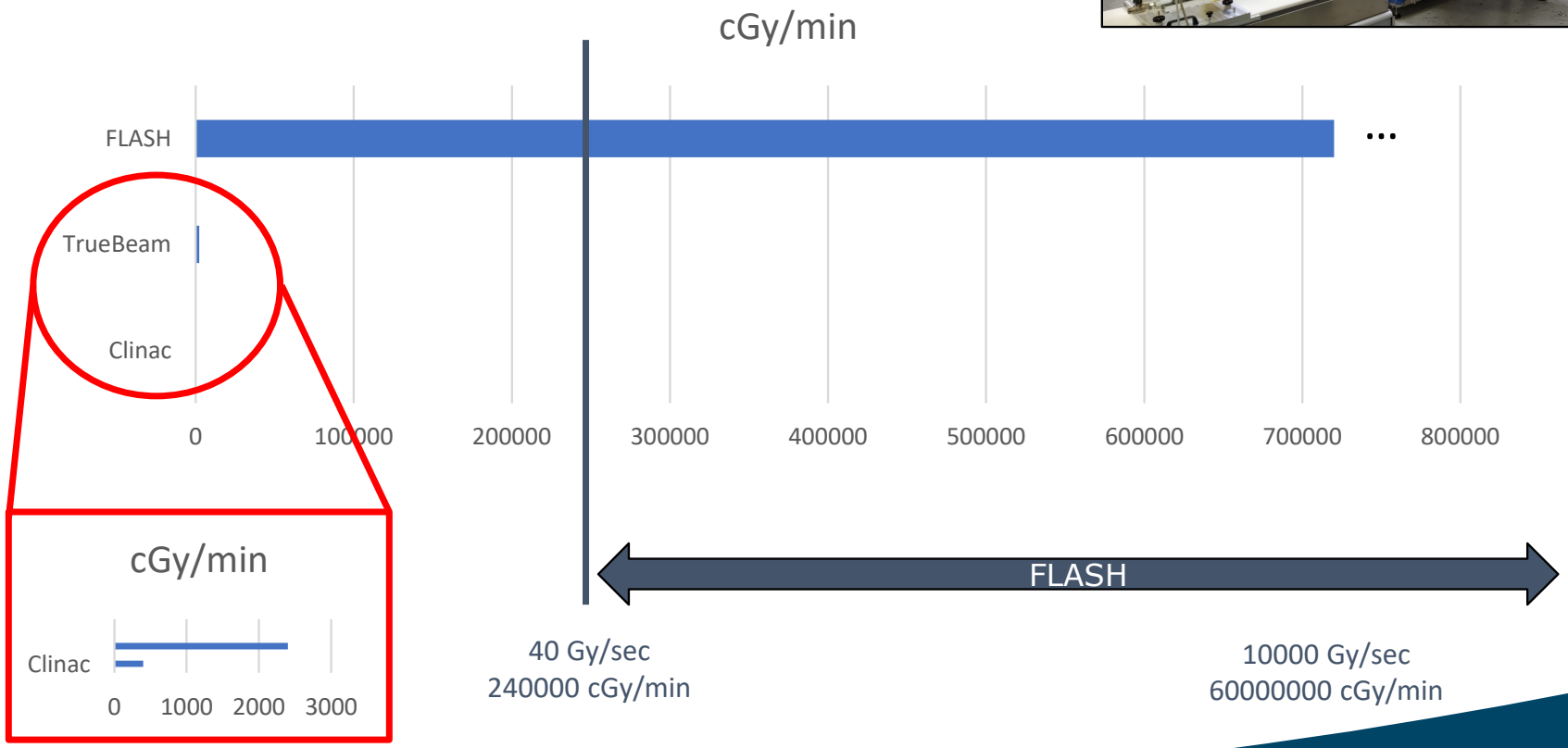
[1]Institut Curie, Centre de Recherche, 91405 Orsay, France. [2]INSERM U612, 91405 Orsay, France. [3]Pathology Laboratory, Ecole Nationale Vétérinaire d'Alfort, Université Paris-Est, 94704 Maisons Alfort, France. [4]Université Paris-XI, 91405 Orsay, France. [5]INSERM U1030, Institut Gustave-Roussy, 94805 Villejuif, France. [6]Institut Curie, Centre de Recherche, 75248 Paris 05, France. [7]INSERM U900, 75248 Paris 05, France. [8]Mines ParisTech, 77305 Fontainebleau, France. [9]CNRS, UMR144, 75248 Paris 05, France. [10]Radio-Oncologie/Radiothérapie, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland. [11]INSERM U967, Commissariat à l'Énergie Atomique (CEA), Division des Sciences du Vivant (DSV), Institut de Radiobiologie Cellulaire et Moléculaire (IRCM), 92265 Fontenay aux Roses, France.
*Corresponding author. E-mail: vincent.favaudon@curie.fr



It’s all about dose rate

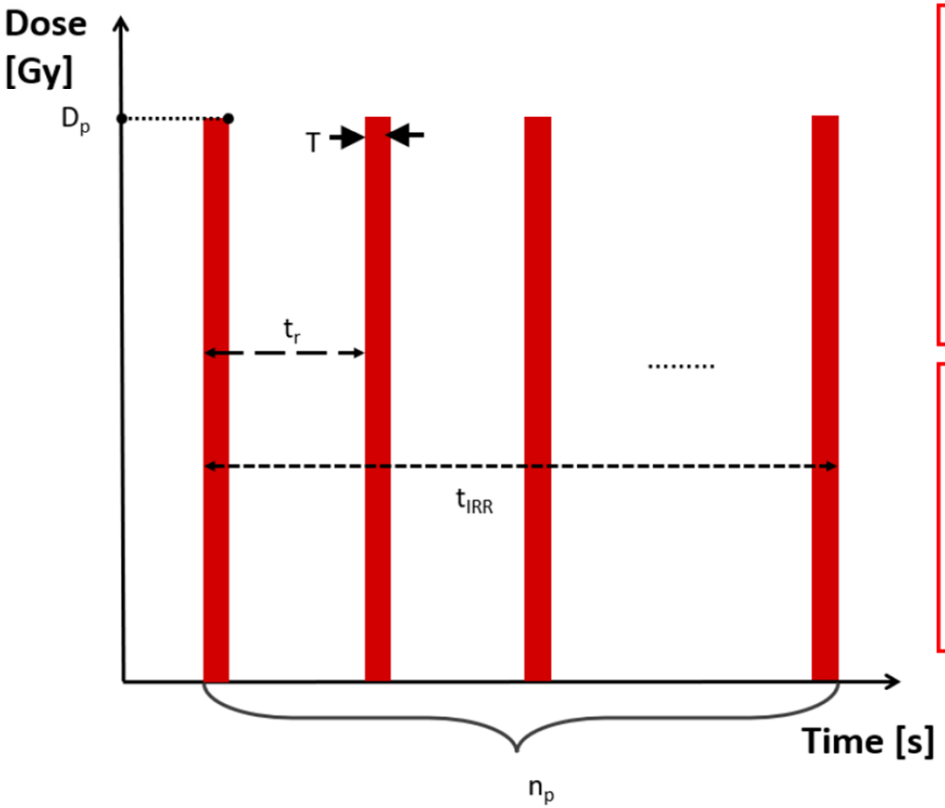
It’s all about dose rate





… but it's more complicated …

Temporal beam structure and dose rates



T Pulse width [s]

D_p Dose per singe pulse [Gy]

PRF Pulse Repetition Frequency [Hz]

n_p number of pulses

t_r time between two pulses = $1/PRF$ [s]

t_{IRR} total irradiation time = $\frac{n_p - 1}{PRF} + T$ [s]

DR Average dose rate [Gy/s]

$$DR = \frac{\text{Tot Dose}}{t_{IRR}} = \frac{n_p \cdot D_p}{t_{IRR}} \approx D_p \cdot PRF$$

IDR Instantaneous dose rate [Gy/s]

$$IDR = \frac{D_p}{T}$$

… but it's more complicated …

High dose-per-pulse electron beam dosimetry — A model to correct for the ion recombination in the Advanced Markus ionization chamber

Kristoffer Petersson,[a)] Maud Jaccard, Jean-François Germond, Thierry Buchillier, and François Bochud

Physics in Medicine & Biology

IPEM Institute of Physics and Engineering in Medicine

ACCEPTED MANUSCRIPT

Physics and biology of ultrahigh dose-rate (FLASH) radiotherapy: topical review

To cite this article before publication: Nolan Matthew Esplen *et al* 2020 *Phys. Med. Biol.* in press https://doi.org/10.1088/1361-6560/

frontiers

FLASH Radiotherapy with electrons: issues related to the production, monitoring and dosimetric characterization of the beam

Fabio Di Martino[1], Patrizio Barca[1], Salvatore Barone[2], Eleonora Bortoli[1], Rita Borgheresi[1], Silvia De Stefano[2], Massimo Di Francesco[2], Luigi Grasso[2], Stefania Linsalata[1], Daniela Marfisi[1], Matteo Pacitti[2] and Giuseppe Felici[2]

RESEARCH ARTICLE — MEDICAL PHYSICS

Development of an ultra-thin parallel plate ionization chamber for dosimetry in FLASH radiotherapy

Faustino Gómez[1,2] | Diego M. Gonzalez-Castaño[2] | Nicolás Gómez Fernández[2] | Juan Pardo-Montero[3,4] | Andreas Schüller[5] | Alessia Gasparini[6,7] | Verdi Vanreusel[6,7,8] | Dirk Verellen[6,7] | Giuseppe Felici[9] | Rafael Kranzer[10,11] | Jose Paz-M

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SCIENTIFIC REPORTS

natureresearch

OPEN

The challenge of ionisation chamber dosimetry in ultra-short pulsed high dose-rate Very High Energy Electron beams

M. McManus[1,2✉], F. Romano[3,1], N. D. Lee[3], W. Farabolini[4,6], A. Gilardi[4], G. Royle[2], H. Palmans[3,1] & A. Subiel[1✉]

A new model for volume recombination in plane-parallel chambers in pulsed fields of high dose-per-pulse

M Gotz[1,3], L Karsch[1,3] and J Pawelke[1,2,3]

[1] OncoRay-National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Fetscherstr. 74, PF 41, 01307 Dresden, Germany
[2] Institute of Radiation Physics, Helmholtz-Zentrum Dresden-Rossendorf, Bautzner Landstraße 400, 01328 Dresden, Germany

RESEARCH ARTICLE — MEDICAL PHYSICS

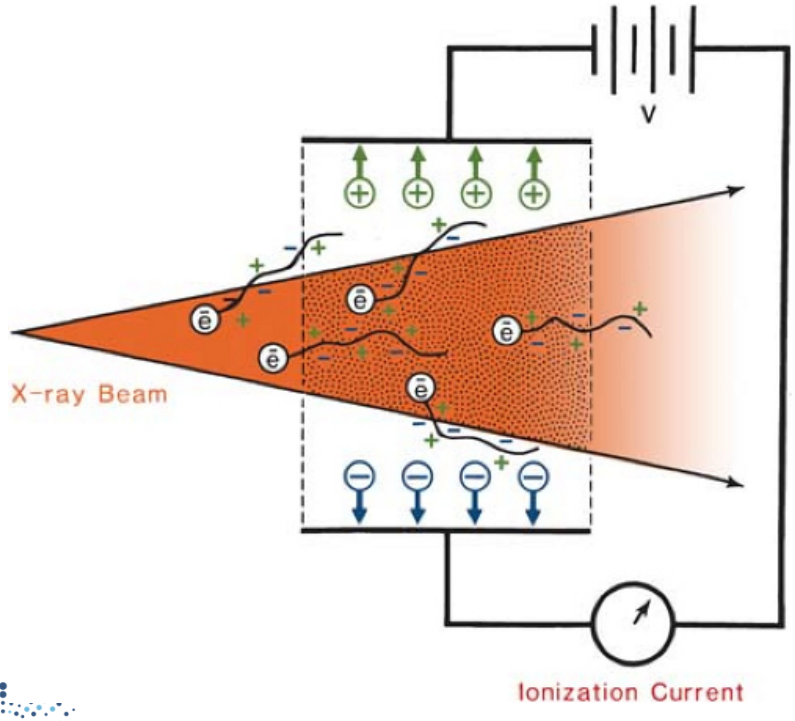
Design, realization, and characterization of a novel diamond detector prototype for FLASH radiotherapy dosimetry

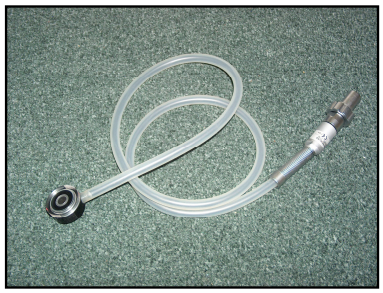
Marco Marinelli[1] | Giuseppe Felici[2] | Federica Galante[2] | Alessia Gasparini[3,4] | Lucia Giuliano[5] | Sophie Heinrich[5] | Matteo Pacitti[2] | Giuseppe Prestopino[1] | Verdi Vanreusel[3,4] | Dirk Verellen[3,4] | Claudio Verona[1] | Gianluca Verona Rinati[1]

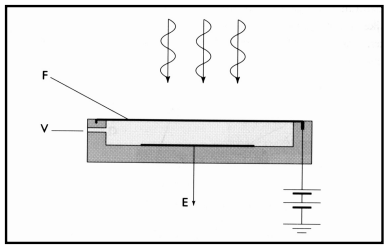
netwerk iridium Topzorg in radiotherapie

It’s all about dose rate

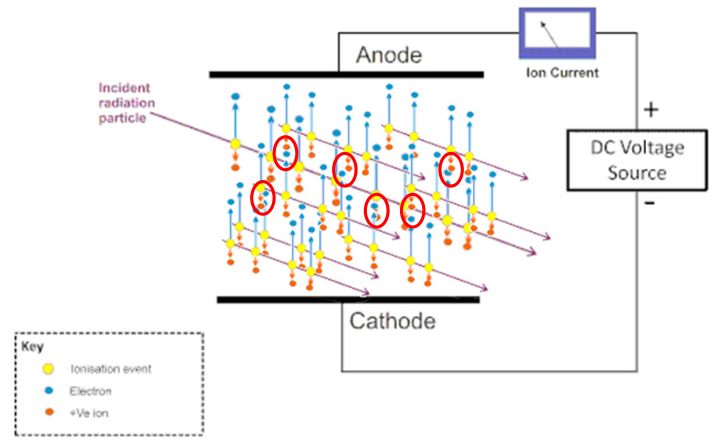
- The basics … k_s - k_{pol}





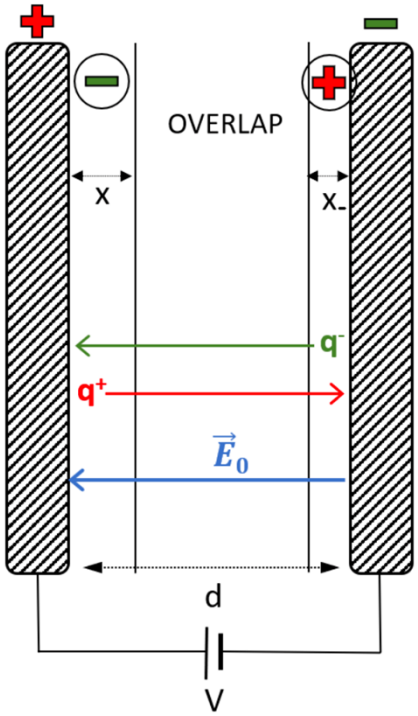


FLASH



… but it's more complicated …

- Recombination effect … and … self shielding



d: interelectrodic distance

V: applied voltage

E_0: electric field (E_0 = V/d)

Physica Medica 103 (2022) 175–180

Contents lists available at ScienceDirect

Physica Medica

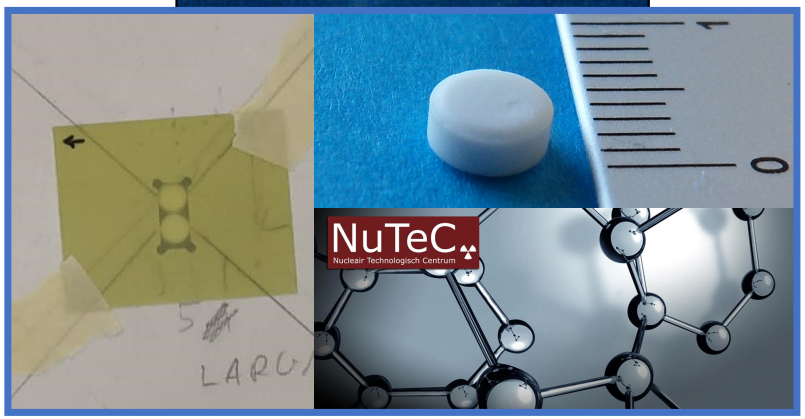
journal homepage: www.elsevier.com/locate/ejmp

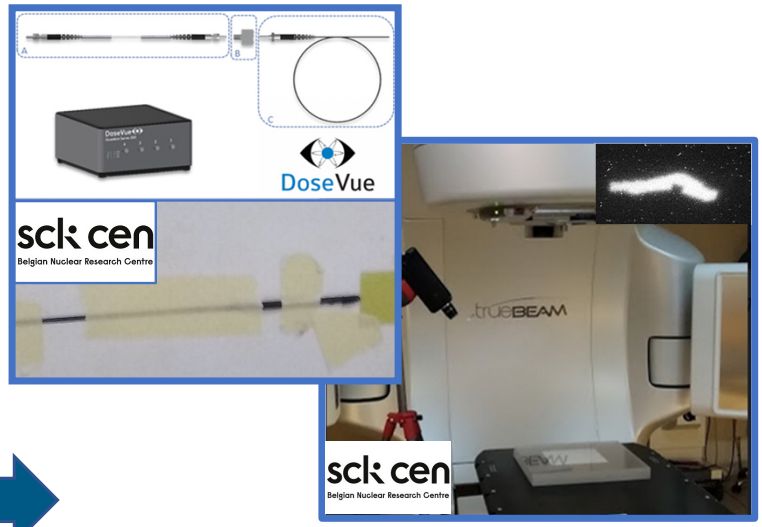
A new calculation method for the free electron fraction of an ionization chamber in the ultra-high-dose-per-pulse regimen

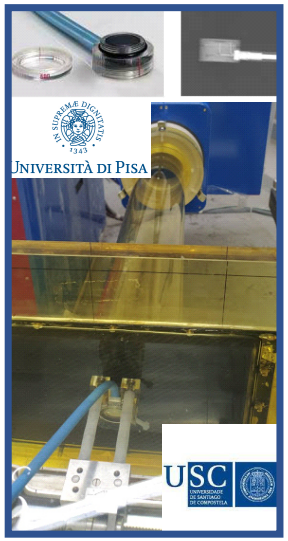
Fabio Di Martino [a,b,d,*], Damiano Del Sarto [b], Salvatore Barone [e], Maria Giuseppina Bisogni [b,c,d], Simone Capaccioli [b,c], Federica Galante [e], Alessia Gasparini [f,g], Giulia Mariani [e], Luigi Masturzo [c,d], Marco Montefiori [c,d], Matteo Pacitti [e], Fabiola Paiar [b,d,h], Jake Harold Pensavalle [c,d], Francesco Romano [i], Stefano Ursino [b,d,h], Verdi Vanreusel [f,g], Dirk Verellen [f,g], Giuseppe Felici [e]

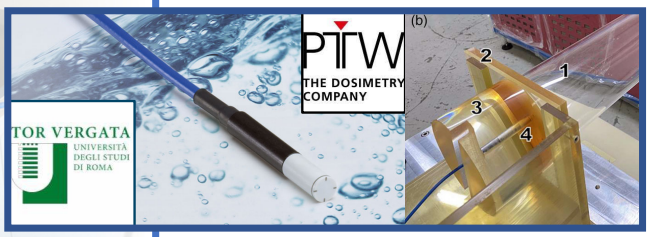
Dose calibration

- ... requires traceability



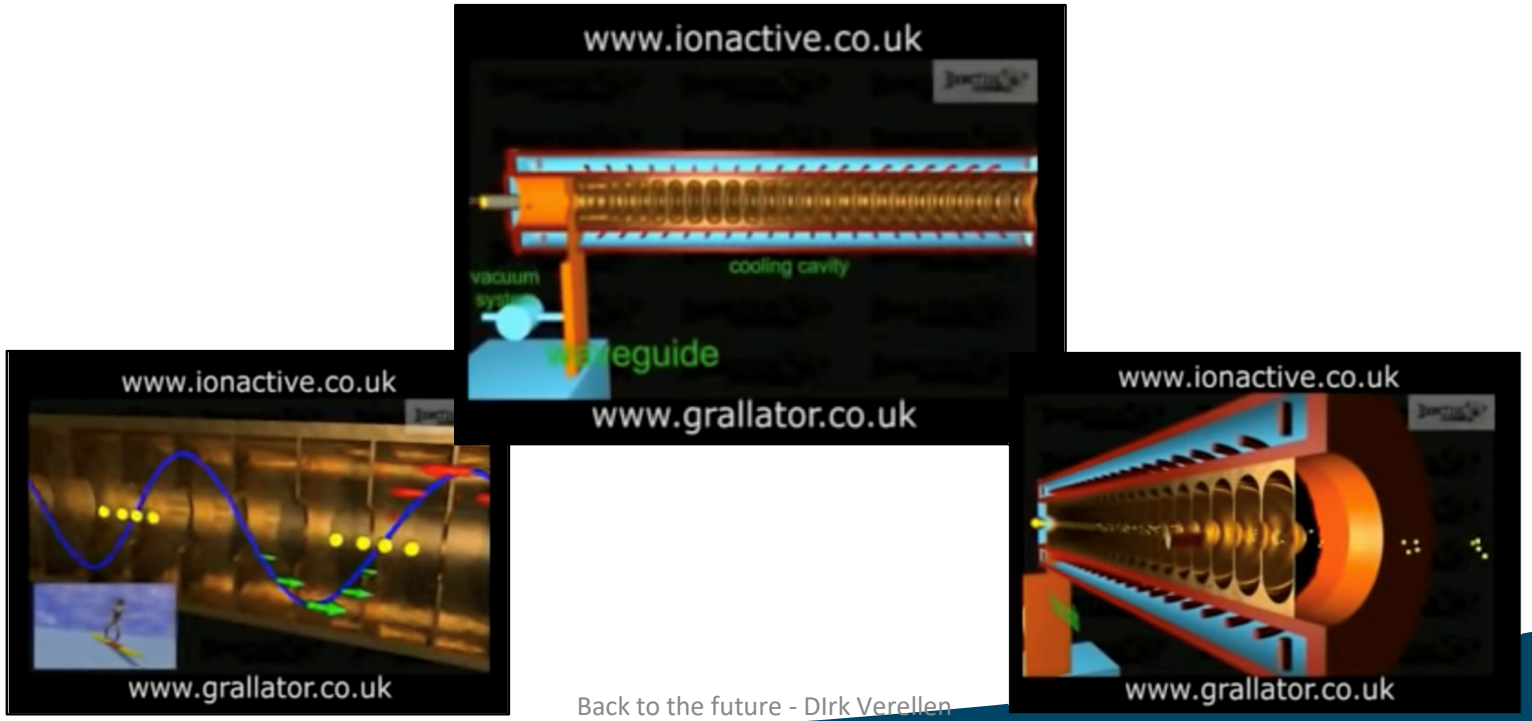






Beam monitoring and real-time controle …

- If you deliver 10Gy with 1 pulse (4.5 µs) …
- … if the pulse is gone … it's gone
  - Beam output, energy, flatness, symmetry, … ????



And of course AI …

Radiotherapy and Oncology 153 (2020) 55–66

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review Article

Overview of artificial intelligence-based applications in radiotherapy: Recommendations for implementation and quality assurance

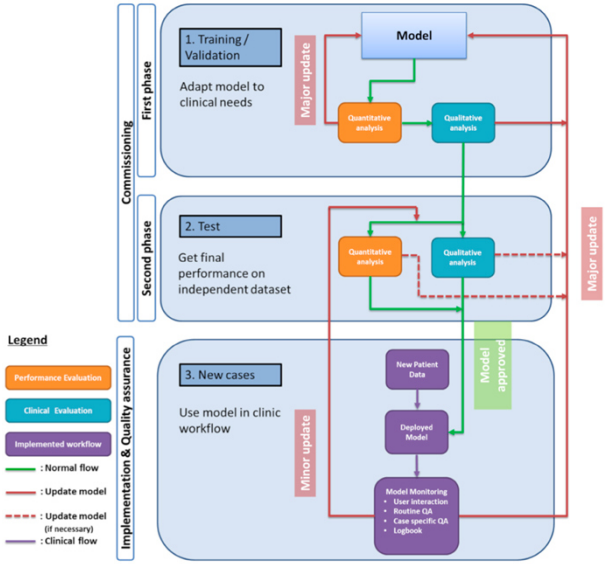
Liesbeth Vandewinckele [a,b,1], Michaël Claessens [c,d,1], Anna Dinkla [e,1,*], Charlotte Brouwer [f], Wouter Crijns [a,b], Dirk Verellen [c,d], Wouter van Elmpt [g]

Physics in Medicine & Biology

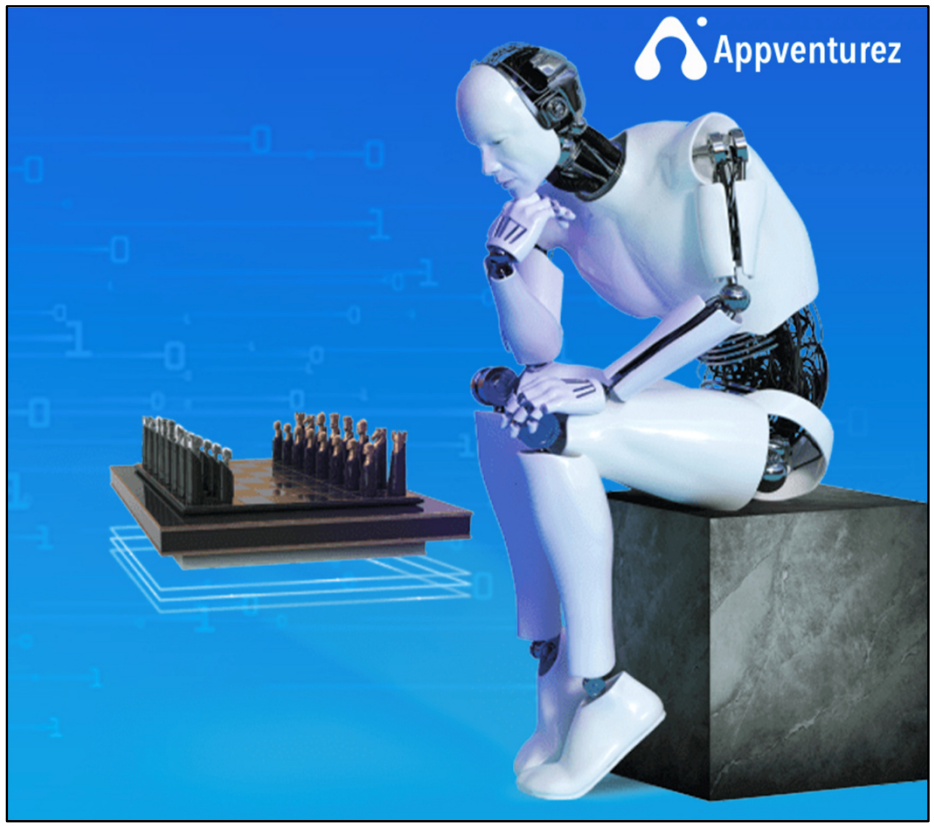
TOPICAL REVIEW · OPEN ACCESS

Towards a safe and efficient clinical implementation of machine learning in radiation oncology by exploring model interpretability, explainability and data-model dependency

To cite this article: Ana Barragán-Montero *et al* 2022 *Phys. Med. Biol.* **67** 11TR01



Rethinking human interaction



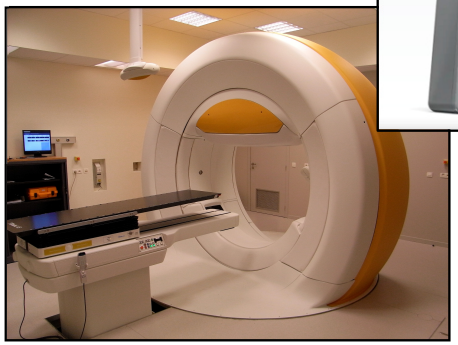
- Similar to the introduction of R&V systems at the end of the previous century:
  - It was introduced to mitigate human errors and reduce repetitive tasks
  - But people started to verify these tasks as if it was human, ... *by performing repetitive tasks ...*
- With large scale introduction of AI (computerized black boxes), the role of human interaction needs rethinking

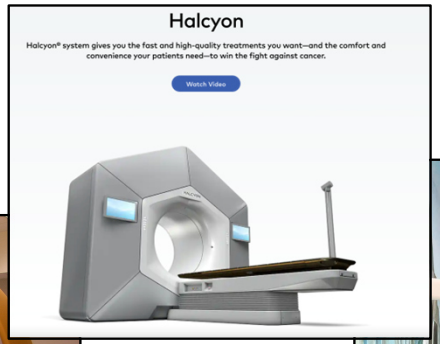
Outline

- Cargo Cult Science
- From early adopters ...
- ... to introducing a new but existing technology/technique
- The process of implementation and regulations

Implementing a new “established” technique

- Vendors are selling complex equipment as **plug&play** to facilities with understaffed-undertrained physicists.
- Hospitals are using internal **procedures and workflows** that are **not adapted** to these new technologies.
- Software and hardware is continuously being **upgraded**.





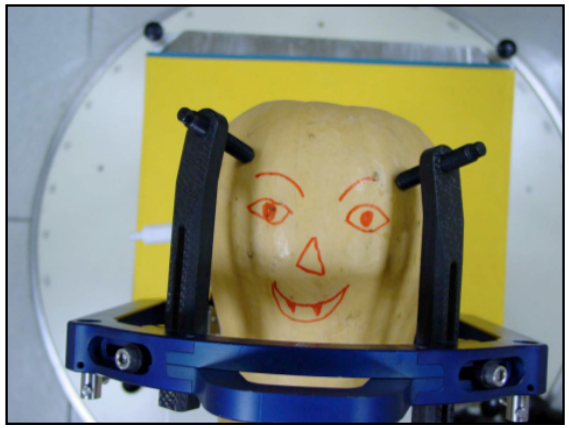
Back to the future - DIrk Verellen

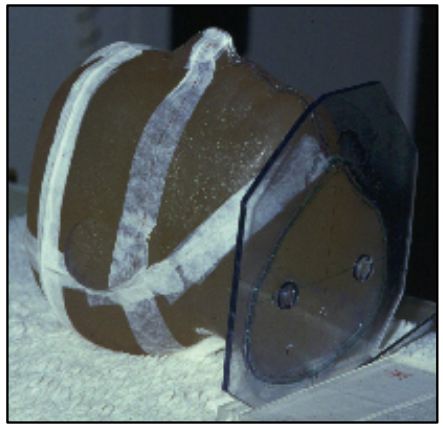
IMRT as an example on evolution of QA

- Technology implementation races ahead of guidelines
  - Small field dosimetry
  - In vivo dosimetry

IMRT as an example

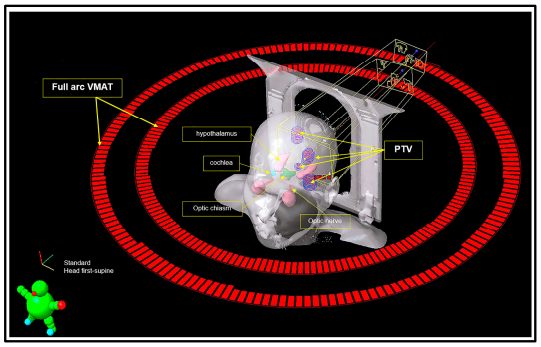
- Phase 1:
  - Being creative … see early adopters

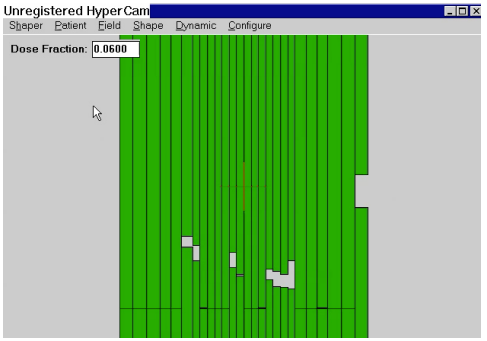


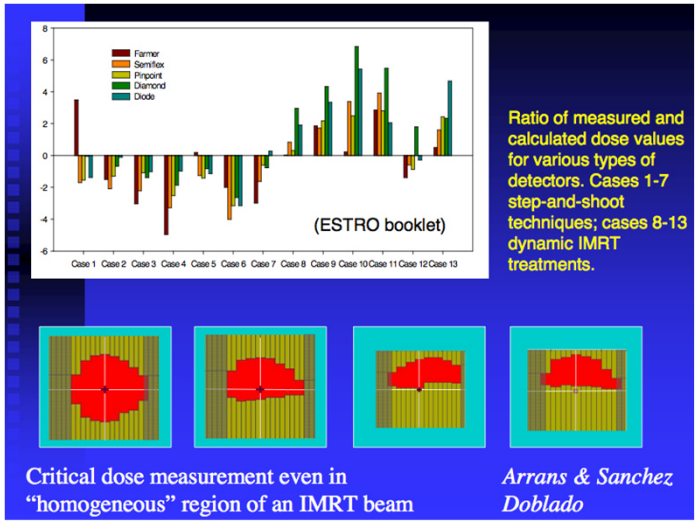


IMRT as an example

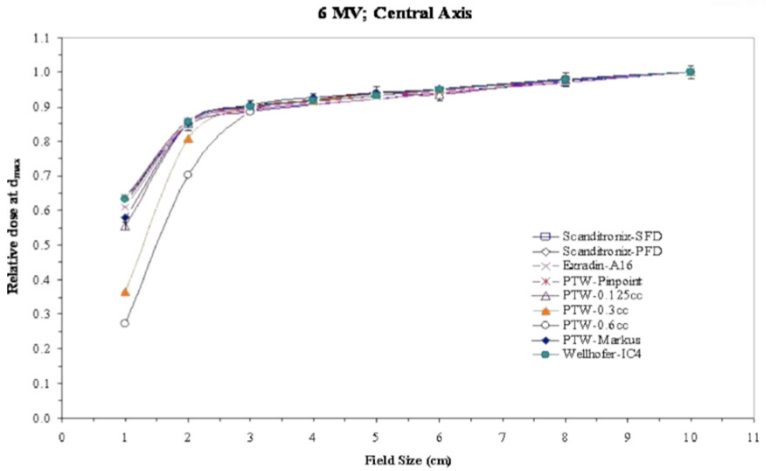
- Phase 2:
  - Make do with what is known and present in the department
- Absolute dose calibration



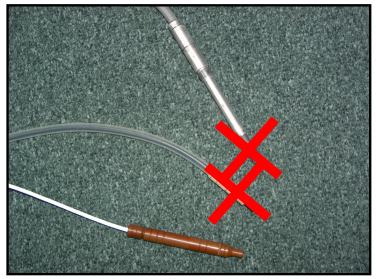




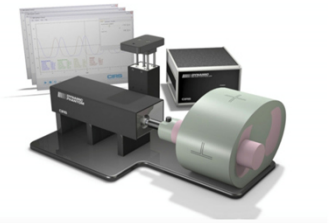
In this case ... size matters



Das IJ, *et al.*, Med Phys, 2008



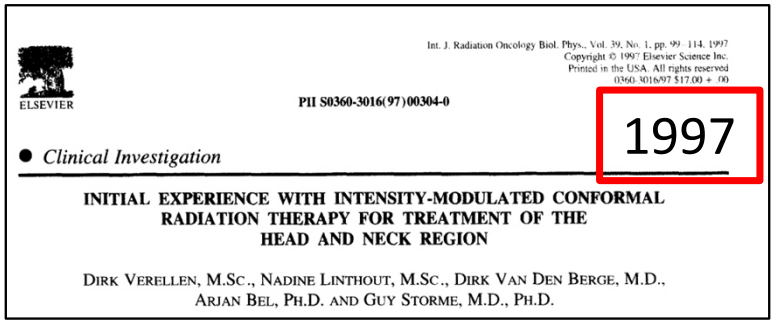
IMRT as an example

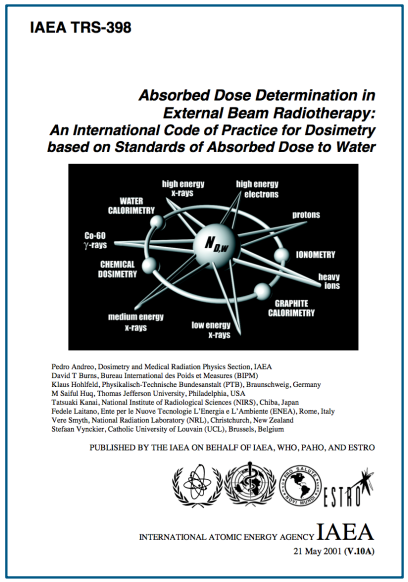



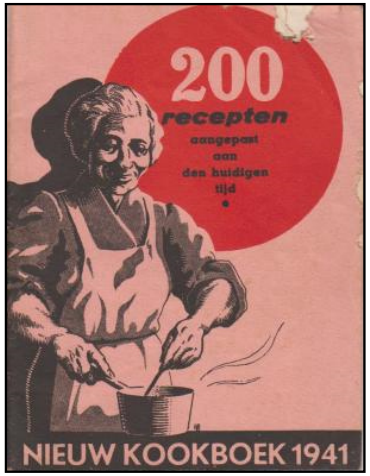

- Phase 2:
  - Make do with what is known and available in the department
- Patient specific QA … *in vivo* dosimetry was no longer feasible …

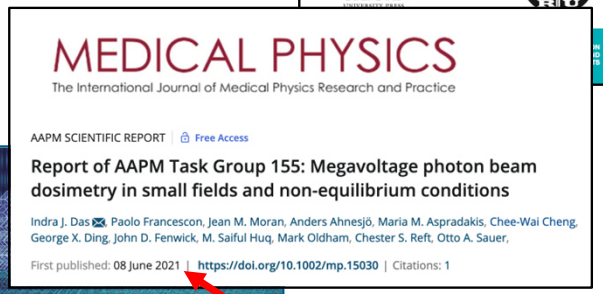
IMRT as an example

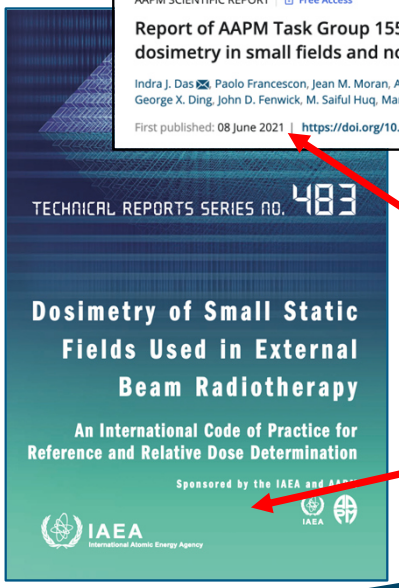
- Phase 3:
  - Finally we have guidelines and mature procedures
- Absolute dose calibration









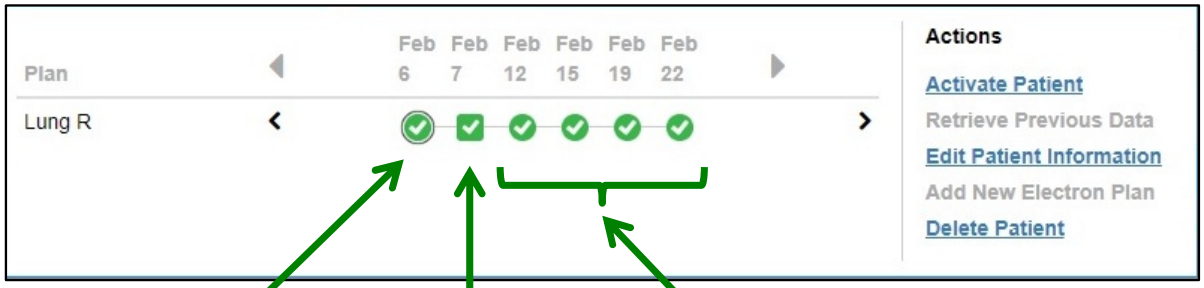


2021

2017

IMRT as an example

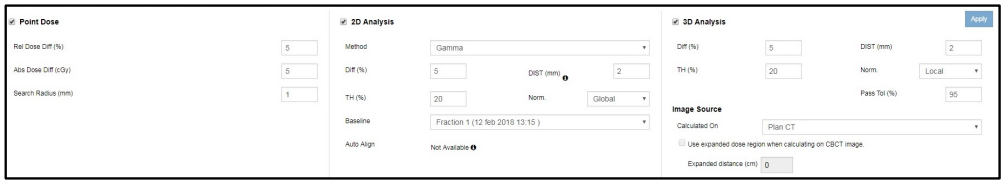
- Phase 3:
  - Finally we have tools for pre-treatment and *in vivo* dosimetry
- Patient specific QA
  - Patient-specific pre-treatment QA and *in vivo* dosimetry are performed for every patient using the PerFraction platform (Sun Nuclear), which includes:



- Independent MU calculation,
- Dose transmission measurements, pre-treatment,
- Dose transmission measurements, during treatment (in vivo)

IMRT as an example

- Patient specific QA

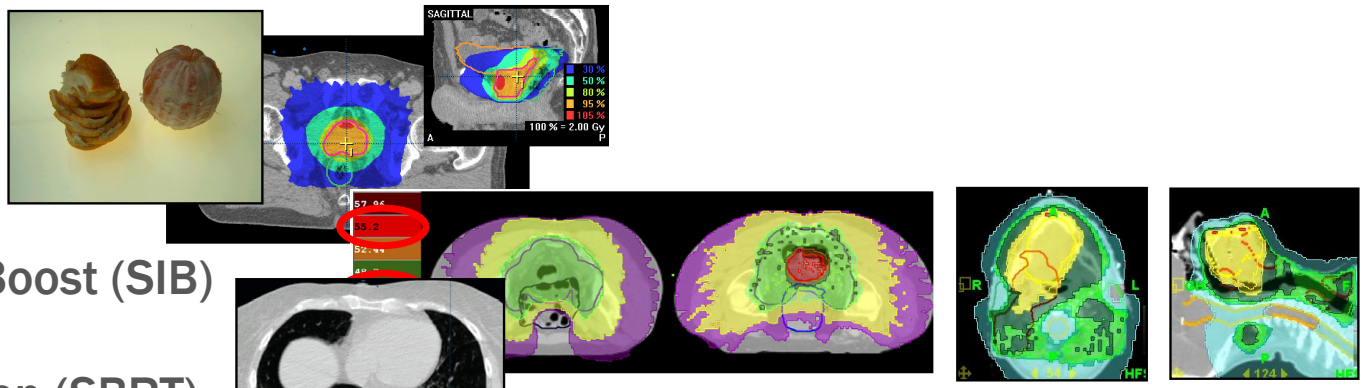


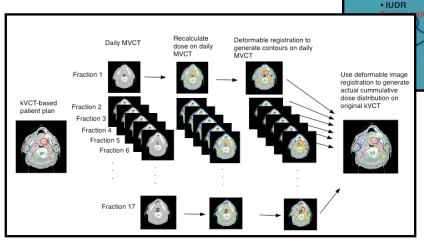
Outline

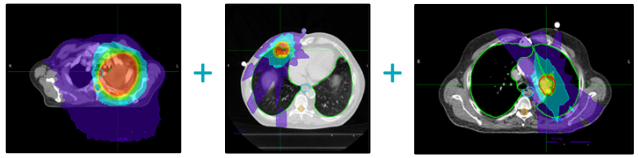
- Cargo Cult Science
- From early adopters ...
- ... to introducing a new but existing technology/technique
- The process of implementation and regulations

Radiotherapy … possibilities Today

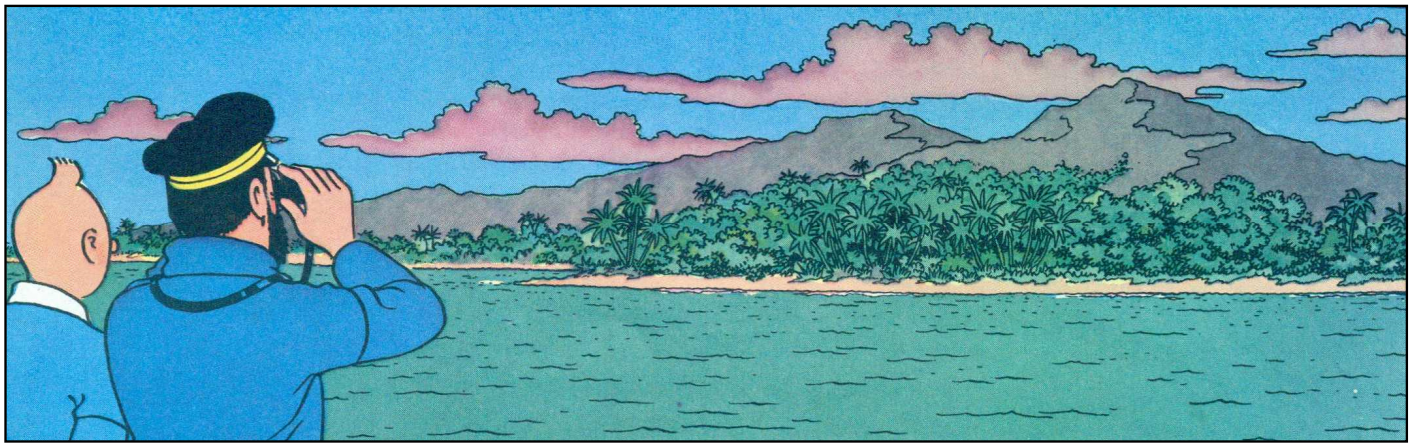
- Margin reduction
  - Dose escalation
  - Conformal avoidance
- Simultaneous Integrated Boost (SIB)
- Reviewed dose fractionation (SBRT)
- Biological Conformal Radiation Therapy (BCRT)
- Adaptive Radiation Therapy (ART)
- Re-irradiation







What are we lookin’ for?



- Ensuring that *what has been planned really has been delivered !!*
  - ***… for each patient!!***
  - **… every fraction!!**
  - **… in a safe way!!**
- Due to the complexity of Radiation Oncology, QA and safety is more than pre-treatment verifications, but process oriented.

Risk management

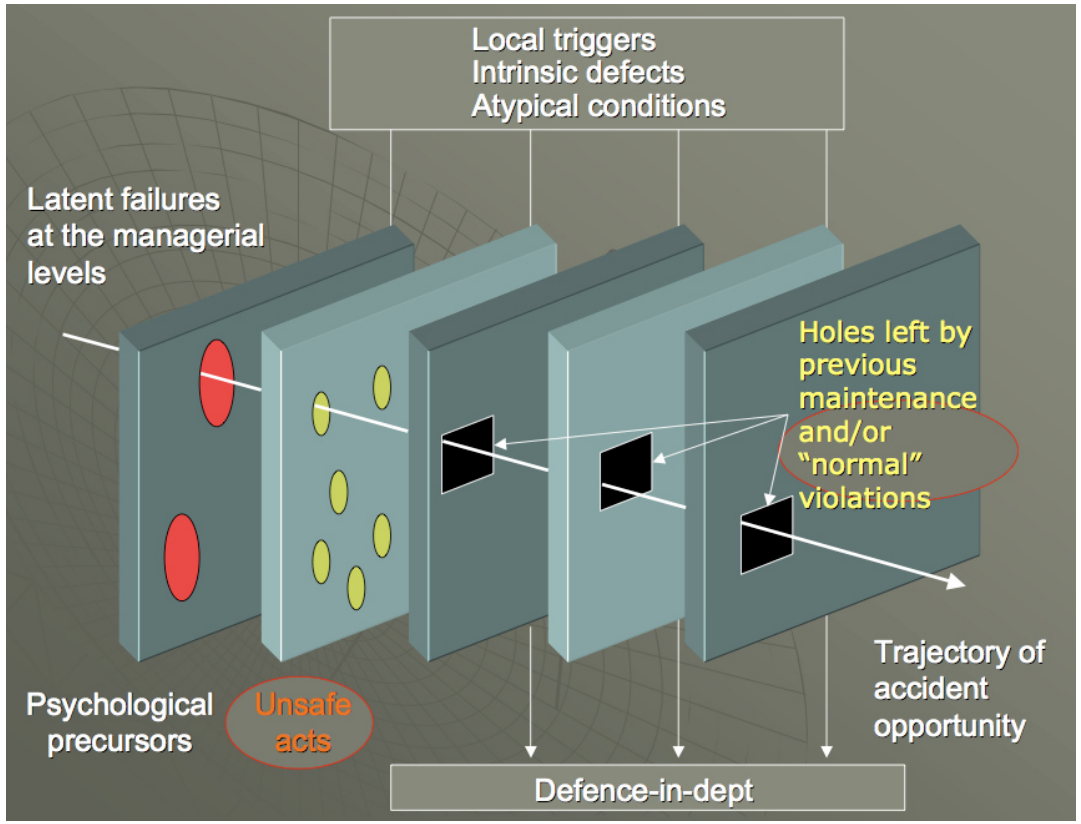
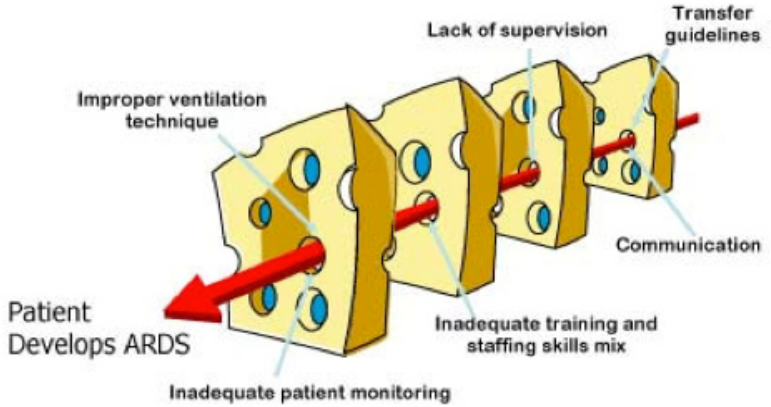


Figure 1. The Swiss cheese model of accident causation [Reason, 2000b].



Risk analysis

- Retrospective risk analysis: root-*cause analysis*
  - **INCIDENT REPORTING**: ROSIS, PRISMA, SAFRON
- Prospective risk analysis: ***process analysis***
  - (H)FMEA: Healthcare Failure Mode and Effects Analysis
- Proper education, proper staffing levels, transparent communication, up to date procedures, E2E testing, in-vivo dosimetry, …

Back to the future - DIrk Verellen

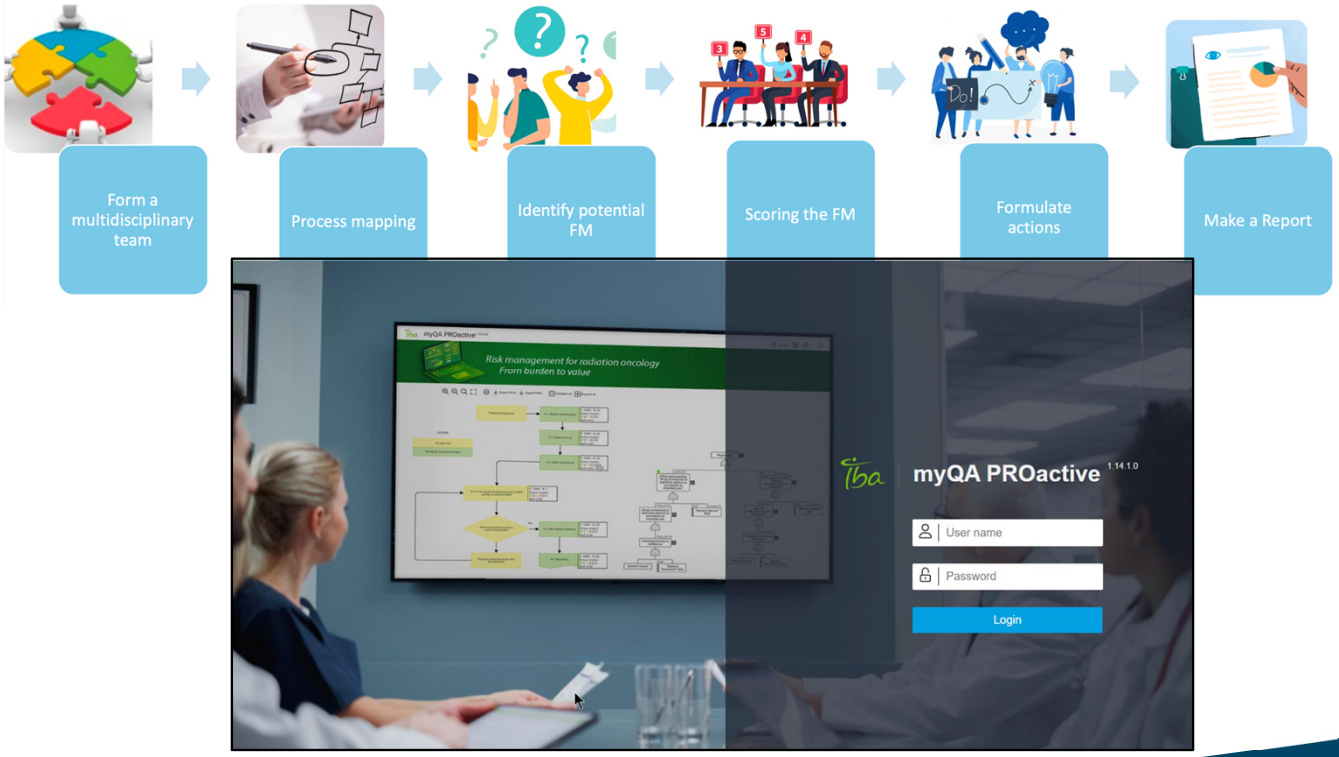
Prospective risk analysis …

- Installing new linac
  - 11 process steps, 362 risk sources, 40 action points
- HDR afterloader
  - 11 process steps, 289 risk sources, 10 action points
- 5 year revision of CT-sim
  - Still 16/45 open aciotn points … (!)
- New TPS
  - 29 process steps, 527 risk sources, 142 action points
- …

Time consuming …

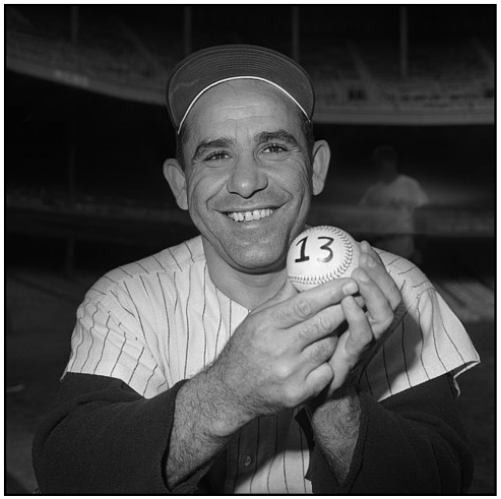
Risk management process

- Finally, some commercial tools become available
- … so, no more excuses.



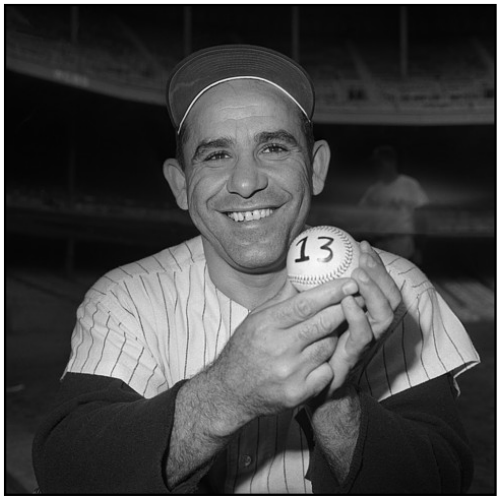
Some Yogi wisdom …

- “If you don't know where you're going, …”



Some Yogi wisdom …

- “If you don't know where you're going, …
  you might not get there.”



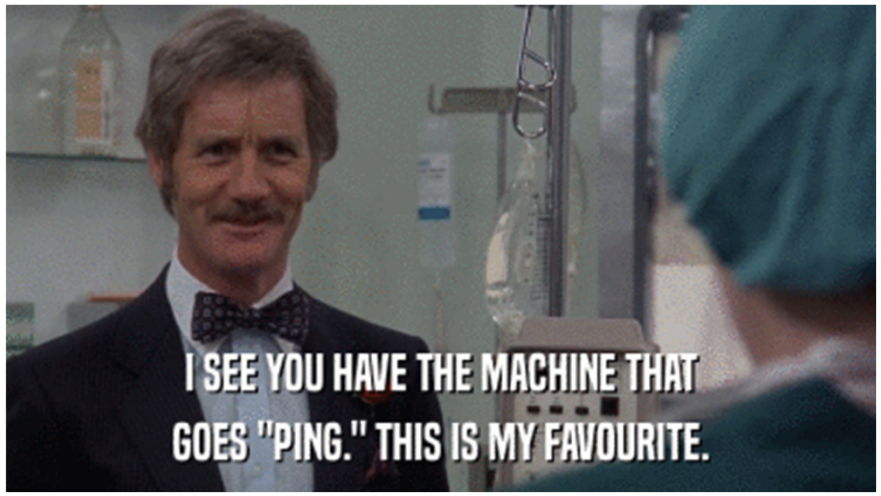
About new developments

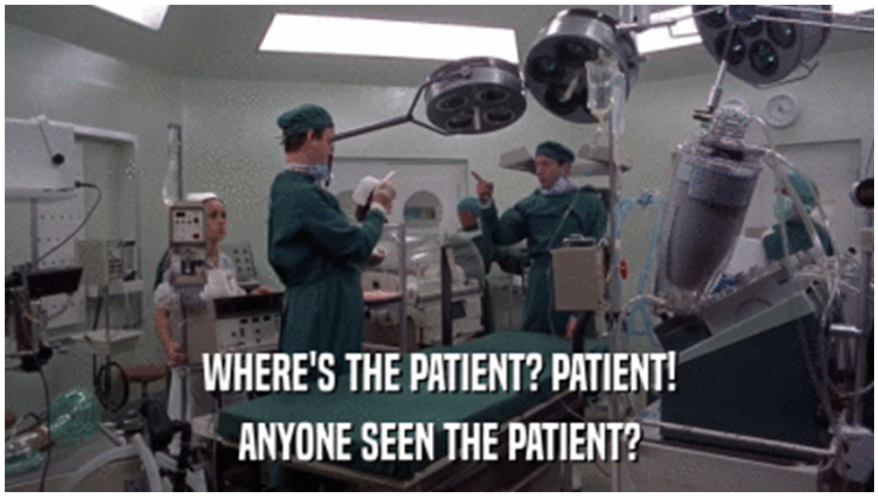
- To quote Terry Pratchett:
  - “New developments cause a rethink. If this bothers you, consider how much damage is being done to the world by people for whom new developments do ***not*** cause a rethink.”
- The danger might be that the focus is too much on the innovation, less on (safe) implementation.

About new developments

- To quote Prof. Dr. Steve Webb:
  - The true challenge is to develop the wisdom to know when to select which [treatment modality] in the clinic.

So, where’s the catch?



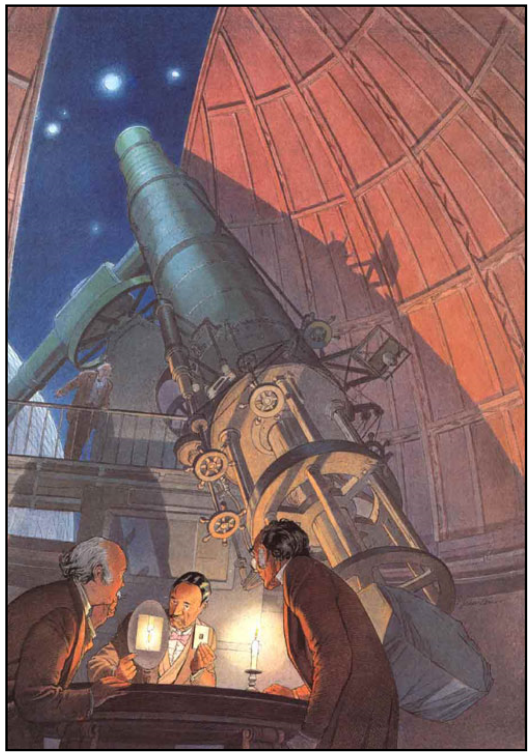


Introducing new technologies/techniques

The most important thing to a patient **is not** the availability of some high technology device, rather **it is** the ability of a team of physicians, physicists, dosimetrists and therapists to use a technology with skill for the benefit of the patient.

Dr. Marc Edwards

It's the TEAM not the BEAM !!!



L' expérience cruciale, F. Schuiten

Acknowledgements