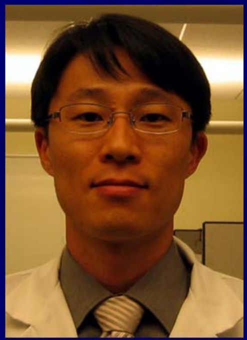
Model Planning and Delivery Uncertainties



[1]Siyong Kim, Ph.D.,
[2]Hosang Jin, Ph.D.,
[3]Jatinder Palta, Ph.D.

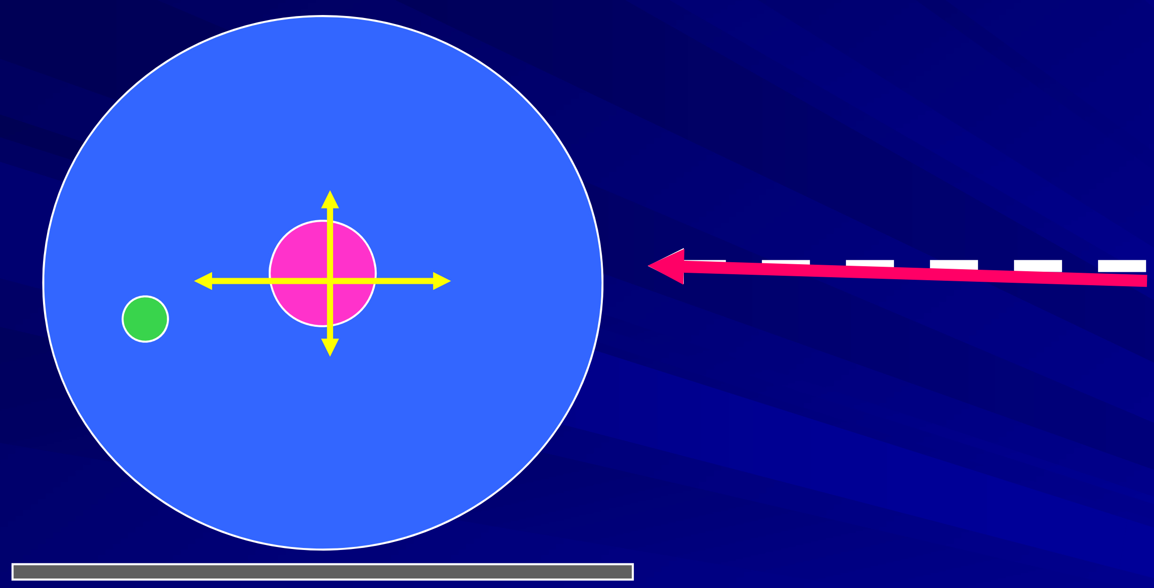
[1]Mayo Clinic, Jacksonville, FL
[2]University of Oklahoma, Oklahoma City, OK
[3]University of Florida, Gainesville, FL

Content

Disclosure

- **Co-founder & interest owner of MT & T, LLC**

Outcome of Uncertainty to Physicists



AP > LAT

AP < LAT

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Judgement

How dare …

Joe-ks.com

Numerous Uncertainty Sources

Source-based Categorization

Cwistraining.org

SOU

Mechanical
Motion

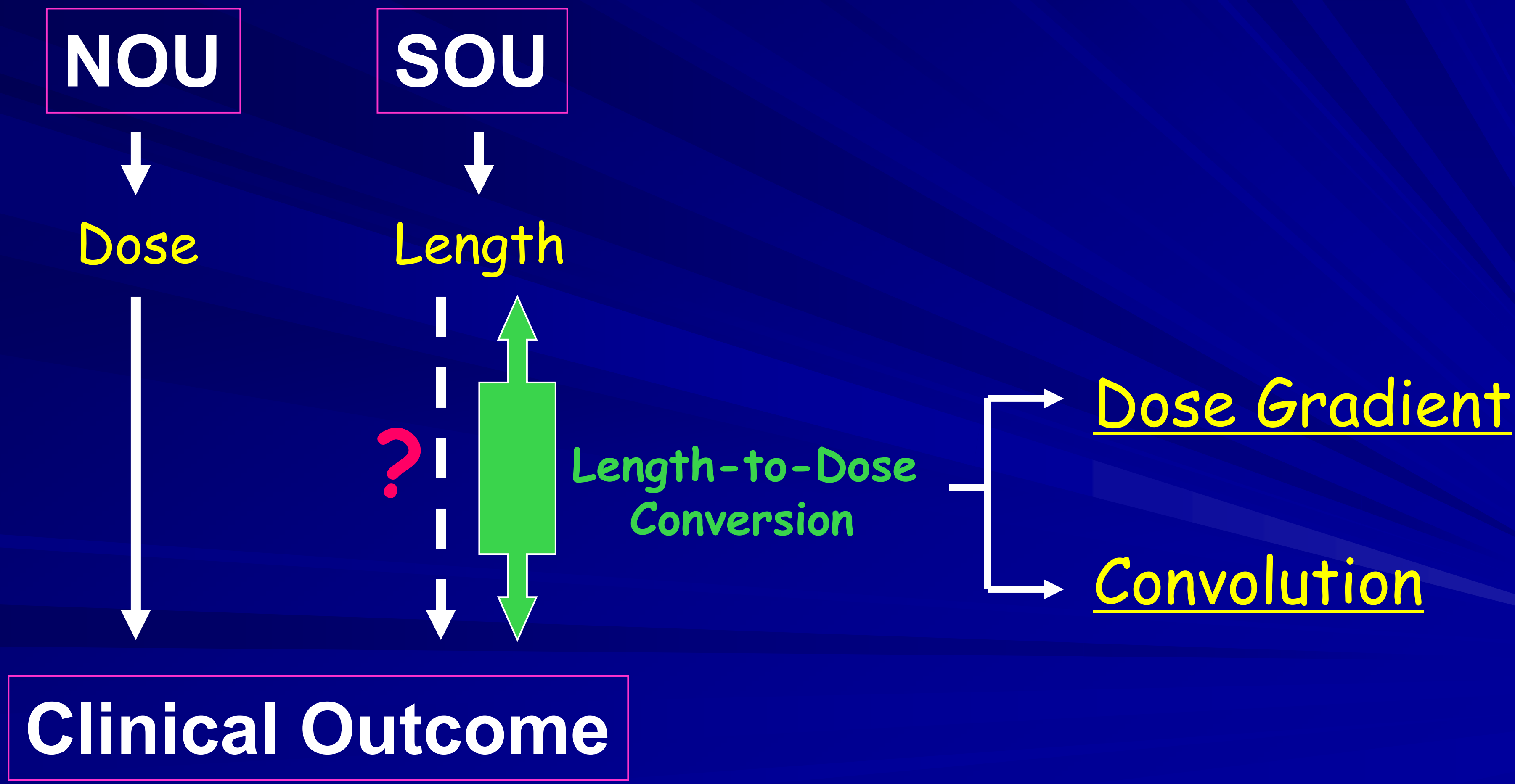
Setup
Finite grid size
Delineation
Registration
.
.
.

NOU

Table in pathway

Output
Algorithm
MLC leakage
Small field
.
.
.

Representing Uncertainty



A Simple Dose Uncertainty Model

Potential Uncertainty – Information that was forgotten

Siyong Kim[1], Hosang Jin[1], Heeteak Chung[1], Jatinder Palta[1] and Sung-Joon Ye[2]

Kim et al. 2004

A novel dose uncertainty model and its application for dose verification

Hosang Jin and Heetaek Chung
Department of Nuclear and Radiological Engineering, University of Florida, Gainesville, Florida 32610

Chihray Liu and Jatinder Palta
Department of Radiation Oncology, University of Florida, Gainesville, Florida 32610

Tae-Suk Suh
Department of Biomedical Engineering, Catholic Medical University, Korea

Siyong Kim[a)]
Department of Radiation Oncology, University of Florida, Gainesville, Florida 32610

Jin et al. 2005

Assumptions

Dose Uncertainty

$$(\sigma^2 = \sigma_{ns}^{\ 2} + \sigma_s^{\ 2})$$

Spatial

proportional to the gradient of Dose

$$\sigma_s = \left| \vec{G}(\vec{r}) \bullet \Delta\vec{r} \right| (cGy)$$

Space oriented dose uncertainty at point, *r*

Dose gradient at *r*

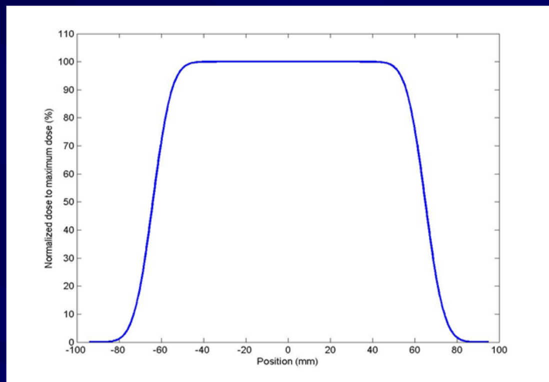
SD of spatial displacement at *r*

Non-spatial

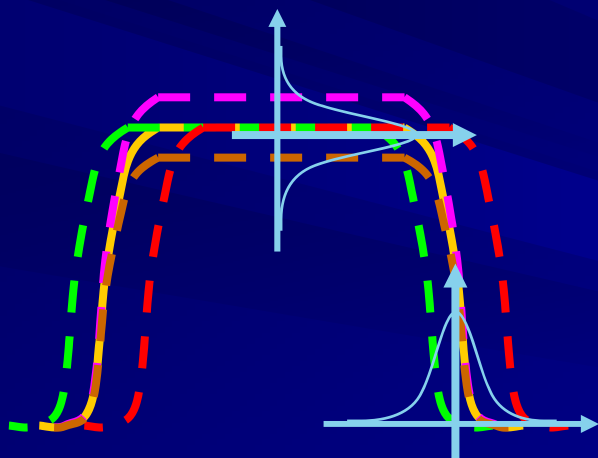
Relative uncertainty is inversely proportional to the level of Dose

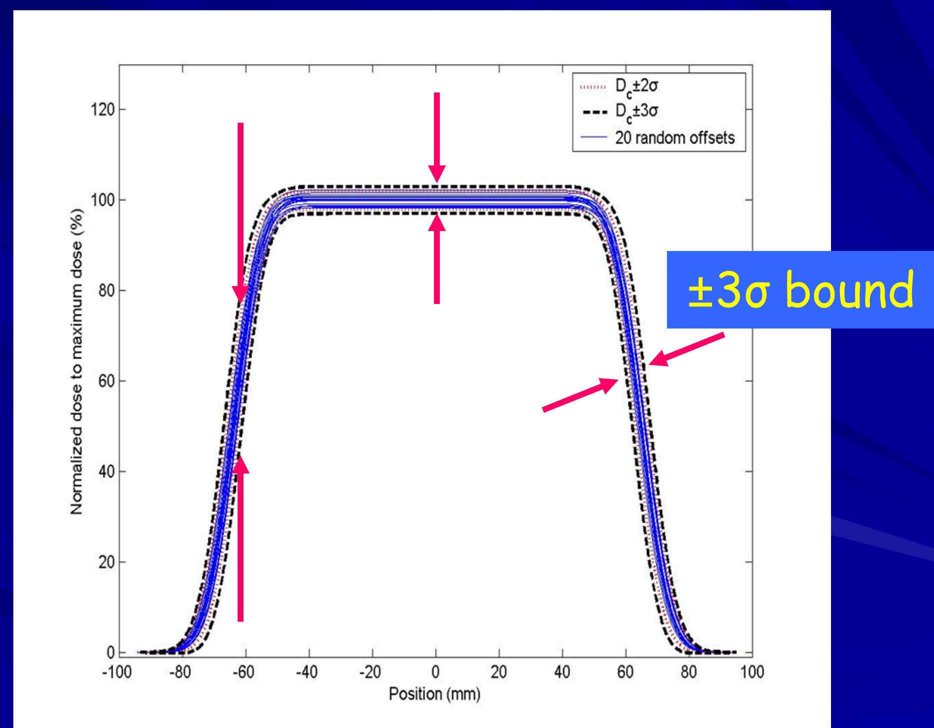
$$\sigma_{ns} = \sigma_{r_o} \sqrt{D\ D_o}\,(cGy)$$

1-D Simulation (A Open Field)



randomly generated 20 dose distributions and 2 uncertainty bounds ($\pm 2\sigma$ and $\pm 3\sigma$)





- NOU

  σ_{ns}=1% at D_{max}
- SOU

  Δx=1 mm → $\sigma_s = (dD/dx)\Delta x$
- Gaussian distribution

Uncertainty Compensation in IMRT QA using Dose Gradient

A dose-gradient analysis tool for IMRT QA

Jean M. Moran,[a] Jeffrey Radawski, and Benedick A. Fraass
Department of Radiation Oncology, University of Michigan Medical Center, Ann Arbor, Michigan 48109-0010 U.S.A.

Moran et al. 2005

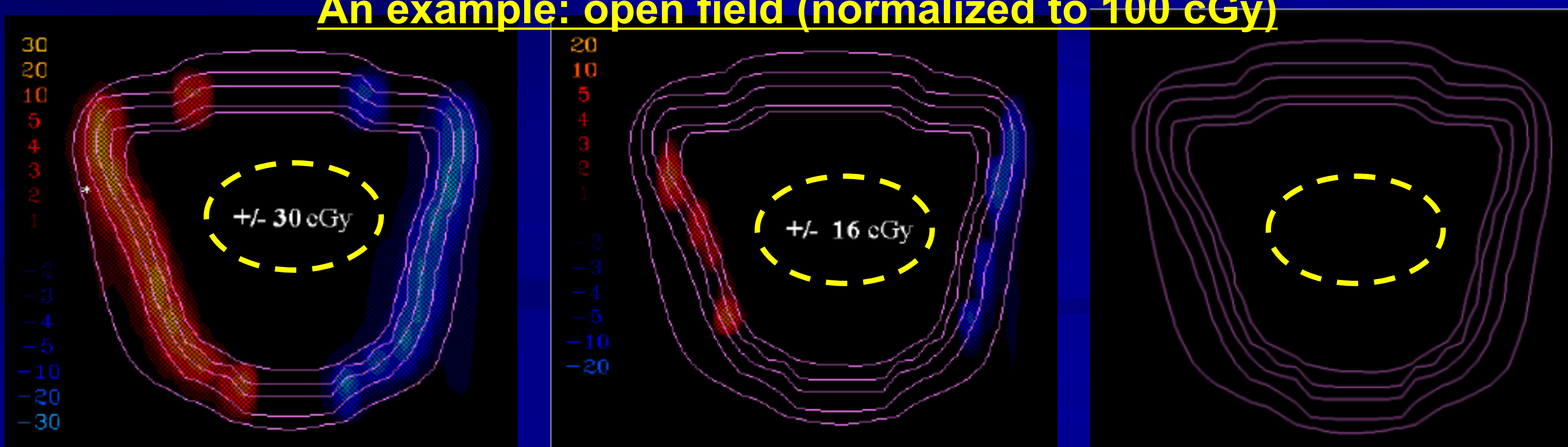
G_i = Generalized gradient at grid point, *i*

$$G_i = Gradient = \sqrt{\sum \left(\frac{\Delta d_{ij}}{\Delta x_{ij}} \right)^2},$$

Δd_{ij} = Dose difference between *i* and each nearest neighbors, *j*

Δx_{ij} = Distance between *i* and *j*

An example: open field (normalized to 100 cGy)



2 mm intentional shift **1 mm G compensation** **2 mm G compensation**

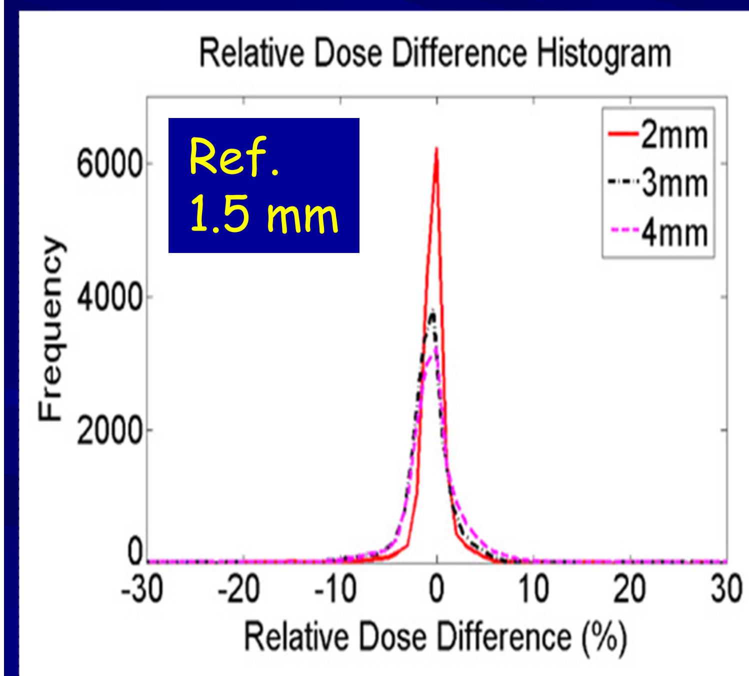
Inherent Uncertainty – Dose Grid Size Effect

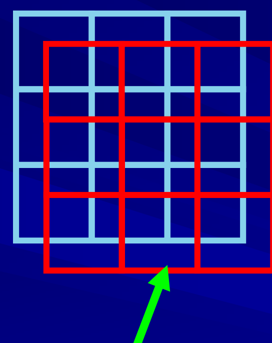
$$I_{grid}(r_p) = \left| \nabla D_{cal}(r_p) \cdot \Delta r \right|$$

Dose variations with varying calculation grid size in head and neck IMRT

Heeteak Chung[1], Hosang Jin[1], Jatinder Palta[2], Tae-Suk Suh[3] and Siyong Kim[2,4]

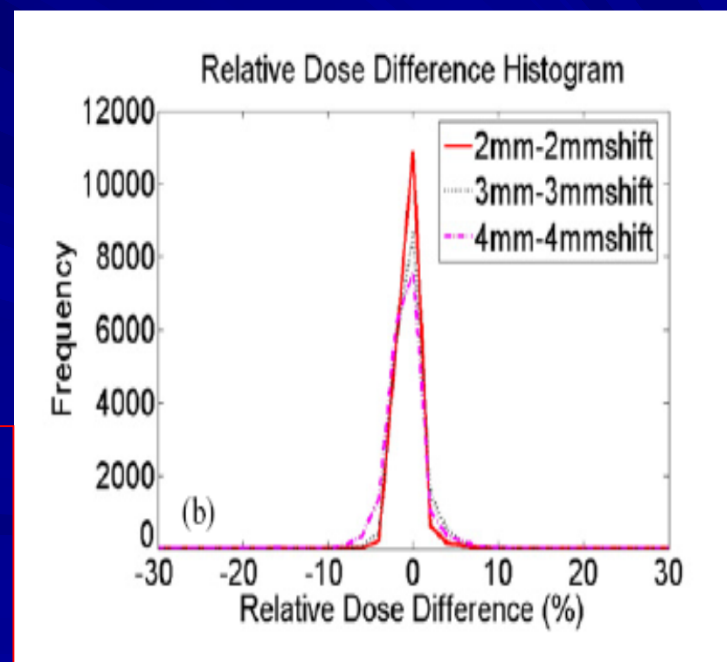
Chung et al. 2006





Grid Origin Shift

2.3%	1.9%
4.6%	2.8%
5.6%	3.8%



Convolution Method

Implementation of random positioning error in computerised radiation treatment planning systems as a result of fractionation

Joseph Leong

Division of Radiation Biophysics, Department of Radiation Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Leong 1987

Expected Dose = Dose ⊗ Spatial Probability Density Function

Application of Convolution Method - Margin Determination

Target margins for random geometrical treatment uncertainties in conformal radiotherapy

A. Bel,[a)] M. van Herk, and J. V. Lebesque
Netherlands Cancer Institute, Antoni van Leeuwenhoek Huis, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

Bell et al. 1996

INCLUSION OF GEOMETRICAL UNCERTAINTIES IN RADIOTHERAPY TREATMENT PLANNING BY MEANS OF COVERAGE PROBABILITY

JOEP C. STROOM, M.SC.,* HANS C. J. DE BOER, M.SC.,* HENK HUIZENGA, PH.D.,† AND ANDRIES G. VISSER, PH.D.*

*University Hospital Rotterdam, Daniel den Hoed Cancer Center, Department of Clinical Physics, Rotterdam, The Netherlands; and †University of Nijmegen, Institute of Radiotherapy, Nijmegen, The Netherlands

Stroom et al. 1999

THE PROBABILITY OF CORRECT TARGET DOSAGE: DOSE-POPULATION HISTOGRAMS FOR DERIVING TREATMENT MARGINS IN RADIOTHERAPY

MARCEL VAN HERK, PH.D., PETER REMEIJER, PH.D., COEN RASCH, M.D, AND JOOS V. LEBESQUE, M.D., PH.D.

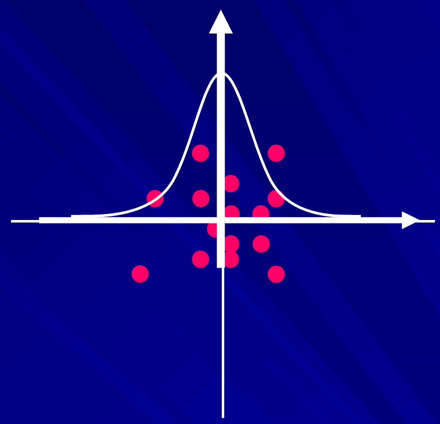
Radiotherapy Department, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Huis, Amsterdam, The Netherlands

van Herk et al. 2000

Geometric Errors

<u>Random errors</u> (treatment execution errors)
= day-to-day variations
= lead to a blurring of dose distribution
= denoted with σ

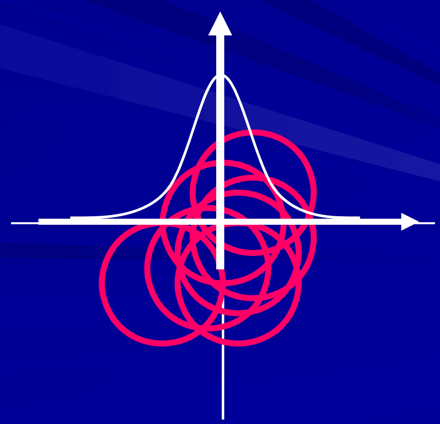
<u>For many fractions</u>



Gaussian

<u>Systematic errors</u> (preparation errors)
= systematic for a single radiotherapy course of a single patient, but stochastic over a group of patients (i.e., for a patient population)
= lead to a displacement of the dose distribution with respect to the target (CTV)
= denoted with Σ

<u>For many patients</u>

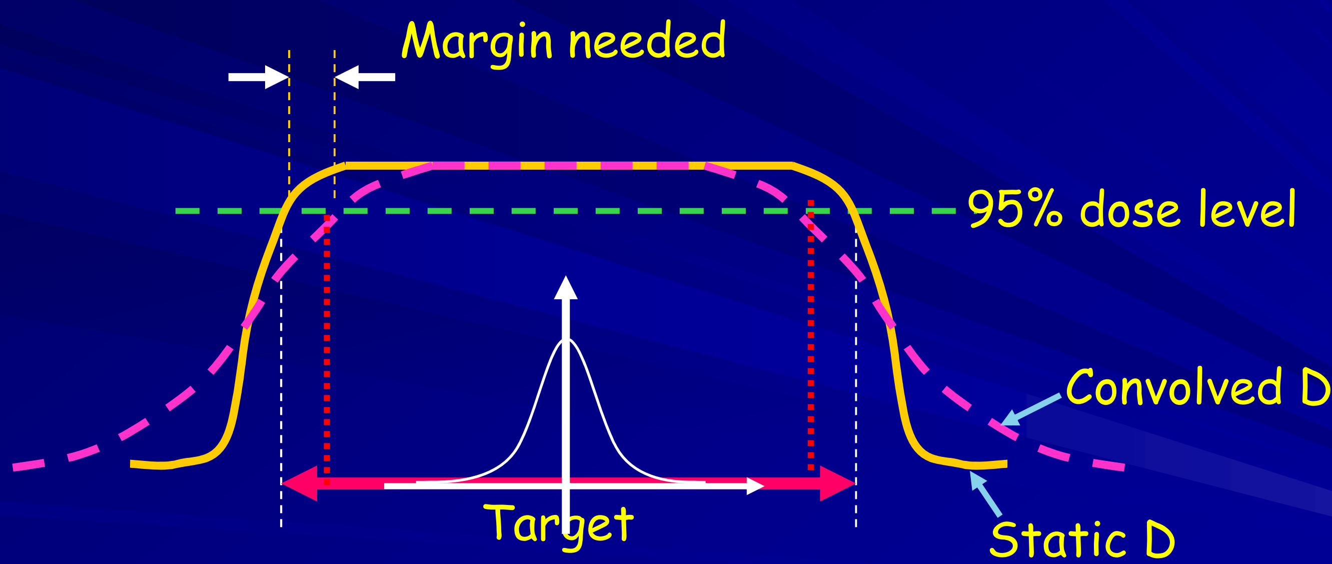


Margin for Random Errors

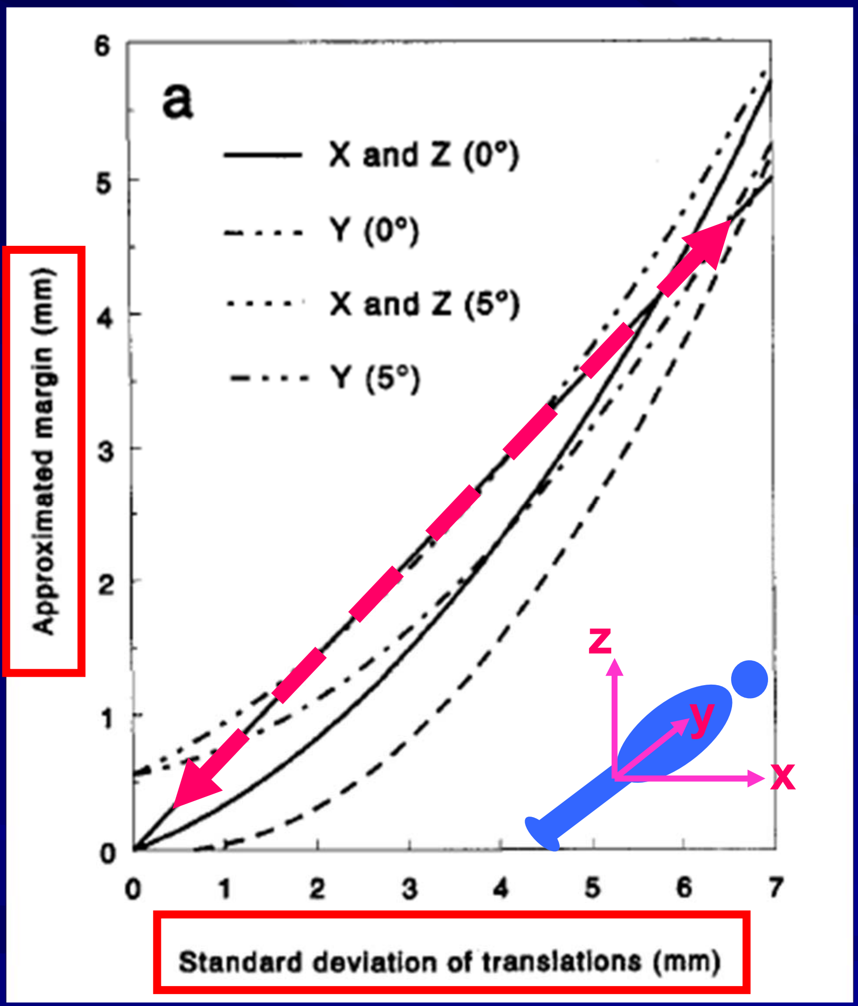
Target margins for random geometrical treatment uncertainties in conformal radiotherapy

A. Bel,[a)] M. van Herk, and J. V. Lebesque
Netherlands Cancer Institute, Antoni van Leeuwenhoek Huis, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

Bell et al. 1996



Margin vs. Random Error (Gaussian SD)



4-field

Margin ≈ 0.7 σ

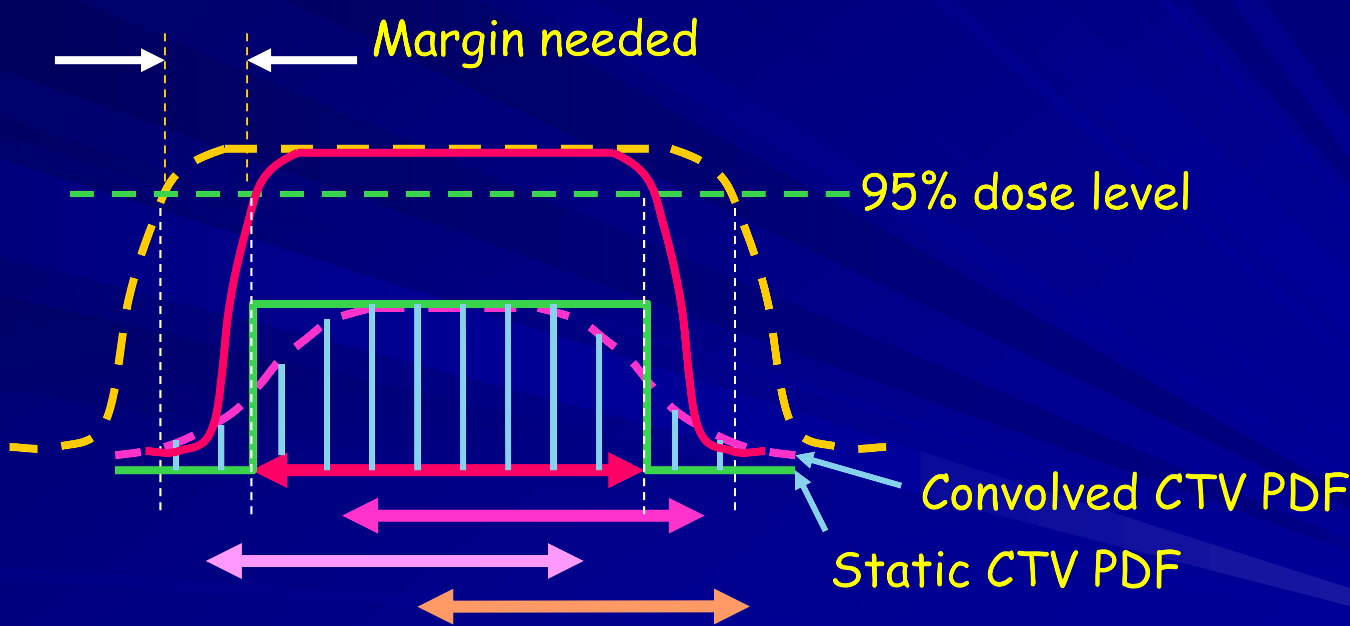
Margin for Systematic Errors

INCLUSION OF GEOMETRICAL UNCERTAINTIES IN RADIOTHERAPY TREATMENT PLANNING BY MEANS OF COVERAGE PROBABILITY

JOEP C. STROOM, M.SC.,* HANS C. J. DE BOER, M.SC.,* HENK HUIZENGA, PH.D.,† AND ANDRIES G. VISSER, PH.D.*

*University Hospital Rotterdam, Daniel den Hoed Cancer Center, Department of Clinical Physics, Rotterdam, The Netherlands; and †University of Nijmegen, Institute of Radiotherapy, Nijmegen, The Netherlands

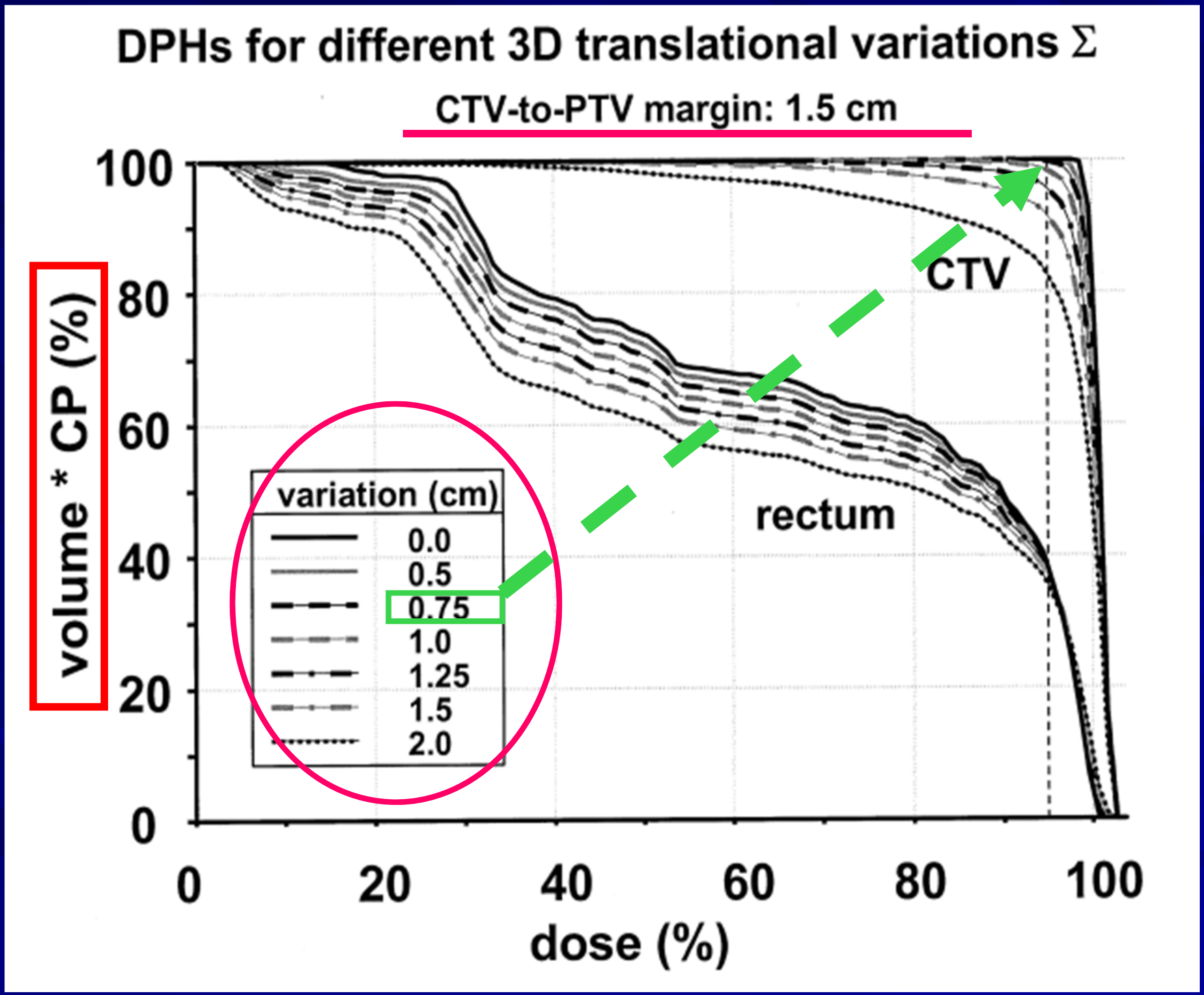
Stroom et al. 1999



<u>Coverage Probability (CP)</u>

- probability for each point to be covered (occupied) by the CTV

DPHs for Various Gaussian Systematic Errors
DPH = Dose Probability Histogram



To ensure
95% dose to 99% CTV

Margin ≈ $2\,\Sigma$

Margin ≈ $2\,\Sigma + 0.7\,\sigma$

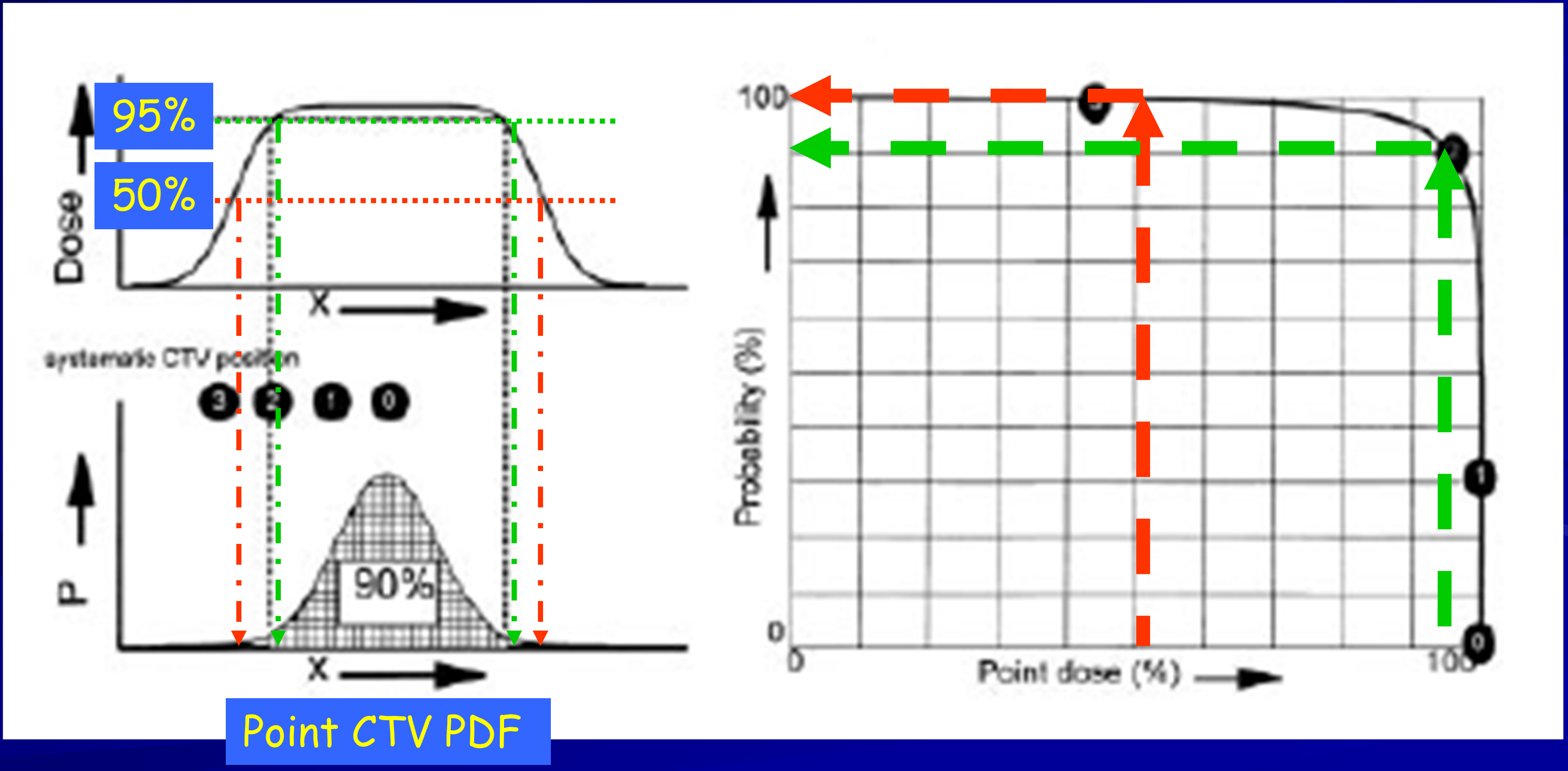
Dose-Population Histogram (point CTV)

THE PROBABILITY OF CORRECT TARGET DOSAGE: DOSE-POPULATION HISTOGRAMS FOR DERIVING TREATMENT MARGINS IN RADIOTHERAPY

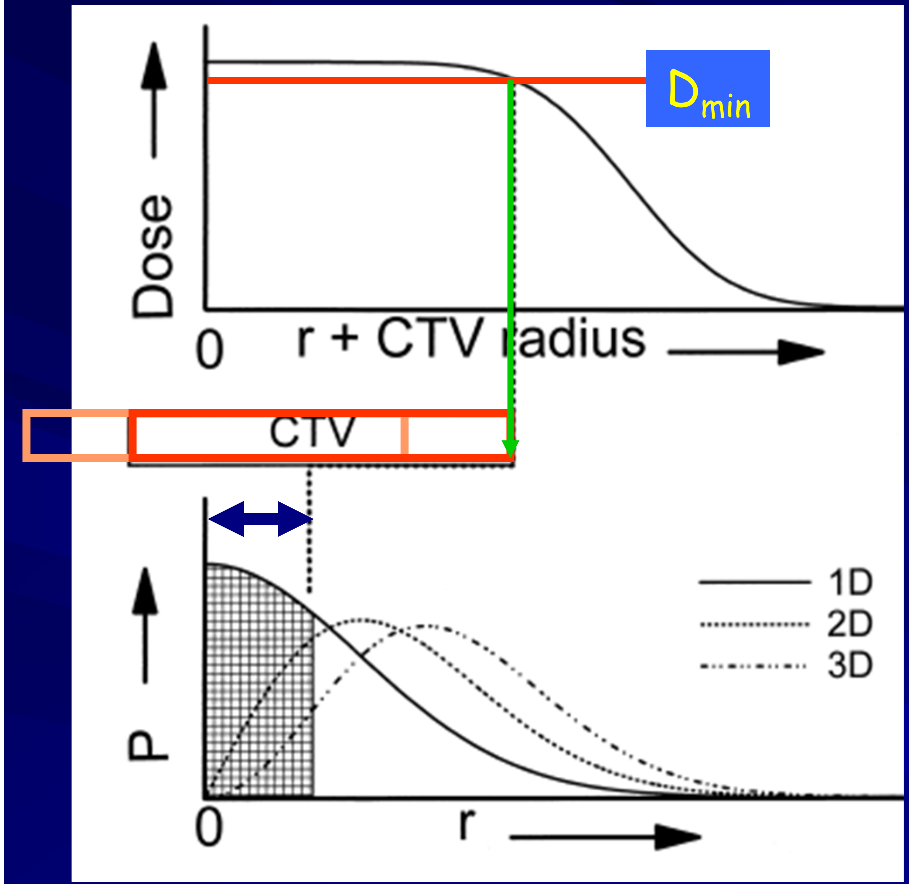
MARCEL VAN HERK, PH.D., PETER REMEIJER, PH.D., COEN RASCH, M.D,
AND JOOS V. LEBESQUE, M.D., PH.D.

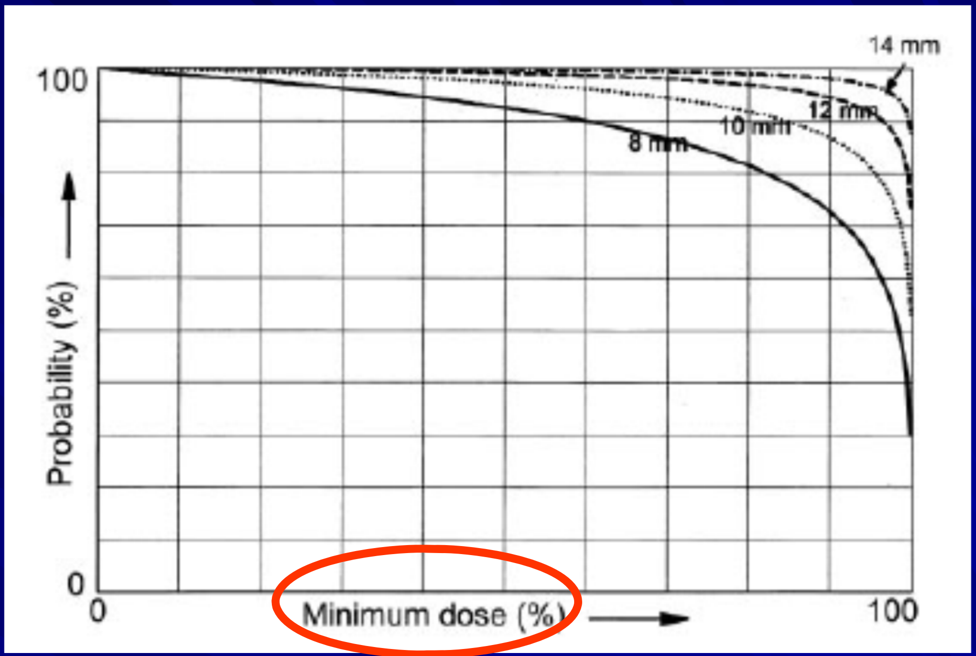
Radiotherapy Department, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Huis, Amsterdam, The Netherlands

van Herk et al. 2000



(Minimum) Dose-Population Histogram





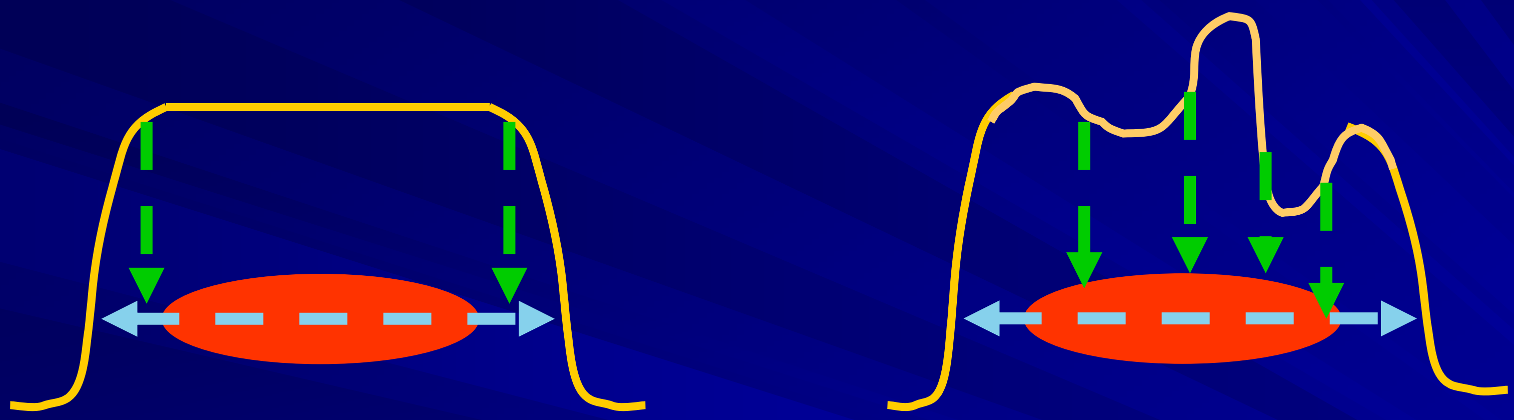
Margin ≈ 2.5 ∑ + 0.7 σ′
$(\sigma'^2 = \sigma_m{}^2 + \sigma_s{}^2)$

To ensure a minimum dose of 95% to the CTV for 90% of patients,

Margin ≈ 2.5 ∑ + 1.64 $(\sigma - \sigma_p)$
$(\sigma^2 = \sigma_m{}^2 + \sigma_s{}^2 + \sigma_p{}^2)$

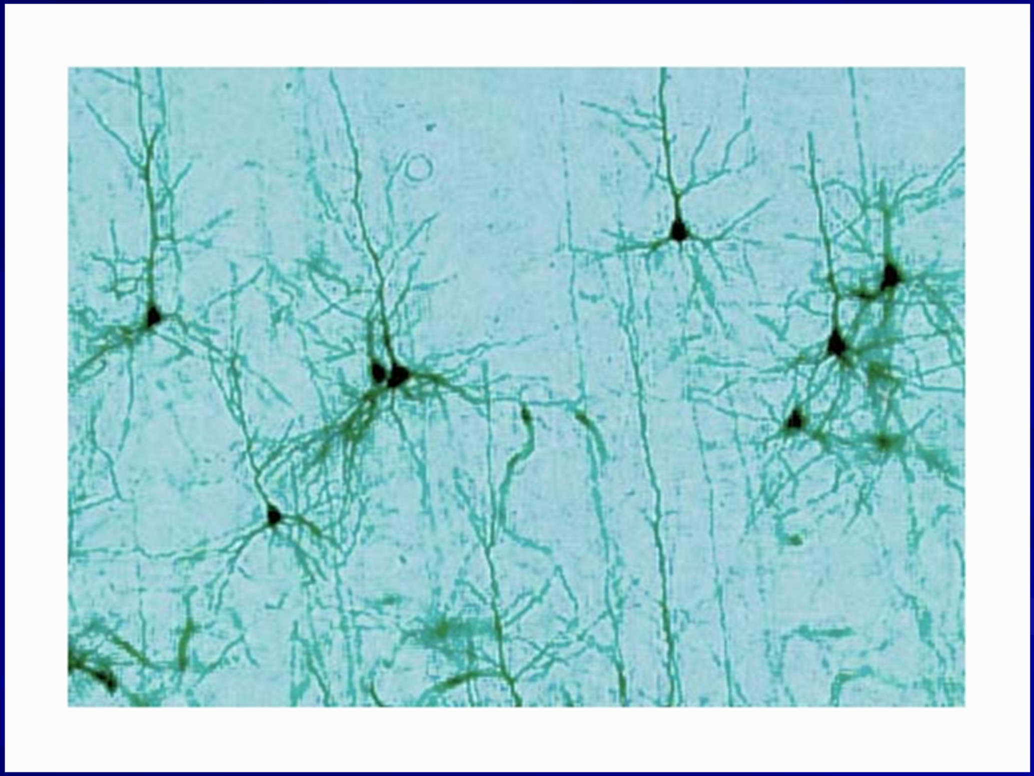
If, σ_p = 3.2 mm
and, $0 \leq \sigma \leq 5$ mm

Conventional Conformal vs. IMRT



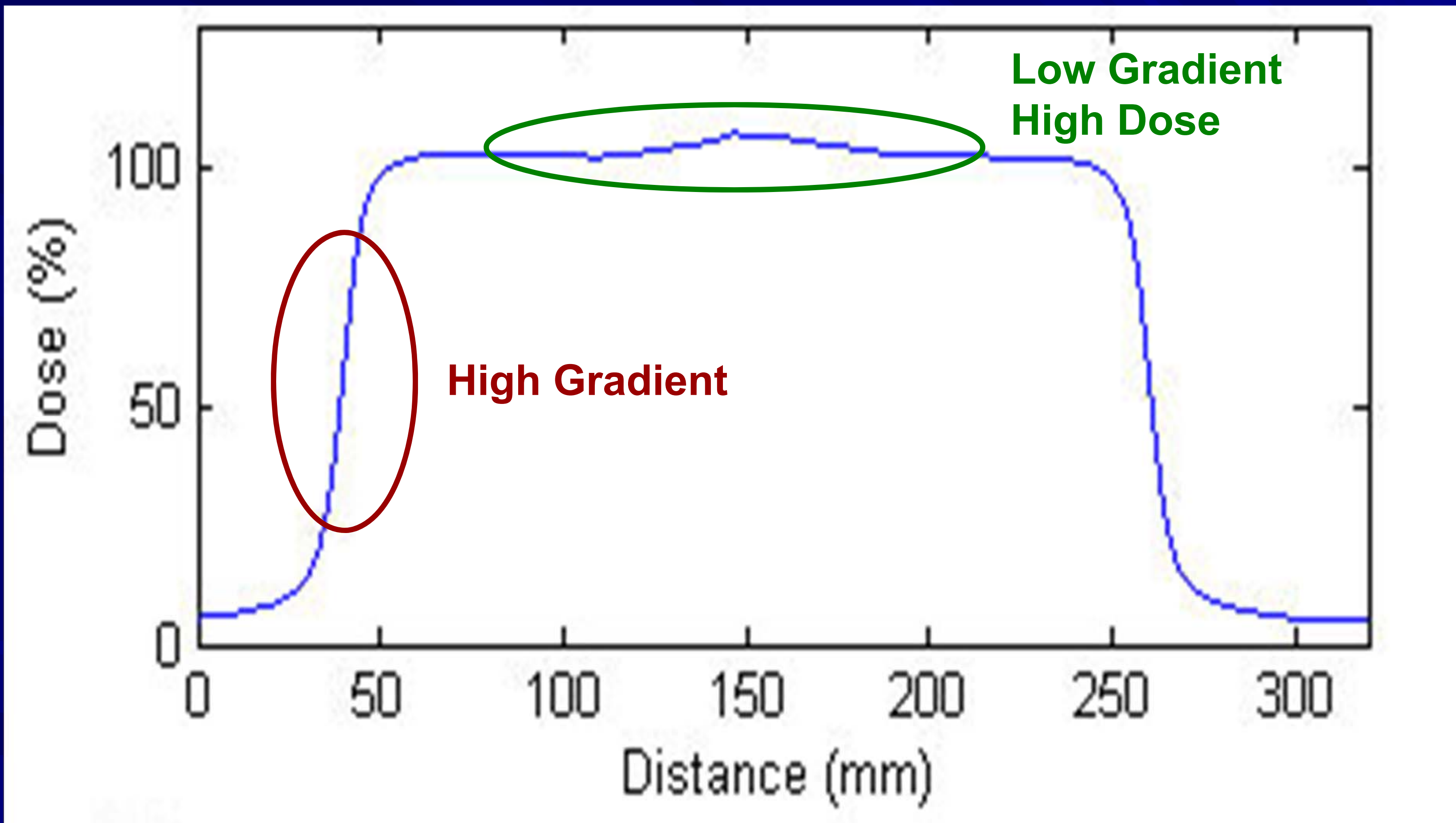
Dose Uncertainty at each point?

Uncertainty Propagation

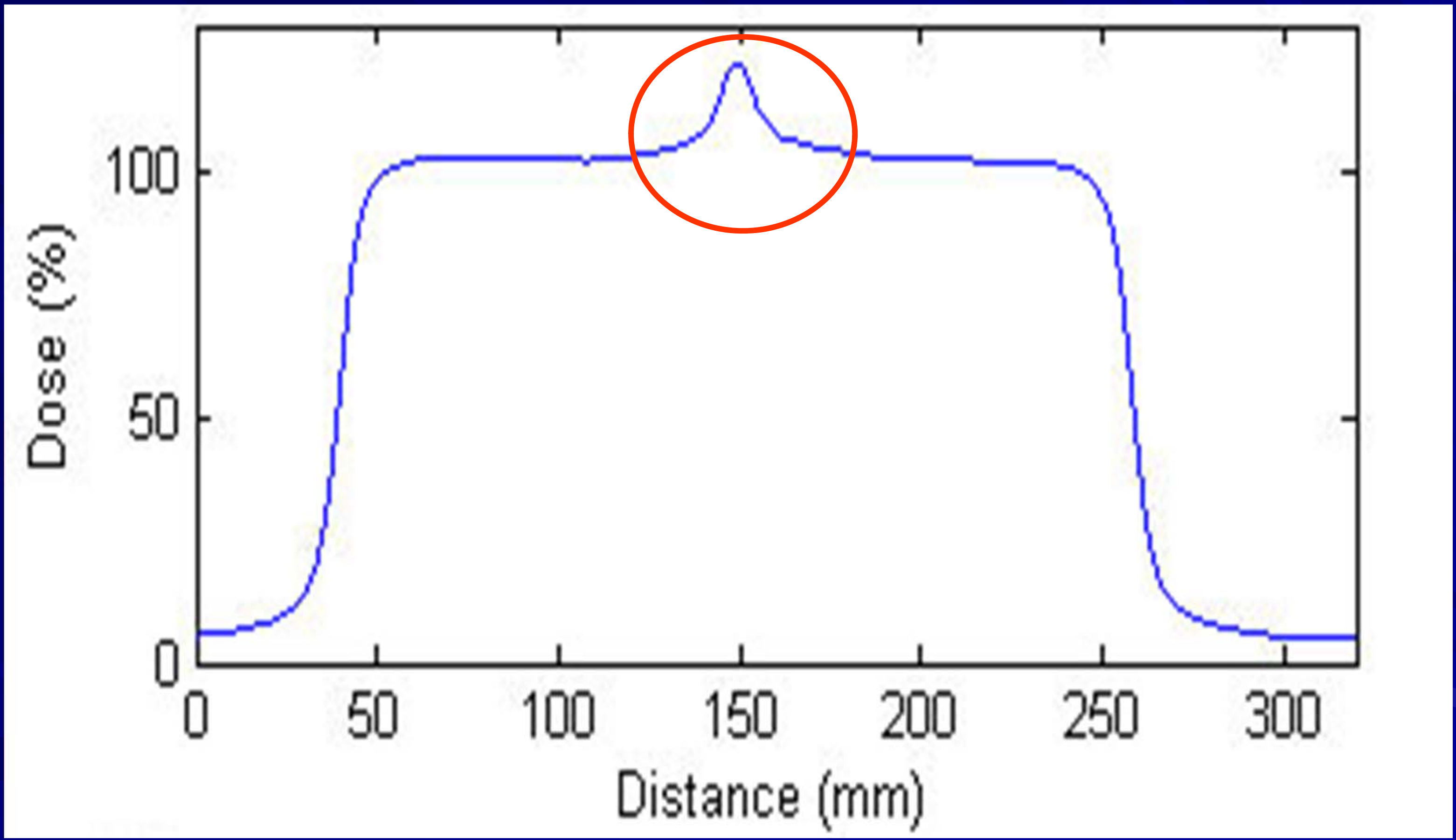


Colinfahey.com

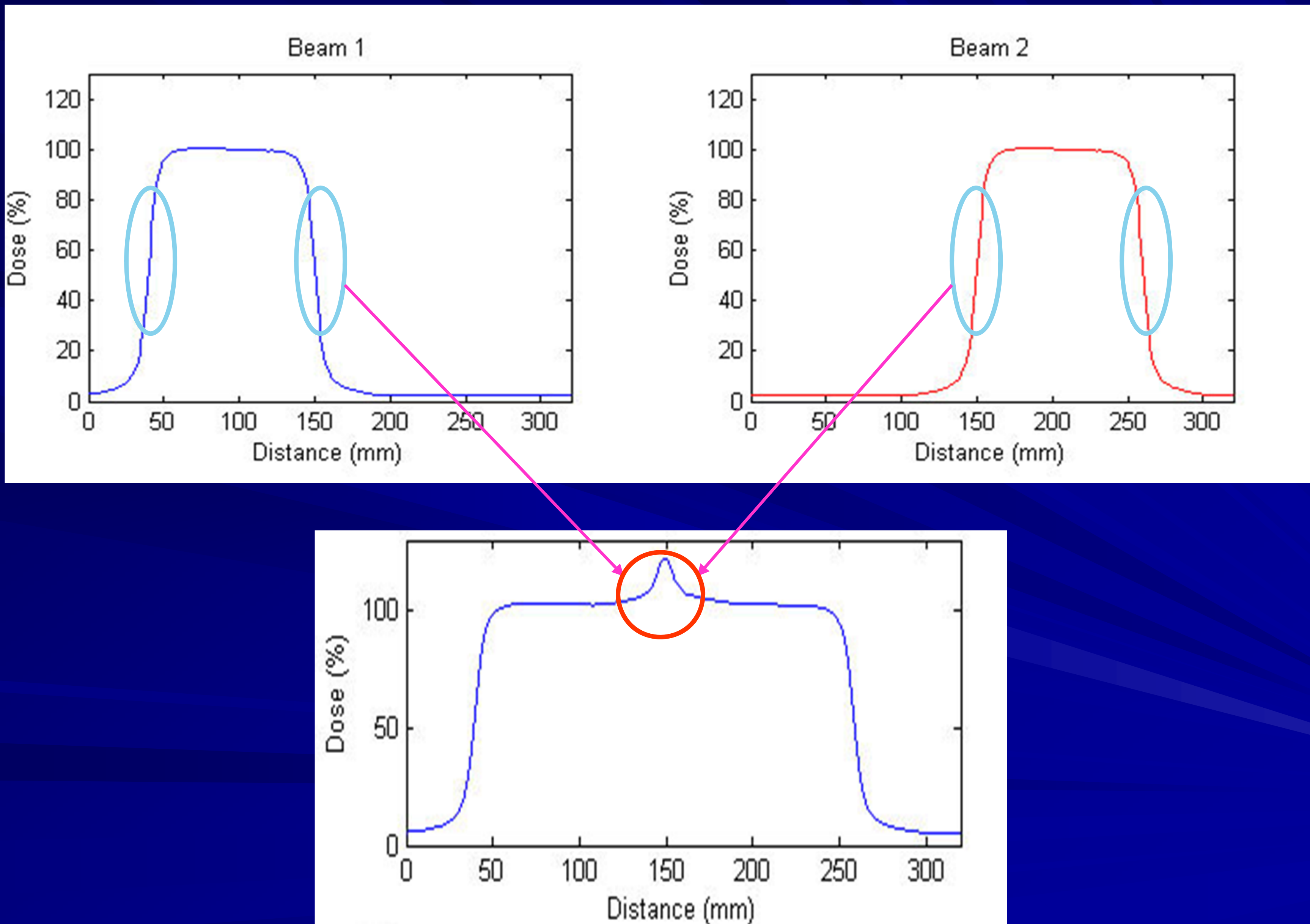
1-D Example - planning



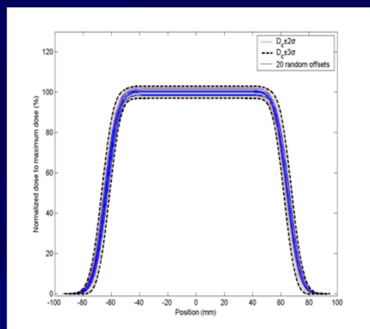
1-D Example - measurement

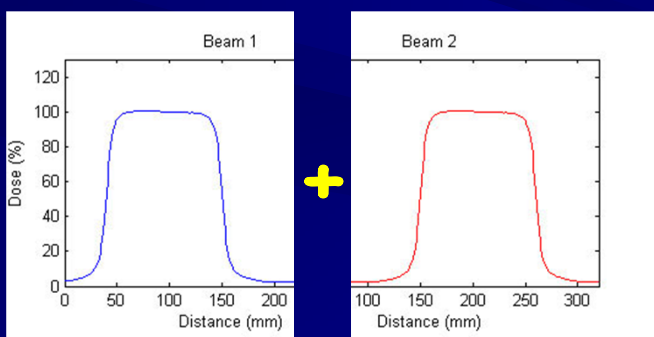


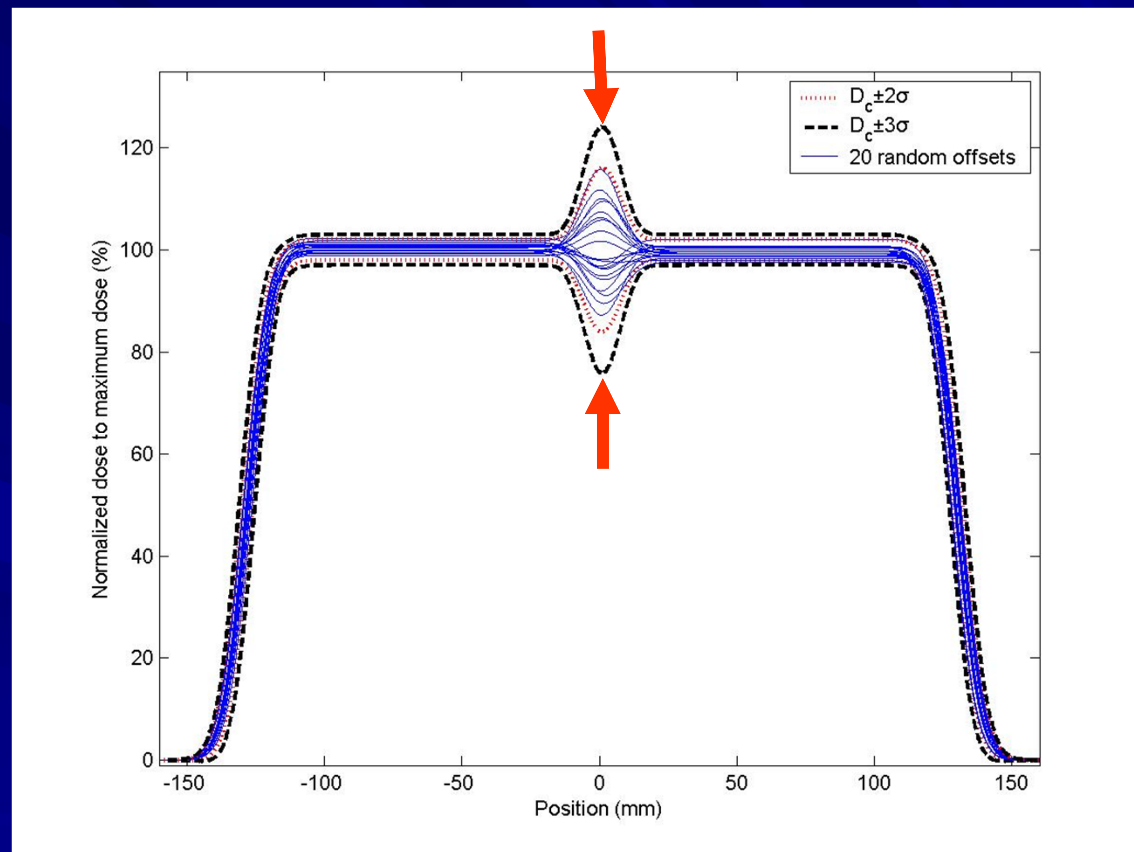
1-D Example : 2 Adjacent Fields



1-D : 2 Adjacent Fields Simulation





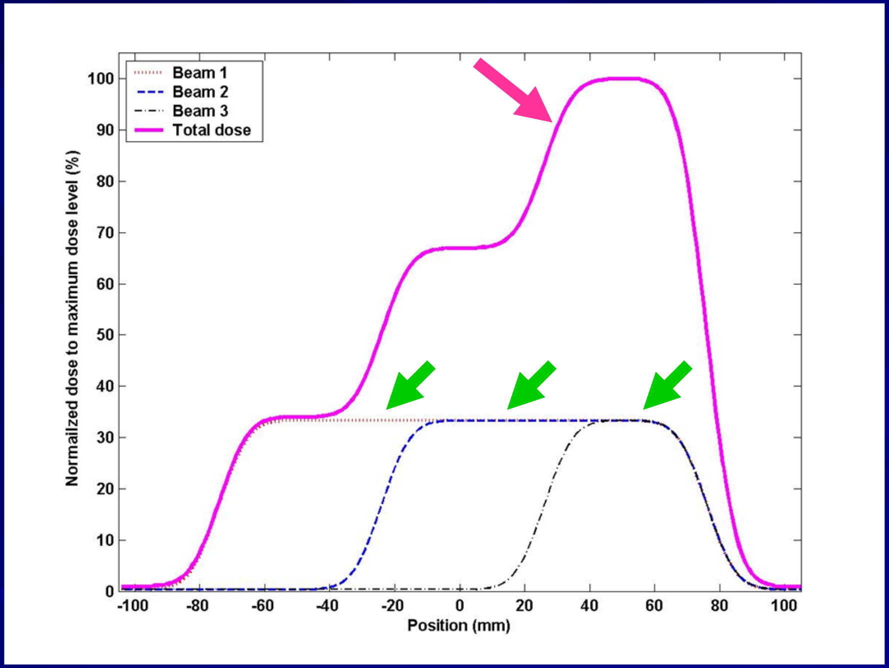


-2σ bound (95.44%): 1 out of 20 random offsets is out of the bound.
-3σ bound (99.74%): contains all the random offsets.

Dose Accumulation History

1-D IMRT Simulation

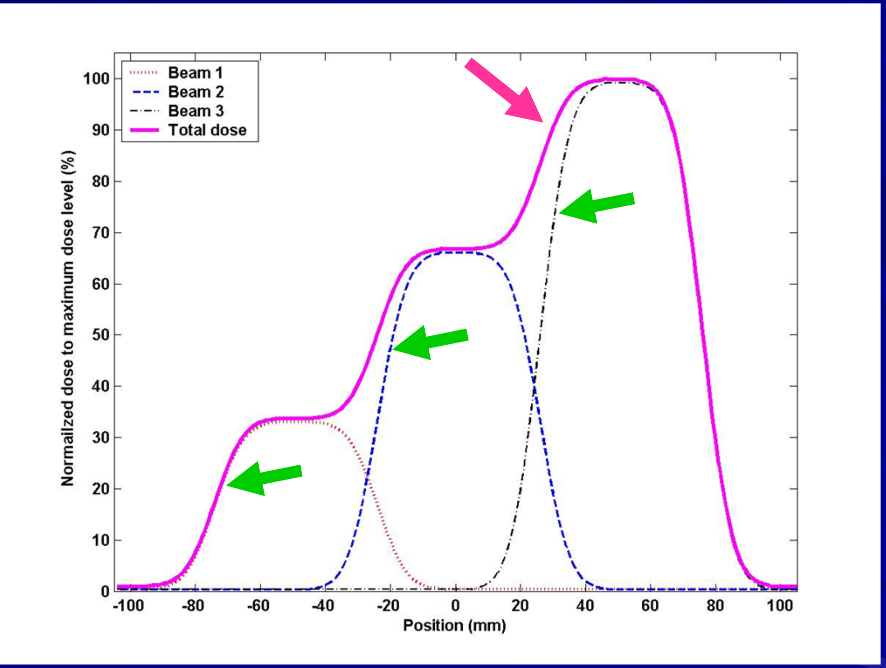
3-Segmented IMRT Field (case 3)



Beam set 1

Different beam width

Same beam fluence

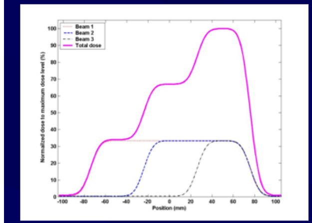


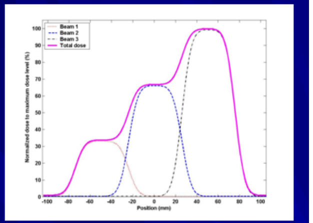
Beam set 2

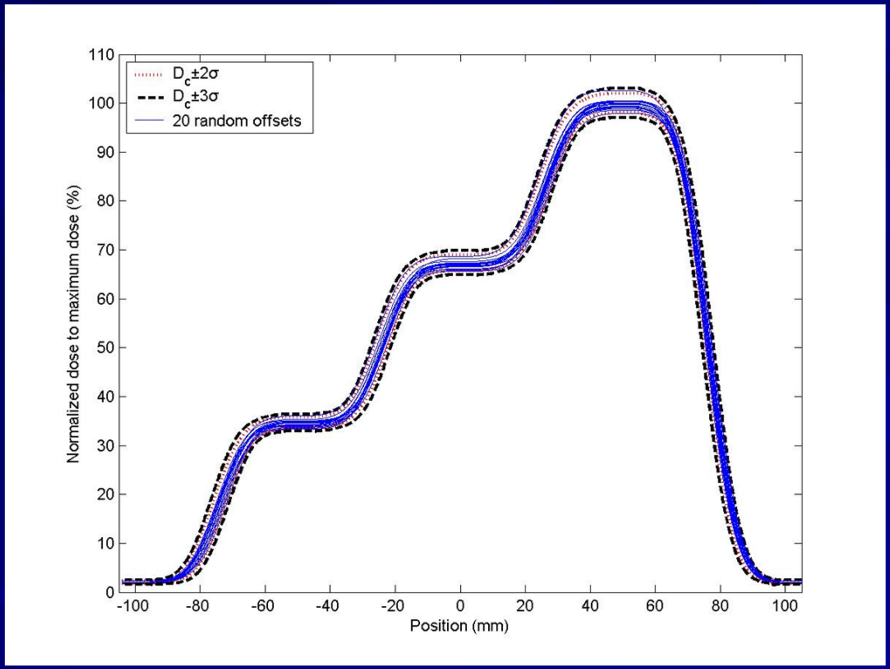
Same beam width

Different beam fluence

Results (1-D: 3 IMRT Beam Fields)



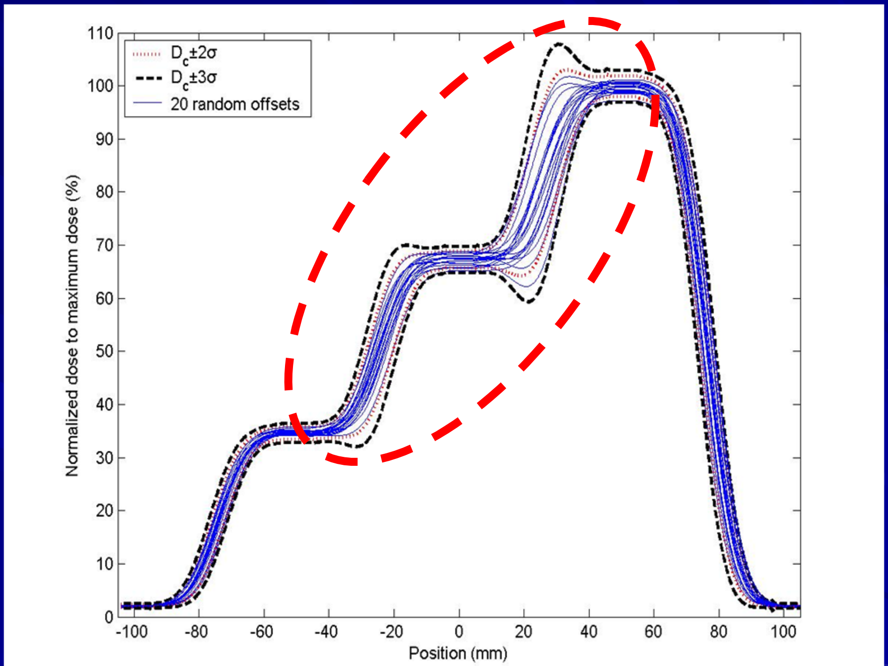




Beam set 1

Different beam widths

Same beam fluences

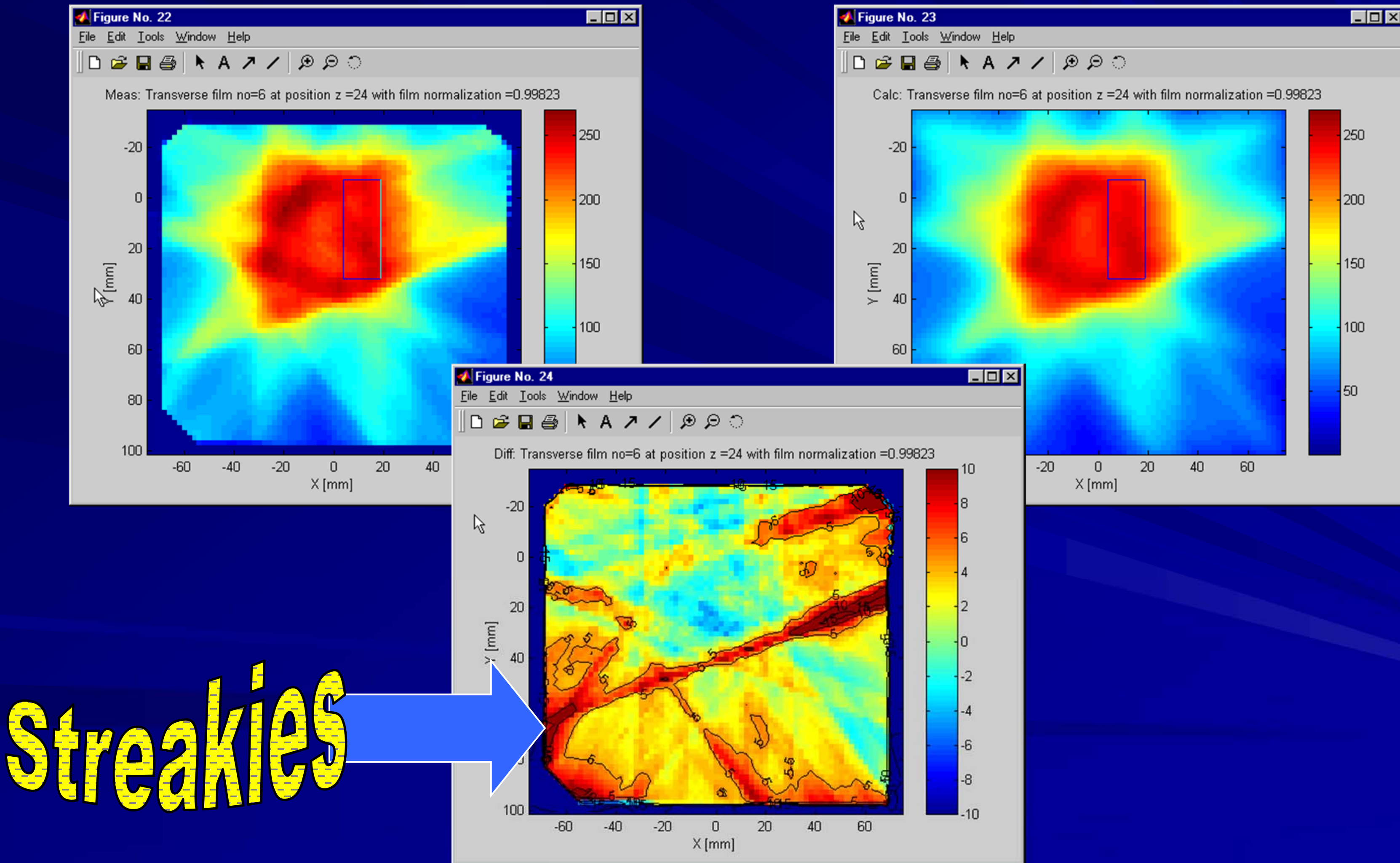


Beam set 2

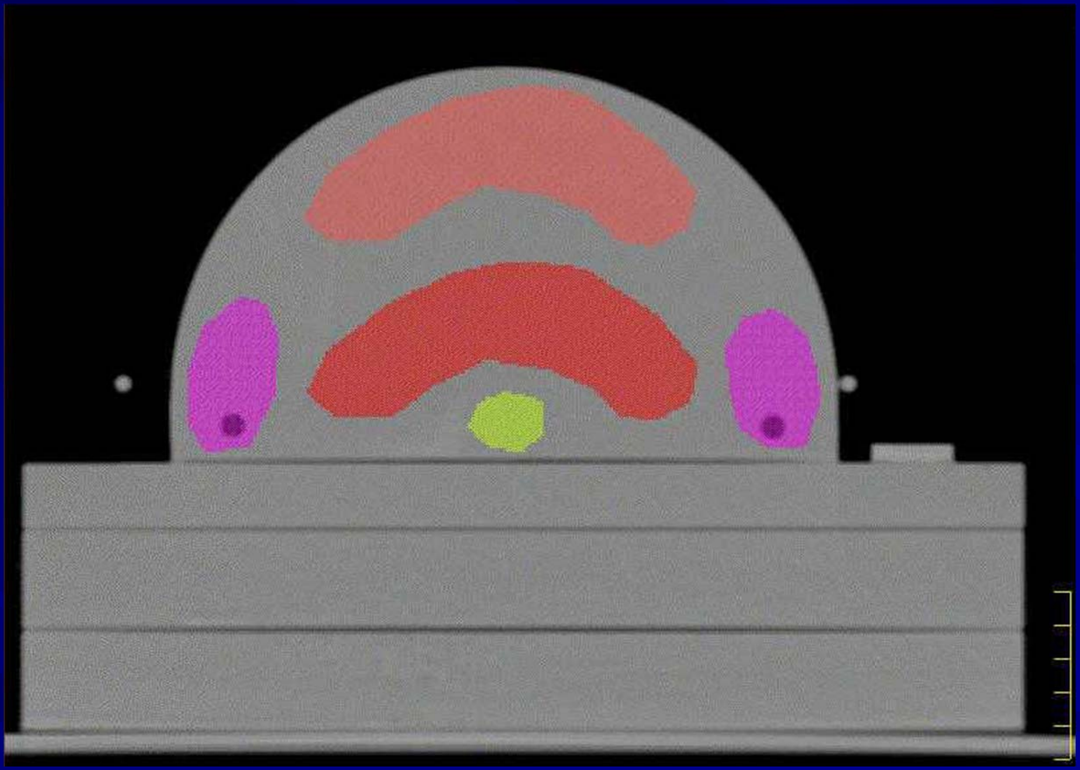
Same beam widths

Different beam fluences

Patient Specific QA: Axial Planes

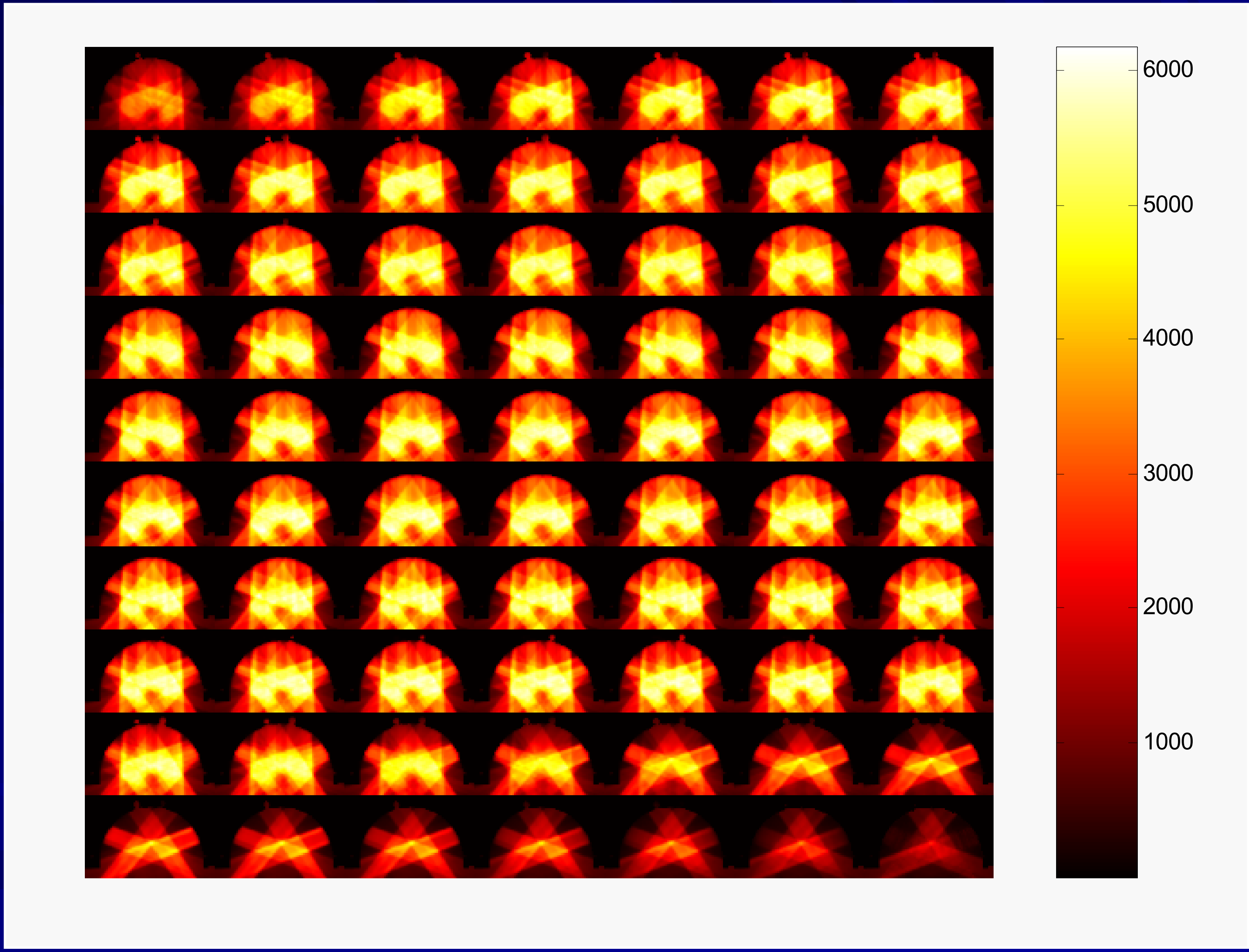


3-D Phantom Study



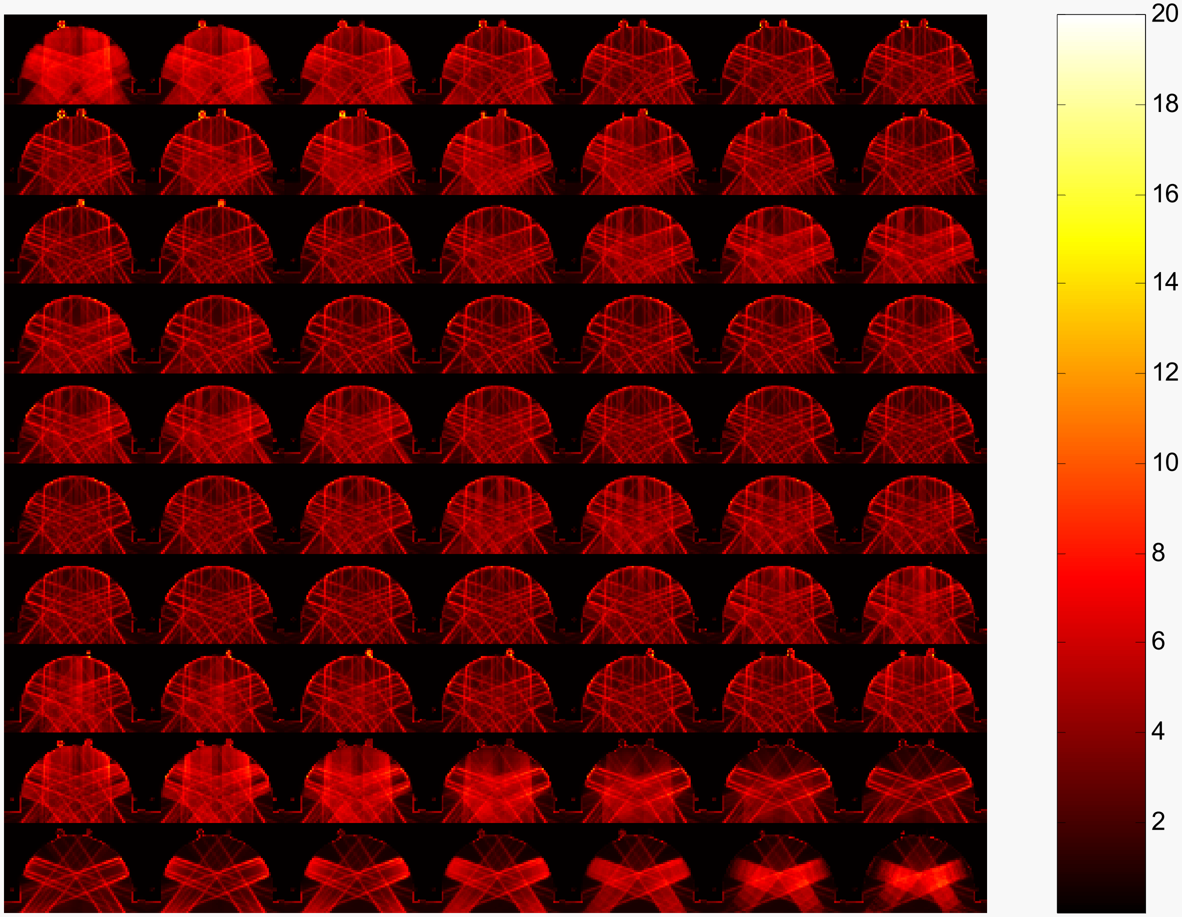
-H&N IMRT case
-5 Angles (Pinnacle)
-Radichromic Film

3-D Phantom Study

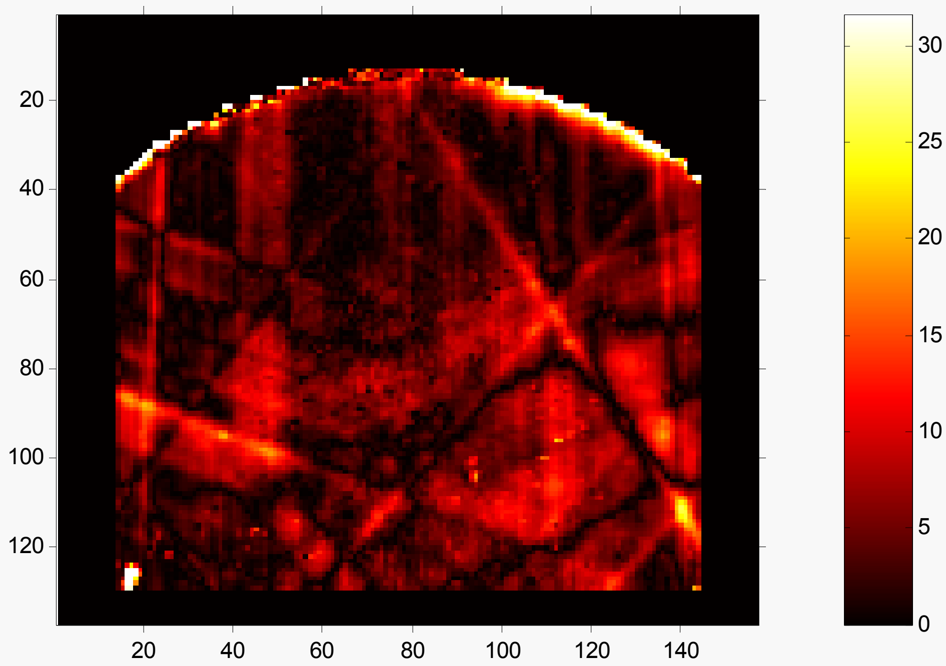


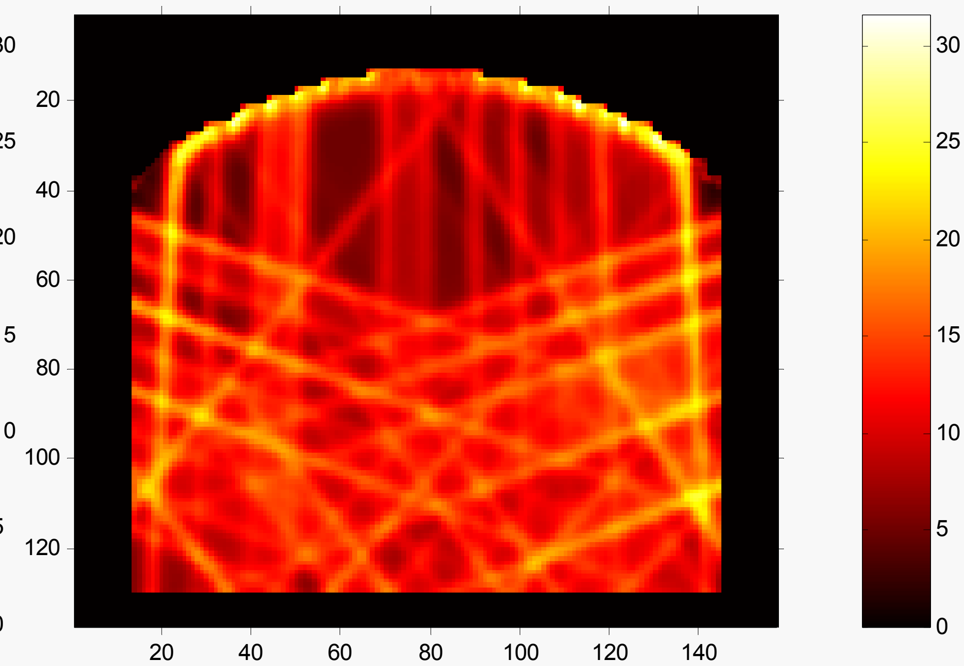
ADAC (Pinnacle) Dose Calculation

3-D dose uncertainty (U^D) map (1σ)



Prediction of Streaks

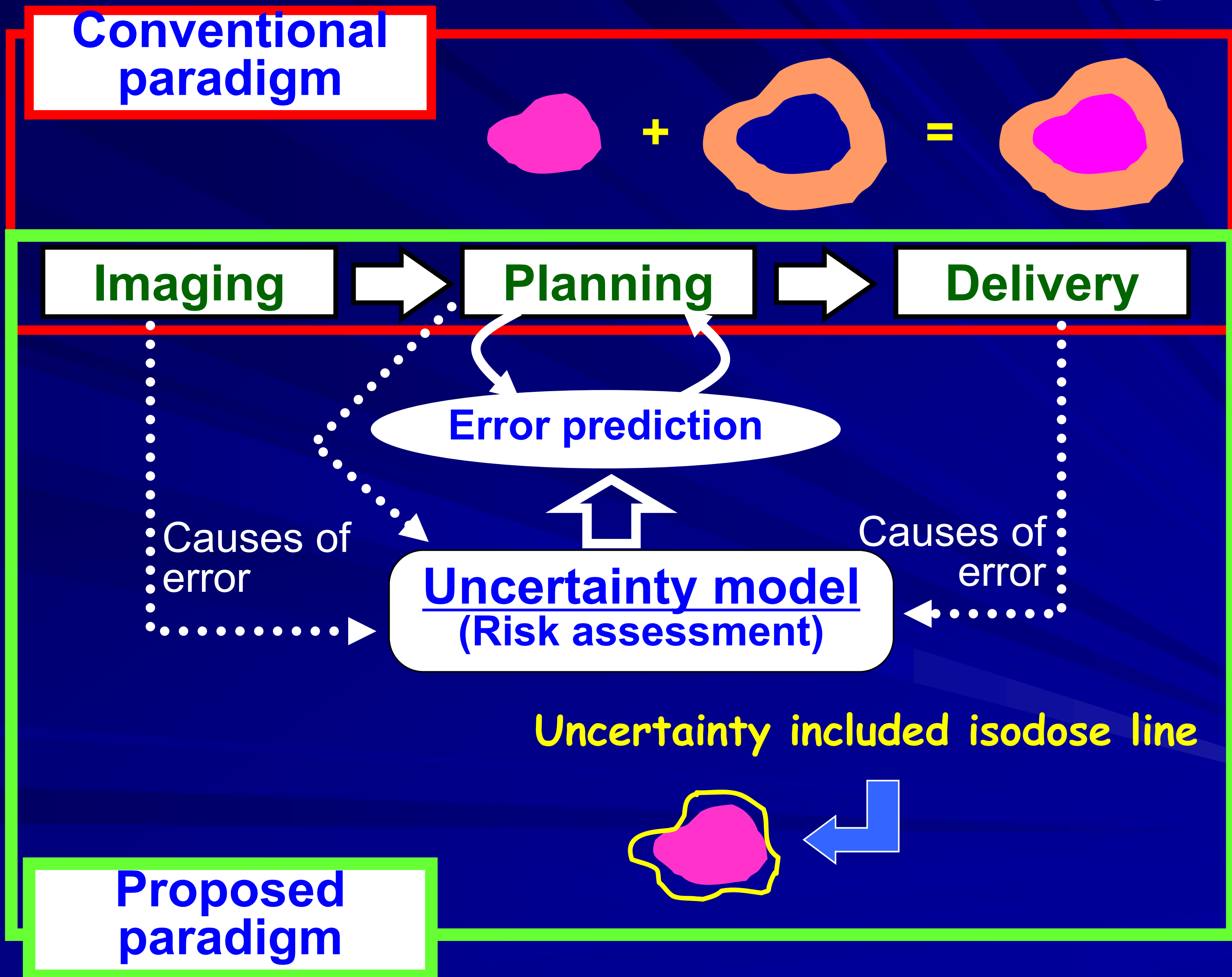




Dose difference

Dose uncertainty

Confidence-Based Planning

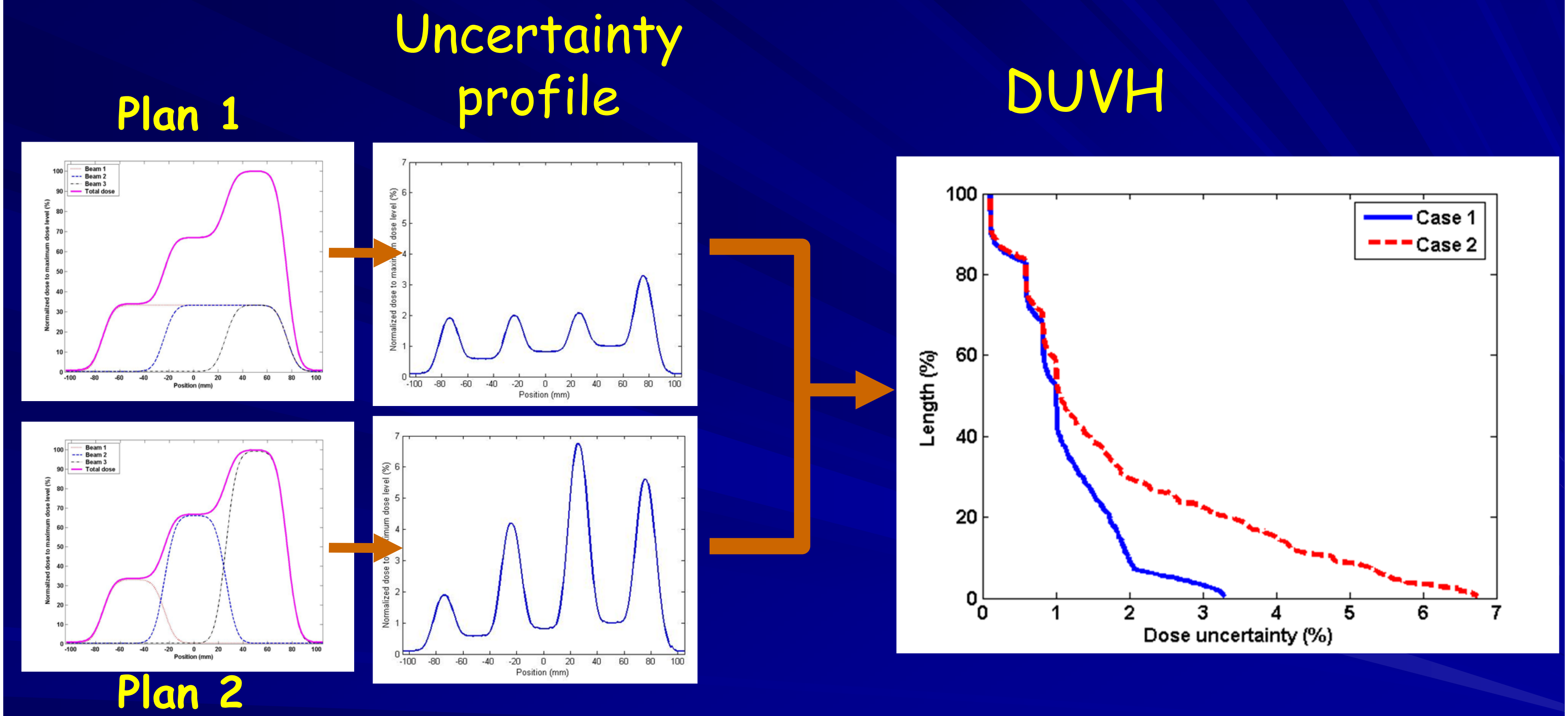


A Long Journey

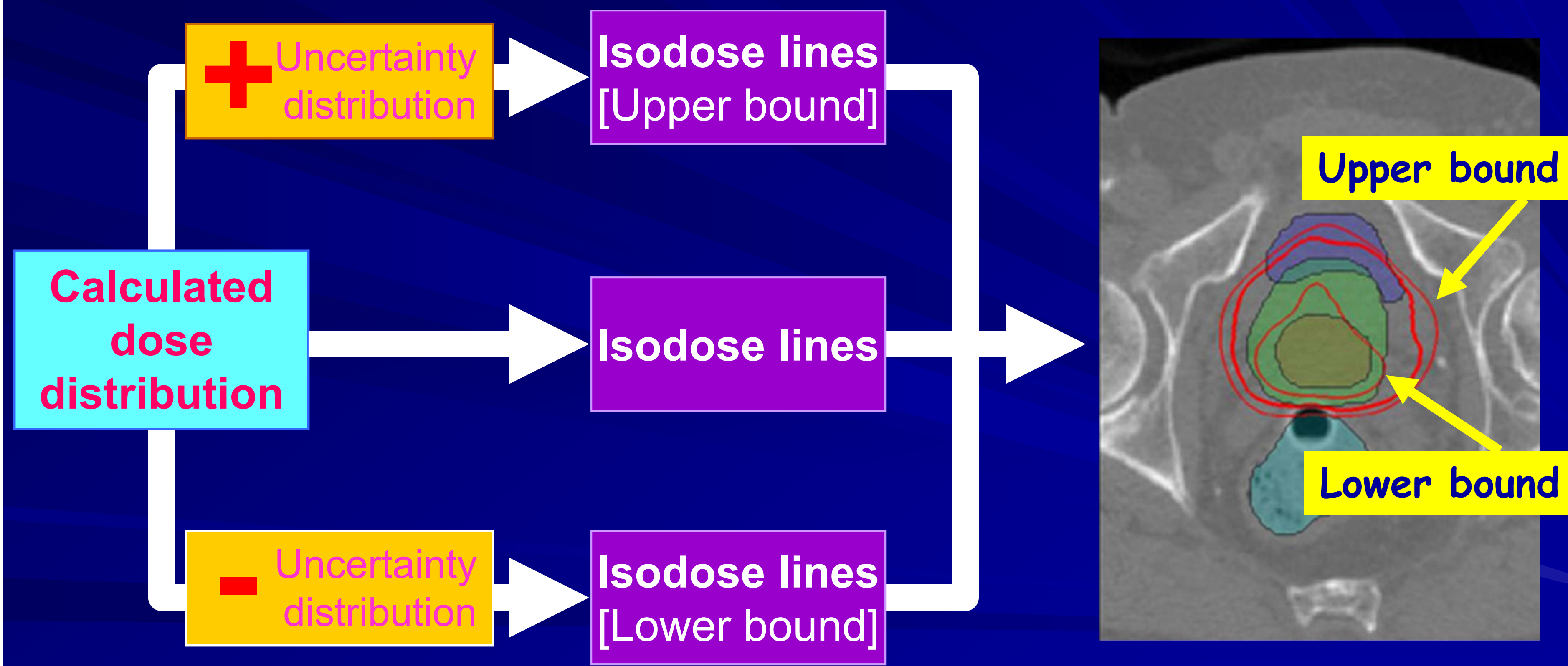
Confidence-Based Planning Evaluation Tools

- **CW-DVH**
  Confidence-weighted dose volume histogram
- **CWDD**
  Confidence-weighted dose distribution
- **DUVH**
  Dose uncertainty volume histogram

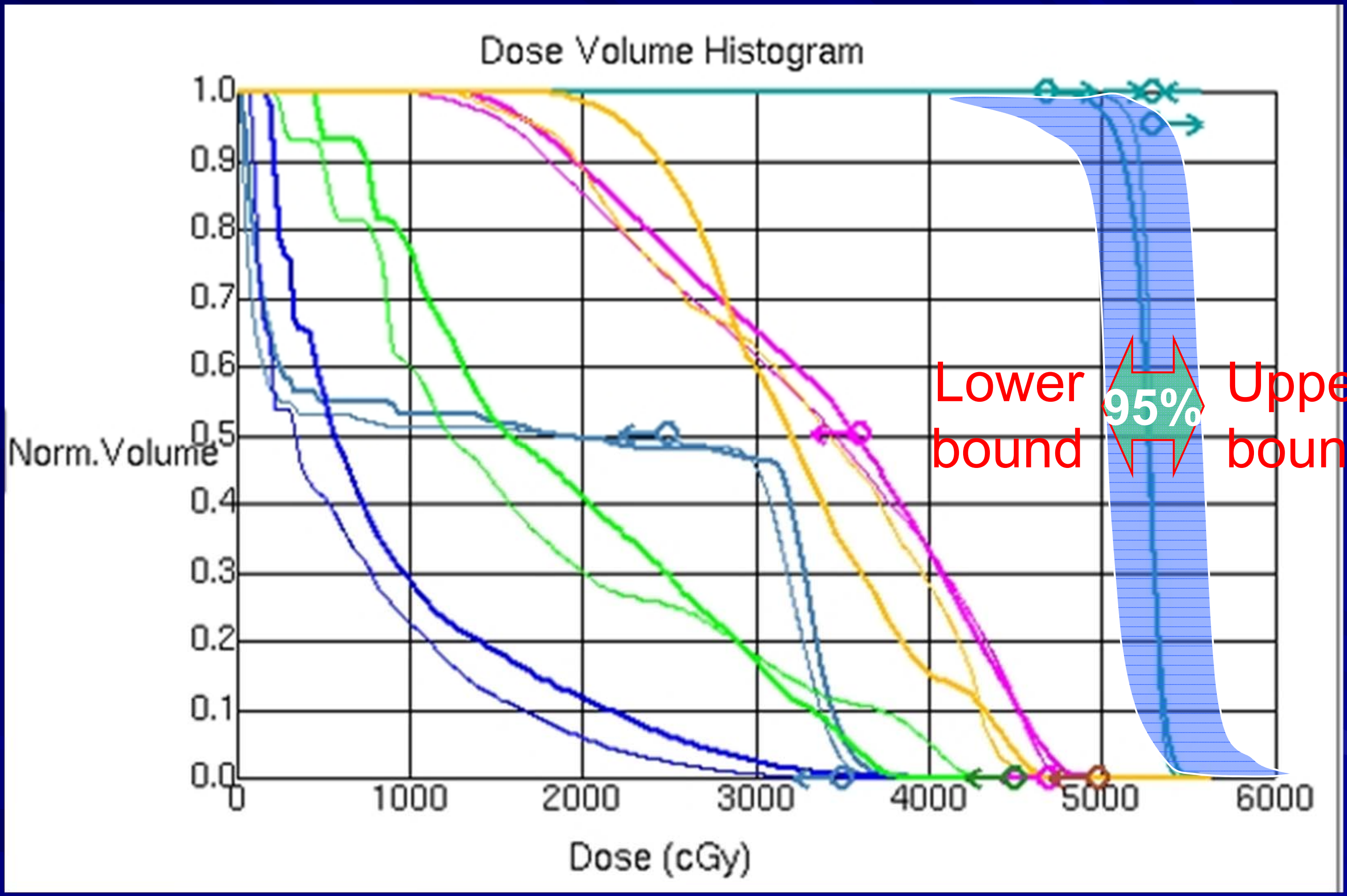
Dose Uncertainty Volume Histogram (DUVH)



Confidence-weighted dose distribution (CWDD)



Confidence-weighted dose volume histogram (CW-DVH)



Clinical study: 8 prostate cases

Plan objectives

Dose of 95% of PTV volume ≥ 100% of prescribed dose
Dose of 99% of PTV volume ≥ 93% of prescribed dose
PTV = CTV + 5 mm in all directions

Patient	Dose (cGy)	Total MU / fraction	# of Fraction	# of Fields	# of sub-fields
P1	7560	372	42	5	30
P2	7560	313	42	5	25
P3	7560	351	42	7	59
P4	7560	314	42	7	54
P5	7800	725	39	7	46
P6	7800	638	39	7	60
P7	7800	389	39	5	29
P8	7800	348	39	5	40

Clinical scenarios

In addition to Inherent Uncertainty of RTP,

Scenario 1

Machine related errors only

Based on in-house QA data

Scenario 2

Machine + Intrafractional errors

Li et al, IJROBP (71), 801-812, 2008;
(based on Calypso)

Scenario 3

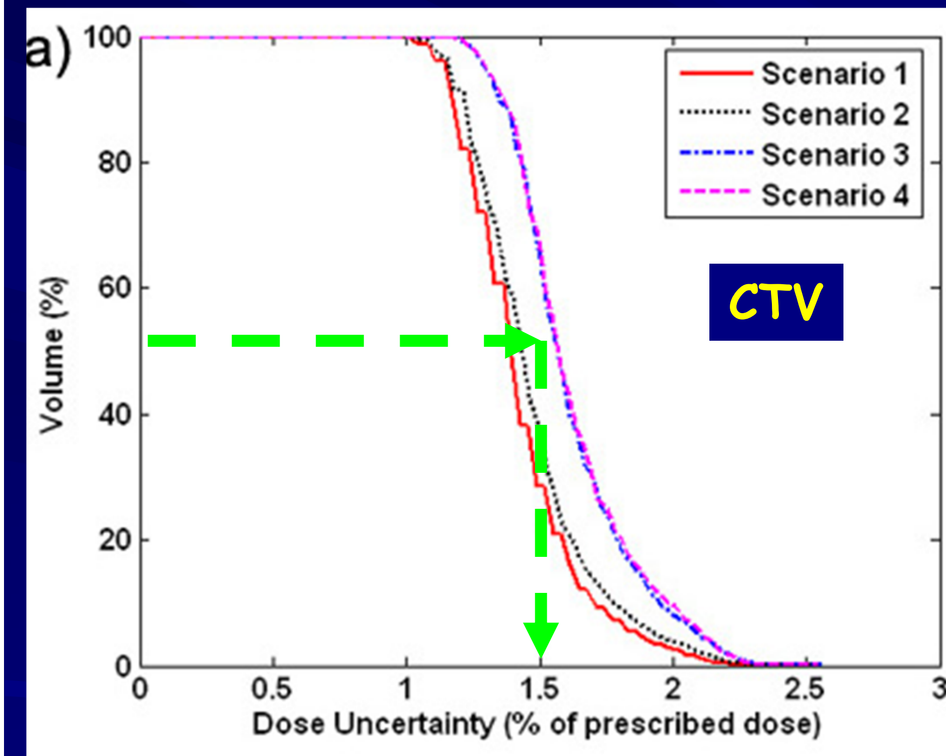
Machine + Interfractional errors

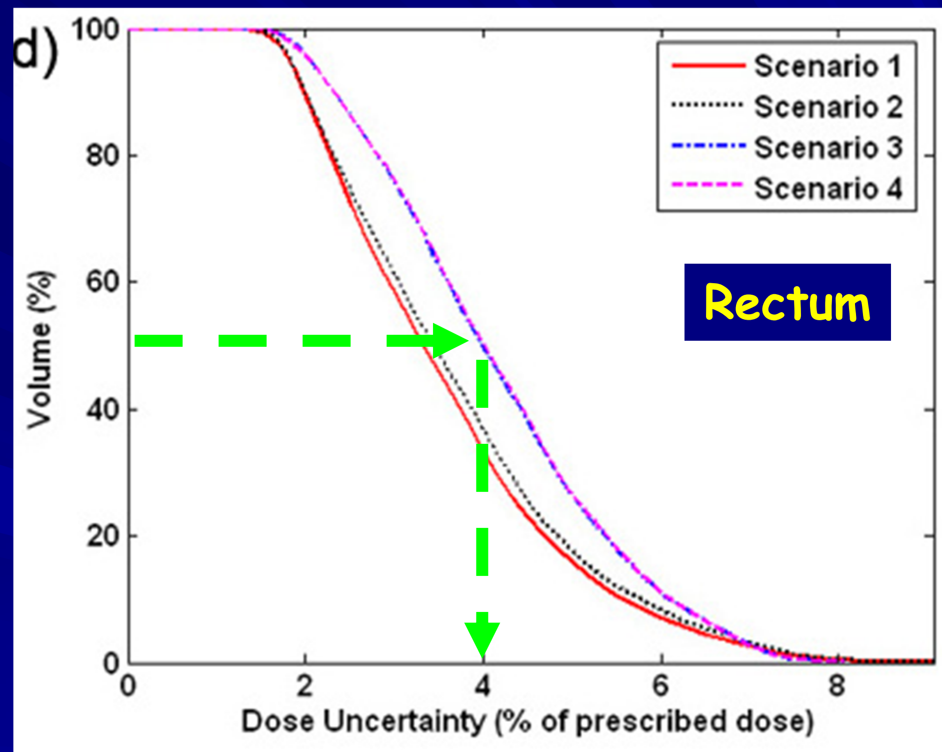
Guckenburger et al, IJROBP (65), 934-942, 2006;
(based on cone-beam CT)

Scenario 4

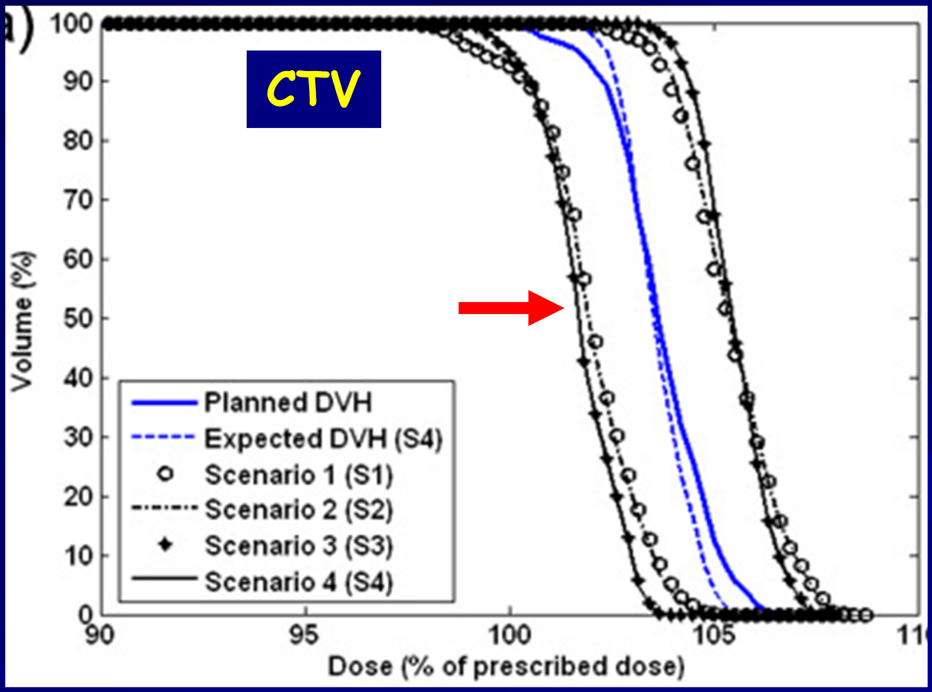
Machine + Intra/Inter-fractional errors

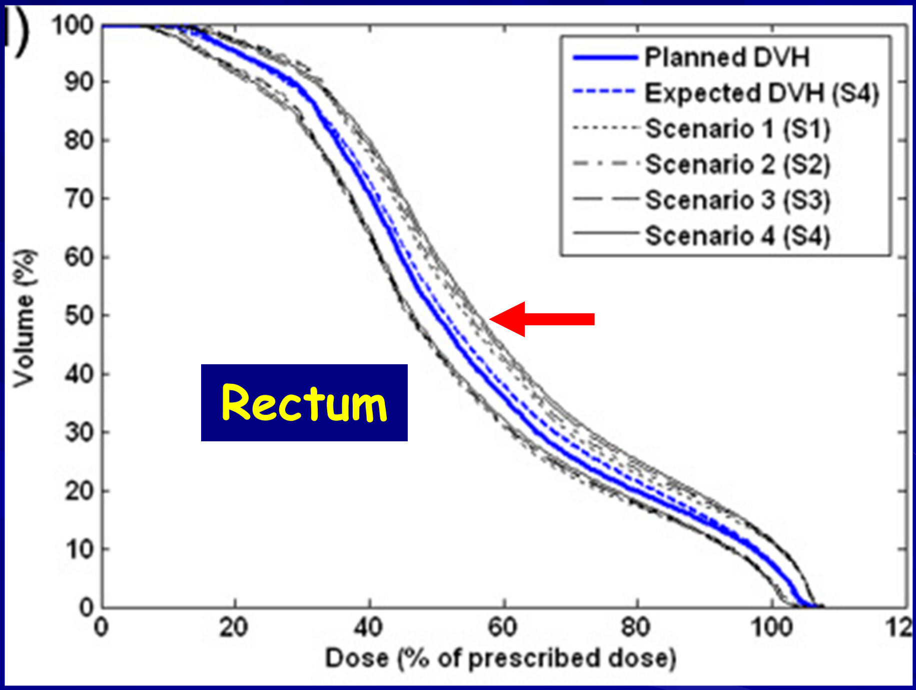
DUVH (P2; 95% confidence level)





CW-DVH (P4; 95% confidence level)

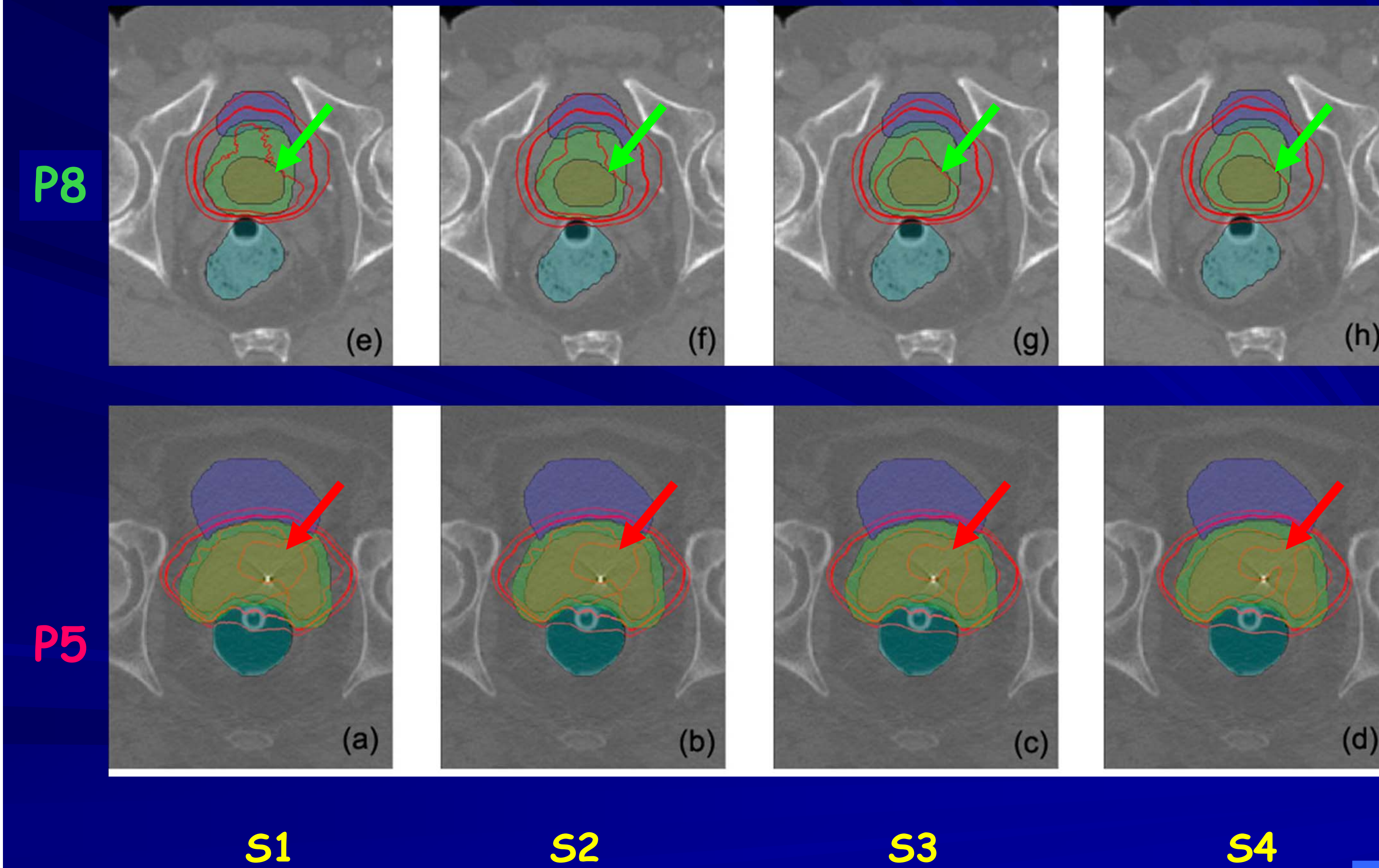




CW-D index (CTV D95 – Lower Bound)

Patient	Plan	S1	S2	S3	S4
	D95 (CTV)	CW-D95 (CTV)			
P1	7644 (101.1%)	7424 (98.2%)	7415 (98.1%)	7414 (98.1%)	7413 (98.0%)
P2	7719 (102.1%)	7600 (100.5%)	7598 (100.5%)	7595 (100.5%)	7591 (100.4%)
P3	7638 (101.0%)	7475 (98.9%)	7475 (98.9%)	7480 (98.9%)	7482 (99.0%)
P4	7692 (101.7%)	7510 (99.3%)	7514 (99.4%)	7558 (100.0%)	7564 (100.1%)
P5	**8004 (102.6%)**	**7395 (94.8%)**	**7381 (94.6%)**	**7313 (93.8%)**	**7312 (93.7%)**
P6	**7992 (102.5%)**	**7461 (95.7%)**	**7461 (95.7%)**	**7445 (95.5%)**	**7452 (95.5%)**
P7	8004 (102.6%)	7757 (99.4%)	7753 (99.4%)	7766 (99.6%)	7767 (99.6%)
P8	7980 (102.3%)	7776 (99.7%)	7775 (99.7%)	7780 (99.7%)	7780 (99.7%)

CWDD



α-DVH

Confidence intervals in dose volume histogram computation

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Henriquez and Castrillon 2010

Alpha-dose volume histogram $\alpha\text{-DVH}_c(x)$ for the region of interest R, dose level x, and confidence value α is defined as the volume contained in R receiving a dose equal to or greater than x with a certainty equal to or greater than $1-\alpha$. The pair of curves $(1-\alpha)-\text{DVH}_c(x)$ and $\alpha-\text{DVH}_c(x)$ set upper and lower limits for the confidence interval of level α.

$$\mathrm{DVH}^{\alpha}{}_{c}(d_j)=\sum_{k=1}^{j-1} H\left[1-\alpha-F\left(\frac{d_j-d_k}{u\cdot d_k}\right)\right]\cdot \mathrm{DVH}_d(d_k)+H\left[1-\alpha-F\left(\frac{d_j-d_j}{u\cdot d_j}\right)\right]\cdot \mathrm{DVH}_d(d_k)$$
$$+\sum_{k=j+1}^{-} H\left[1-\alpha-F\left(\frac{d_j-d_k}{u\cdot d_k}\right)\right]\cdot \mathrm{DVH}_d(d_k)$$

$$\mathrm{DVH}^{\alpha}{}_{c}(d_j)\underset{u\to 0}{\longrightarrow}\sum_{k=1}^{j-1} H[1-\alpha-1]\cdot \mathrm{DVH}_d(d_k)+H[1-\alpha-F(0)]\cdot \mathrm{DVH}_d(d_j)$$
$$+\sum_{k=j+1}^{-} H[1-\alpha-0]\cdot \mathrm{DVH}_d(d_k).$$

$H[1-\alpha-F(0)]=1$ if $\alpha<1/2$, and $H[1-\alpha-F(0)]=0$, otherwise, since F is the distribution function of a standardized variable and $F(0)=1/2$. Thus,

$$\mathrm{DVH}^{\alpha}{}_{c}(d_j)\underset{u\to 0}{\longrightarrow}\mathrm{DVH}_d(d_j)+\sum_{k=j+1}^{-} H[\alpha]\cdot \mathrm{DVH}_d(d_k)=\sum_{k=j}^{-}\mathrm{DVH}_d(d_k)=\mathrm{DVH}_c(d_j)\qquad \alpha<\frac{1}{2}$$
$$\mathrm{DVH}^{\alpha}{}_{c}(d_j)\underset{u\to 0}{\longrightarrow}\sum_{k=j+1}^{-} H[\alpha]\cdot \mathrm{DVH}_d(d_k)=\sum_{k=j+1}^{-}\mathrm{DVH}_d(d_k)=\mathrm{DVH}_c(d_{j+1})\qquad \alpha\geq\frac{1}{2}$$

There are two obvious extreme cases for $\mathrm{DVH}^{\alpha}{}_{c}$: $\alpha=1$ and $\alpha=0$.

$$\mathrm{DVH}^{1}{}_{c}(d_j)=\sum_{k=1}^{-} H\left[1-1-F\left(\frac{d_j-d_k}{u\cdot d_k}\right)\right]\cdot \mathrm{DVH}_d(d_k)$$
$$=\sum_{k=1}^{-} 0\cdot \mathrm{DVH}_d(d_k)=0,$$

$$\mathrm{DVH}^{0}{}_{c}(d_j)=\sum_{k=1}^{-} H\left[1-0-F\left(\frac{d_j-d_k}{u\cdot d_k}\right)\right]\cdot \mathrm{DVH}_d(d_k)$$
$$=\sum_{k=1}^{-} 1\cdot \mathrm{DVH}_d(d_k)=V.$$

In the first case, the confidence level is 0 and no point can be assigned to any dose level. In the second case, any point can be assigned to any dose level. When $\alpha=0.5$, since $F(0)=1/2$,

$$\mathrm{DVH}^{1/2}{}_{c}(d_j)=\sum_{k=1}^{-} H\left[\frac{1}{2}-F\left(\frac{d_j-d_k}{u\cdot d_k}\right)\right]\cdot \mathrm{DVH}_d(d_k)$$
$$=\sum_{k=j}^{-} 1\cdot \mathrm{DVH}_d(d_k)=\mathrm{DVH}_c(d_j).$$

Therefore, the original DVH_c is the median $\mathrm{DVH}^{\alpha}{}_{c}$.

Different distribution functions were used to obtain the corresponding expressions for $\mathrm{DVH}^{\alpha}{}_{c}$ from Eq. (1). They are described in the following subsections.

II.B. Rectangular uncertainty model

This probability distribution is important in uncertainty evaluation because it deals with a situation where it is clear that no value can be found outside an interval, but no information is available about probability within its boundaries.[17] The simplest assumption is a constant probability density inside the interval. This distribution is useful when dealing with computer calculations. Its density function (with mean 0 and variance 1) is

$$f_r(w)=\begin{cases}\dfrac{1}{2\sqrt{3}} & w\in[-\sqrt{3},\sqrt{3}]\\ 0 & w\notin[-\sqrt{3},\sqrt{3}]\end{cases}$$

and its distribution function is

$$F_r(w)=\begin{cases}0 & w<-\sqrt{3}\\ \dfrac{w+\sqrt{3}}{2\sqrt{3}} & -\sqrt{3}\leq w<\sqrt{3}\\ 1 & \sqrt{3}\leq w\end{cases}.$$

Details of this derivation are shown in the Appendix. The α-dose volume histogram for a rectangular distribution is

$$\mathrm{DVH}^{\alpha}{}_{c,r}(d_j)=\sum_{d_k>\frac{d_j}{1+\sqrt{3}\cdot u\cdot(2\alpha-1)}}\mathrm{DVH}_d(d_k)$$
$$=\mathrm{DVH}_c\left(\frac{d_j}{1+\sqrt{3}\cdot u\cdot(2\alpha-1)}\right).\qquad (2)$$

Again, it is easy to obtain a standard DVH when $u=0$, and also when $\alpha=0.5$. It can be observed from the formula that

Dose-expected Volume Histogram (DeVH)

A NOVEL METHOD FOR THE EVALUATION OF UNCERTAINTY IN DOSE–VOLUME HISTOGRAM COMPUTATION

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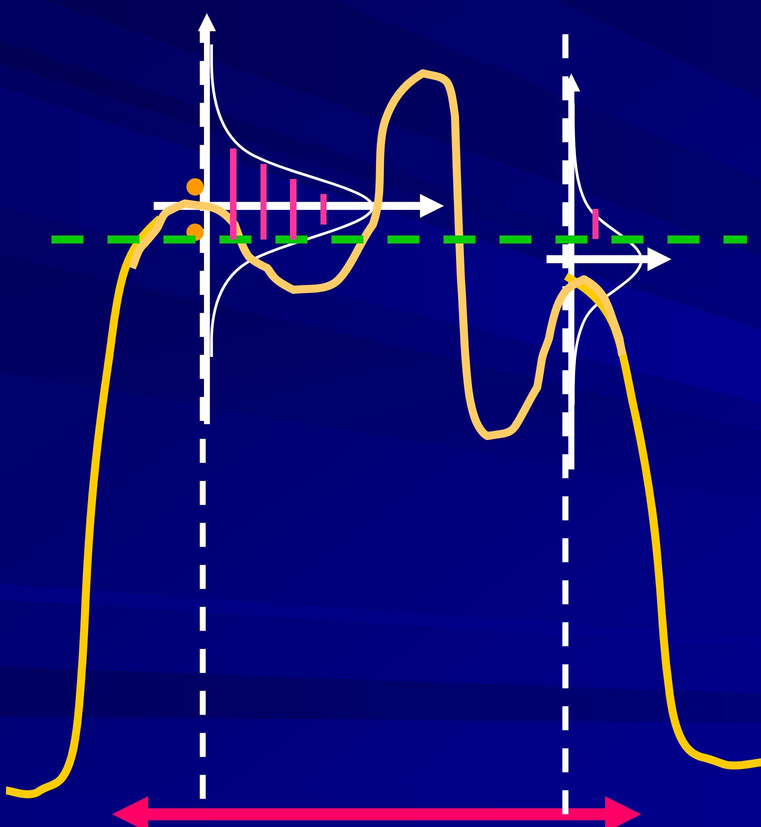
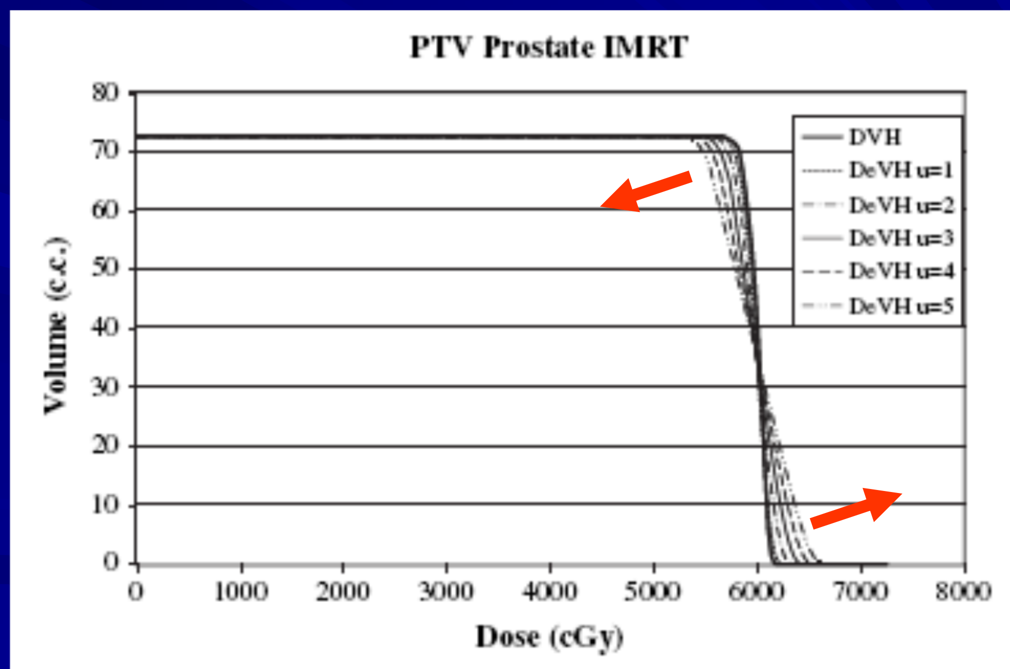
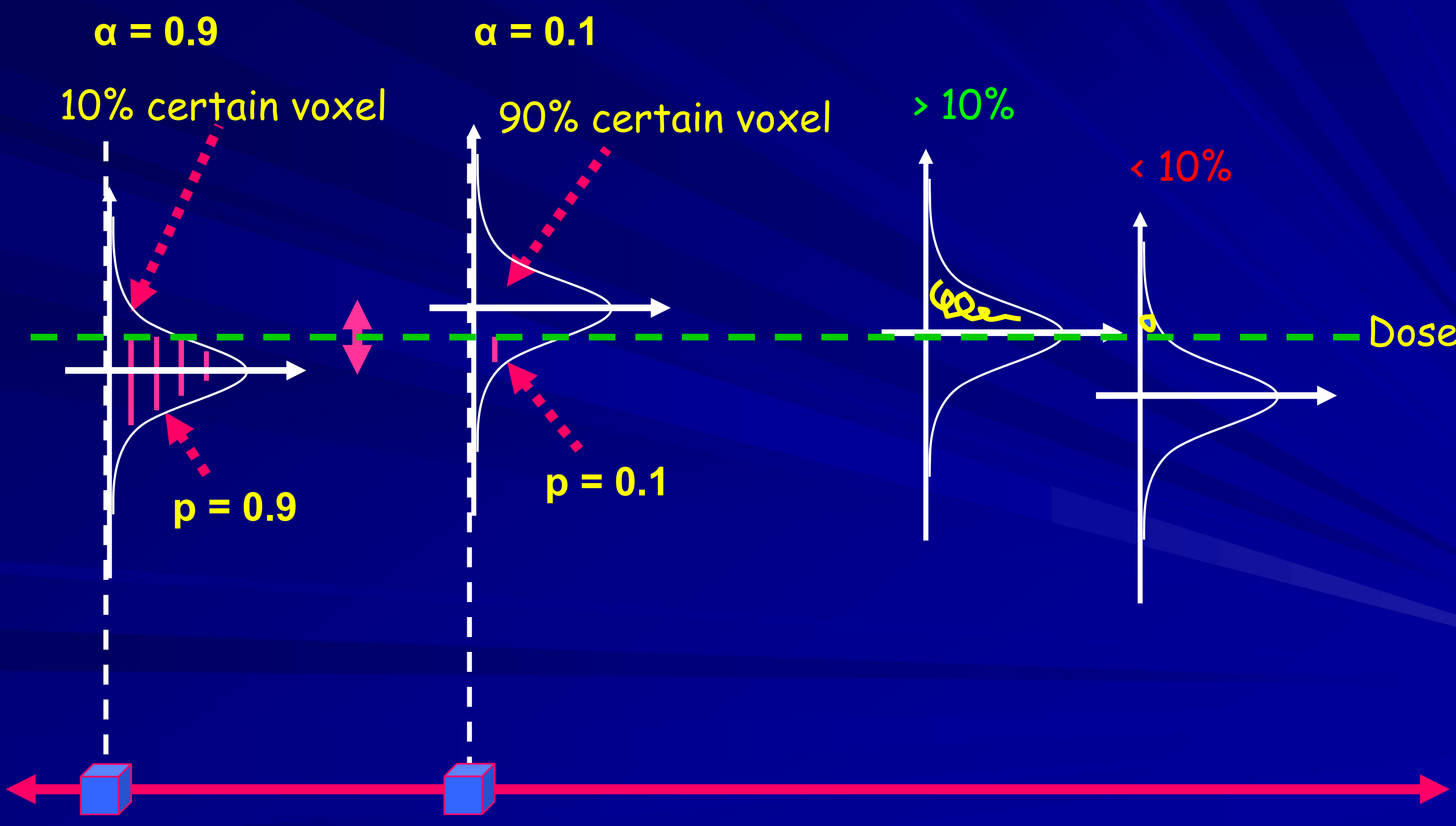
Henriquez and Castrillon 2008



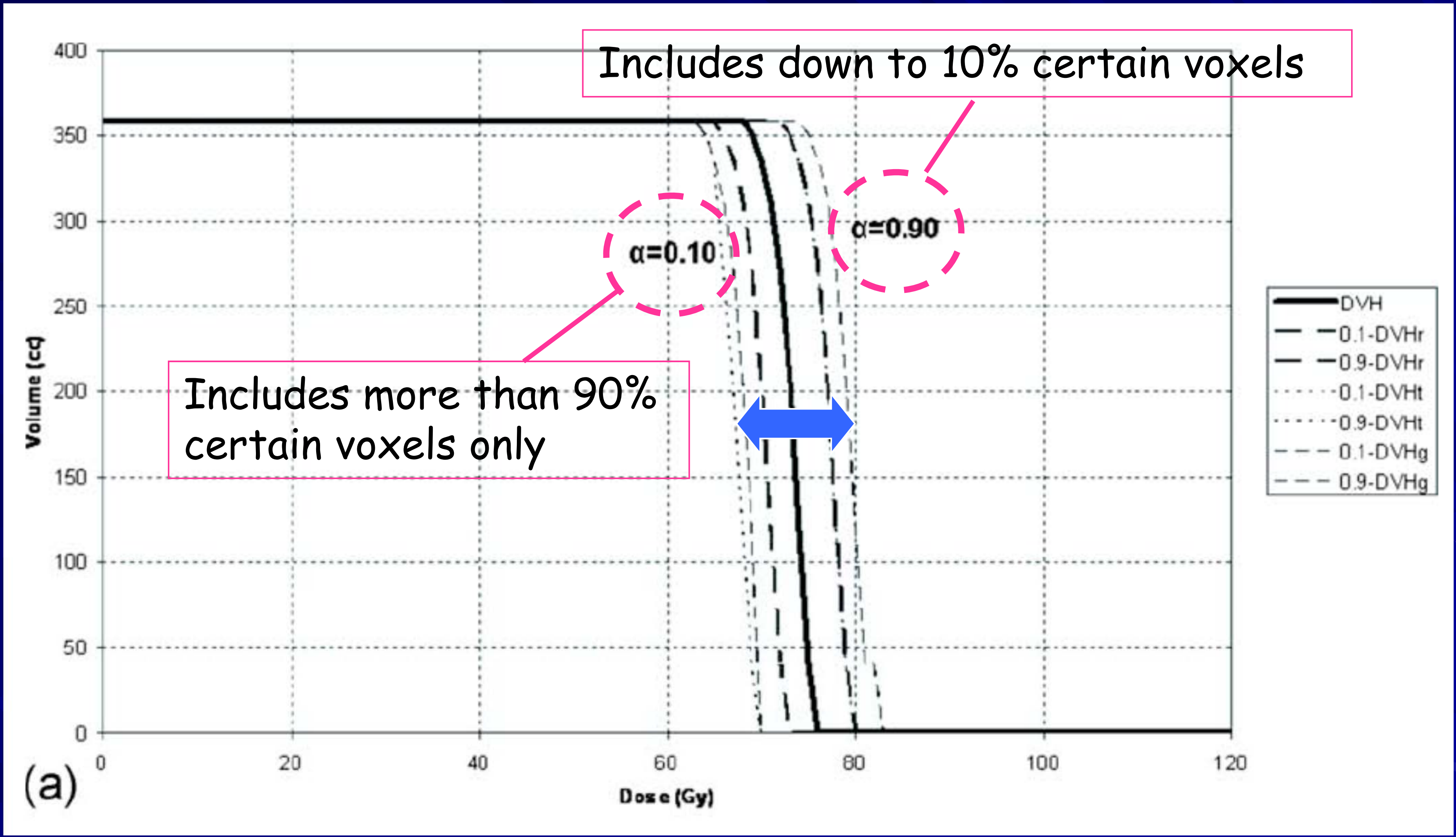


α-DVH

Take "1- α" certainty as the threshold



α-DVH



Prerequisite – Known Dose Uncertainty PDF

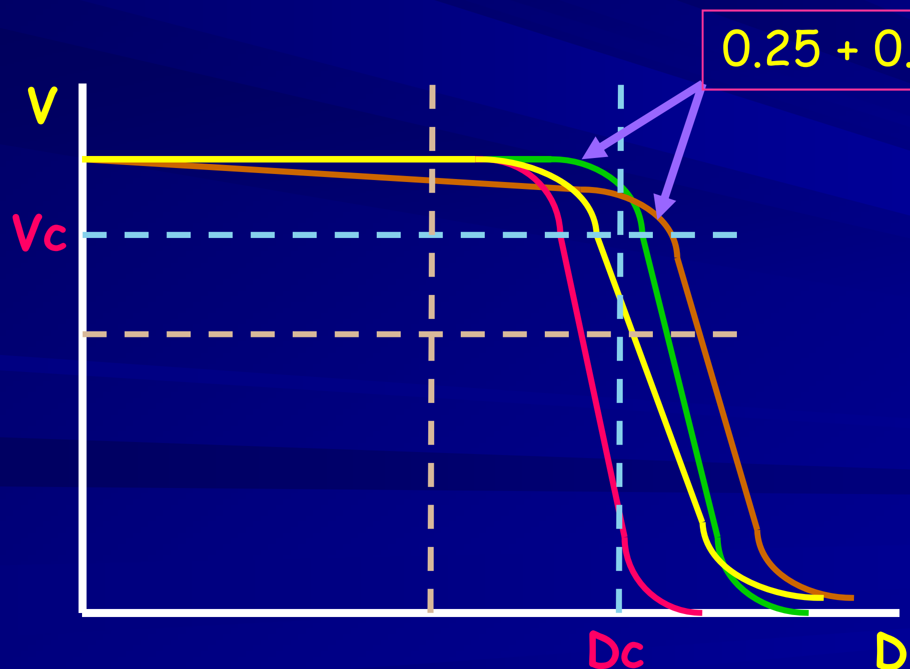
Dose-Volume Population Histogram (DVPH)

Dose–volume population histogram: a new tool for evaluating plans whilst considering geometrical uncertainties

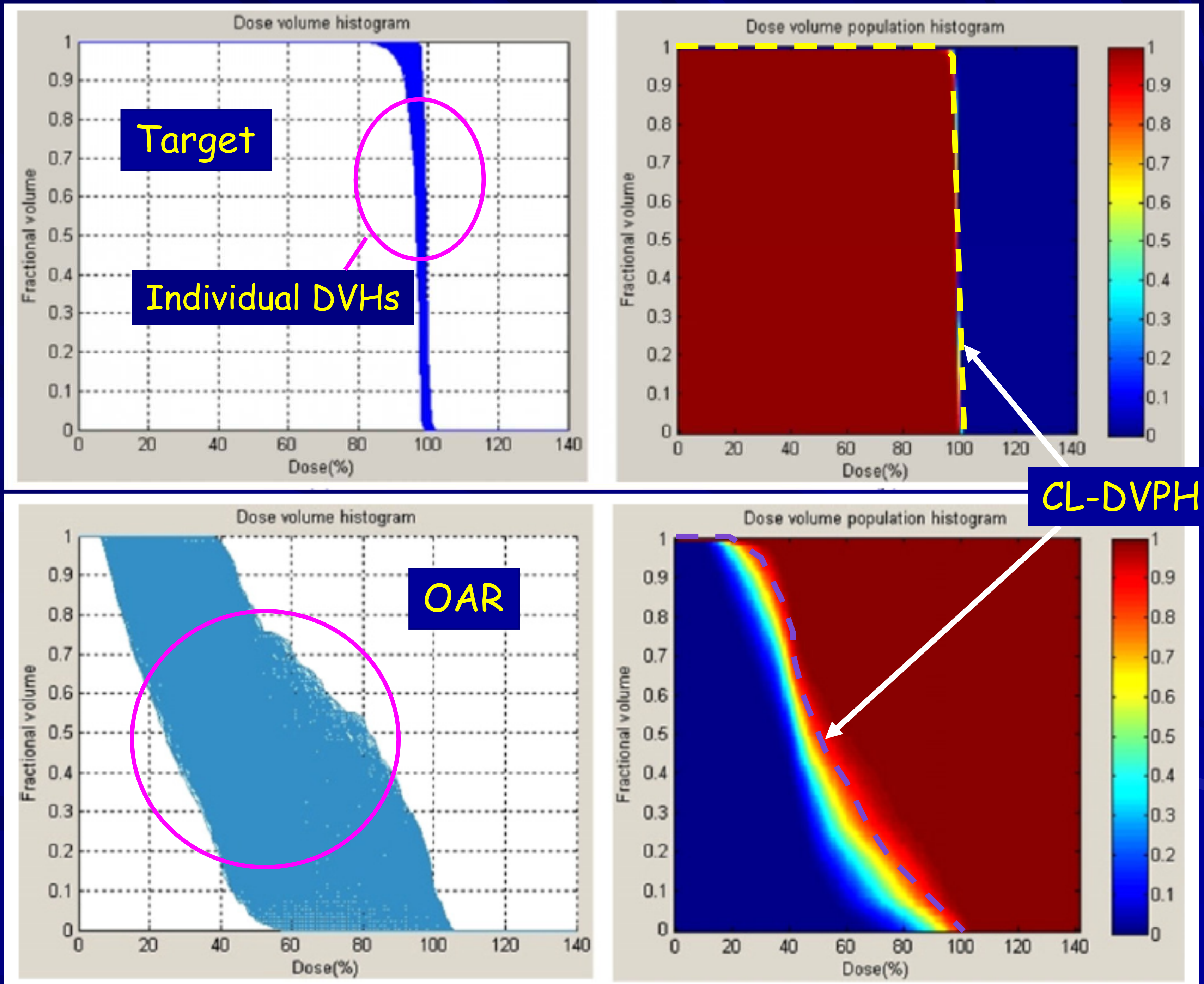
Nguyen et al. 2009

T B Nguyen[1,2], A C F Hoole[1], N G Burnet[2] and S J Thomas[1]

<u>Simulate many cases with systematic error</u>

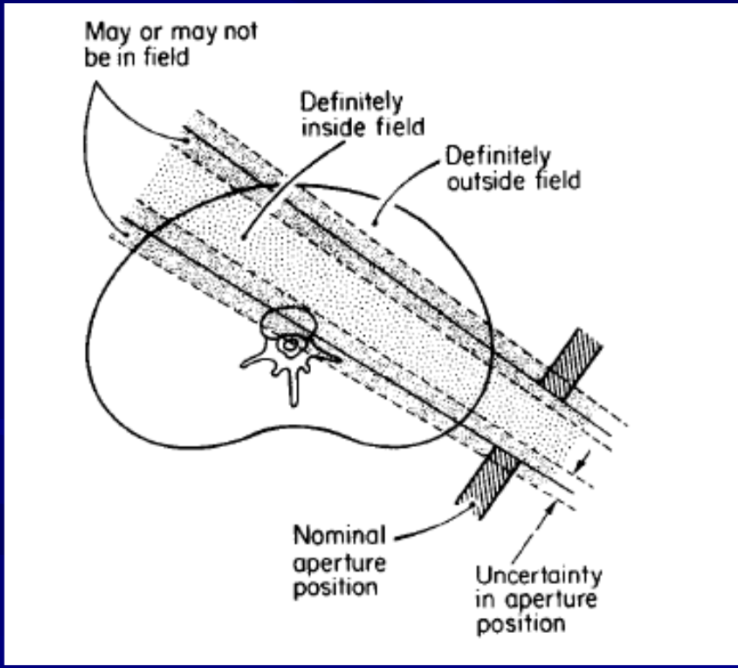


With enough cases considering both systematic and random setup errors, a DVPH can be obtained.


Dose volume histogram
Target
Individual DVHs
Fractional volume
Dose(%)
Dose volume population histogram
Fractional volume
Dose(%)
CL-DVPH
Dose volume histogram
OAR
Fractional volume
Dose(%)
Dose volume population histogram
Fractional volume
Dose(%)

Uncertainty in Bound Concept

Goitein 1985



For each plan,
3 calculations are suggested;

1 at the nominal condition and
2 extreme conditions in confidence level

Summary

- Spatial uncertainty can be converted to dose uncertainty in reasonable accuracy.
- The *a priori* dose uncertainty model is able to provide dose uncertainty map in 3-D space.
- The clinical example demonstrated that the local dose uncertainty could be significantly different among the prostate IMRT plans although they met the same plan objectives, indicating the necessity of uncertainty evaluation.
- The uncertainty-based plan-evaluation tools provide an intuitive and quantitative inspection of the potential risk of the plans.
- If dose uncertainties are explicitly incorporated in planning *a priori*, the potential risk existing in radiotherapy can be better managed.

Thankyou!

Let's visit Florida !

Used Data

Table 2. SOU inputs of the uncertainty model (mean ± SD)

	x (mm)	y (mm)	z (mm)	Pitch (θ_x; degree)	Roll (θ_y; degree)	Yaw (θ_z; degree)
Machine	−0.1 ± 0.3	0.0 ± 0.3	0.0 ± 0.3	Refer to Fig. 1 for angular deviations of gantry and collimator angle at each gantry angle		
Intrafraction*	0.0 ± 0.3	−0.4 ± 0.7	−0.5 ± 0.6	—	—	—
Interfraction	−0.2 ± 2.6	0.1 ± 2.3	−1.0 ± 3.3	−0.2 ± 1.2	0.5 ± 1.0	0.1 ± 0.7

Abbreviation: Ref . = reference; SD = standard deviation

Note: The coordinate system is based on the International Electrotechnical Commission (IEC) fixed coordinate system (see Fig. 1 in Ref. 18)

* Data are for Group 3 in Ref. 21.