From 2D to 3D:

What we learned and current physics needs and challenges

Núria Jornet

Servei de Radiofísica i Radioprotecció

Hospital de la Santa Creu i Sant Pau

Barcelona

Can you keep a secret? …

Our information was 2D

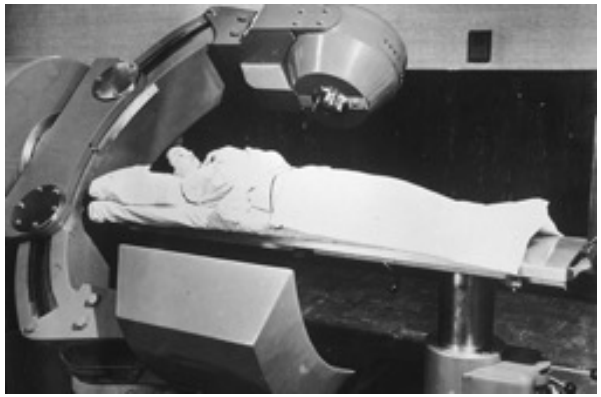
We had planar X-ray images : Patient anatomy collapsed in 2D

We calculated the dose distribution on one plane (slice) containing beam axis

But we never treated patients with 2D RT!!

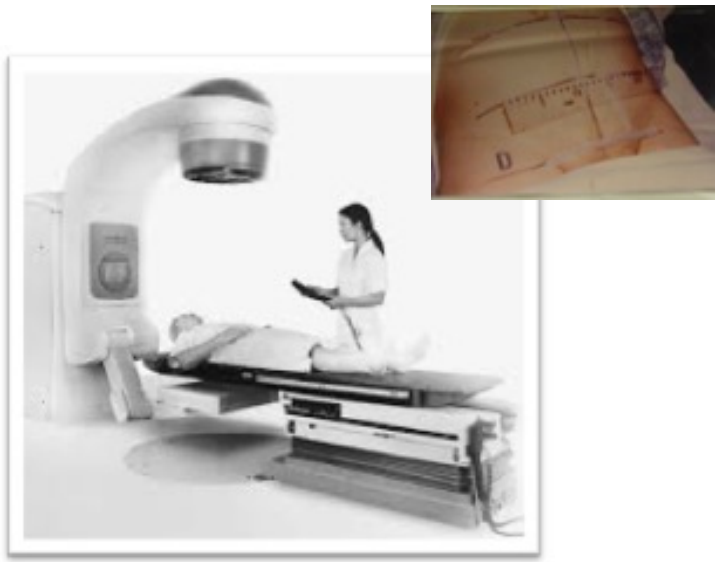
Patients are 3D

Beam delivery was 3D



Can you keep a secret? …

Patient information for treatment planning: the 2D era

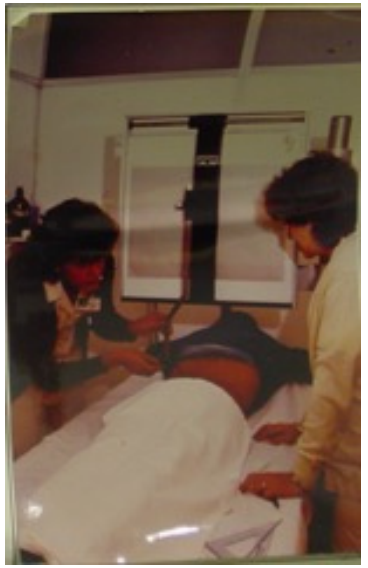


RT- simulator
2D X ray images
Fluoroscopy

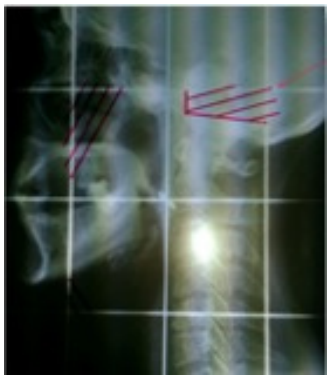
Mimics the treatment unit
Gantry, collimator rotation
Wires simulating field size

Contour plotter

Patient contour on central axis

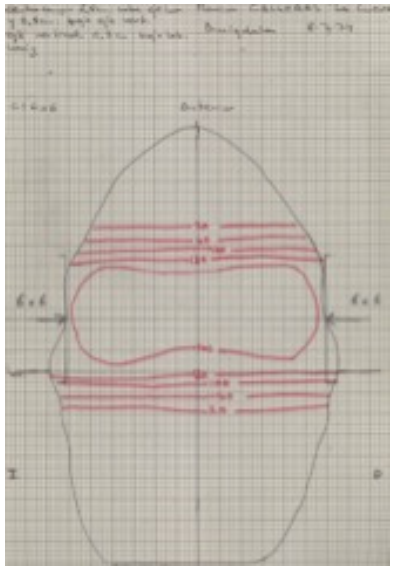


Patient information for treatment planning: the 2D era



RT- simulator
2D X ray images

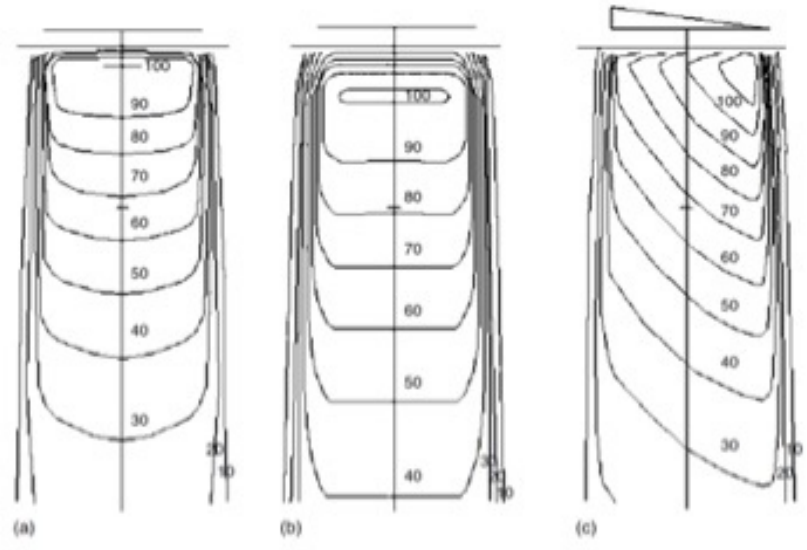
Anatomical references



Contour plotter

Contour on central axis
Patient: water /no heterogeneities considered

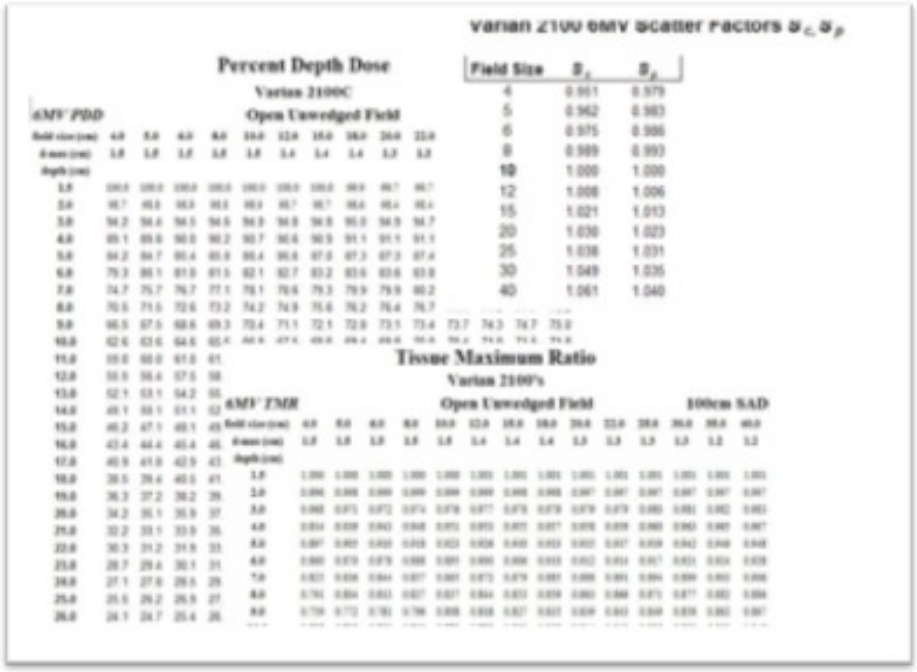
Beam information for treatment planning: the 2D era



6MV X rays

25MV X rays

6MV X rays
45º wedge


Varian 2100 6MV Scatter Factors S_c, S_p

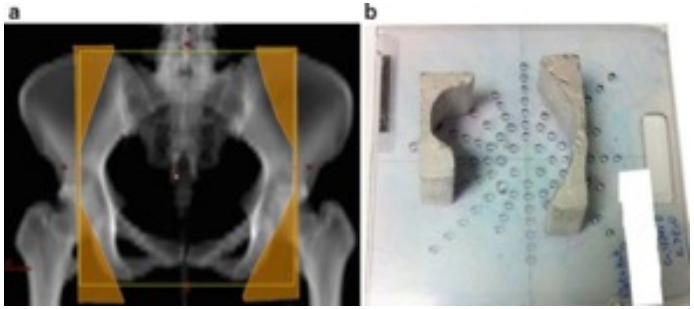
Percent Depth Dose
Varian 2100C
6MV PDD
Open Unwedged Field

Field Size	S_c	S_p
4	0.951	0.979
5	0.962	0.983
6	0.975	0.986
8	0.989	0.993
10	1.000	1.000
12	1.008	1.006
15	1.021	1.013
20	1.030	1.023
25	1.038	1.031
30	1.049	1.035
40	1.061	1.040

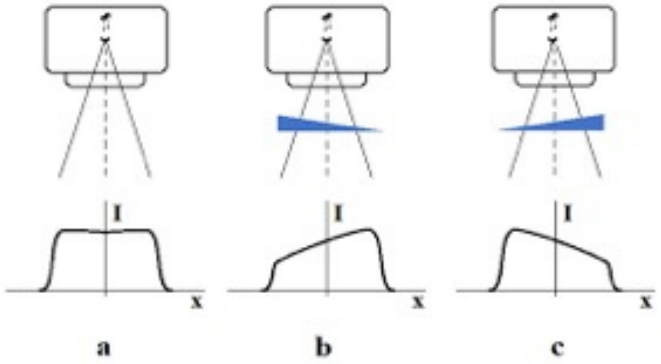
Tissue Maximum Ratio
Varian 2100's
6MV TMR
Open Unwedged Field
100cm SAD

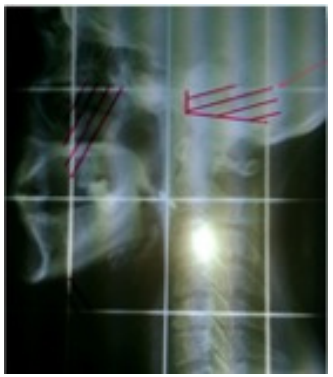
Beam modifiers: the 2D era

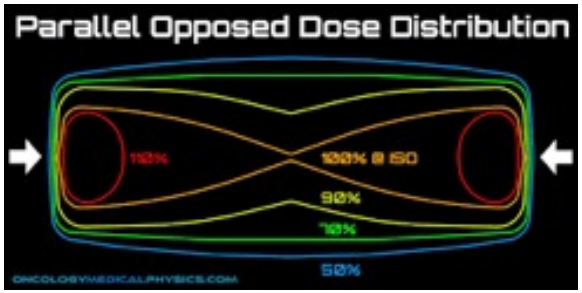
Field shaping: Pb corner blocks/Cerrobend blocks

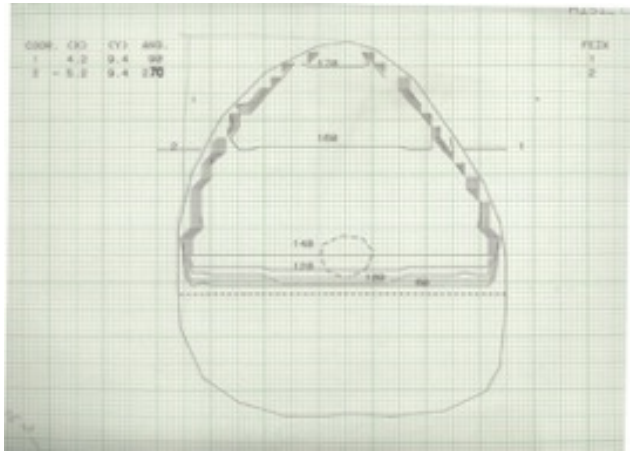


Fluence modifiers (1D): Physical wedges









Treatment planning 2D era

- First compute equivalent squares of the fields:

$$EqSq = \left(LW/_{L+W}\right) = \left(\times 20\times 18/_{20+18}\right) = 19.0$$

- Then look up Output Factors and TMRs
  - FS = 19 cm^2 Depth = 8 cm
- Substitute in:

$$MU = Dose/_{Sc \times Sp \times TMR \times OAF \times TF}$$

Assumes SAD Calibration

- And you're done!

6MV TMR — **Open Unwedged Field**

field size (cm)	4.0	5.0	6.0	8.0	10.0	12.0	15.0	18.0	20.0
d-max (cm)	1.5	1.5	1.5	1.5	1.5	1.4	1.4	1.4	1.3
depth (cm)									
1.5	1.000	1.000	1.000	1.000	1.000	1.001	1.001	1.001	1.001
2.0	0.996	0.998	0.999	0.999	0.999	0.999	0.998	0.998	0.997
3.0	0.968	0.971	0.972	0.974	0.976	0.977	0.978	0.979	0.979
4.0	0.934	0.939	0.943	0.948	0.951	0.953	0.955	0.957	0.958
5.0	0.897	0.905	0.910	0.918	0.923	0.926	0.930	0.933	0.935
6.0	0.860	0.870	0.878	0.888	0.895	0.900	0.906	0.910	0.912
7.0	0.825	0.836	0.844	0.857	0.865	0.872	0.879	0.885	0.888
8.0	0.791	0.804	0.813	0.827	0.837	0.844	0.853	0.859	0.863

Field Size	S_c	S_p
4	0.951	0.979
5	0.962	0.983
6	0.975	0.986
8	0.989	0.993
10	1.000	1.000
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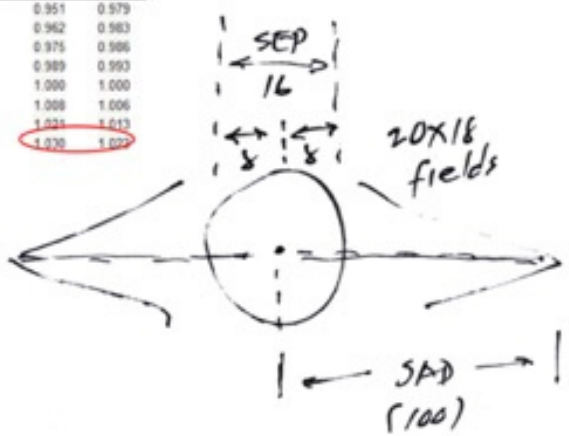
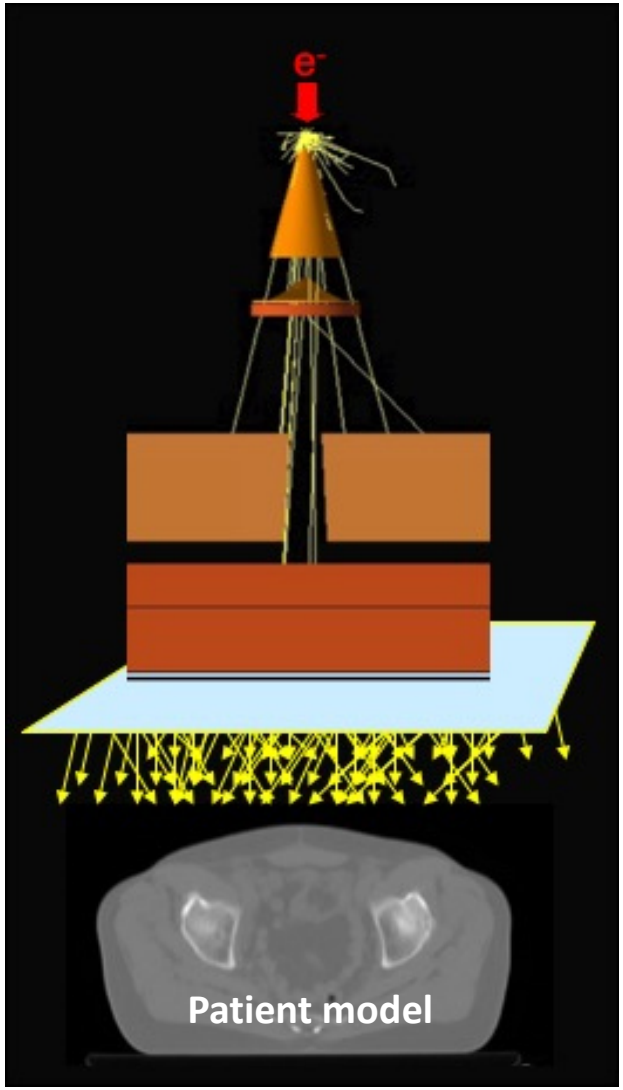


Treatment planning on 2D: what was needed, how was it done.

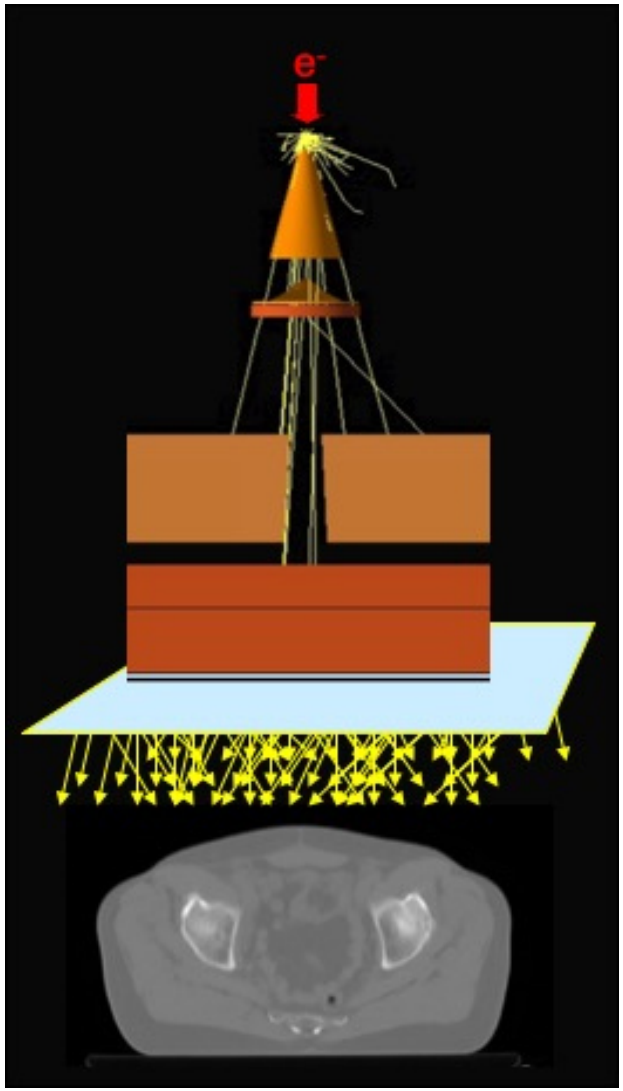
2D treatment planning	3D treatment planning
Patient positioning/immobilization	Patient positioning/immobilization
Patient contour (central slice)	CT imaging
Beam portal (x-rays)	Volume delineation
Design of Cerrobend blocks (anatomical references 2D)	
Dose prescription (ICRU point)	Dose prescription (volumetric)
Dose optimization: None (maybe field weights/wedges)	Dose optimization: Manual or inverse planning (IMRT/VMAT)
Dose calculation: 1 plane…	Dose calculation: All planes! (3D)



Dose calculation

Beam model: Head model and MLC model

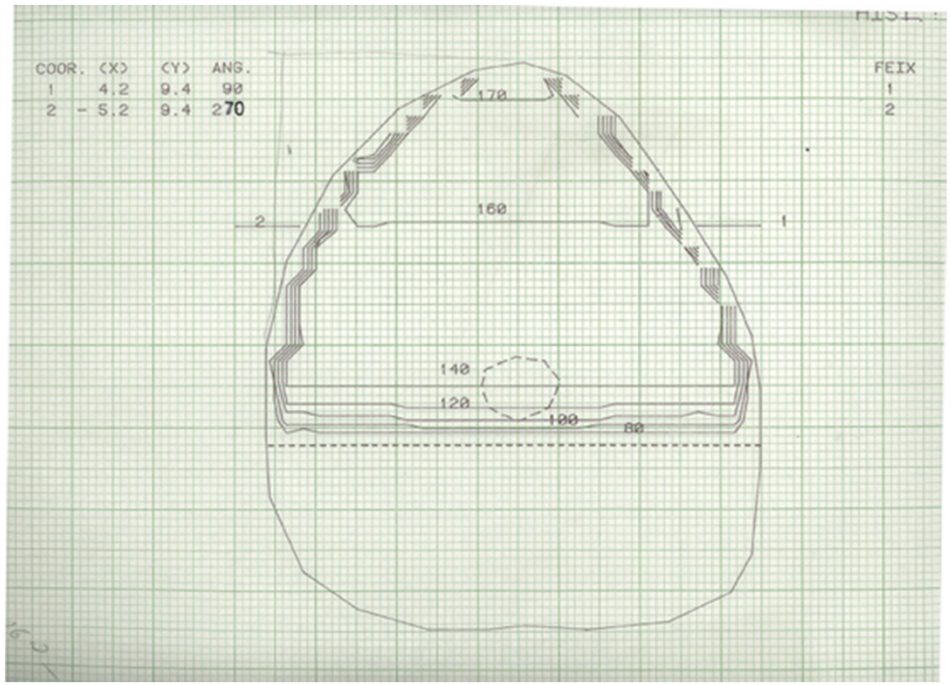
Radiation transport (dose deposition)



Dose calculation

	2D	3D
Head model	Direct use of dose profiles/output factors	Multisource (description of sources extracted from measured dose profiles /output factors) Description of individual particles
Dose deposition	Non-existing Superposition of isodose curves with corrections of surface obliquity Hand calculation of treatment time	Dose calculations from fluence using kernel superpositions or explicit transport equations
Patient model	Non-existing 1 contour through beam central axis Patient water equivalent	3D set of images Mass and/or electron density information

Treatment plan design



Need to choose

Number of beams
Field size
Gantry angle
Wedges
Weight

Resulted

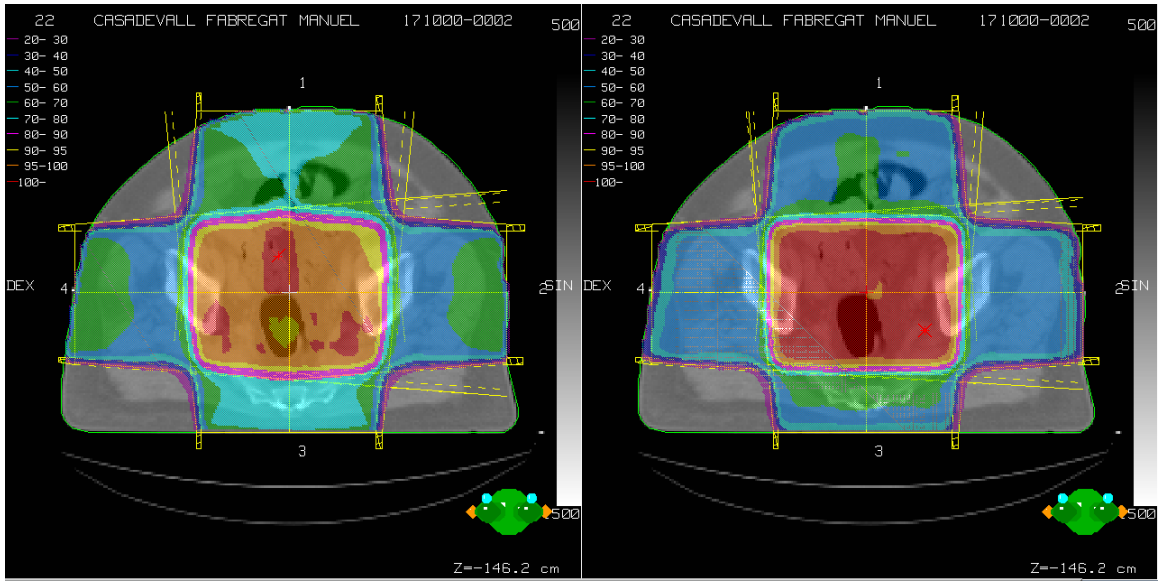
Standard disposition of the beams/weights

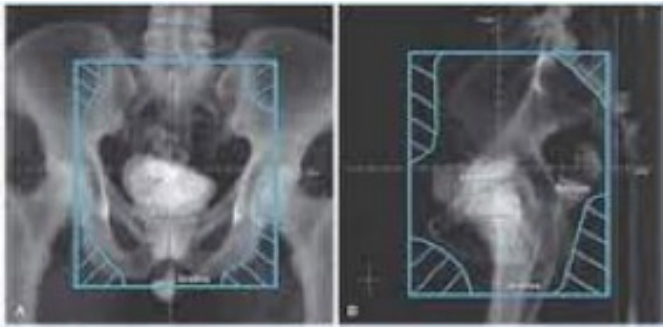
Dose distributions in water

Similar dose distributions

No variability due to the dose engine/calculation algorithm

Treatment plan design moving from: 2D to 3D





2D planning

No treatment volumes defined	Reduction of the variability between RO
No treatment OARs defined	Reduction of the variability between RO
No dose engine used	No differences between treatment planning systems
Standard disposition of the beams	Similar dose distributions

MAIN sources of variability were:

1. Patients
2. Treatment delivery (immobilization systems, treatment verification)

Treated volume >> CTV

2D planning

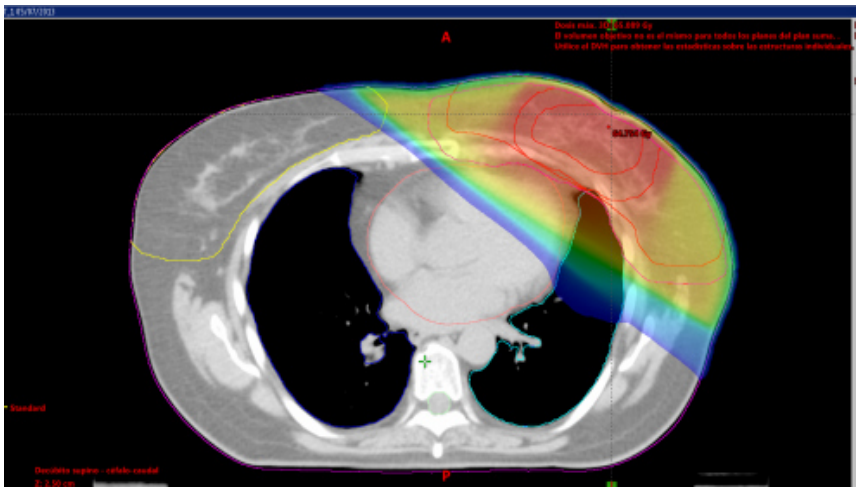
Very limited treatment individualization

Less heterogeneity in clinical practice

Limited information to study correlation between the treatment and clinical outcome

What were the consequences?

DVH depended on the dose distribution and correlated with clinical results



D_{mean} =12.5 Gy

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Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D., Ulla Blom-Goldman, M.D., Dorthe Brønnum, R.N., Candace Correa, M.D., David Cutter, F.R.C.R., Giovanna Gagliardi, Ph.D., Bruna Gigante, Ph.D., Maj-Britt Jensen, M.Sc., Andrew Nisbet, Ph.D., Richard Peto, F.R.S., Kazem Rahimi, D.M., Carolyn Taylor, D.Phil., and Per Hall, Ph.D.

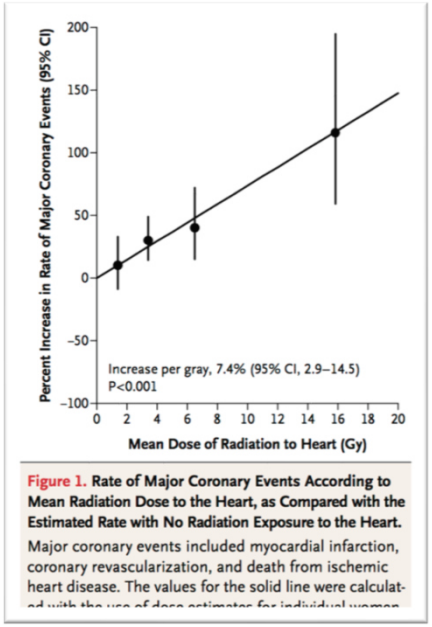
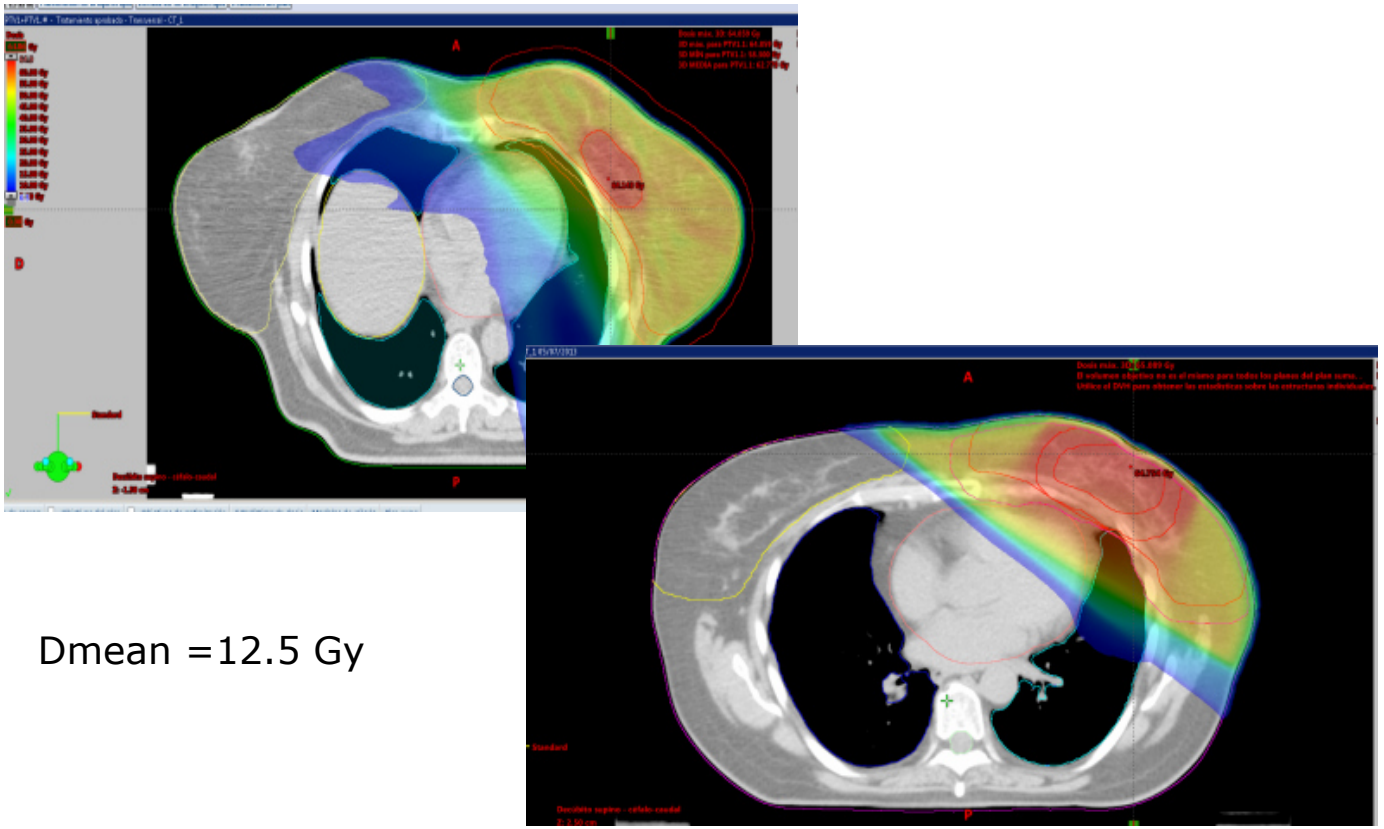


Figure 1. Rate of Major Coronary Events According to Mean Radiation Dose to the Heart, as Compared with the Estimated Rate with No Radiation Exposure to the Heart.

Major coronary events included myocardial infarction, coronary revascularization, and death from ischemic heart disease. The values for the solid line were calculat-

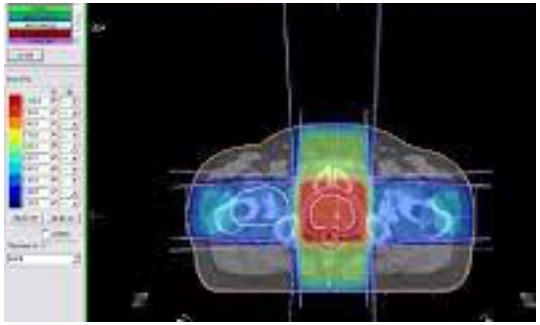
2023: Can the dose distribution have an impact on the heart toxicity?

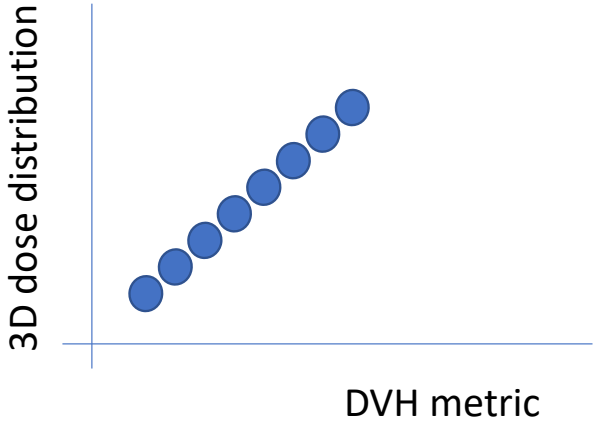


Dmean =12.5 Gy

How robust are DVH end points to changes in treatment techniques?

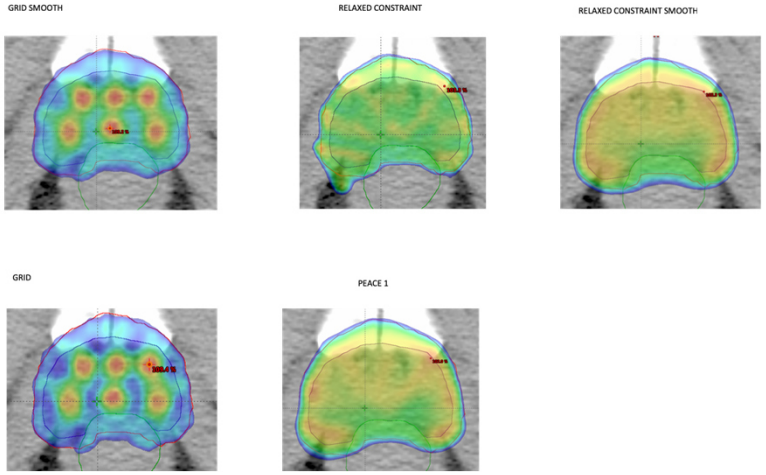
- At a point in time the treatment technique were very similar
- Dose distributions were very similar
- DVH described in fact similar spatial dose distributions → good surrogate of the underlying dose distribution

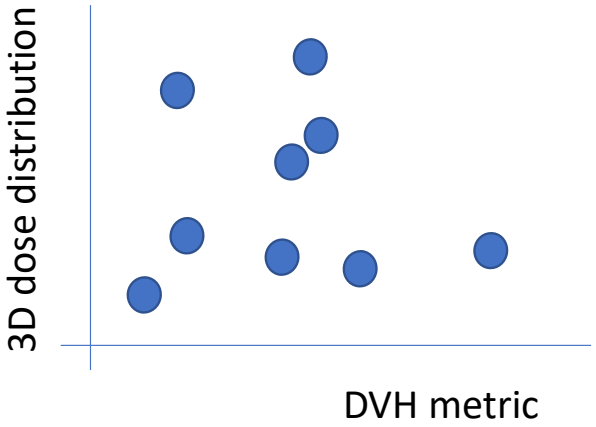




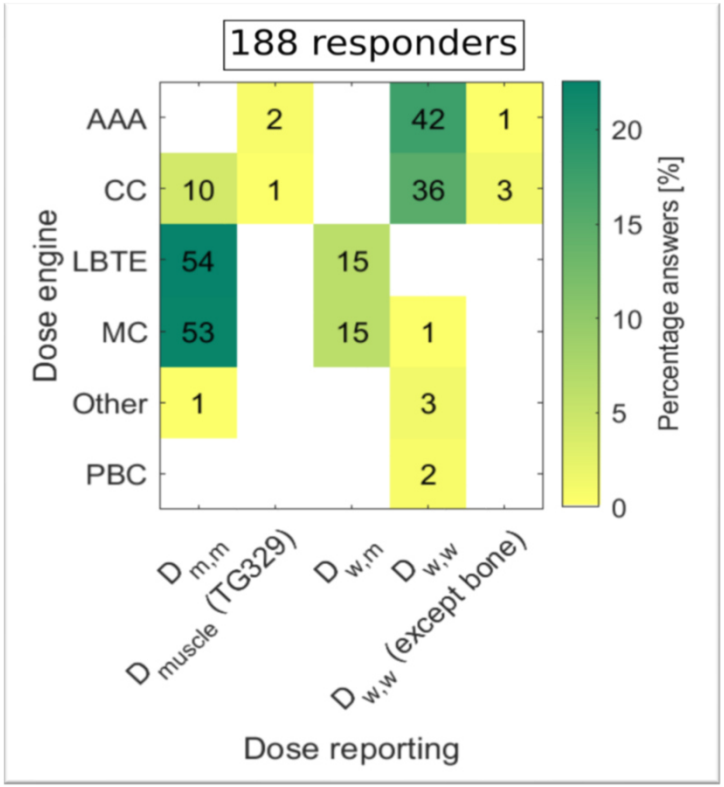
How robust are DVH end points to changes in treatment techniques?

- Different techniques
- Introduction of IMRT/VMAT
- The same two histograms can correspond to very different 3D dose distributions



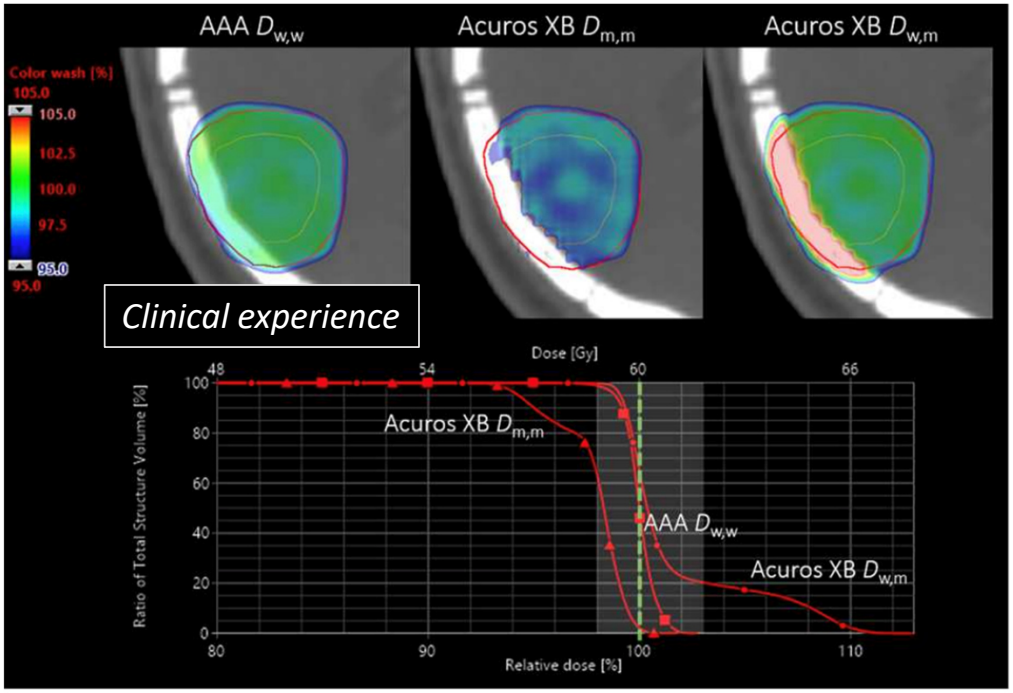


Variability in dose distributions due to the dose engine and dose reporting quantity



Results on the survey by the ESTRO physics workshop group on SBRT practice

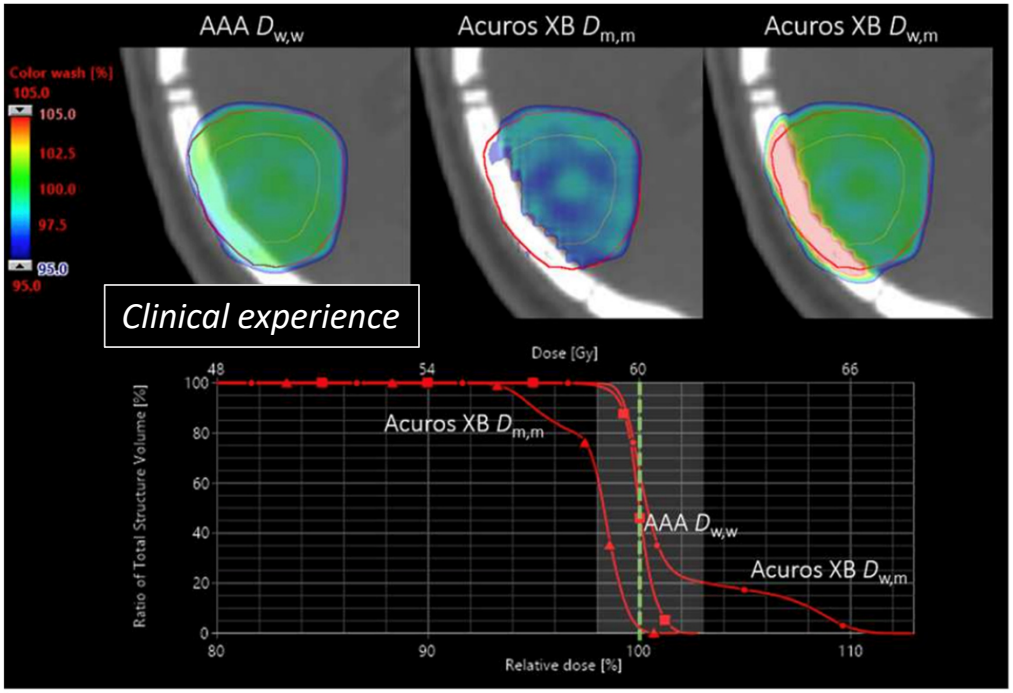
Impact on the dose quantity in toxicity



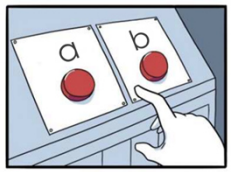
Evaluation and acceptability criteria
Based on the clinical experience from previous dose calculation algorithms and mainly $D_{w,w}$

Jurado-Bruggeman D et al. Med Phys. 2022;49(1):648-665
Jurado-Bruggeman D, Muñoz-Montplet C. Phys Imaging Radiat Oncol. 2023;26:100443.

Impact on the dose quantity in toxicity



Diego Jurado PhD defense



a Correct

b Accept

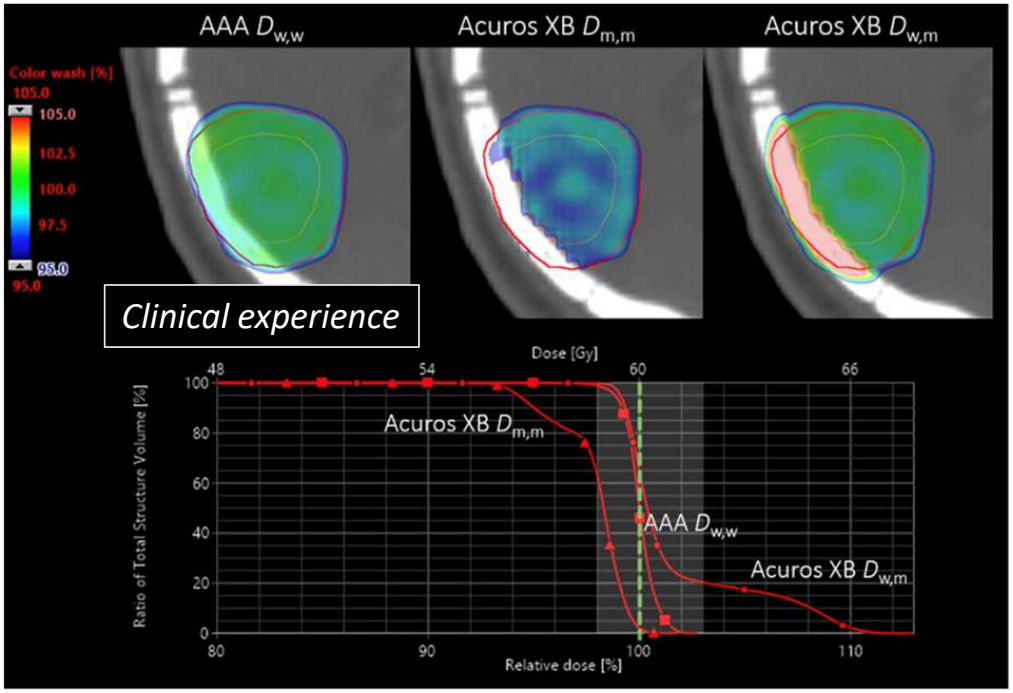
Dm,m bone: increase fluence

Dw, m bone: decrease fluence

Patient will be treated differently

Clinical outcome??

Impact on the dose quantity in toxicity



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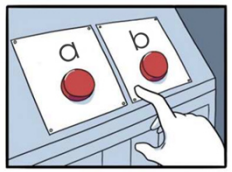

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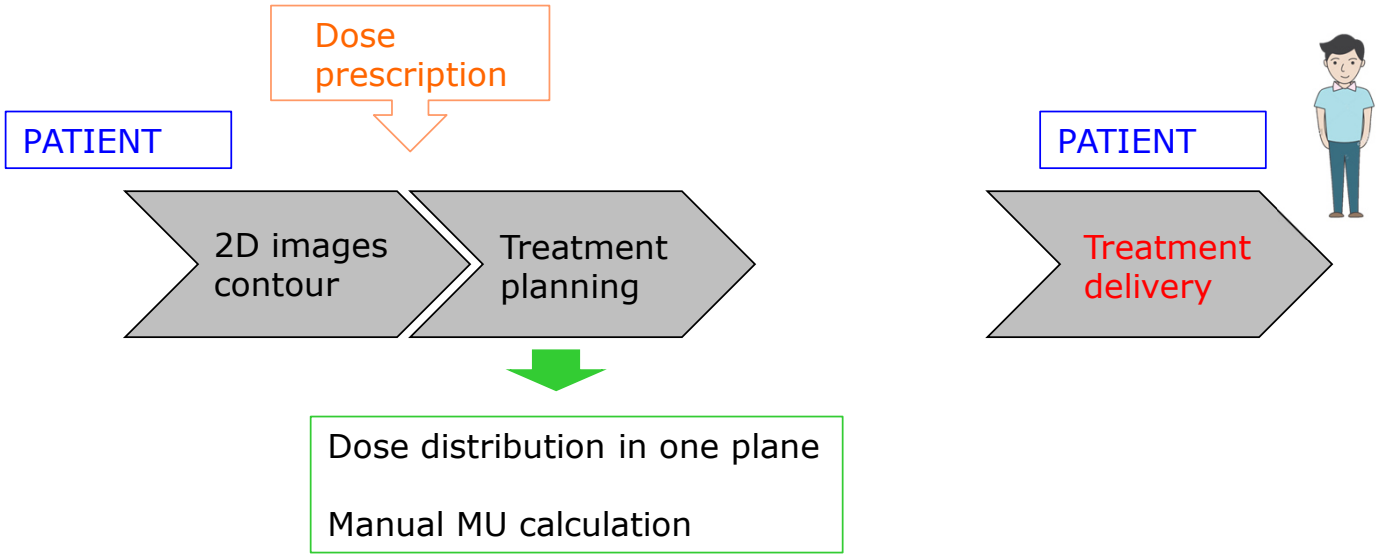
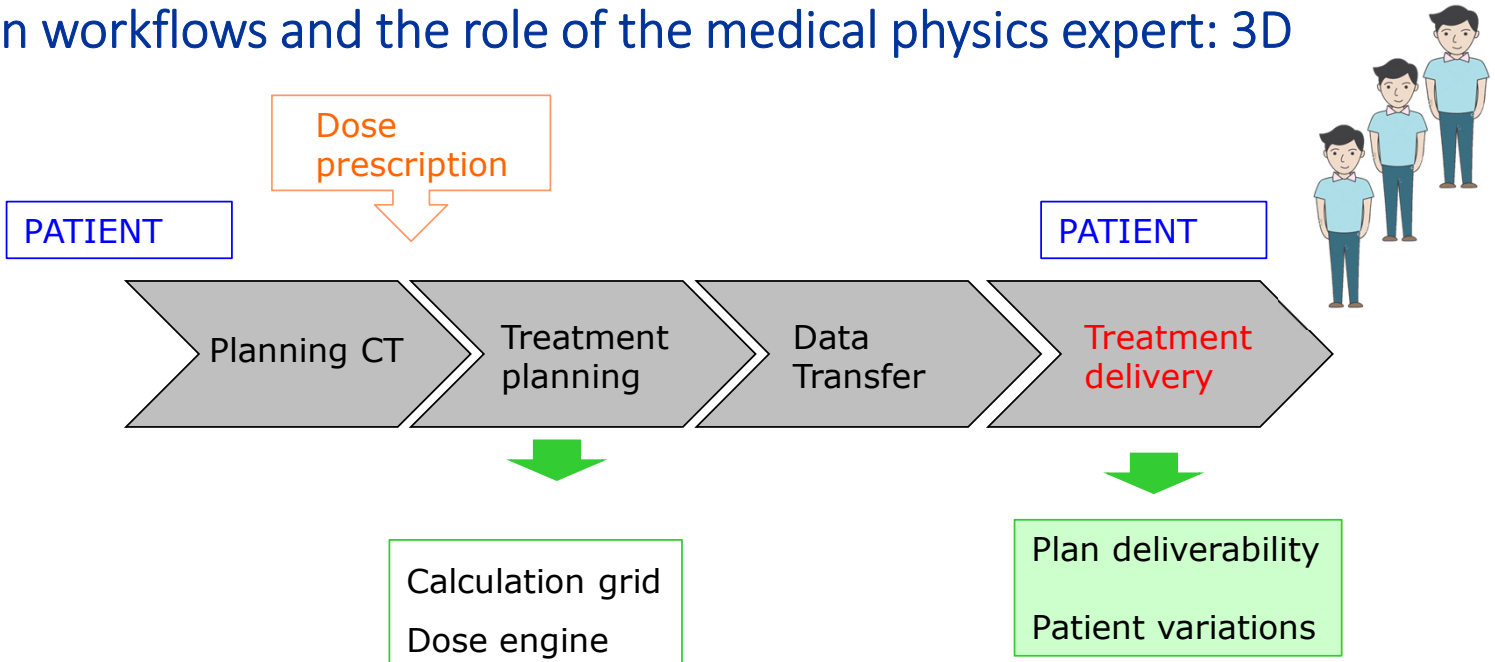
Patient will be treated differently

Clinical outcome??

Impact on workflows and the role of the medical physics expert: 2D



Impact on workflows and the role of the medical physics expert: 3D



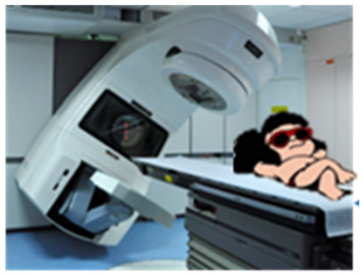
Impact on workflows and the role of the medical physics expert: Patient specific QA

Plan Design (TPS)

Plan Check
DVH metrics
Plan parameters

Independent dose calculation
Point doses
3D dose calculation

Pre-treatment verification
Treatment Unit



IGRT

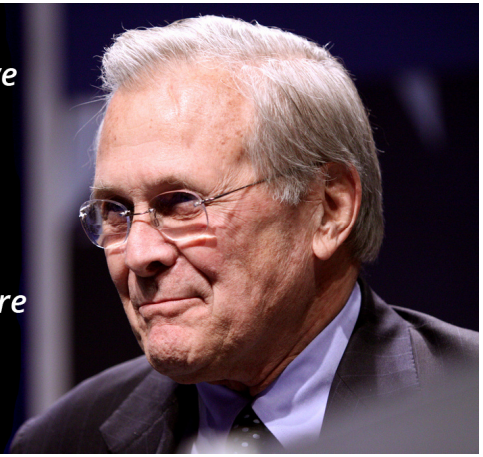
In vivo dosimetry (IVD)

There are known knowns; there are things we know that we know.

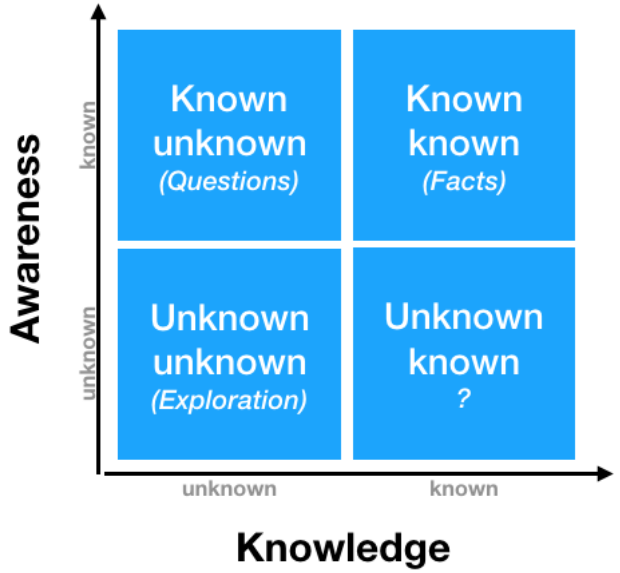
There are known unknowns; that is to say, there are things that we now know we don't know.

But there are also unknown unknowns – there are things we do not know we don't know.

-Donald Rumsfeld



Knowns / Unknowns	Knowns	Unknowns
Knowns	**Known Knowns** Things we are aware of and understand.	**Known Unknowns** Things we are aware of but don't understand.
Unknowns	**Unknown Knowns** Things we understand but are not aware of.	**Unknown Unknowns** Things we are neither aware of nor understand.



What we know: Known Knowns

- Importance of getting right the patient model for radiation transport accuracy
- Importance of understanding the dose calculation engine and the dose quantity we are using to report dose
- Importance of the plan quality evaluation:
  - Dose distribution (not only fulfillment of DVH based dose constraints)
  - Robustness
  - Complexity
- Patients vary through the course of treatment and even if during one fraction
- If we have 4D dimensions we should not base our prescriptions/plan evaluation in 1D metrics (i.e. heart D_{mean})

What we think we know (but we should know better…) “unknown knows”

- How should we accumulate the delivered dose taking into account patient variations?
- How should we handle non-invariance of the dose distribution with patient variation (shifts/inter/intrafraction patient anatomical variations?
- How should we handle CTV-PTV margins in low density regions (lung) for dose optimization?
- How should we produce robust plans and how can we evaluate robustness?

What we know we don’t know (“known unknowns”)

- Do the spatial features of the dose distribution have clinical impact?
- Which is the best dose quantity for plan optimization?
- Which is the best dose quantity for reporting?
- Patient models from CBCT and MRI giving accurate information for radiation transport.
- Dose accumulation algorithms; how to handle tumor regression/loss of weight

What we know we don't know ("known unknowns")

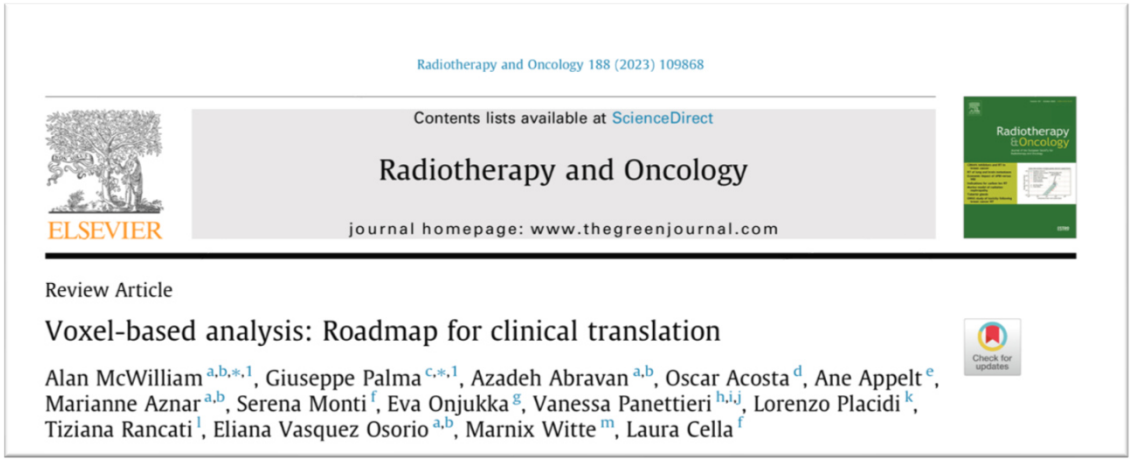
- How to integrate efficiently all the patient data and technology possibilities to
  - 1. Tailor the dose distribution to the patient, taking into account tumor characteristics, co-morbidities, intrafraction variability, patient changes during the treatment.
  - 2. Know the dose delivered to the patient at treatment completion.

IN an ACCURATE and EFFICIENT WAY

What we don’t know we don’t know (“unknown unknowns”)

HOW?

- Not forgetting dosimetry as the core of MPE education and training
- Networks of experts
- Collaboration with industry



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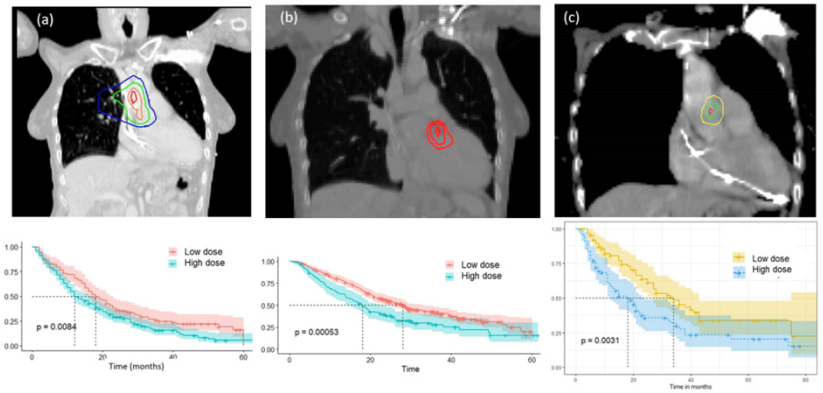
Review Article

Voxel-based analysis: Roadmap for clinical translation

Alan McWilliam [a,b,*,1], Giuseppe Palma [c,*,1], Azadeh Abravan [a,b], Oscar Acosta [d], Ane Appelt [e], Marianne Aznar [a,b], Serena Monti [f], Eva Onjukka [g], Vanessa Panettieri [h,i,j], Lorenzo Placidi [k], Tiziana Rancati [l], Eliana Vasquez Osorio [a,b], Marnix Witte [m], Laura Cella [f]



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