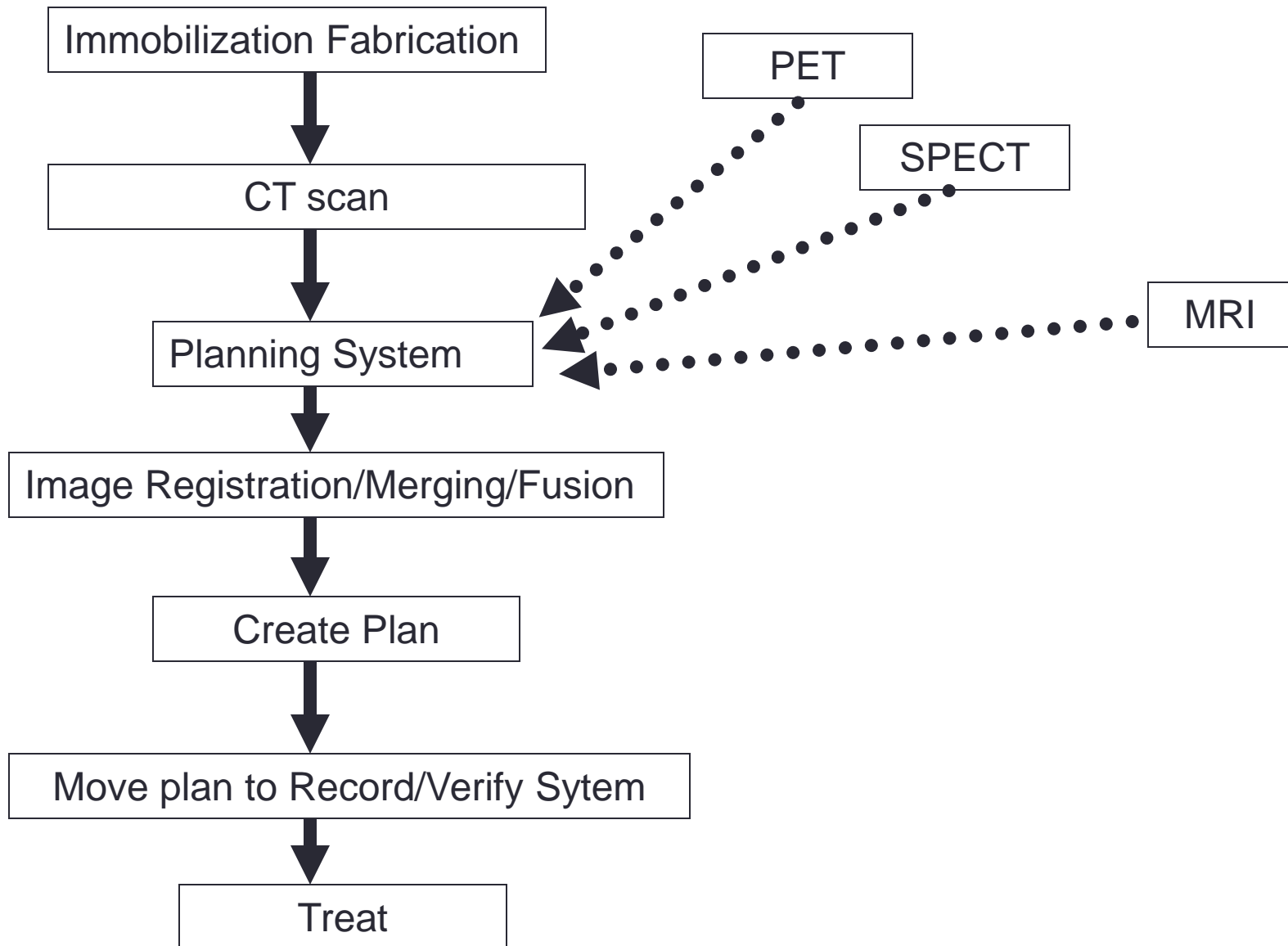


# Advanced Treatment Planning

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Duke University





In 3D/IMRT planning:

- Primary dataset is from CT

Secondary datasets could be from:

- Magnetic Resonance Imaging
- Magnetic Resonance Spectroscopy
- Positron Emission Tomography
- Single Photon Emission Computed Tomography

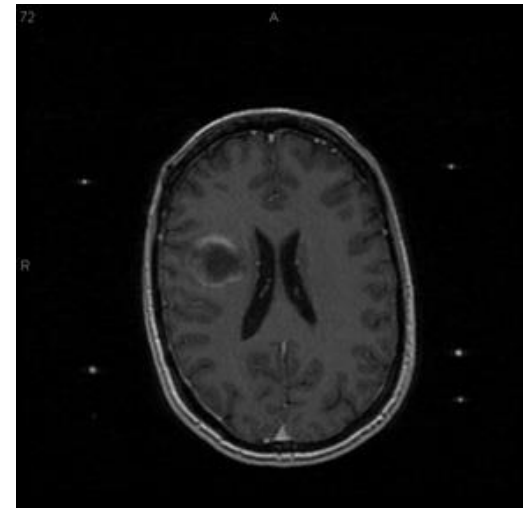
Primary CT dataset is used by the planning system for beam-patient interactions (energy deposition).

Secondary datasets are used to augment the information in CT, i.e., to superimpose specific information from the secondary dataset onto the primary dataset – IMAGE FUSION/REGISTRATION.

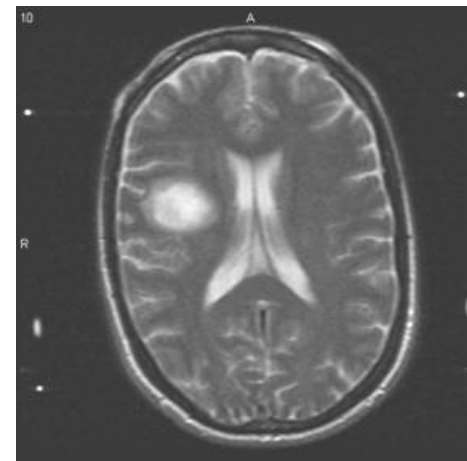
# Magnetic Resonance Imaging



T1 – weighted image



T1

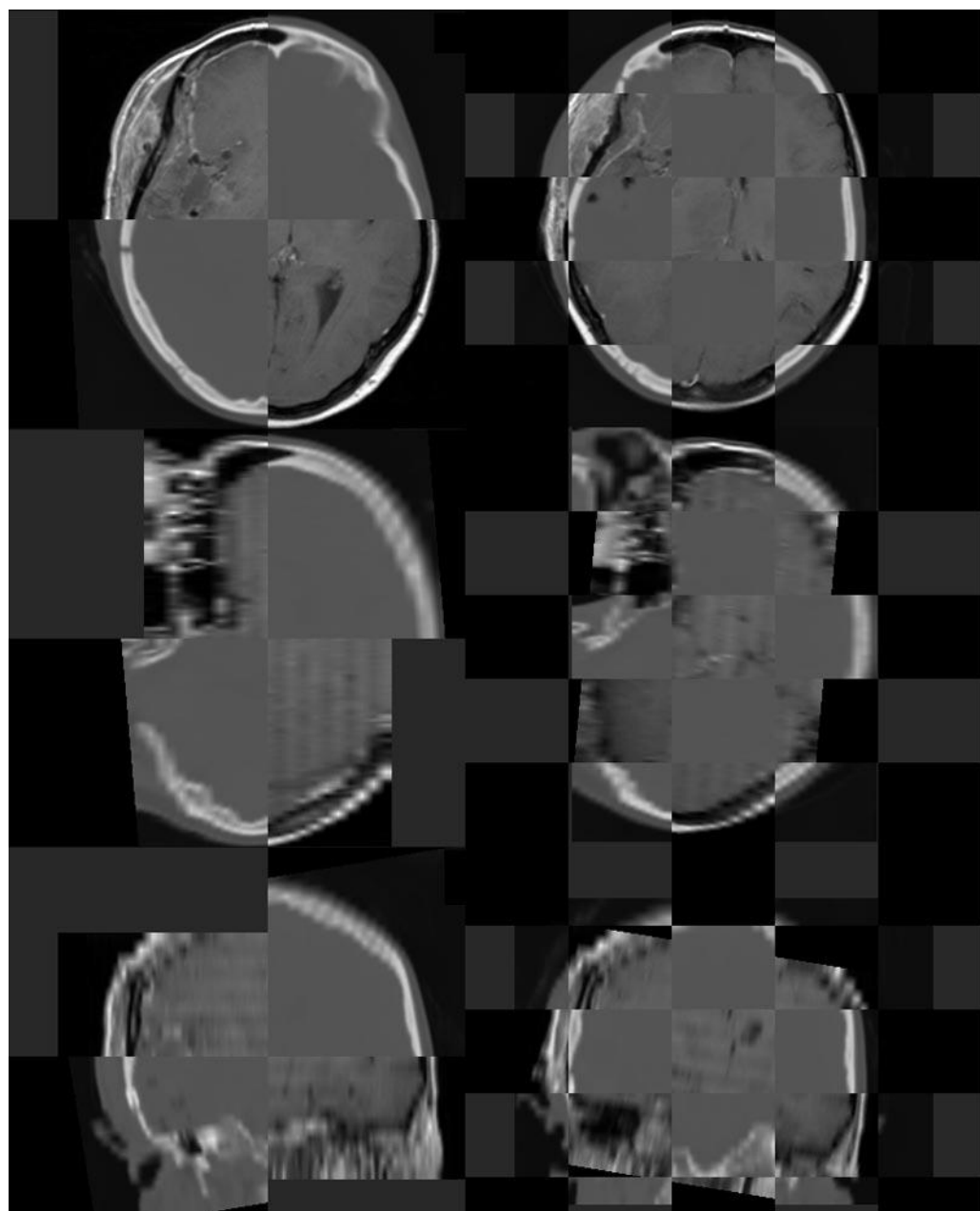


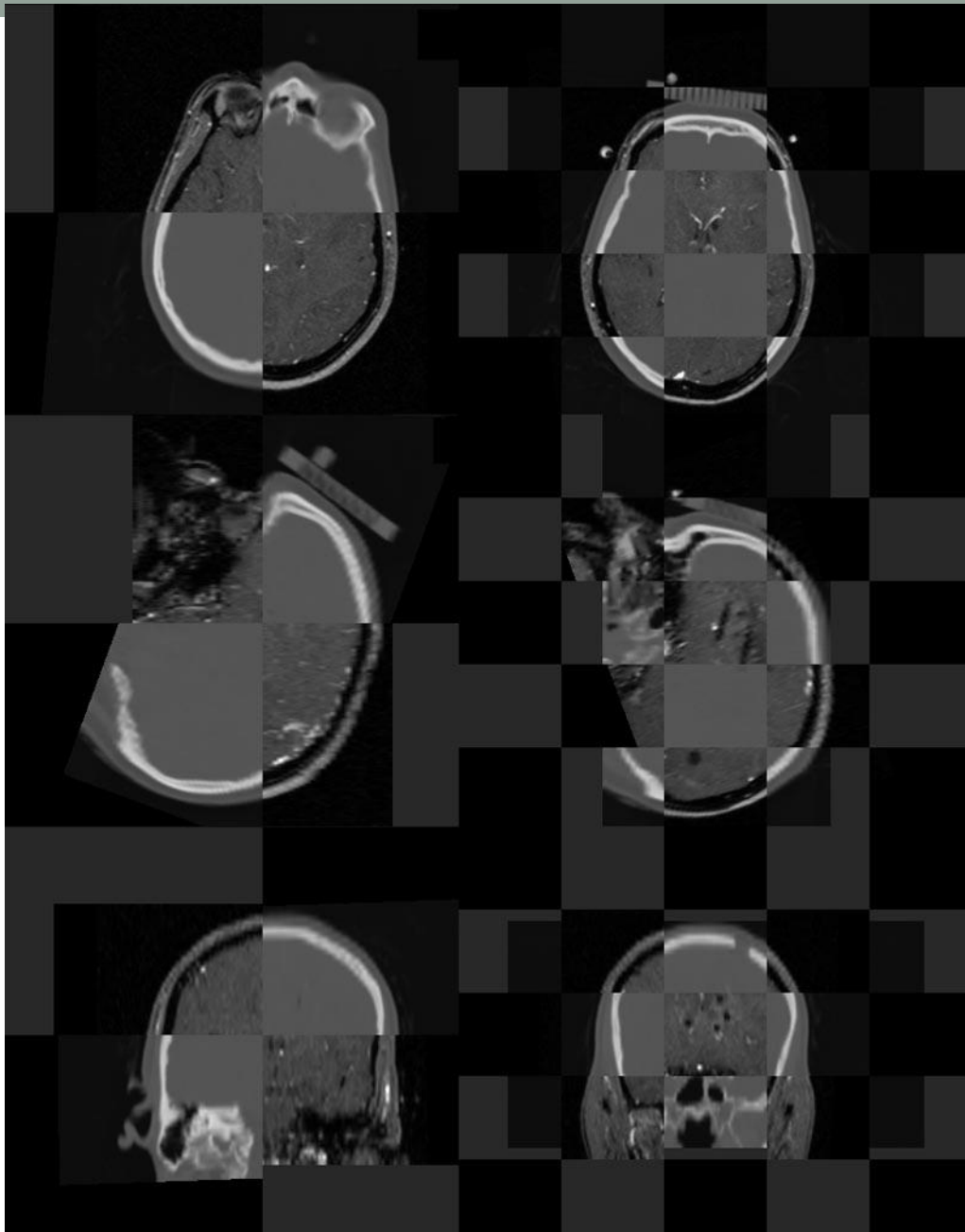
T2

## Manual MR to CT Image Registration

- CT and MR images are registered to each other within the planning system.
- Manual motion consists of translating and rotating the MR image in all three views: coronal, sagittal, transverse.
- Frequently, it is not possible to obtain a complete match, due to the patient being in different positions in the two modalities.
- If the patient is in different positions, match as best as possible in the region of interest (tumor).

We will talk about different image registration methodologies later on .....

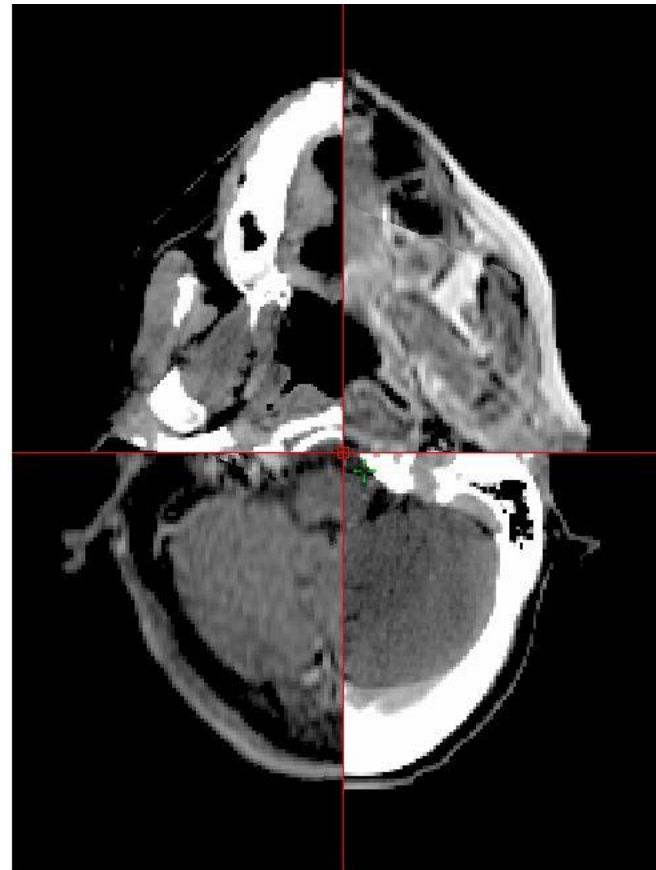


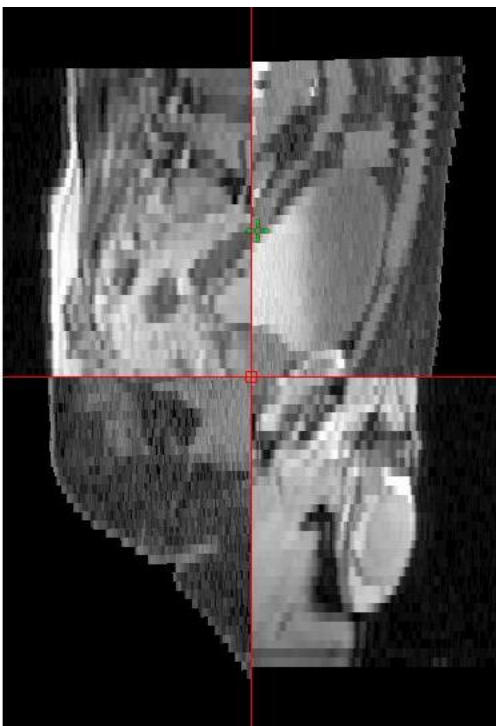
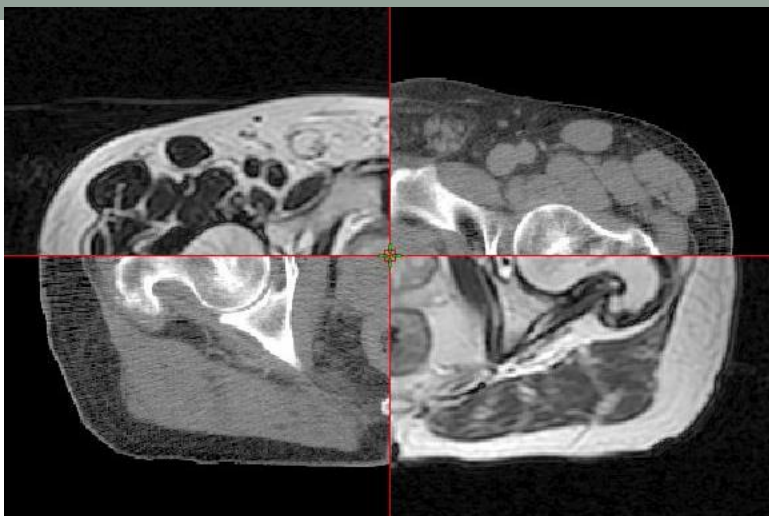


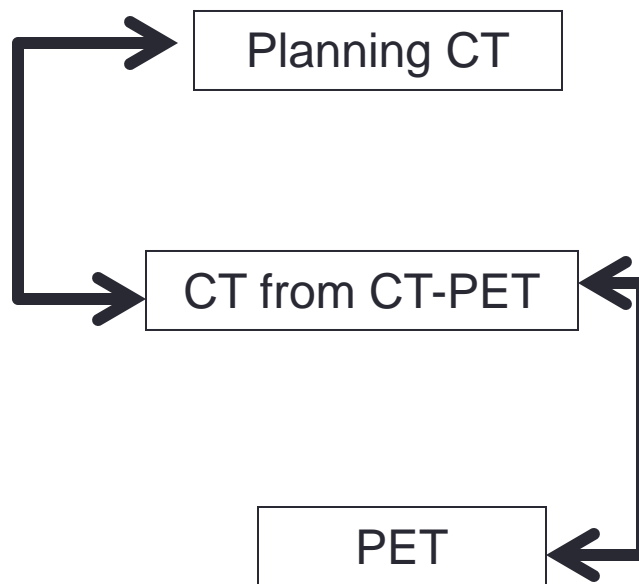
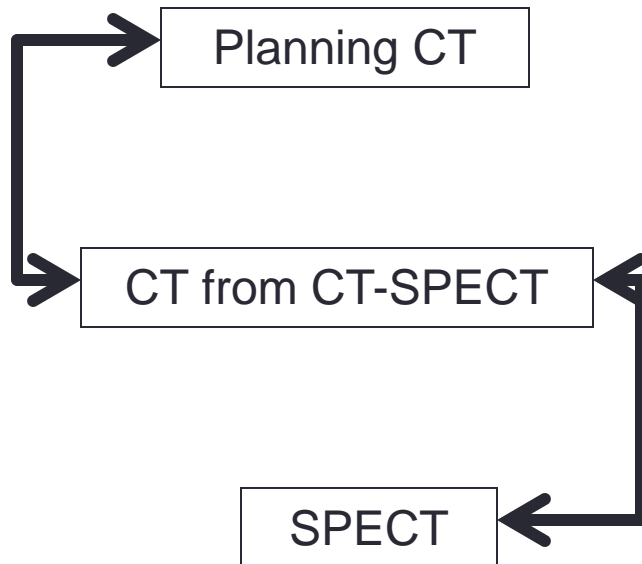
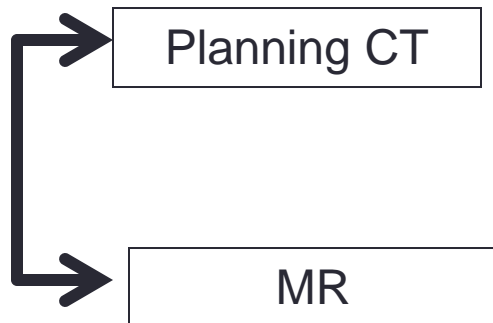
After merging, physician draws tumor on MR image. MR tumor contour is then transformed into CT coordinates and displayed in CT image.

If the tumor appears on both CT and MR, physicians draw tumor on both CT and MR and usually designate the “final” tumor as a union from these modalities.

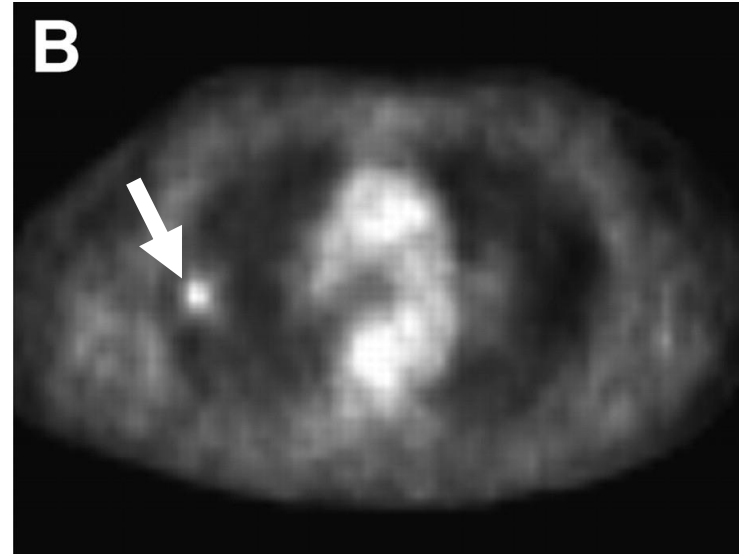
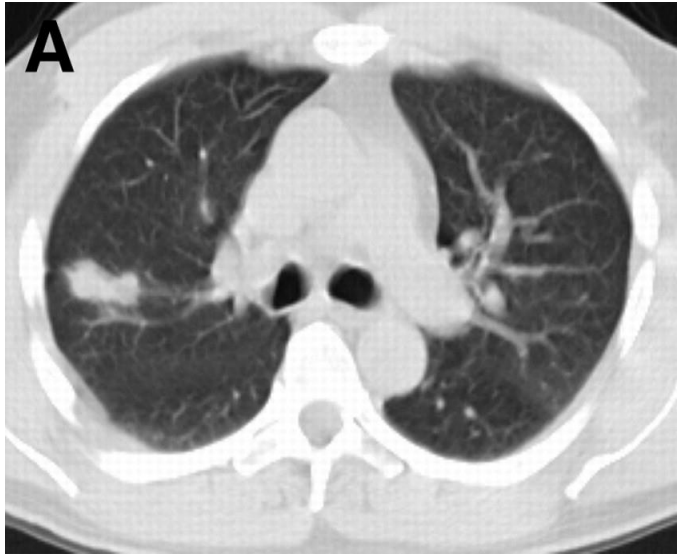








## Positron emission tomography



### PET radionuclides:

$^{11}\text{C}$  (20 min) ,  
 $^{13}\text{O}$  (10 min),  
 $^{15}\text{N}$  (2 min),  
 $^{18}\text{F}$  (110 min),  
 $^{64}\text{Cu}$  (12.7 hrs)  
 $^{62}\text{Cu}$  (9.7 min)

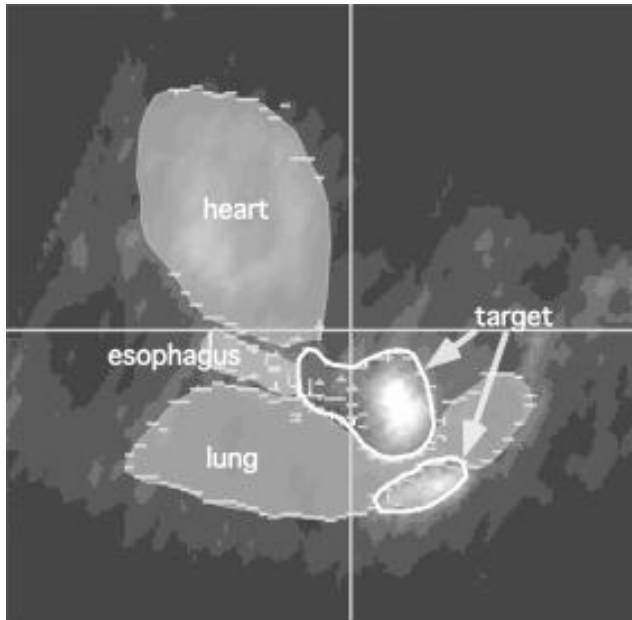
### Functionality imaged:

Metabolism: [F-18]FDG

Proliferation: [F-18]FLT

Hypoxia: [F-18]FMISO, [Cu-64/62]ATSM, [F-18]FAZA

## Positron emission tomography



In example of FDG-PET above, union of CT and PET information is considered as target.

$$SUV = \frac{C(\mu Ci / ml)}{(ID(\mu Ci) / w(Kg))}$$

dose in pixel

injected dose

patient weight

$SUV > 2.5 \Rightarrow$  tumor ??

Really need kinetic analysis to assess rate transfer coefficient!

## Parameters that determine consistency of nuclear medicine “product”

Patient parameters in time period (hours/days) prior to administration of radiopharmaceutical: Food intake , physical activity, glucose level (for PET in mg/dL).

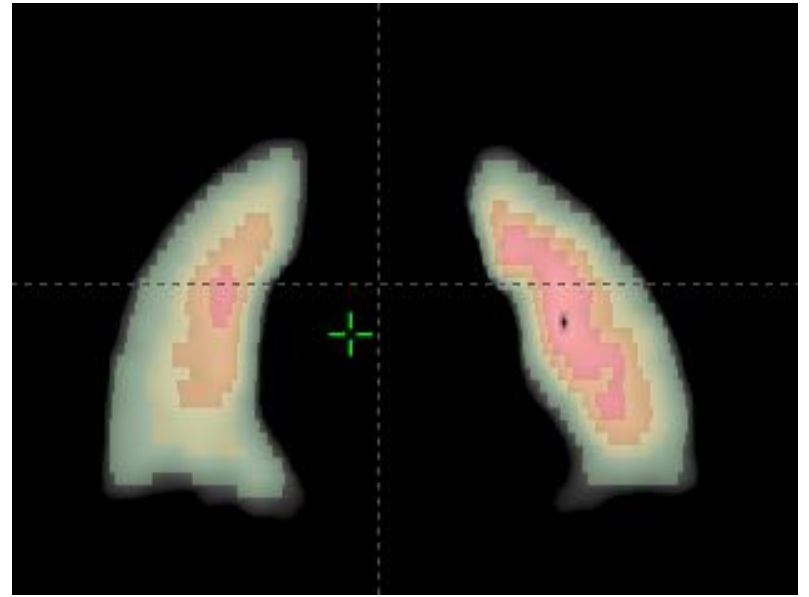
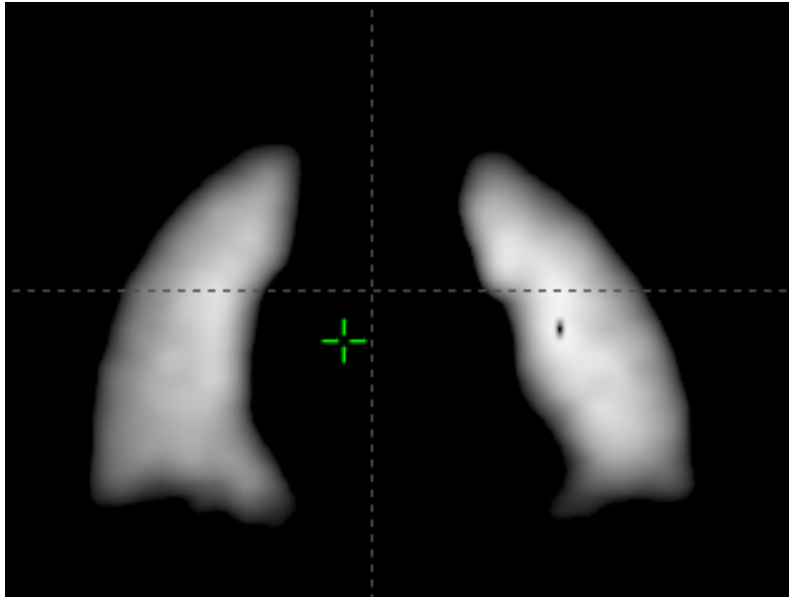
Dose administration parameters: Radiopharmaceutical dose administered (mCi/Kg), patient weight (Kg), route of administration, other drugs (muscle relaxants, pain medication, etc.)

Patient parameters in time period immediately post administration of radiopharmaceutical: Length of time period between radiopharmaceutical administration and scanning, room temperature, physical activity.

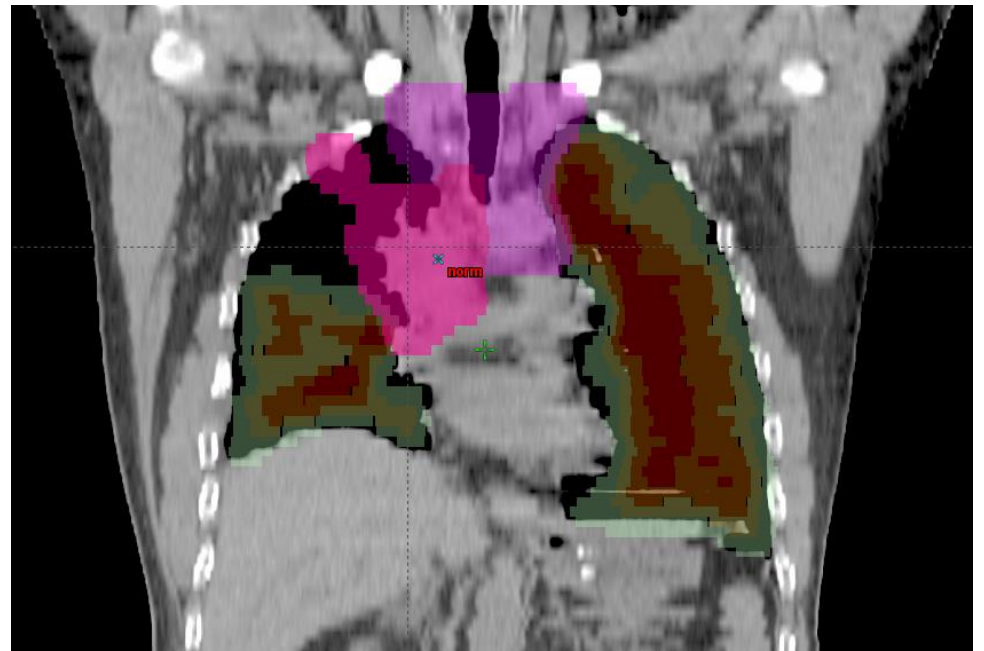
Imaging parameters: attenuation correction (via CT for CT-PET /CT-SPECT), image acquisition time (consistent time required for absolute quantities such as SUV/ SPECT signal), motion correction/ respiratory gating, image processing parameters (detector efficiency, system dead time, random coincidences, scatter, attenuation, sampling nonuniformity, and image smoothing).

Parameters in registration of PET/SPECT images to planning CT image: Immobilization (preferably same as for RT), alignment of PET/SPECT to CT in a combined modality machine.

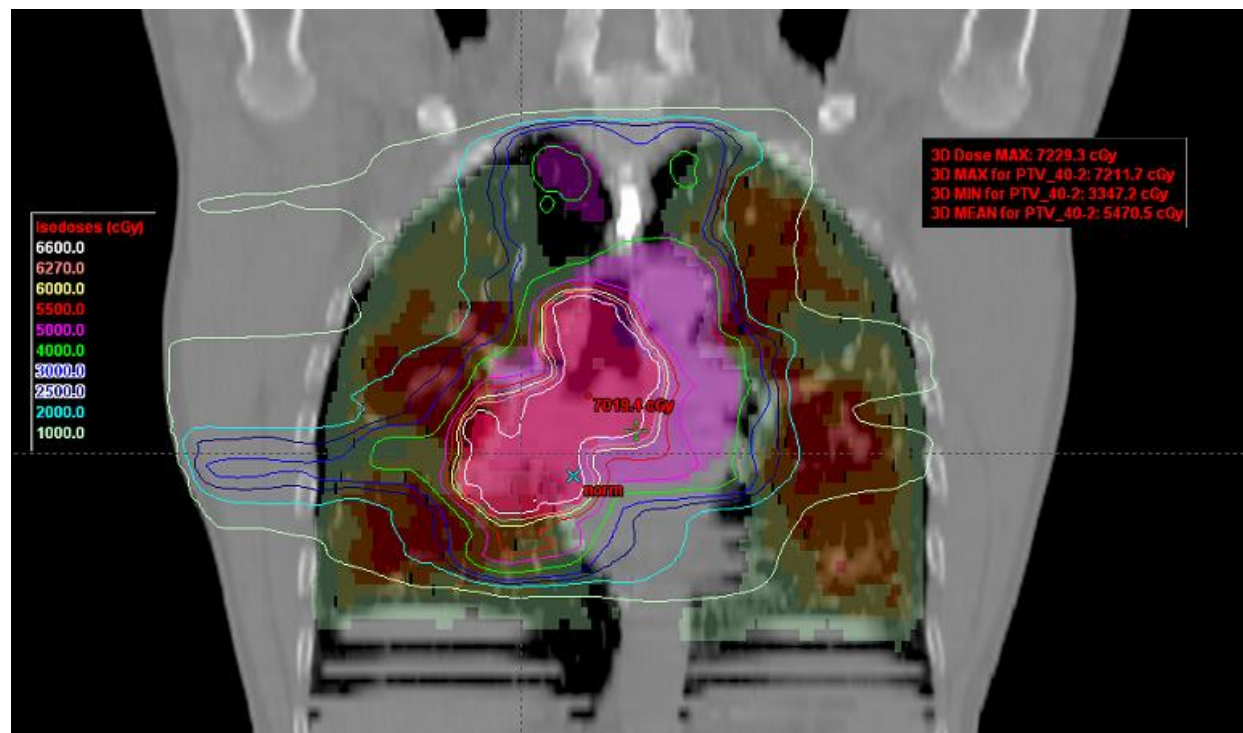
## SPECT



heterogeneous SPECT.....





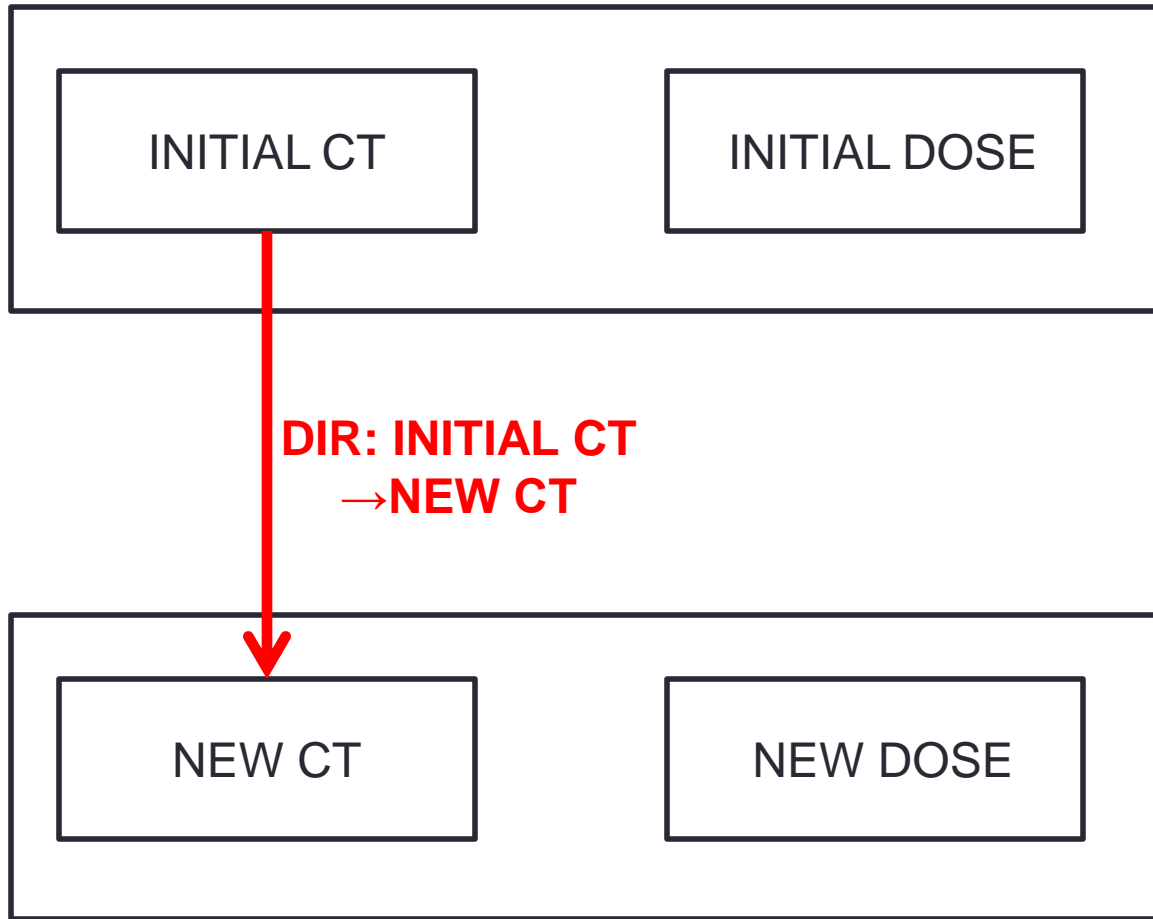


## Deformable Image Registration (DIR)

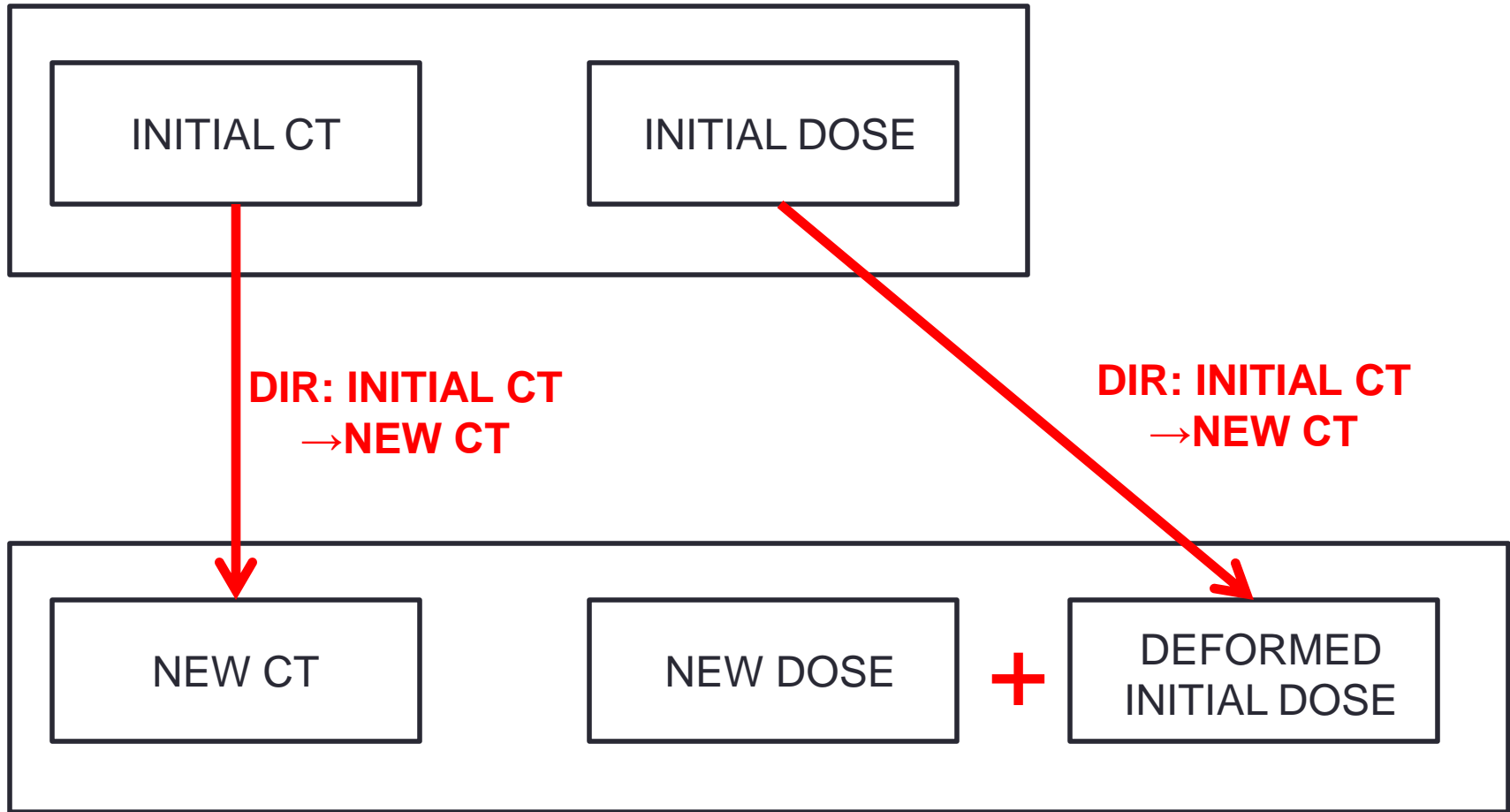
In what situations would DIR be useful?

- Patient comes back for re-treatment after some years and we need to “deform” old dose from old CT set onto new CT set to gauge how much more dose can be given.
- Patient anatomy changes during treatment. New CT set is acquired and new plan generated. Initial dose from initial CT set needs to be deformed to new CT set so the new plan dose and initial plan dose can be summed.

## Deformable Image Registration (DIR)



## Deformable Image Registration (DIR)



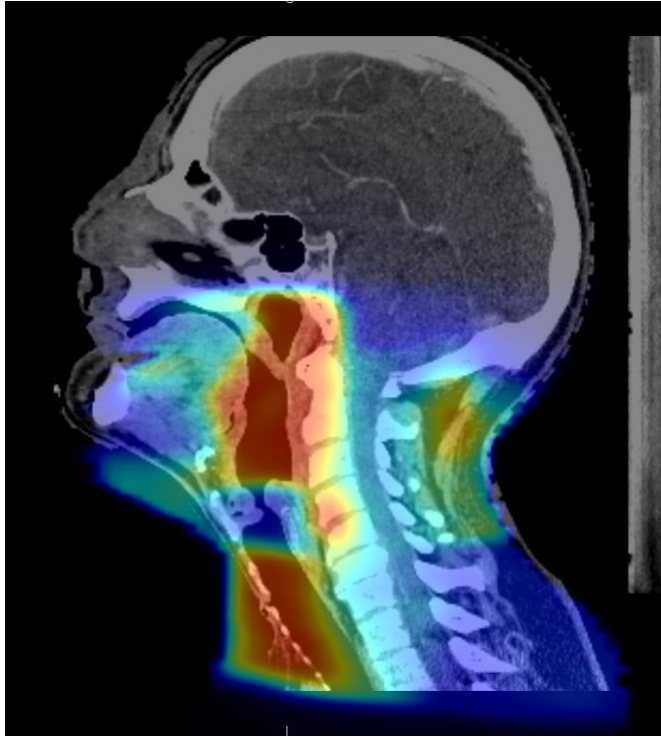
## Deformable Image Registration (DIR)



NEW CT

OLD CT

## Deformable Image Registration (DIR)



OLD DOSE  
SUPERIMPOSED ONTO  
NEW CT (RIGID  
REGISTRATION)



OLD DOSE  
SUPERIMPOSED ONTO  
NEW CT (DEFORMABLE  
REGISTRATION)

## Deformable Image Registration (DIR)

Things to watch out for ...

- DIR algorithms are yet to be fully physically validated.
- Some DIRs can result in non-physical “volume folding”.
- Deformations can be achieved in many different ways, so which one is closest to ground truth?

Commercial algorithms with DIR capability: Velocity AI, MIM VoxAlign, Raysearch, Varian.

Be careful..... DIR dose accumulation results should be taken as a “guideline”, rather than absolute truth.

## Image registration categories

- Purely manual - rigid registration.
- Purely automatic – rigid/deformable registration.
  - *Feature-based image registration.*
  - *Intensity-based image registration (most commonly used).*
- Semi-manual (automatic + manual) – rigid registration.
  - *Purely automatic followed by manual “tweaking”.*



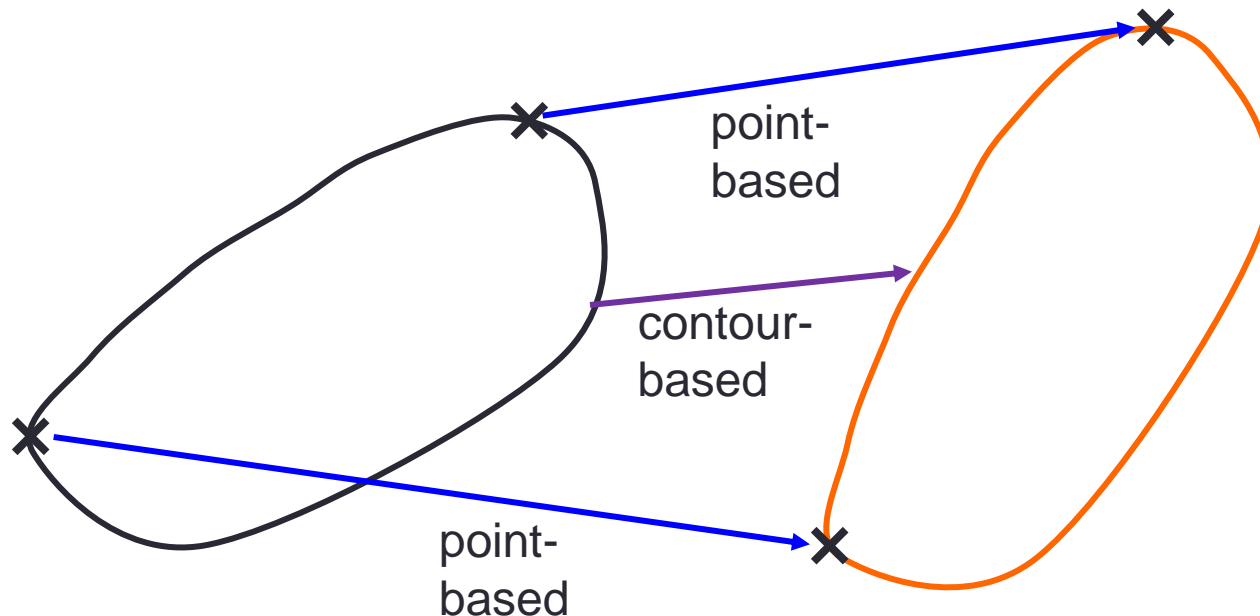
## ➤ Automatic Image Registration Techniques

- Feature-based image registration

- ❖ *Point-based matching (usually 2D images).*

- ❖ *Contour-based matching (based on manual or automatic segmentation).*

- ❖ *Chamfer (edge) matching, using edge detection software.*



## Feature-based image registration: Example of 2D point-based registration:

Anatomic feature-based registration for patient set-up in head and neck cancer radiotherapy. Sharp et. al, Physics in Medicine and Biology, 2005, Vol. 50, 4667-4679

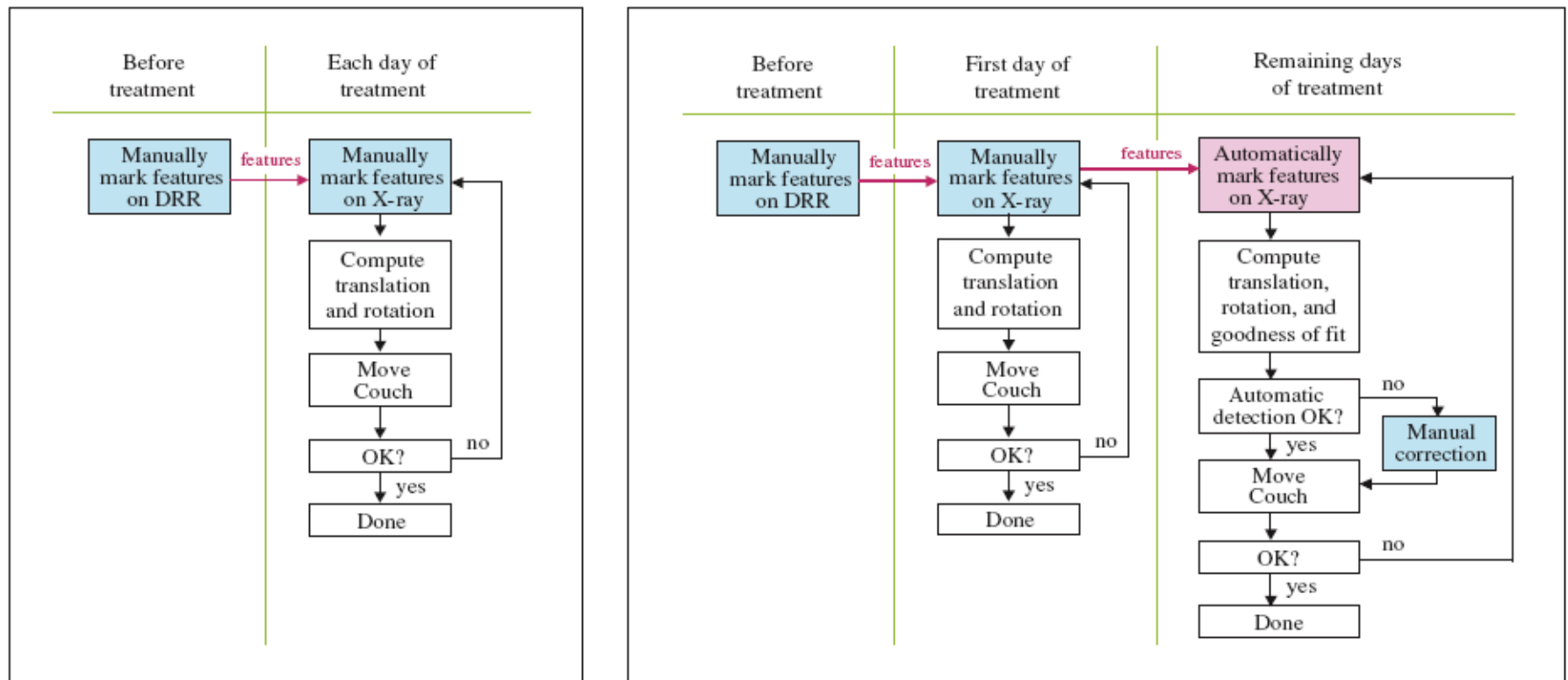
### **Abstract**

Modern radiotherapy equipment is capable of delivering high precision conformal dose distributions relative to isocentre. One of the barriers to precise treatments is accurate patient re-positioning before each fraction of treatment. At Massachusetts General Hospital, we perform daily patient alignment using radiographs, which are captured by flat panel imaging devices and sent to an analysis program. A trained therapist manually selects anatomically significant features in the skeleton, and couch movement is computed based on the image coordinates of the features. The current procedure takes about 5 to 10 min and significantly affects the efficiency requirement in a busy clinic. This work presents our effort to develop an improved, semi-automatic procedure that uses the manually selected features from the first treatment fraction to automatically locate the same features on the second and subsequent fractions. An implementation of this semi-automatic procedure is currently in clinical use for head and neck tumour sites. Radiographs collected from 510 patient set-ups were used to test this algorithm. A mean difference of 1.5 mm between manual and automatic localization of individual features and a mean difference of 0.8 mm for overall set-up were seen.

## Feature-based image registration: Example of 2D point-based registration:

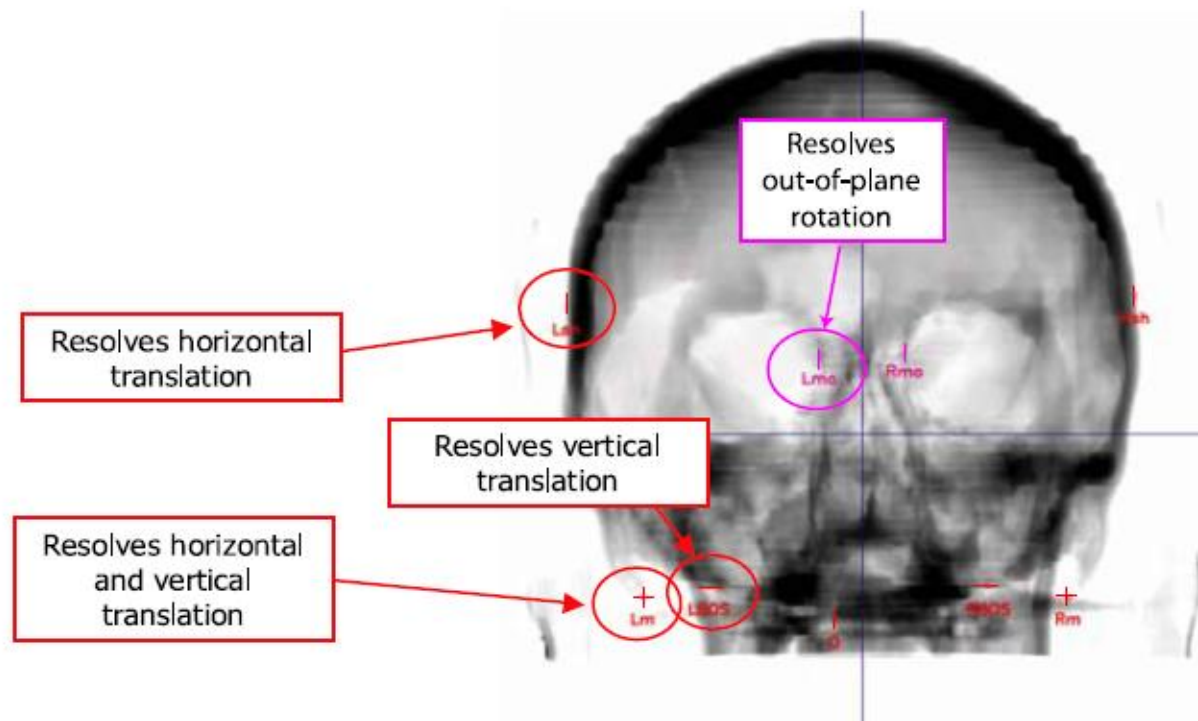
Anatomic feature-based registration for patient set-up in head and neck cancer radiotherapy.

Sharp et. al, Physics in Medicine and Biology, 2005, Vol. 50, 4667-4679



**Figure 1.** Current clinical process (left) and proposed clinical process (right).

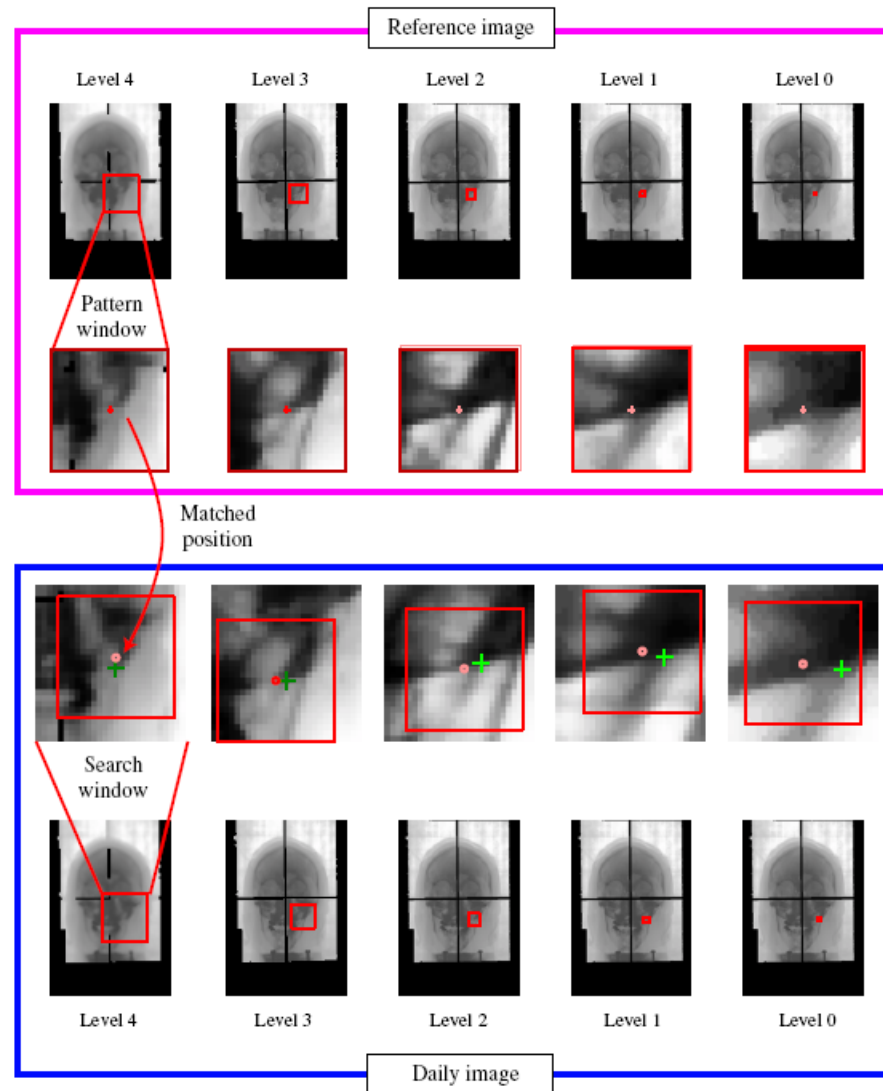
## Feature-based image registration: Example of 2D point-based registration:



Anatomic feature-based registration for patient set-up in head and neck cancer radiotherapy.

Sharp et. al, Physics in Medicine and Biology, 2005, Vol. 50, 4667-4679

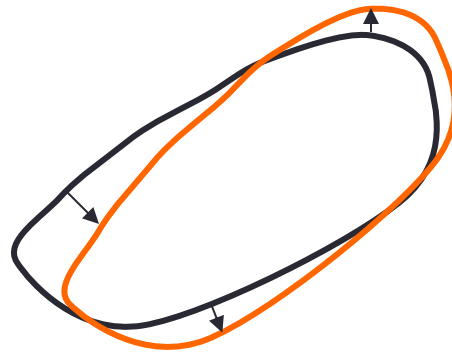
## Feature-based image registration: Example of 2D point-based registration:



**Figure 6.** For each feature, and at each resolution, a pattern window is defined in the reference image, and matched within a search window in the daily image. The computed match position at each level is shown by a circle. For comparison, the manually selected location of the same feature is marked with a plus sign.

## Feature-based image registration: Contour-based matching

Matches one contour to another (in 2D or 3D), so as to minimize the “difference” between them. (For example, difference could be the sum of square of distances from each point on one contour to the nearest point on the other contour).



Procedure is more laborious (hence slower) than point matching, since it requires human interaction for contour drawing.

Can be made less human-dependent by using automatic segmentation algorithms. However, automatic segmentation can be very error prone!

## Feature-based image registration: Contour-based matching

### Scenario:

- Patient is planned with CT image. Contours of interest are drawn on planning CT image.
- Images are acquired prior to each treatment (using either cone-beam computed tomography or CT-on-rails). Contours are drawn on these images.
- Contour-to-contour matching is performed between the planning CT and pre-treatment CT.
- Patient is shifted based on the contour matching, and then treated.



← bony matching or “soft tissue” (prostate) matching (based on your protocol). Increasingly, centers are adopting soft tissue matching.

## Feature-based image registration: Contour-based matching

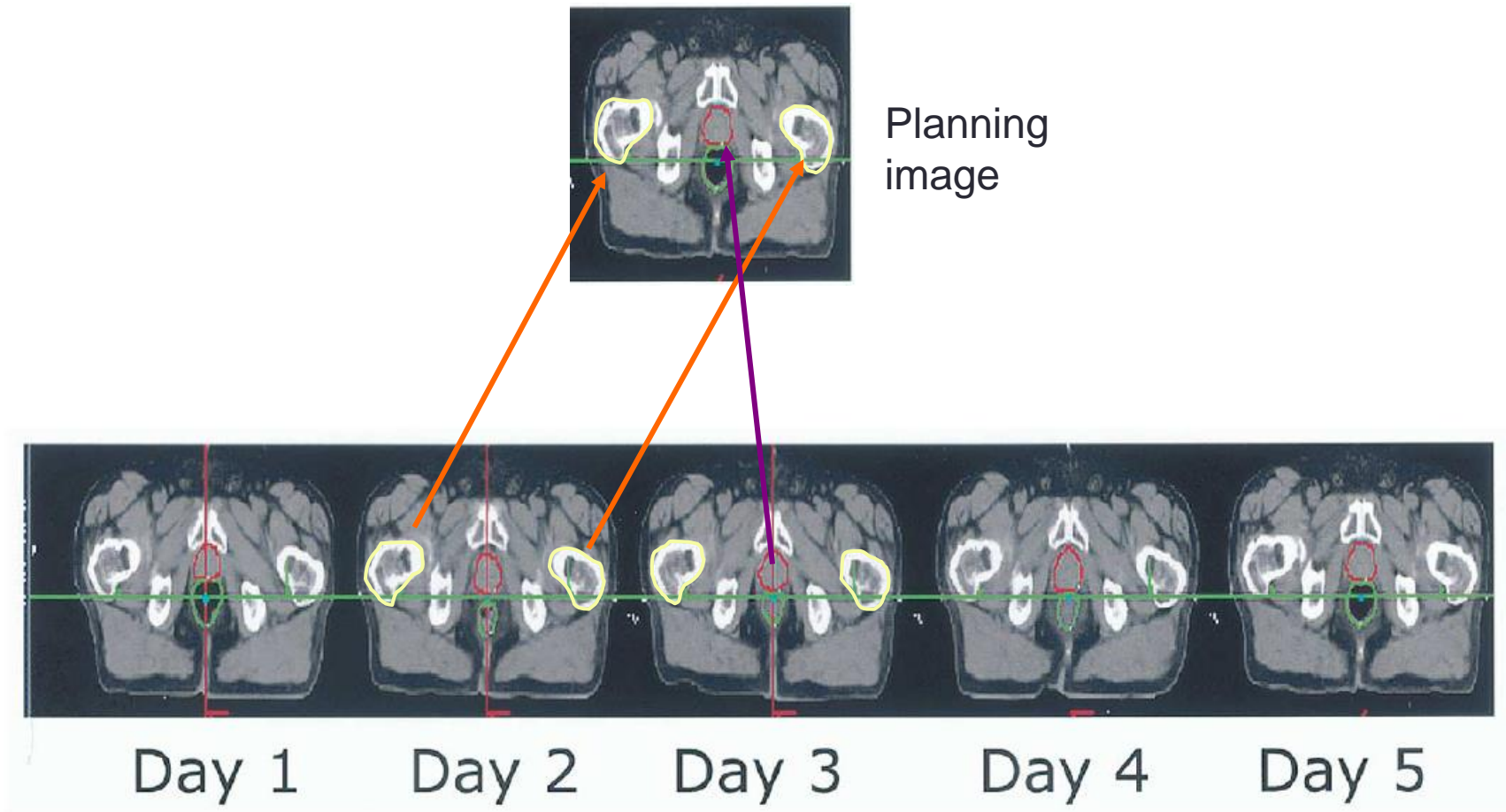
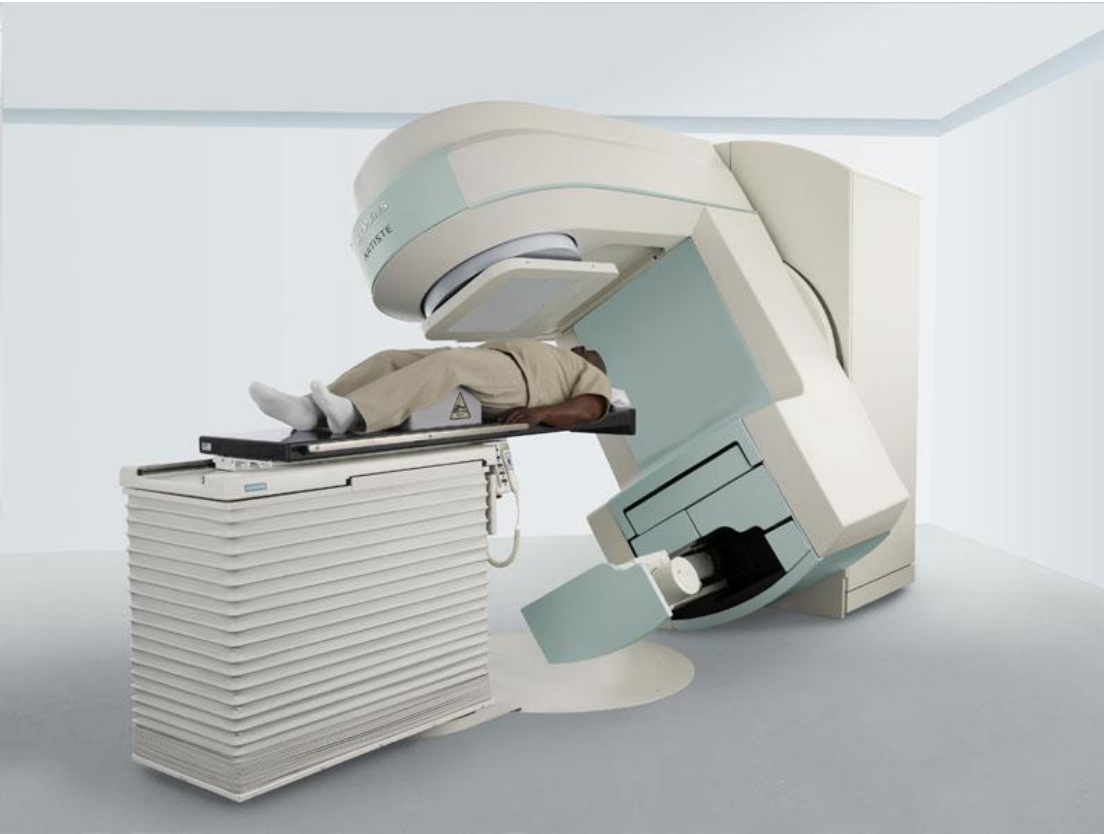


Fig. 3. Prostate and rectum position for 5 consecutive treatment days. Prostate outlined in red; rectum in green.

→ = bony matching

→ = soft tissue matching





SIEMENS ARTISTE



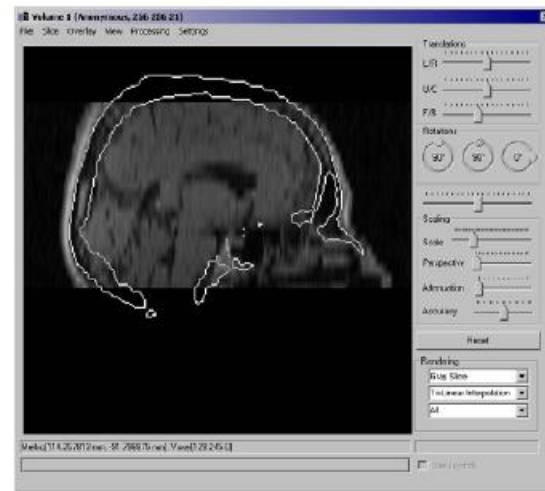
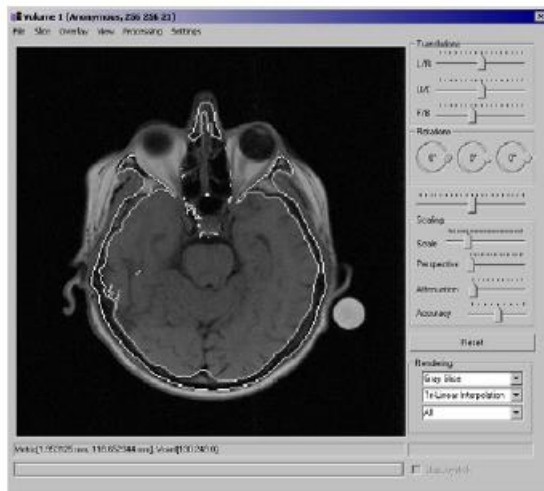
VARIAN CBCT SYSTEM

## Feature-based image registration: Chamfer-based matching

Use edge detection software to extract only the ridges/edges in the image.

Match the edges/ridges to each other.

Decreases the complexity from a full image to just a set of features.



## Intensity-based image registration

### ➤ Squared error

- minimizes the sum of squares of differences between intensity of images at corresponding pixel values
- Can only be used within the same imaging modality.

### ➤ Correlation

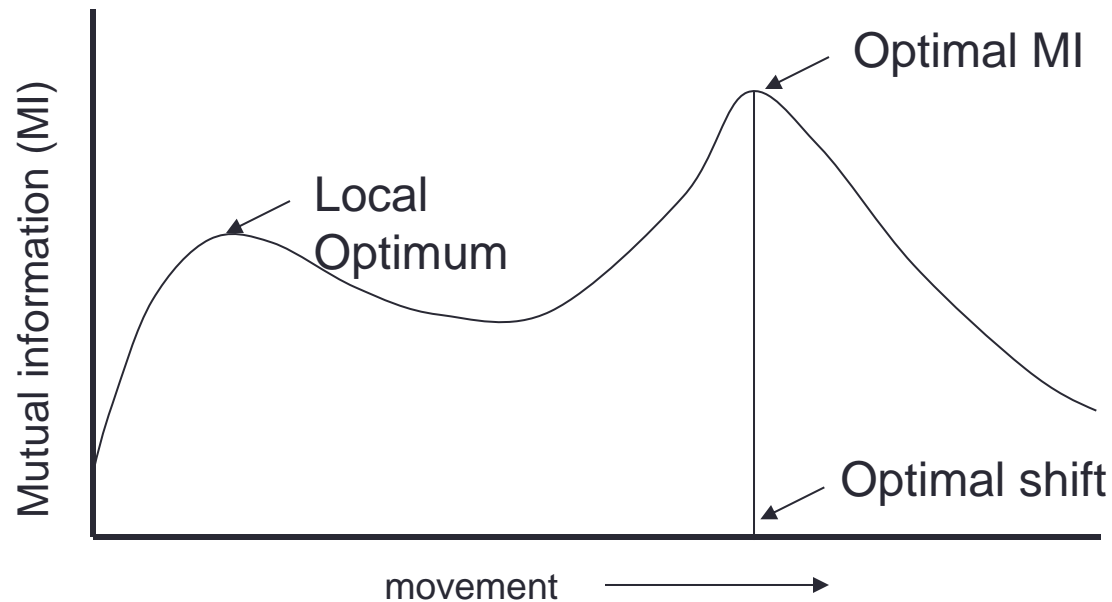
- Maximizes the correlation in coincidence of image intensities.
- Can be used between dissimilar imaging modalities, provided pixel intensities have the same relative order.

### ➤ Mutual information

- Maximizes the mutual information between two images.
- Can be used between dissimilar imaging modalities.

Optimization is used to move one image with respect to another, until the chosen criterion (above) is optimized (minimized/maximized)

For rigid body shift, there are 6 variables: 3 translations and 3 rotations.



As you can see, there is the danger of optimization techniques getting “stuck” at local optima.

## Intensity-based image registration: squared error (minimization)

Example: assume that the image on the right is the target image.....

$$SE = \sum_{i,j} \left( I_{i,j}^{\text{moving}} - I_{i,j}^{\text{target}} \right)^2$$

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

moving image

-

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

target image

## Intensity-based image registration: squared error (minimization)

Example: assume that the image on the right is the target image.....

$$SE = \sum_{i,j} \left( I_{i,j}^{\text{moving}} - I_{i,j}^{\text{target}} \right)^2$$

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0

moving image

-

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

target image

=

0	1	2	2	2	2	2	2	1	0
0	0	1	2	2	2	2	1	0	0
0	0	0	1	2	2	1	0	0	0
0	0	0	0	1	1	0	0	0	0
0	0	0	0	-1	-1	0	0	0	0
0	0	0	-1	-2	-2	-1	0	0	0
0	0	-1	-2	-2	-2	-2	-1	0	0
0	-1	-2	-2	-2	-2	-2	-2	-1	0
-1	-2	-2	-2	-2	-2	-2	-2	-2	-1
-1	-1	-1	-1	-1	-1	-1	-1	-1	-1

SE = 156

## Intensity-based image registration: squared error (minimization)

Imagine that the moving image is shifted down by one pixel .....

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0

moving image

-

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

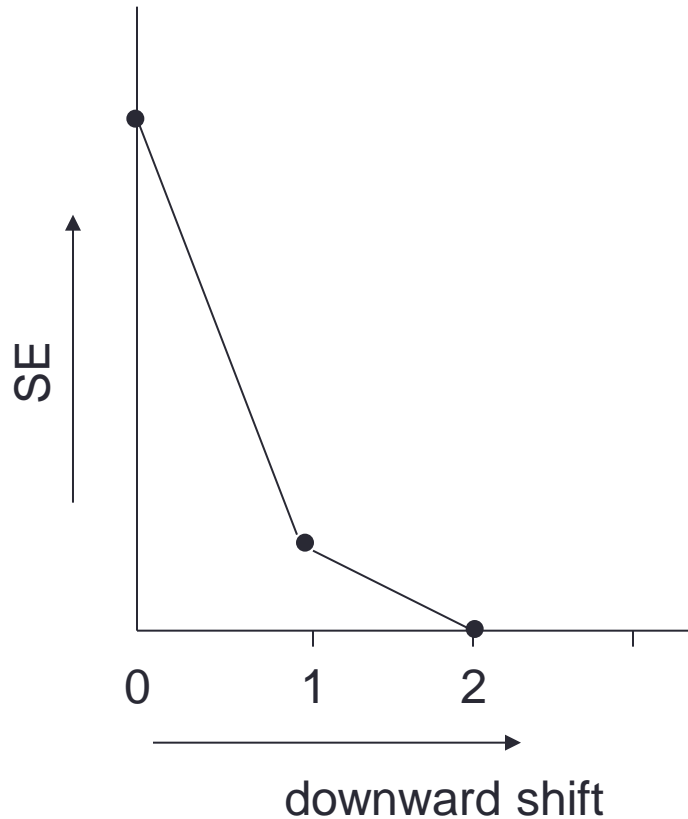
target image

=

0	1	1	1	1	1	1	1	1	0
0	0	1	1	1	1	1	1	0	0
0	0	0	1	1	1	1	0	0	0
0	0	0	0	1	1	0	0	0	0
0	0	0	0	0	0	0	0	0	0
0	0	0	0	-1	-1	0	0	0	0
0	0	0	-1	-1	-1	-1	0	0	0
0	0	-1	-1	-1	-1	-1	-1	0	0
0	-1	-1	-1	-1	-1	-1	-1	-1	0
-1	-1	-1	-1	-1	-1	-1	-1	-1	-1

SE = 50

## Intensity-based image registration: squared error (minimization)



An optimization algorithm would make these shifts “intelligently”. For example, gradient descent algorithms would sequentially choose shift directions that lie close to the steepest descent path.



## Intensity-based image registration: cross-correlation (maximization)

In general, the cross-correlation between two variables  $x$  and  $y$  (equal number of entries for each variable) is:

$$CC = \frac{\overset{\text{expectation}}{E}((x - \overset{\text{mean of } y}{\bar{x}})(y - \bar{y}))}{\underset{\text{std dev of } y}{\sigma_x \sigma_y}}$$

$$CC = \frac{\sum_i (x_i - \bar{x})(y_i - \bar{y})}{\left(\sum_i (x_i - \bar{x})^2\right)^{1/2} \left(\sum_i (y_i - \bar{y})^2\right)^{1/2}}$$

list of pixel values in moving image

list of pixel values in target image

## Intensity-based image registration: cross-correlation (maximization)

For a 0 pixel shift .....

moving image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0

$$\bar{x} = 1.92$$

target image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

$$\bar{y} = 2.20$$

$$CC = 0.5812$$

## Intensity-based image registration: cross-correlation (maximization)

For a 1 pixel shift .....

moving image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0

$$\bar{x} = 2.10$$

target image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

$$\bar{y} = 2.20$$

$$CC = 0.8443$$

## Intensity-based image registration: cross-correlation (maximization)

For a 2 pixel shift .....

moving image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

$$\bar{x} = 2.2$$

target image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

$$\bar{y} = 2.2$$

$$CC = 1.0000$$

## Intensity-based image registration: Mutual Information (MI) (maximization)

$$MI(A, B) = \sum_{i_a, i_b} p_{AB}(i_a, i_b) \log_2 \left( \frac{p_{AB}(i_a, i_b)}{p_A(i_a) p_B(i_b)} \right)$$

image A  
(moving)

image B  
(target)

intensity  
level in  
image A

The diagram illustrates the components of the Mutual Information (MI) formula. Three arrows point from text labels to specific parts of the equation: one from 'image A (moving)' to the 'A' in  $MI(A, B)$ , one from 'image B (target)' to the 'B' in  $MI(A, B)$ , and one from 'intensity level in image A' to the  $i_a$  term in the joint probability  $p_{AB}(i_a, i_b)$ .

Entropy of information (Shannon entropy) is a measure of information content.

$$H = -\sum p \log(p)$$

For example, if there are 2 alphabets in a word:

$$A = 0.5, B = 0.5$$

$$H = -0.5 \times \log(0.5) - 0.5 \times \log(0.5) = 0.69$$

$$A = 0.8, B = 0.2$$

$$H = -0.8 \times \log(0.8) - 0.2 \times \log(0.2) = 0.50 \text{ (less information!)}$$

Trivia: the English language is 75% redundant, i.e., information is duplicated.

## Intensity-based image registration: Mutual Information (MI) (maximization)

For a 0 pixel shift .....

moving image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0

target image

1	1	1	1	1	1	1	1	1	1
1	2	2	2	2	2	2	2	2	1
1	2	3	3	3	3	3	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	5	5	4	3	2	1
1	2	3	4	4	4	4	3	2	1
1	2	3	3	3	3	3	3	2	1
1	2	2	2	2	2	2	2	2	1
1	1	1	1	1	1	1	1	1	1

$$\begin{array}{cccccc}
 0 & 1 & 2 & 3 & 4 & 5 \\
 \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow \\
 count_A = \{20, 24, 20, 20, 12, 4\}
 \end{array}$$

$$count_B = \{0, 36, 28, 20, 12, 4\}$$

$$p_A = \{0.20, 0.24, 0.20, 0.20, 0.12, 0.04\} \quad p_B = \{0, 0.36, 0.28, 0.20, 0.12, 0.04\}$$

$$\begin{array}{c}
 \text{moving} \\
 \longleftrightarrow \\
 \text{count}_{AB} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 12 & 16 & 2 & 6 & 0 & 0 \\ 8 & 2 & 12 & 2 & 4 & 0 \\ 0 & 6 & 2 & 8 & 2 & 2 \\ 0 & 0 & 4 & 2 & 4 & 2 \\ 0 & 0 & 0 & 2 & 2 & 0 \end{bmatrix} \begin{array}{c} \updownarrow \\ \text{target} \end{array}
 \end{array}$$

$$p_{AB} = \begin{bmatrix} 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 \\ 0.12 & 0.16 & 0.02 & 0.06 & 0.00 & 0.00 \\ 0.08 & 0.02 & 0.12 & 0.02 & 0.04 & 0.00 \\ 0.00 & 0.06 & 0.02 & 0.08 & 0.02 & 0.02 \\ 0.00 & 0.00 & 0.04 & 0.02 & 0.04 & 0.02 \\ 0.00 & 0.00 & 0.00 & 0.02 & 0.02 & 0.00 \end{bmatrix}$$



$$\begin{aligned}
 p_A &= \{0.20, & 0.24, & 0.20, & 0.20, & 0.12, & 0.04\} \\
 p_{AB} &= \begin{bmatrix} 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 \\ 0.12 & 0.16 & 0.02 & 0.06 & 0.00 & 0.00 \\ 0.08 & 0.02 & 0.12 & 0.02 & 0.04 & 0.00 \\ 0.00 & 0.06 & 0.02 & 0.08 & 0.02 & 0.02 \\ 0.00 & 0.00 & 0.04 & 0.02 & 0.04 & 0.02 \\ 0.00 & 0.00 & 0.00 & 0.02 & 0.02 & 0.00 \end{bmatrix} p_B = \begin{Bmatrix} 0, \\ 0.36, \\ 0.28, \\ 0.20, \\ 0.12, \\ 0.04 \end{Bmatrix}
 \end{aligned}$$

$$\text{MI} = 0.5889$$

For a 0 pixel shift:  $MI = 0.5889$

For a 1 pixel shift:  $MI = 0.9004$

For a 2 pixel shift:  $MI = 2.0620$

For 2 images that are exactly the same (same modality, same pixel intensity distribution), the maximum MI value is dependent on the way the image “looks”, i.e., there is no predefined maximum.

This is different from cross-correlation, where the maximum CC value is = 1 for the same imaging modality.

## 3D Dose Computation Algorithms

Clarkson type methods: Based on a very basic empirical calculation strategy (refer to Khan). Fast, but least accurate of methods.

Pencil beam algorithm: Used for fast 3D computation, IMRT optimization. Based on fitting the unknown parameters of some physically “realistic” pencil beam function.

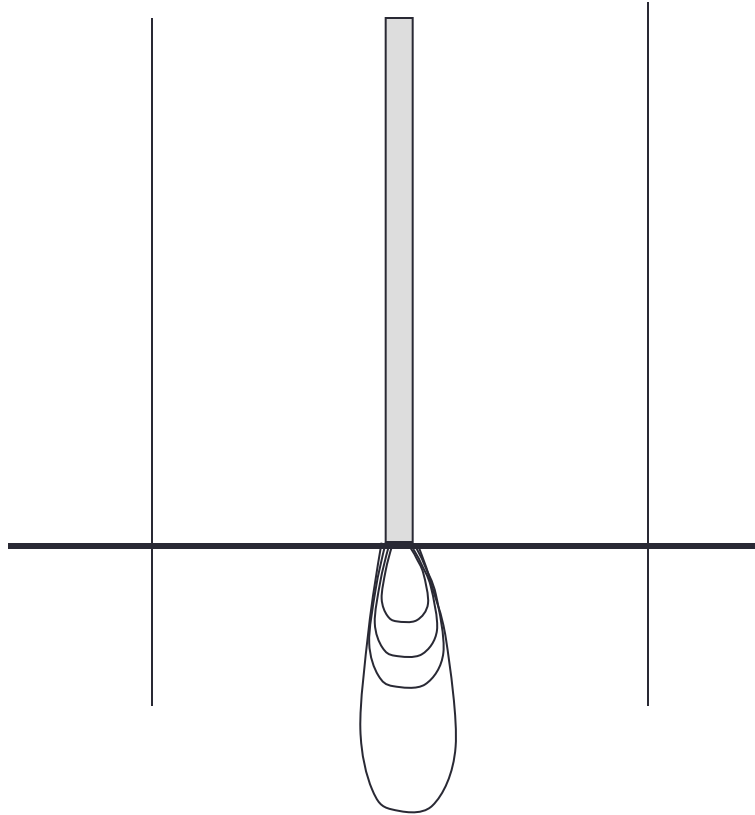
Convolution-superposition algorithm: 3D/ IMRT. Based on more rigorous physical principles than Pencil beam algorithm (fewer assumptions). More accurate/slower than pencil beam.

Monte Carlo: 3D/IMRT retrospective verification (not IMRT optimization – too slow!). Almost no assumptions. Most accurate. Very slow. (some commercial systems are coming up with Monte Carlo for electron dosimetry).

Computational  
Expense



## Pencil Beam Algorithm



The contribution from each “pencil” can be multiplied by its corresponding fluence and then added together to compute dose from the full beam.

We shall start with a pencil beam model that does not account for off-axis beam quality change, and add in this effect later on.

Several different pencil beam algorithms are currently being utilized.

*Medical physics*

## Photon pencil kernel parameterisation based on beam quality index

Tufve Nyholm<sup>a</sup>, Jörgen Olofsson<sup>a</sup>, Anders Ahnesjö<sup>a,b</sup>, Mikael Karlsson<sup>a,\*</sup>

<sup>a</sup>Department of Radiation Sciences, Radiation Physics, Umeå University, Umeå, Sweden, <sup>b</sup>Nucletron Scandinavia, Uppsala, Sweden

Ahnesjö et al.

uses depth dose measurements and phantom scatter factors to estimate the energy distribution, and then uses the spectrum to get a radially parameterised pencil beam kernels from Monte Carlo simulations [5,6].

Based  
on this  
original  
model

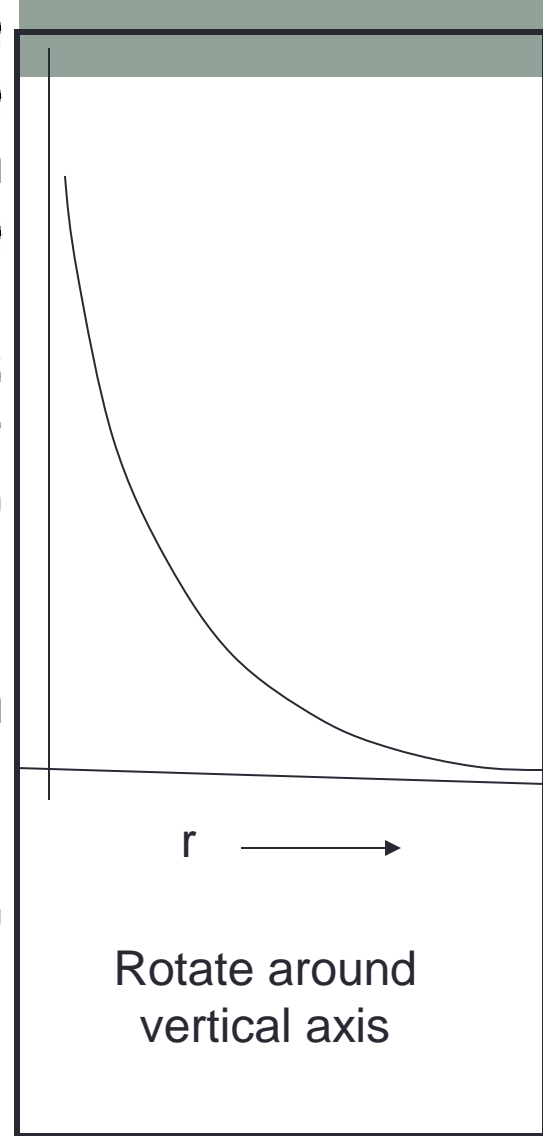
$\frac{\text{TMR}(\text{FS}=10, d=20)}{\text{TMR}(\text{FS}=10, d=10)}$

The aim of this work is to derive a parameterisation of a pencil dose deposition kernel expressed in terms of the beam quality index  $\text{TPR}_{20/10}$ , in order to simplify commissioning, and reduce the risk for errors.

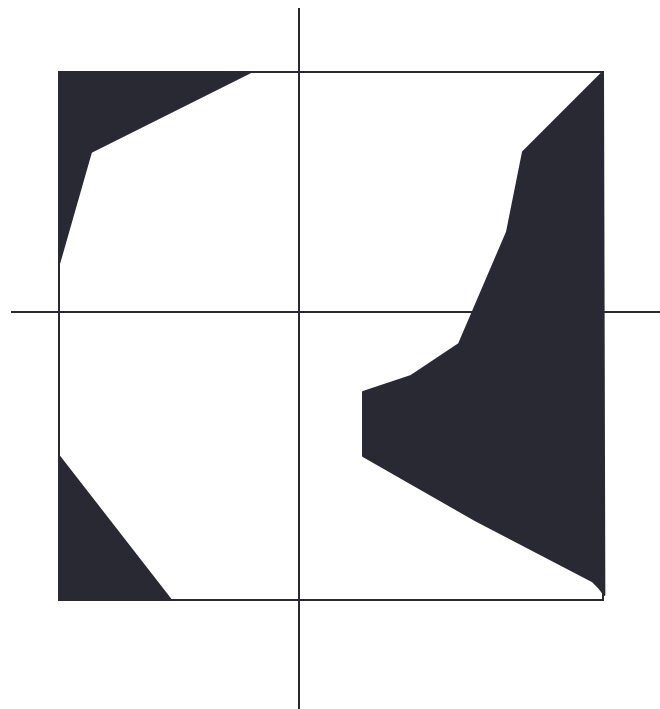
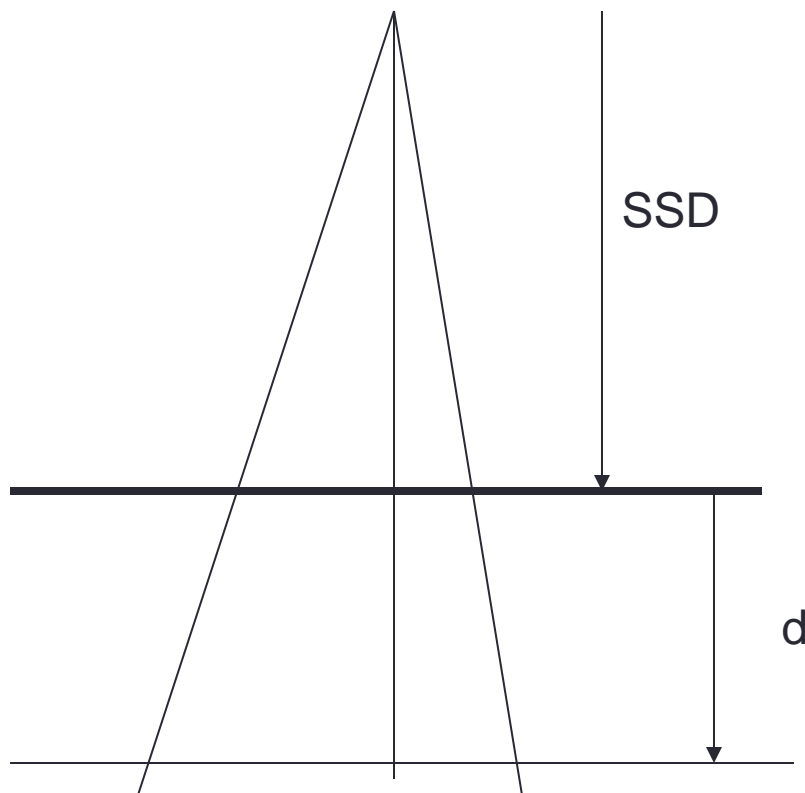
This work is based on data measured by customers of the Helax TMS (Nucletron) for beam characterization. The processing of the data for these customers have been performed centralized through the vendor, which have resulted in an extensive database of measured and processed data [10]. The parts of the measured datasets used in this work are depth doses and output factors in water and air for four different field sizes ( $5 \times 5$ ,  $10 \times 10$ ,  $15 \times 15$  and  $20 \times 20 \text{ cm}^2$ ). The beam characterization process produces a set of pencil kernel values for each individual beam. The pencil kernels are based on a radial parameterisation according to

$$\frac{p}{\rho}(r, d) = \left( \frac{A(d)\exp[-a(d)r] + B(d)\exp[-b(d)r]}{r} \right) \quad (1)$$

where  $d$  is the calculation depth,  $r$  is the radius, and  $A$ ,  $B$ ,  $a$ , and  $b$  are depth dependent parameters which are tabulated for depth ( $d$ ) between 0.075 and 50 cm in 0.15 cm steps. The parameterisation provides a separation between primary and scatter dose, such that the first term models the primary and the second the scatter dose.

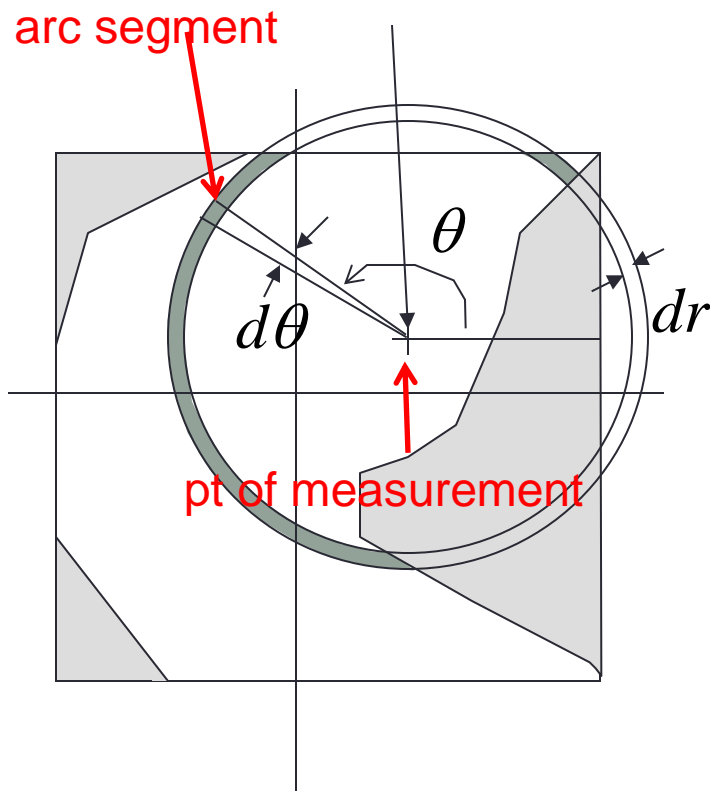


How do you compute the dose at any point from some beam shape?



Contribution of dose from each arc segment is added to the point of measurement.

Arc segments are included in the open section and included with attenuation in the blocked sections.



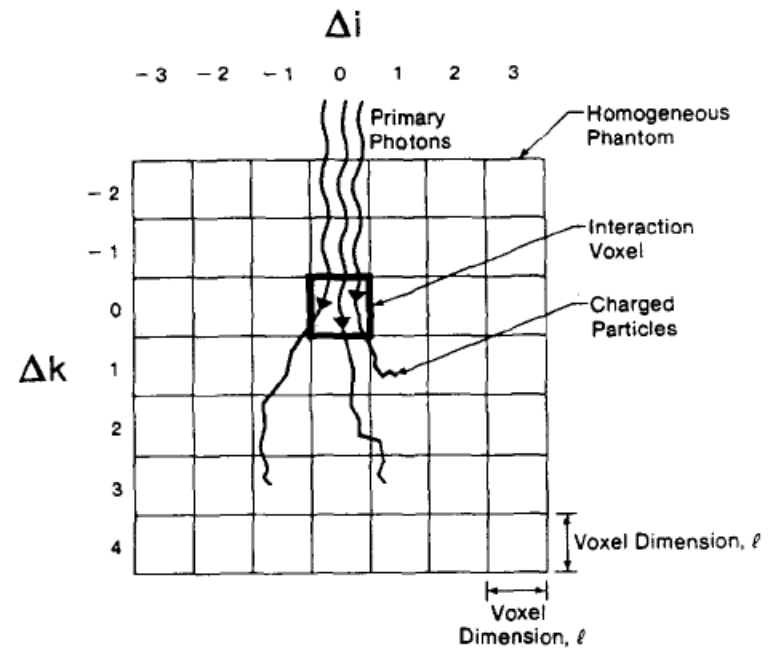
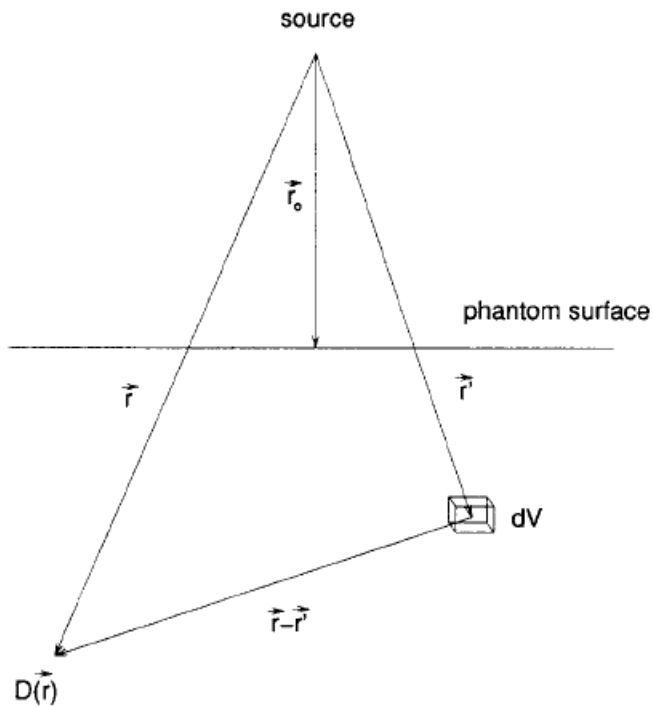
Integrate for each ring the part that has fluence.

Start with a ring radius =  $dr$ , and keep increasing ring radius in steps of  $dr$ , until the ring is completely without fluence.

Dose can be computed to points inside or outside block.



# Convolution Superposition Algorithm



creates a dose  
interaction kernel

# **A convolution method of calculating dose for 15-MV x rays**

T. R. Mackie,<sup>a)</sup> J. W. Scrimger, and J. J. Battista

*Department of Medical Physics, Cross Cancer Institute, Edmonton, Alberta, Canada T6G 1Z2*

(Received 1 May 1984; accepted for publication 14 August 1984)

Arrays were generated using the Monte Carlo method representing the energy absorbed throughout waterlike phantoms from charged particles and scatter radiation set in motion by primary interactions at one location. The resulting "dose spread arrays" were normalized to the collision fraction of the kinetic energy released by the primary photons. These arrays are convolved with the relative primary fluence interacting in a phantom to obtain three-dimensional dose distributions. The method gives good agreement for the 15-MV x-ray dose in electronic disequilibrium situations, such as the buildup region, near beam boundaries, and near low-density heterogeneities.

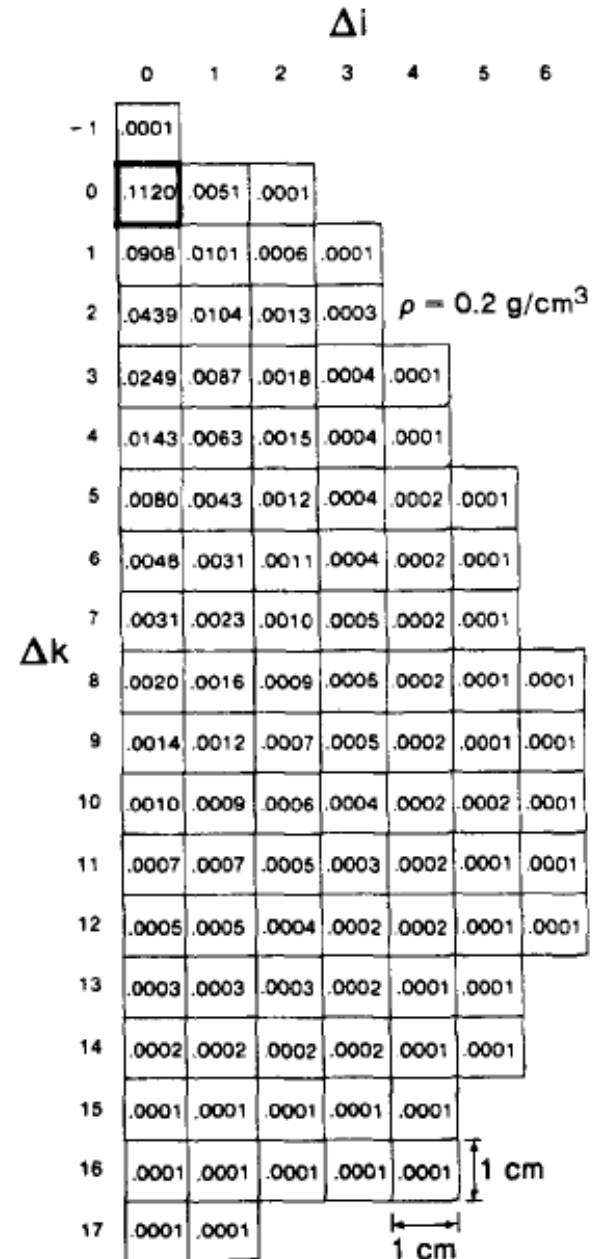
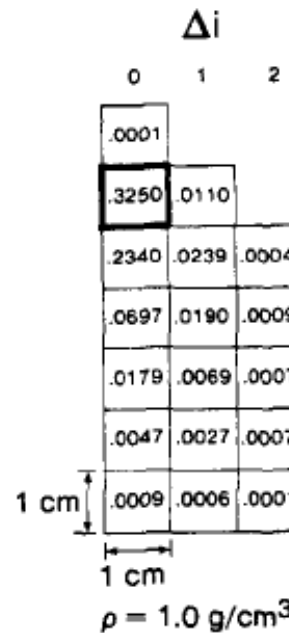
## PRIMARY DOSE SPREAD ARRAY

Kernels for 15 MV beam,  
with different voxel sizes.

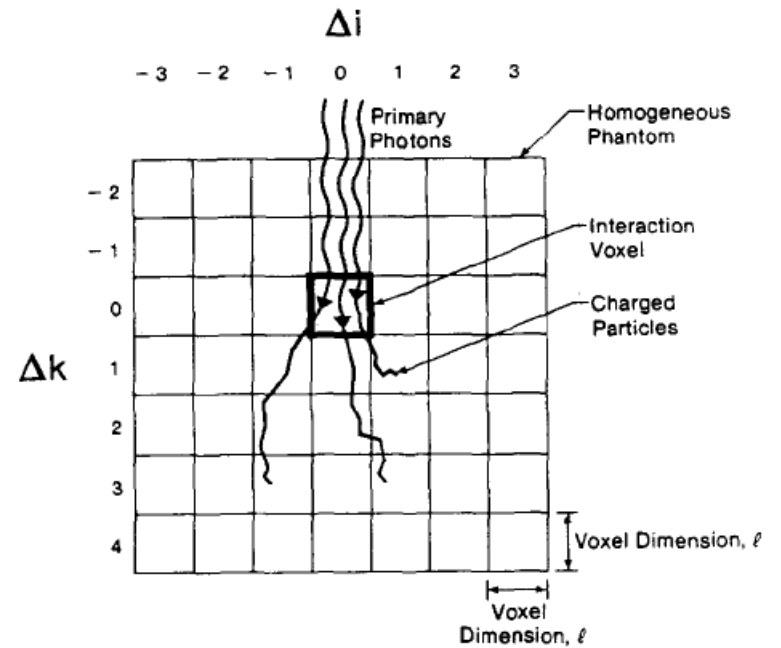
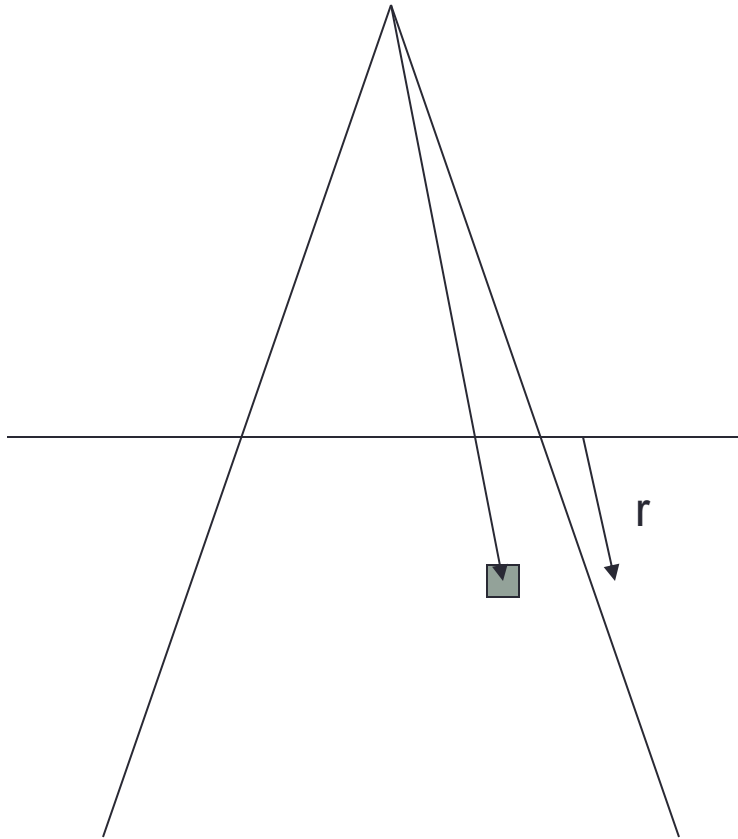
The kernels are only given in  
2 dimensions, but they are  
quadrilaterally symmetric.

Value in each pixel is  
normalized to TERMA (total  
energy released per unit  
mass).

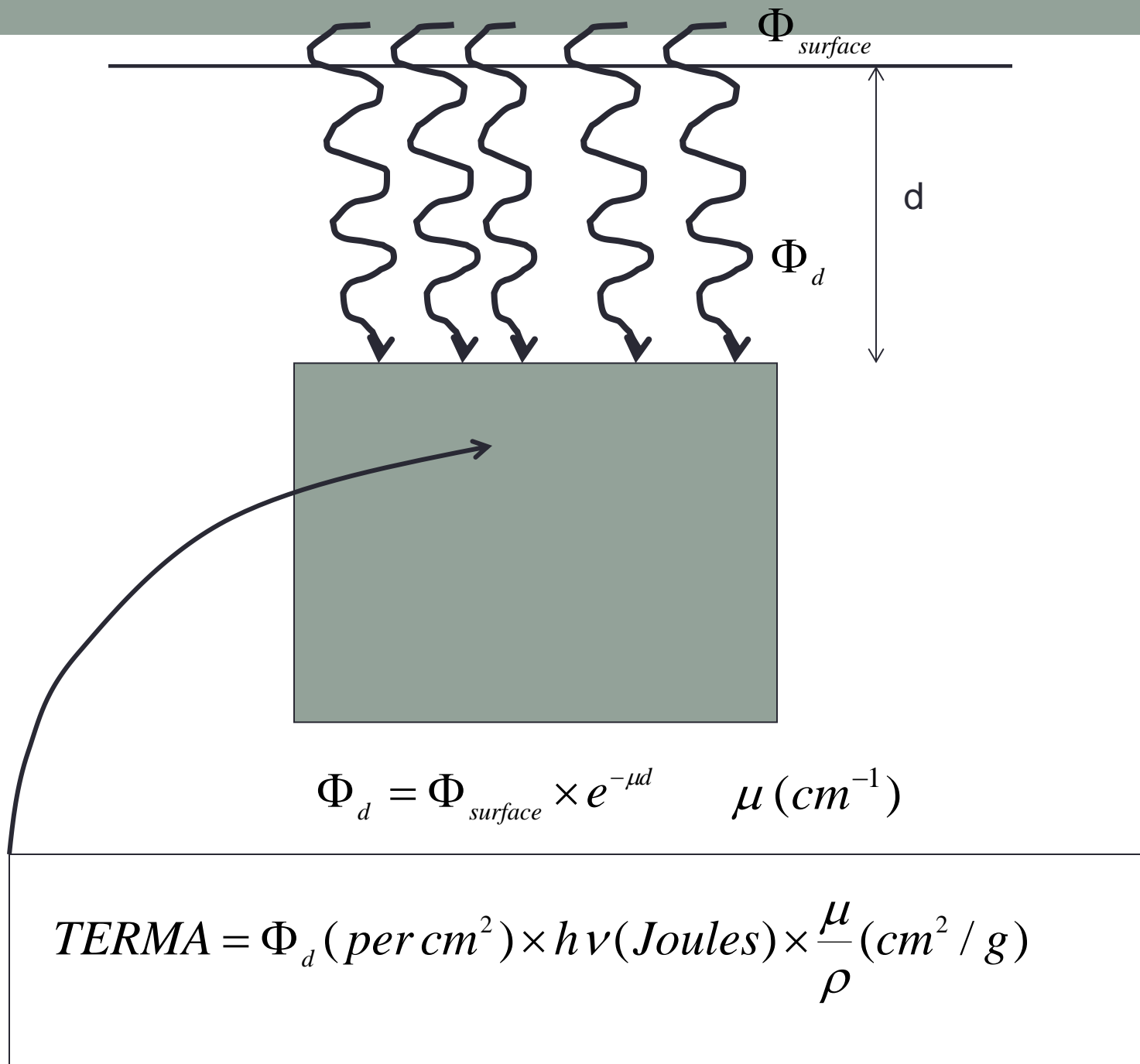
A primary dose spread array (analogous to the point  
spread array used in image processing) is the three-dimen-  
sional spatial distribution of energy deposited by electrons  
and positrons which spread from the site of the primary pho-  
ton interactions. It is generated by tracking the motion of



How do you figure out TERMA for a voxel?



$$\text{TERMA} = \text{fluence@voxel} \times \text{photon\_energy} \times (\text{mass\_attenuation/density})$$



### **III. SCATTER DOSE SPREAD ARRAYS**

The Monte Carlo program used to determine the primary dose spread arrays is also used to follow scattered photons and charged particles produced by the scatter photon interactions. The first scattered dose is scored separately from higher order multiple scatter. The dose due to first-scatter photons, which is deposited relatively close to the primary interaction site, is placed in a truncated first-scatter (TFS) dose spread array. The first-scatter dose deposited relatively far from the primary interaction site is included with multiple scatter in a residual first- and multiple-scatter (RFMS) dose spread array. Positron annihilation photons are treated

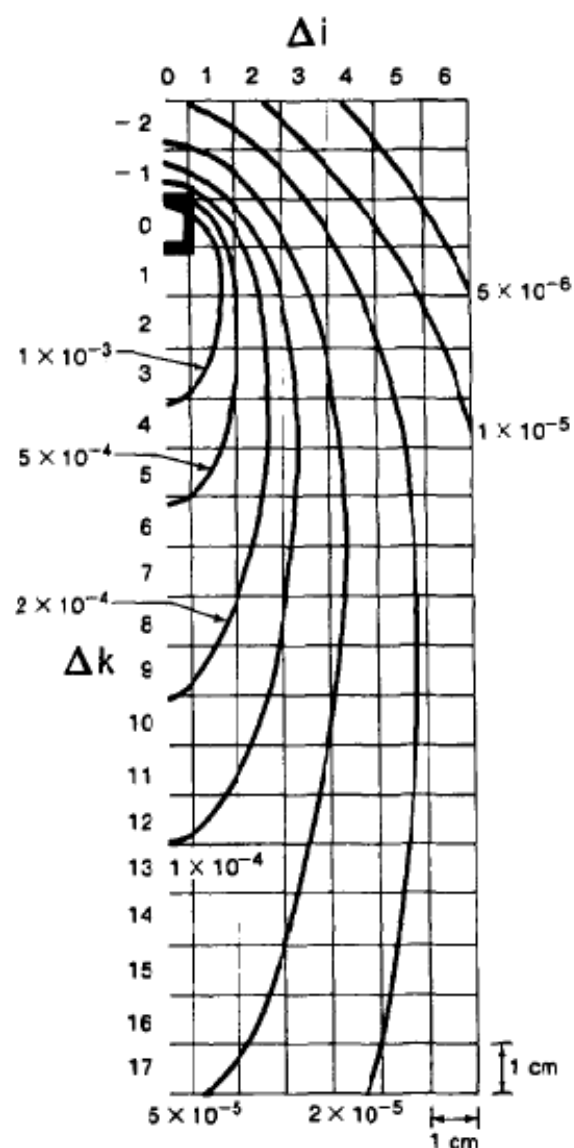


FIG. 4. Truncated first-scatter (TFS) dose spread array in isodose format.  $\rho = 1.0 \text{ g/cm}^3$ ;  $\rho \cdot l = 1.0 \text{ g/cm}^2$ .

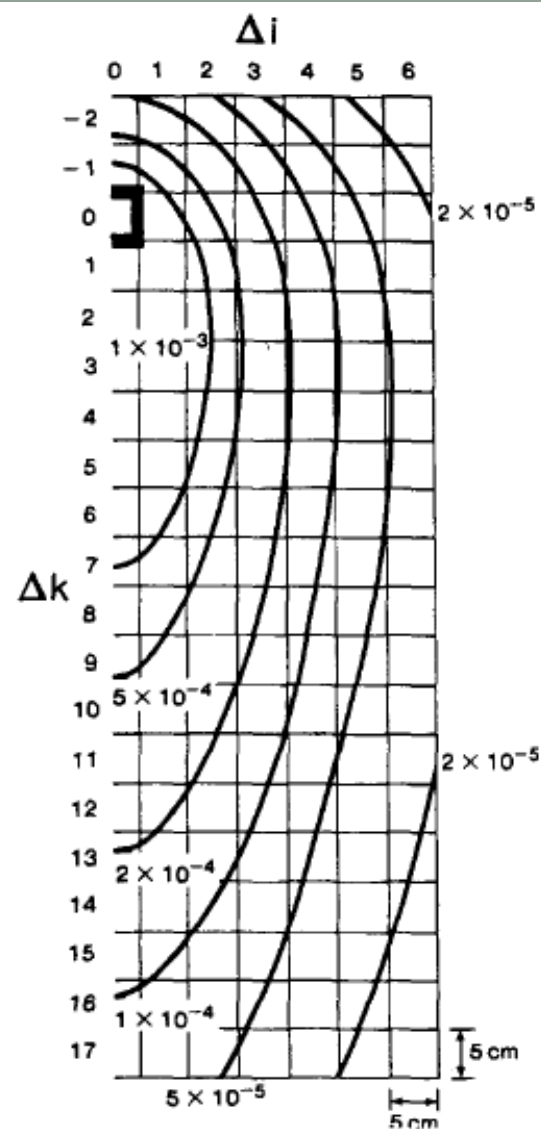


FIG. 5. Residual first- and multiple-scatter (RFMS) dose spread array in isodose format.  $\rho = 1.0 \text{ g/cm}^3$ ;  $\rho \cdot l = 5.0 \text{ g/cm}^2$ .

## Accounting for Tissue Heterogeneities

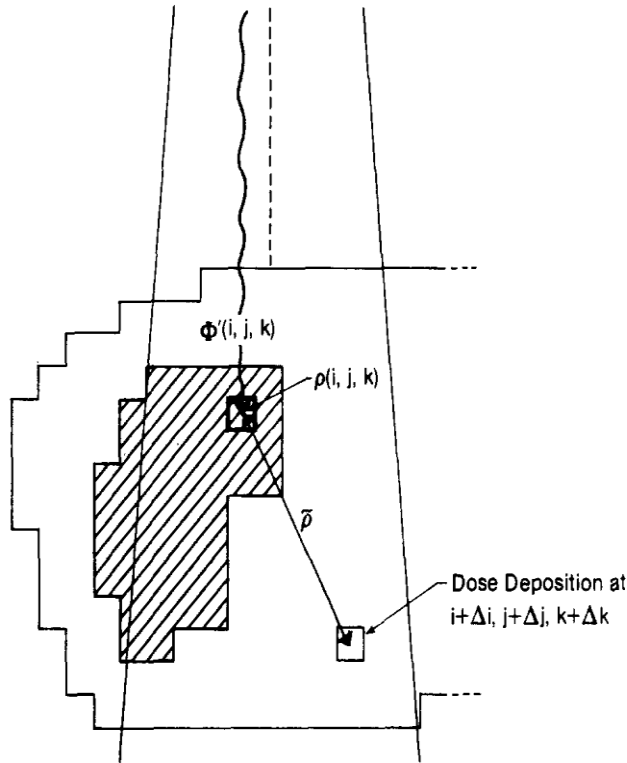


FIG. 11. Illustration of the extension of the algorithm to waterlike heterogeneous media.  $\tilde{\rho}$  is the average density between the interaction and dose deposition voxels.

Dose contribution  $(i + \Delta i, j + \Delta j, k + \Delta k)$

$$\propto \Phi'(i, j, k) \frac{\rho(i, j, k)}{\tilde{\rho}} Ap(\tilde{\rho} \cdot l, \Delta i, \Delta j, \Delta k). \quad (8)$$

(Note that the dose spread array value  $Ap(\tilde{\rho} \cdot l, \Delta i, \Delta j, \Delta k)$  is not invariant for the same value of  $\Delta i, \Delta j, \Delta k$  at different values of  $i, j, k$  because  $\tilde{\rho}$  changes throughout the phantom. Convolution with a noninvariant kernel is called superposition.) The factor  $\rho(i, j, k) / \tilde{\rho}$  takes into account the difference in the amount of kinetic energy released in the heterogeneous interaction voxel compared to the amount set in motion in the interpolated homogeneous voxel of density  $\tilde{\rho}$ . Otherwise, the calculation is carried out in the same manner as in a homogeneous phantom. Therefore, this procedure avoids the need to first compute the dose in water and then calculate a correction for inhomogeneity, separately.



# Investigation of the convolution method for polyenergetic spectra

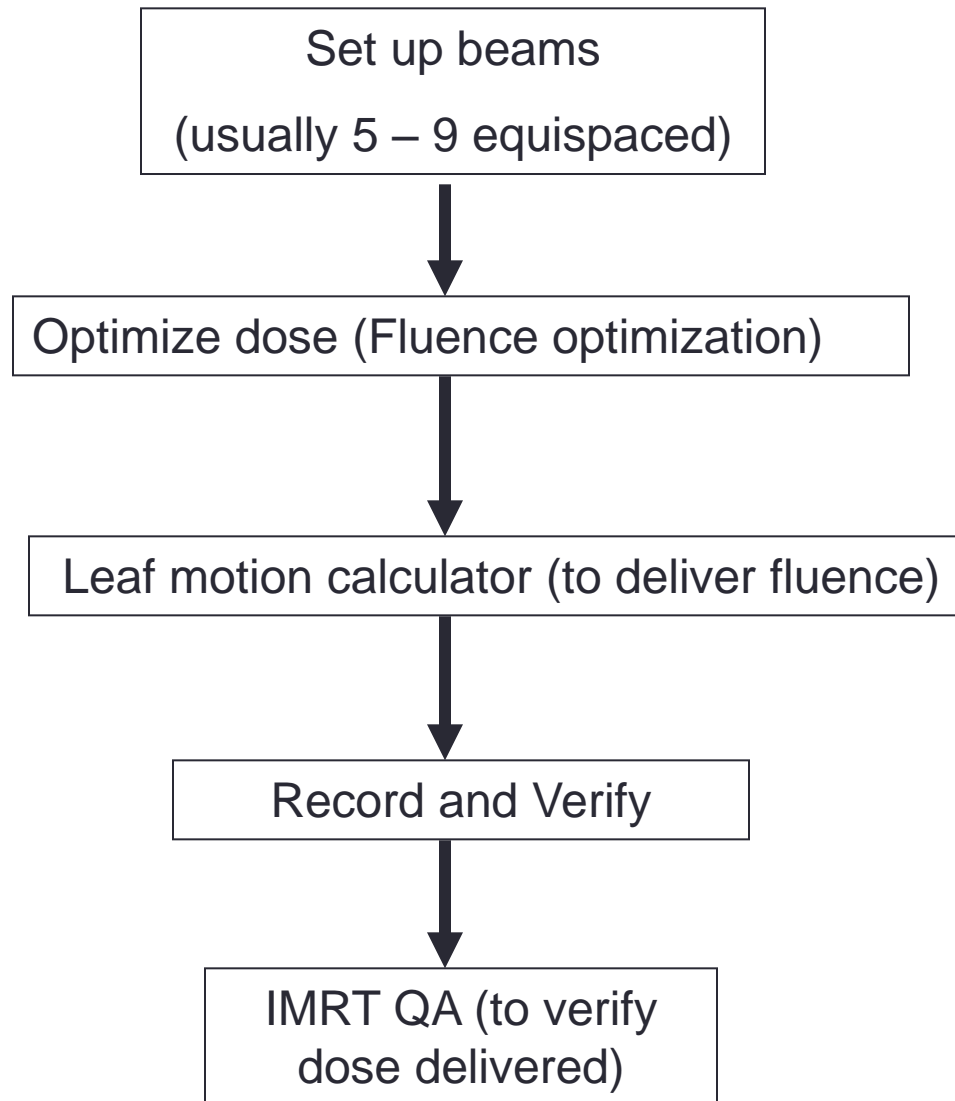
Nikos Papanikolaou, T. Rockwell Mackie, Carol Meger-Wells, Mark Gehring,  
and Paul Reckwerdt

*Department of Medical Physics, University of Wisconsin, Madison, Wisconsin 53706*

(Received 2 July 1992; accepted for publication 17 May 1993)

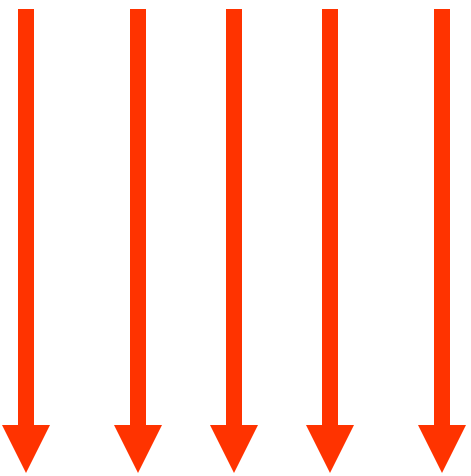
The distribution of absolute dose per unit fluence from polyenergetic photon beams impinging upon a water phantom was calculated using two convolution approaches that properly account for beam hardening effects. Dose deposition kernels calculated previously using the EGS4 Monte Carlo code are convolved with the primary term to give the dose for monoenergetic photon beams of energies ranging from 100 keV to 50 MeV. A polyenergetic dose distribution is composed of separately calculated monoenergetic components, which are appropriately weighted with the fluence spectrum to yield the polyenergetic dose distribution. Alternatively, a single convolution for the polyenergetic beam is considered, where a composite polyenergetic kernel is convolved with the respective polyenergetic term. The effects of the polyenergetic kernel variance due to beam hardening as well as the effect of tilting the kernels for a diverging beam geometry were also examined. The depth dose data produced using the two proposed methods were compared with measured data and Monte Carlo simulations and showed good agreement.

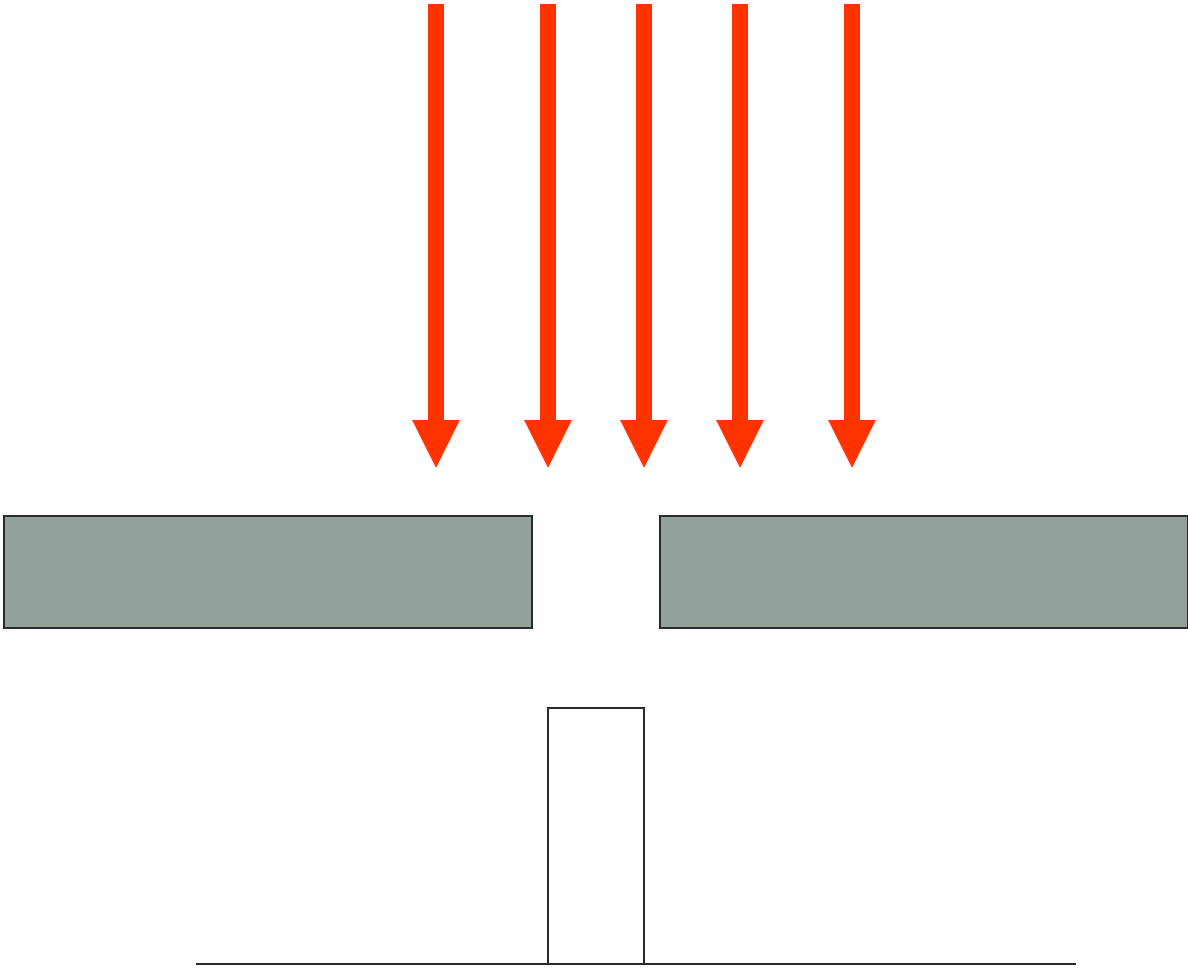
## IMRT PLANNING

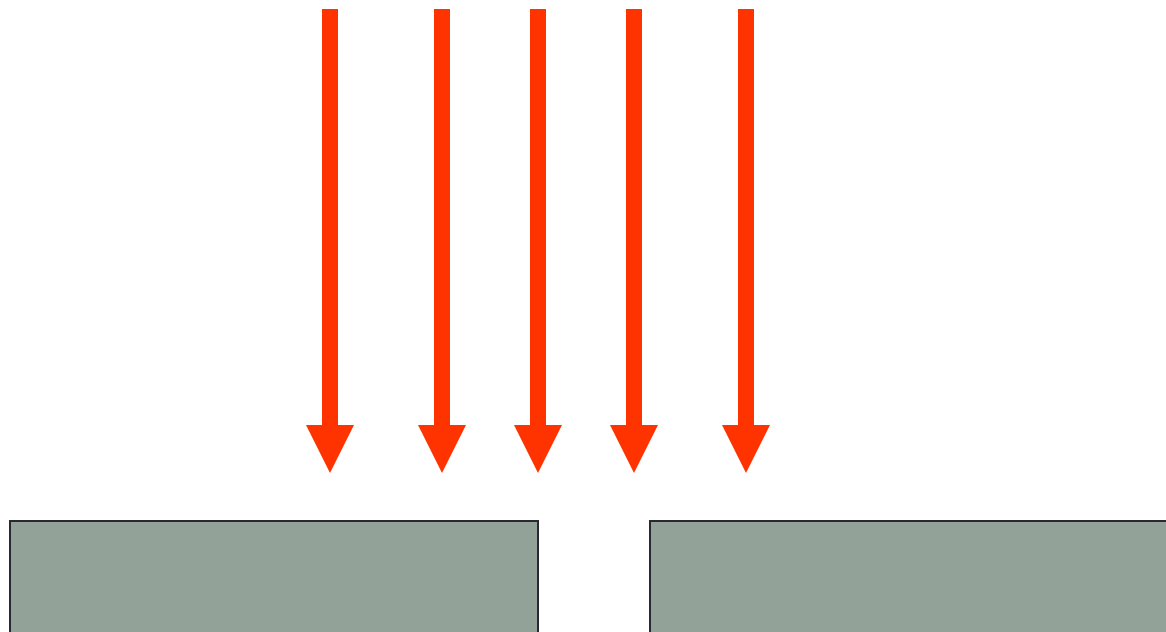


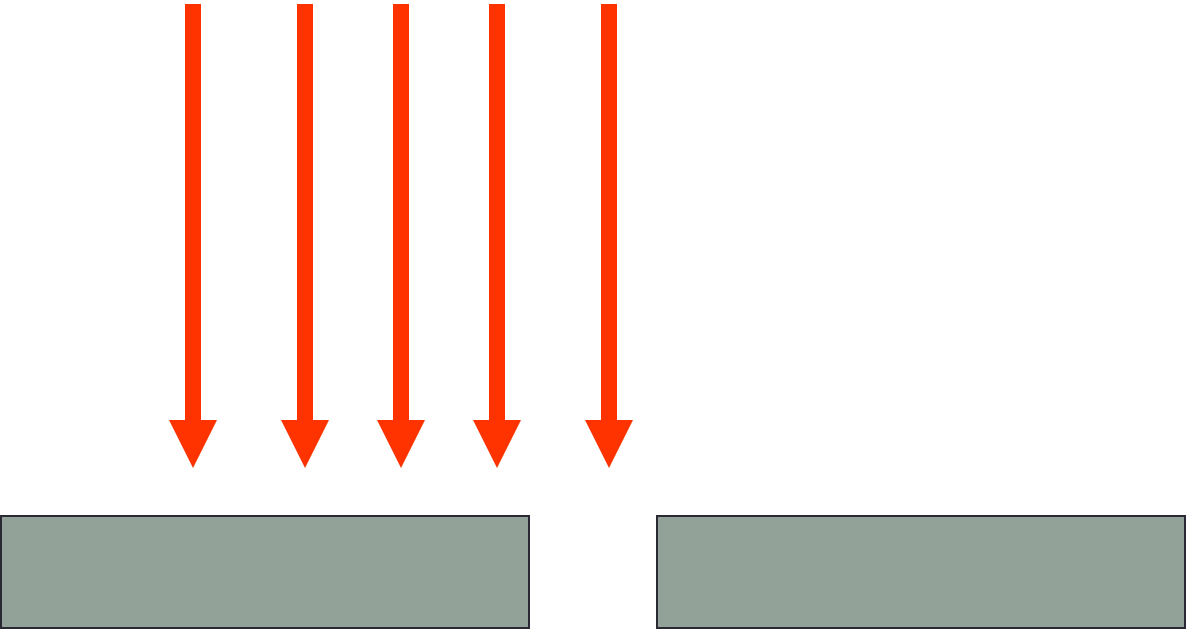
**leaf**

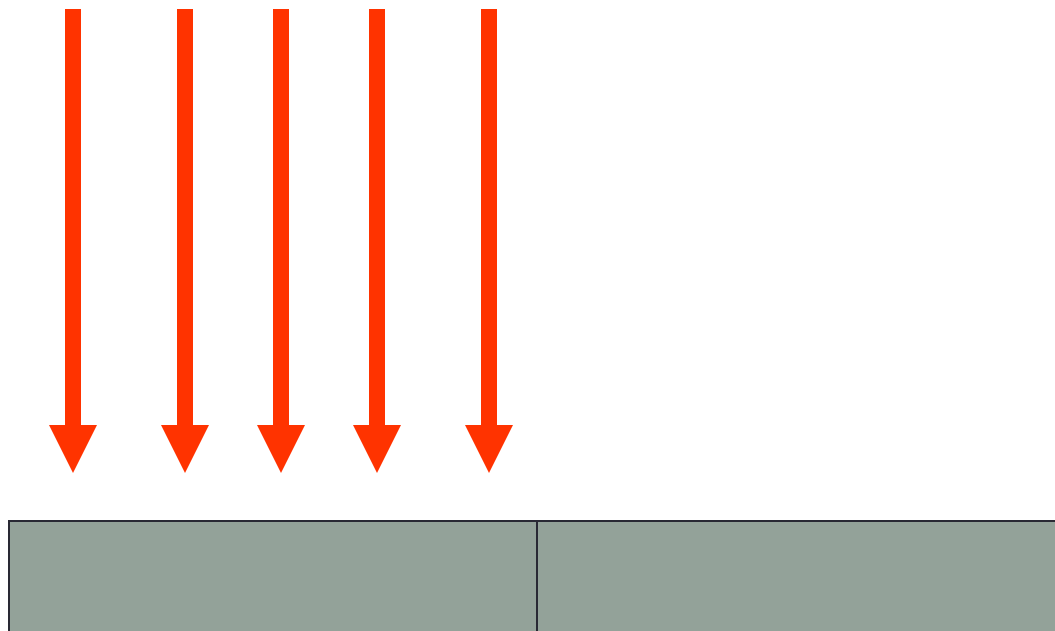
**leaf**

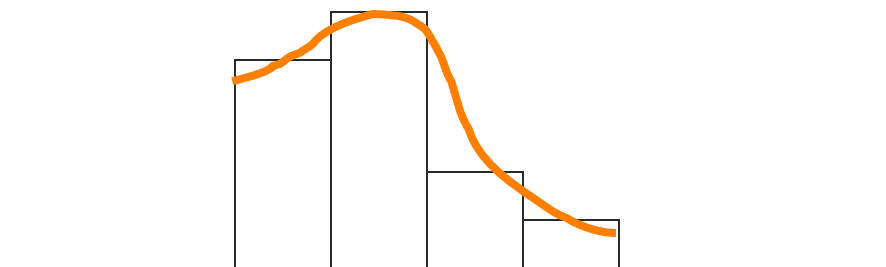




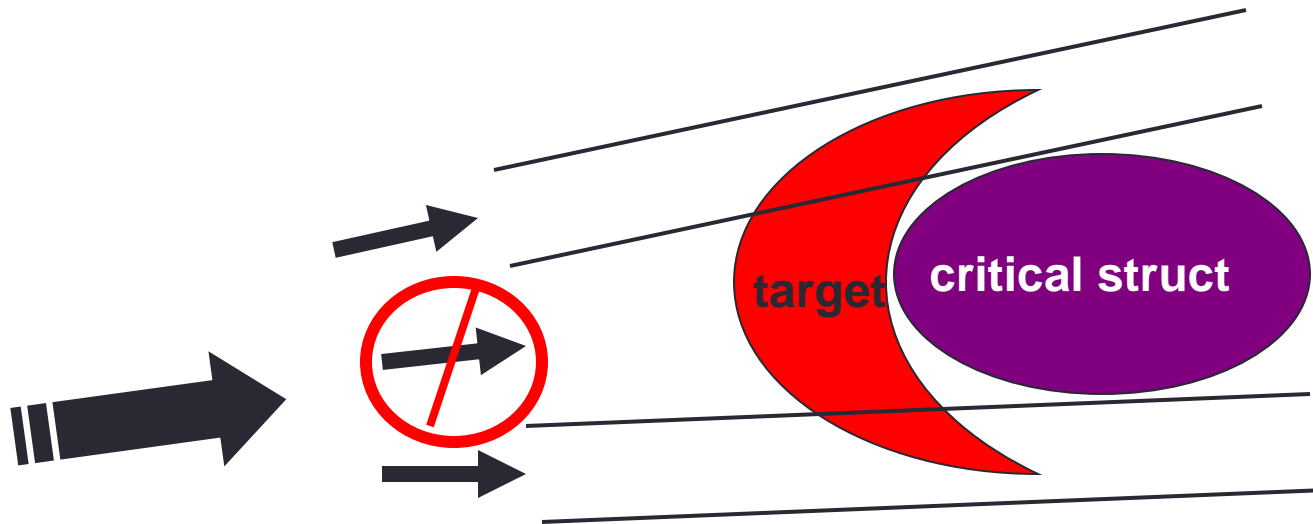






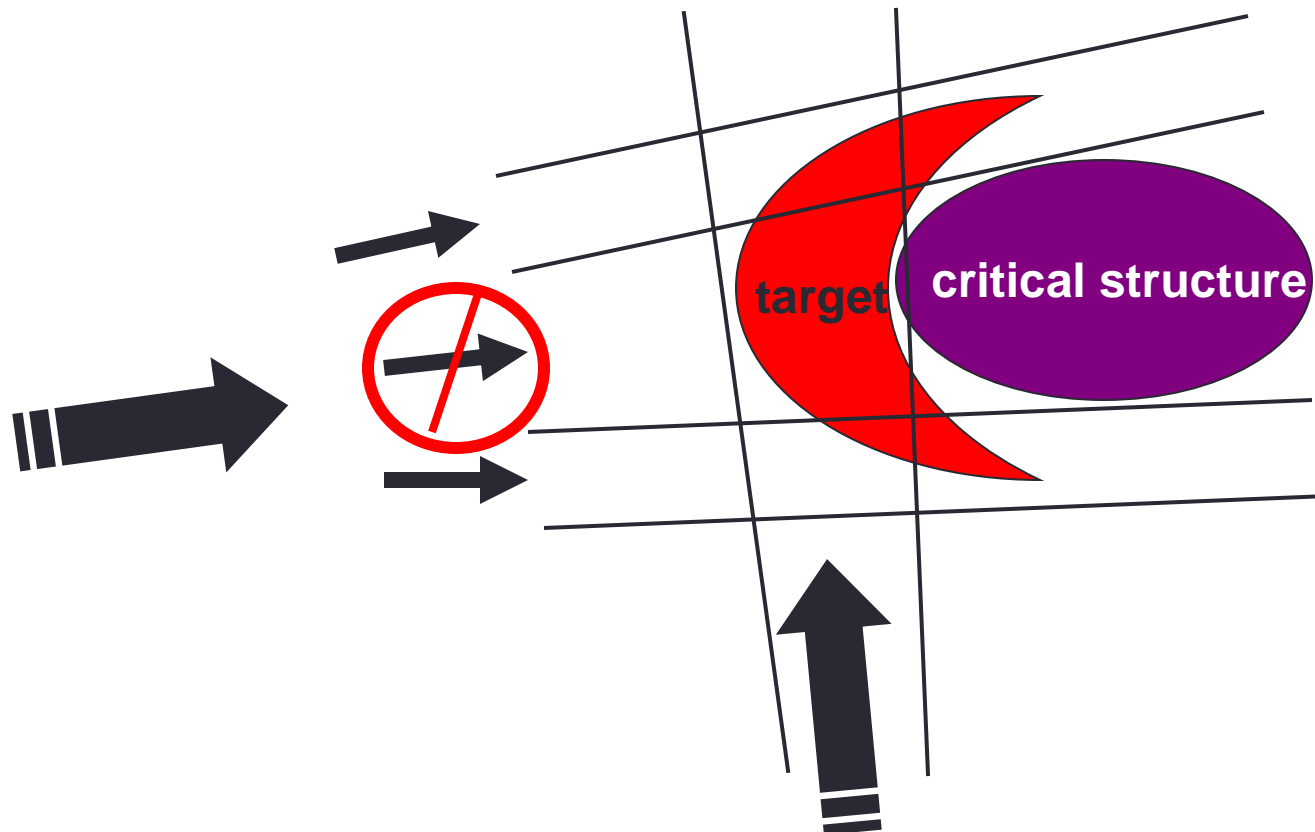






**Q: How is the radiation cutoff/ reduced in the central area?**

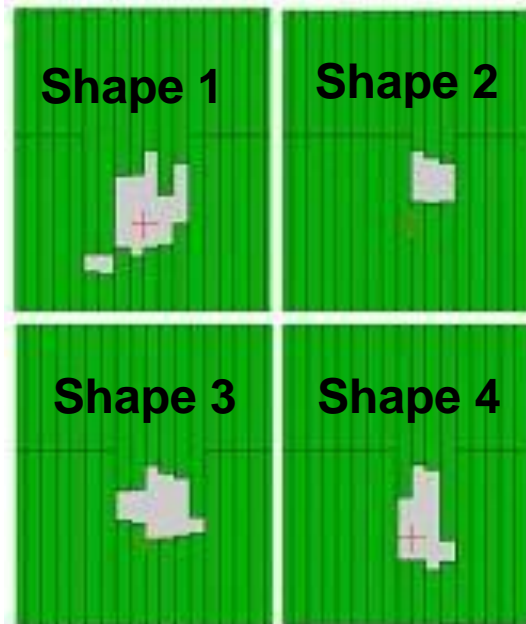
**A: Using multileaf collimators.**



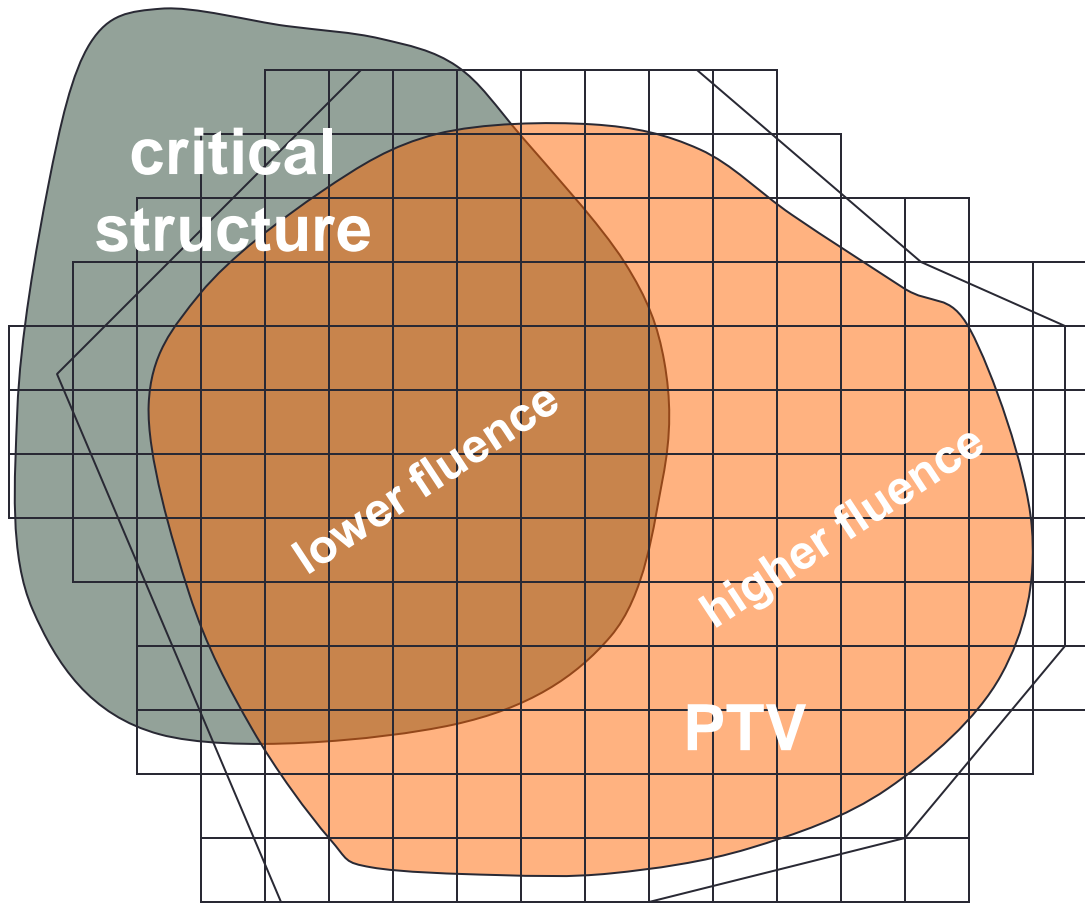
## Two methods for delivering modulated dose

Dynamic dose delivery: leaves move while radiation is on.

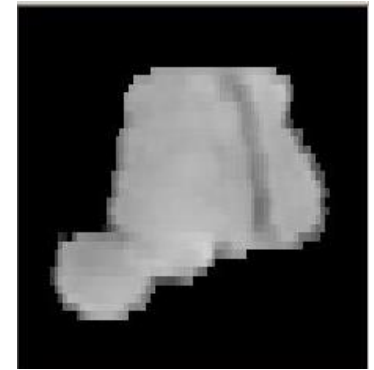
Static step-and-shoot: leaves are fixed while radiation is on, i.e., leaves move to take on different shapes while radiation is off.



## Fluence modulation



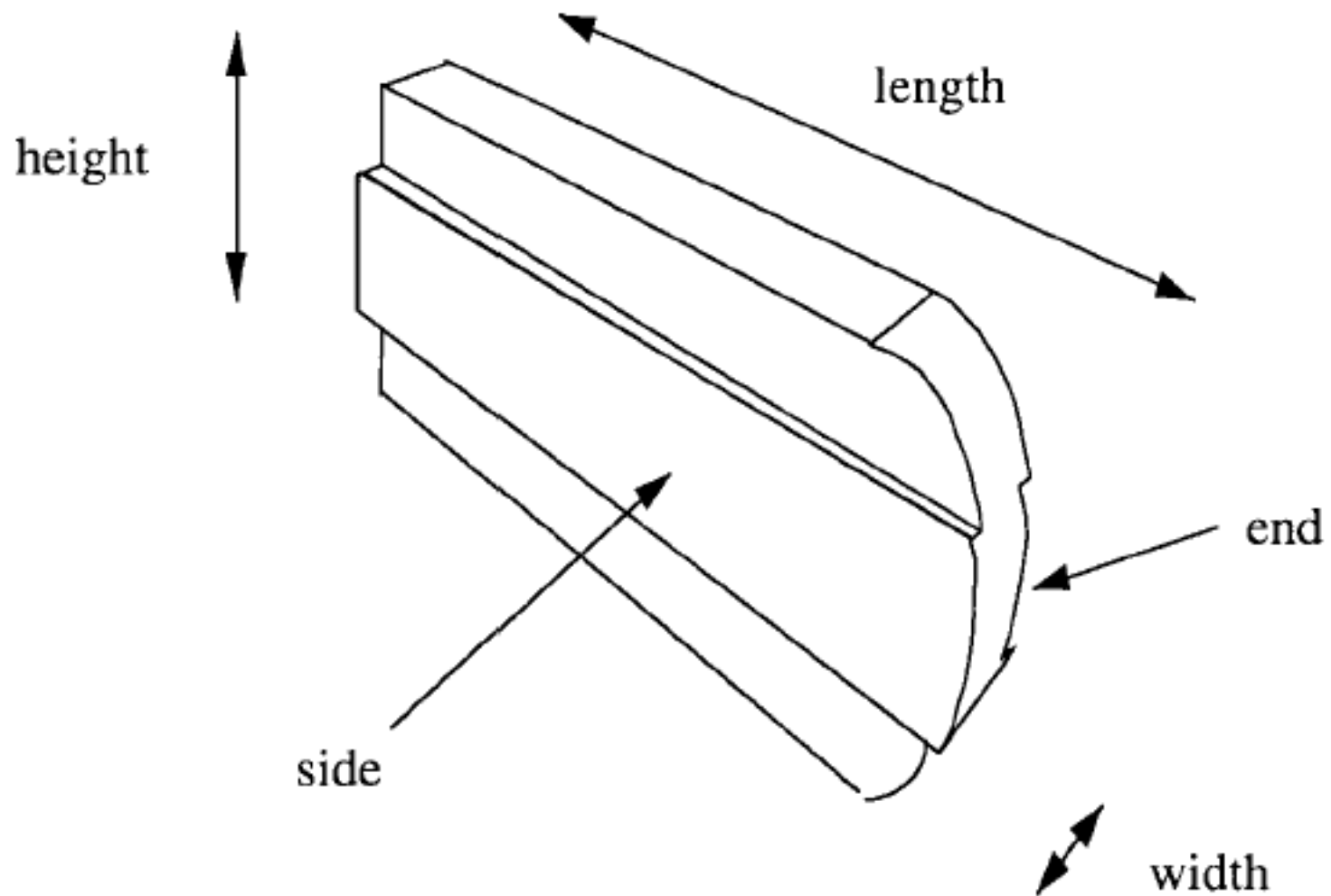
Beam's eye view (BEV)



Fluence map picture

The fluence in each grid element can be changed (modulated) to achieve a desired dose distribution. Grid covers the target with an 8 – 10 mm margin.

## VARIAN MLC LEAF



## Varian 120 leaf Millennium MLC

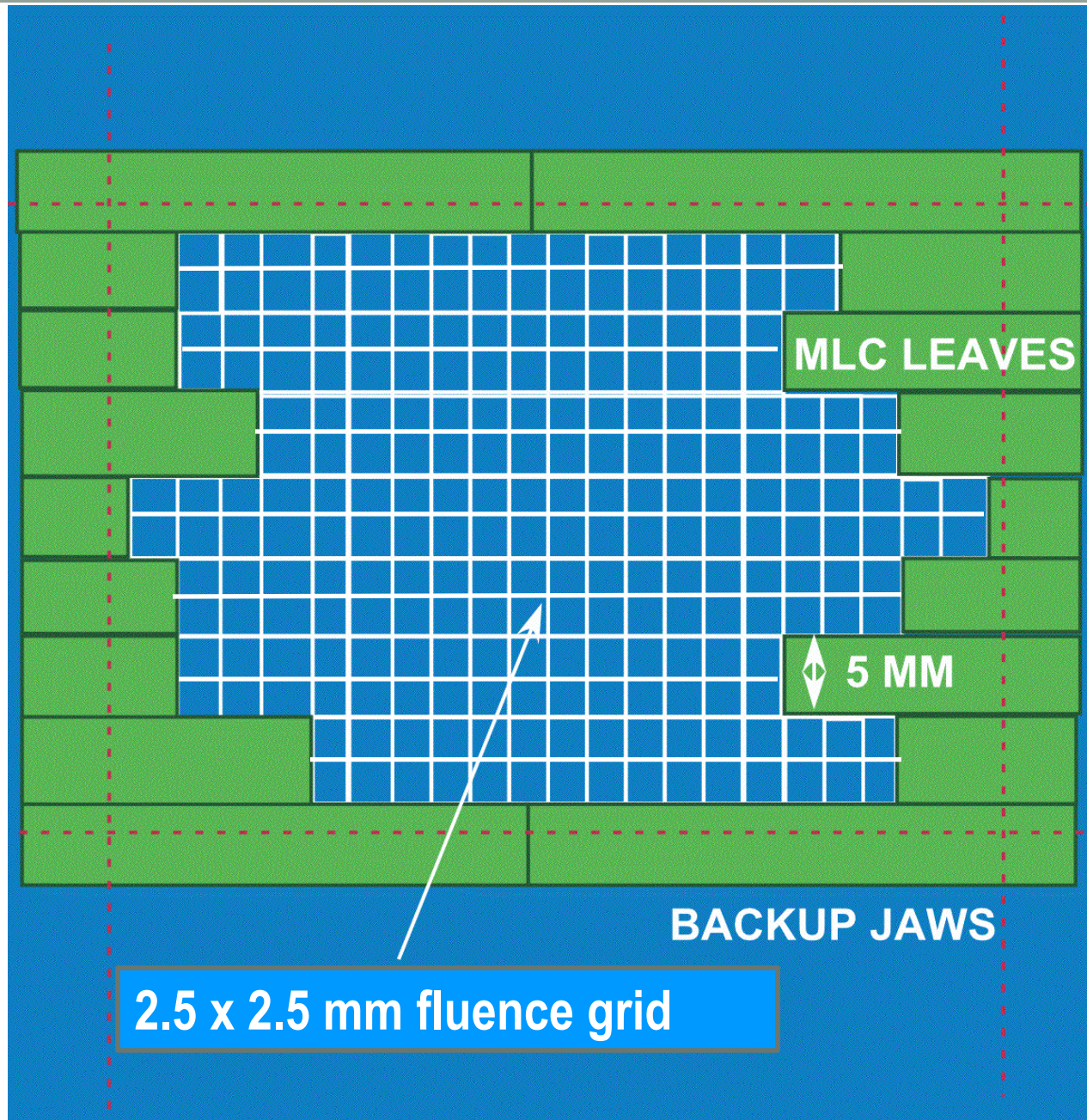


10 leaves:  
1 cm at iso

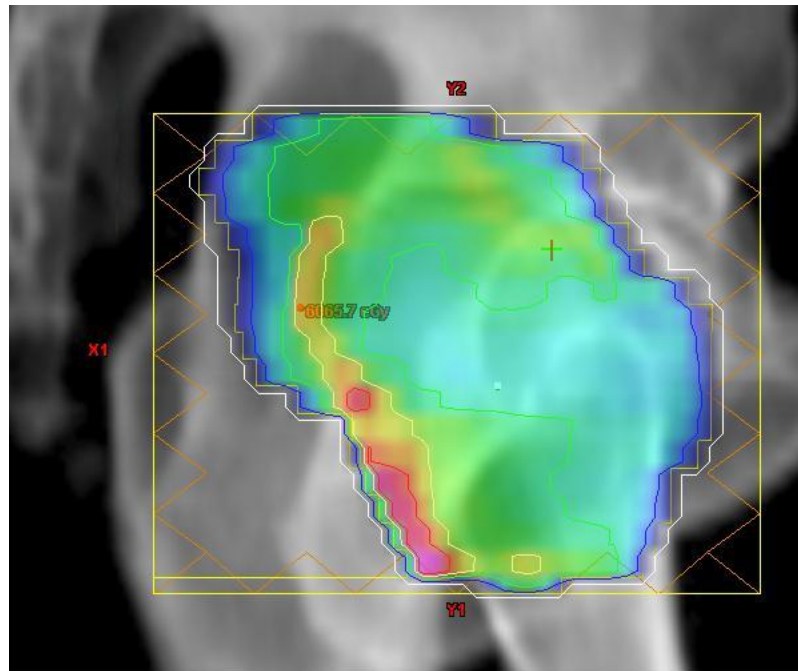
40 leaves per side:  
0.5 cm projection at  
isocenter

10 leaves:  
1 cm at iso





# FLUENCE DISTRIBUTION - PROSTATE





## IMRT Optimization

Modulate the beamlet weights (fluence) so as to achieve certain target and critical structure objectives.

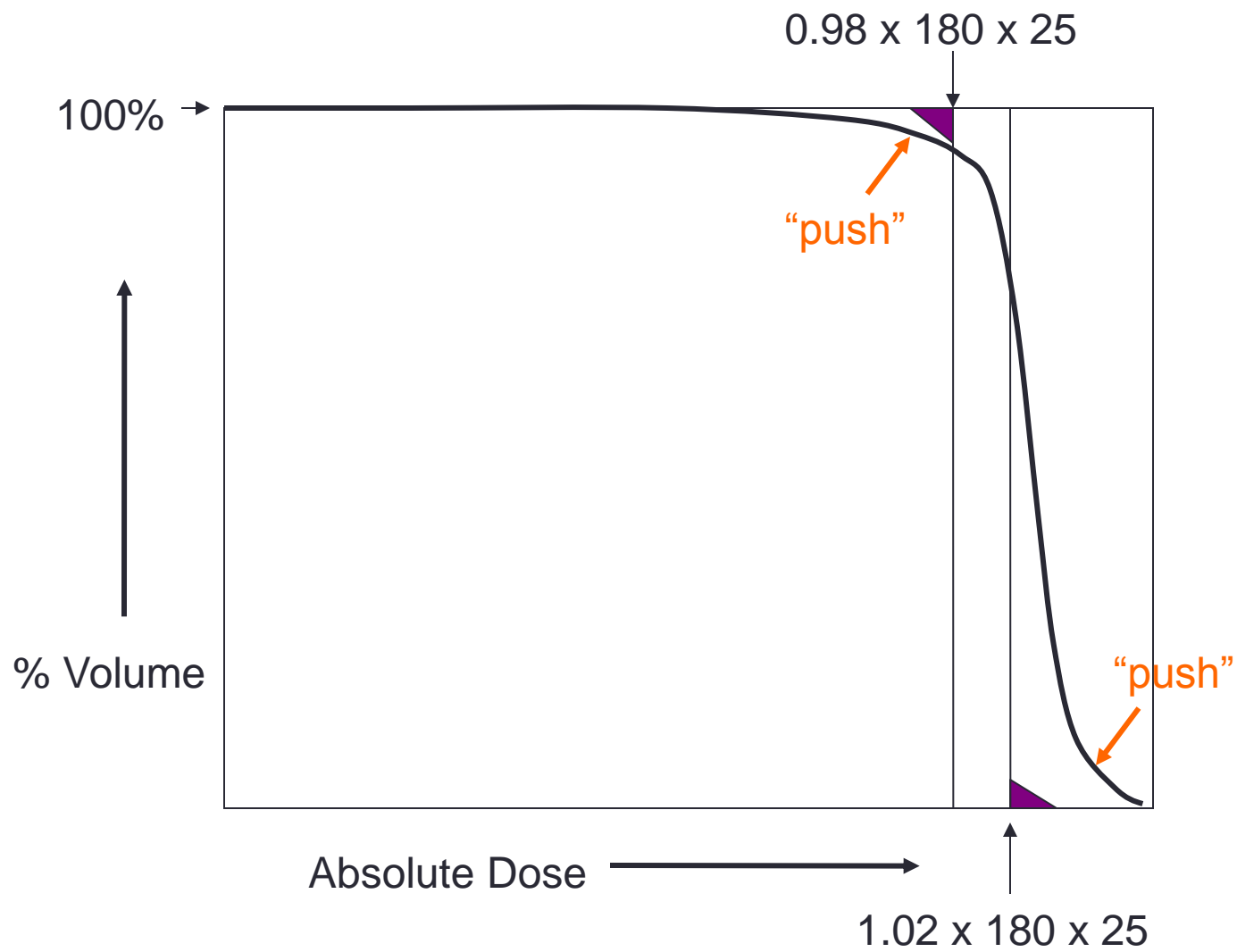
What are the target objectives?

Assume that there is a single PTV that is required to be given a prescription dose of  $D$  cGy/ fx to  $N$  fractions (e.g., 180 cGy/ fx to 25 fractions).

The target objective for this case is that 100% of PTV should be greater than some lower percentage of the prescription dose (e.g., 98%), and that 0% of PTV should not exceed some higher percentage of target dose (e.g., 102%).

How is this target objective represented in the IMRT DVH optimization window?

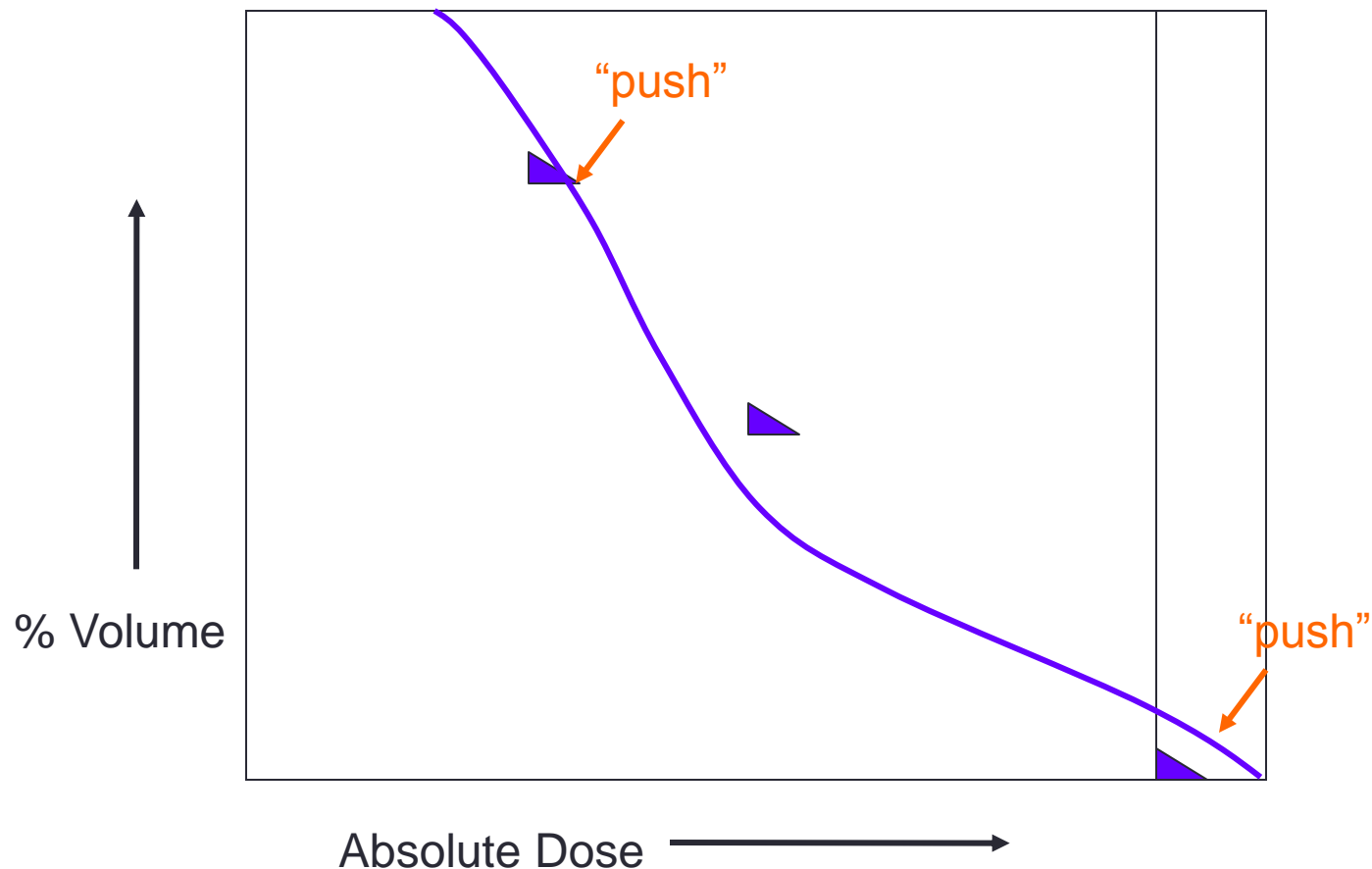




## What are critical structure constraints?

Maximum dose constraint: 0% of structure allowed to be above some dose  $D$  Gy.

Dose-volume constraint:  $x\%$  of structure allowed to be above some dose  $D$  Gy.



## How do you value constraints (importance of a constraint)?

Priority score: 0 (no importance) – 100+ (very important)

Each constraint (for each structure) must be assigned a priority score.

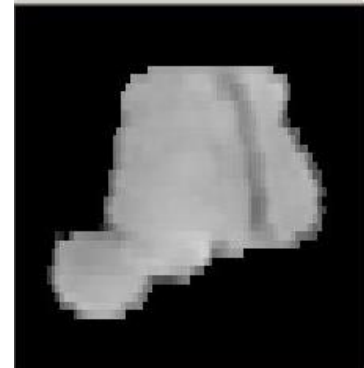
Once all constraints are satisfied, the priority scores essentially become inactive.

If some constraints are not satisfied, the priority scores tell the optimizer how to balance off between those constraints that are not yet satisfied.

## Constraint priorities can be thought of as relative weights, so why do absolute priority values matter?

Structure (target/ critical structure) priorities are balanced against fluence map smoothness.

Raising structure priorities too high can result in a very “choppy” fluence pattern. The choppiest a fluence pattern, the harder it is for the hardware to deliver it, i.e., the actual delivered dose could be quite different from what the optimization “promises”.



Fluence map  
picture

## Structures and Objectives

☐ Use Normal Tissue ObjectivePriority: 

Normal Tissue Objective Parameters...

<input checked="" type="checkbox"/>	PTV_40	Volume [cc]:	646	Points:	21517	Resolution [mm]:	3.00
	Upper	Volume [%]:	0.0	Dose [cGy]:	4060.0	Priority:	100
	Lower	Volume [%]:	100.0	Dose [cGy]:	3940.0	Priority:	100
<input type="checkbox"/>	PTV_66	Volume [cc]:	237	Points:	7893	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-1	Volume [cc]:	19	Points:	2000	Resolution [mm]:	2.06
<input type="checkbox"/>	SPECT7-2	Volume [cc]:	99	Points:	3302	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-3	Volume [cc]:	212	Points:	7055	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-4	Volume [cc]:	304	Points:	10119	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-5	Volume [cc]:	331	Points:	11020	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-6	Volume [cc]:	346	Points:	11517	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-7	Volume [cc]:	495	Points:	16487	Resolution [mm]:	3.00
<input type="checkbox"/>	body	Volume [cc]:	22497	Points:	222191	Resolution [mm]:	4.50
	Upper	Volume [%]:	0.0	Dose [cGy]:	4000.0	Priority:	250
<input checked="" type="checkbox"/>	esphogus	Volume [cc]:	30	Points:	2000	Resolution [mm]:	2.38
	Upper	Volume [%]:	30.0	Dose [cGy]:	3000.0	Priority:	80
	Upper	Volume [%]:	0.0	Dose [cGy]:	4000.0	Priority:	80
<input checked="" type="checkbox"/>	heart	Volume [cc]:	530	Points:	17651	Resolution [mm]:	3.00
	Upper	Volume [%]:	46.0	Dose [cGy]:	2281.2	Priority:	80
<input checked="" type="checkbox"/>	lung	Volume [cc]:	1702	Points:	56732	Resolution [mm]:	3.00
	Upper	Volume [%]:	34.2	Dose [cGy]:	1561.9	Priority:	90
	Upper	Volume [%]:	16.0	Dose [cGy]:	2553.3	Priority:	90
<input type="checkbox"/>	penalty	Volume [cc]:	462	Points:	15398	Resolution [mm]:	3.00
	Upper	Volume [%]:	0.0	Dose [cGy]:	3200.0	Priority:	90
<input checked="" type="checkbox"/>	penalty2	Volume [cc]:	131	Points:	4365	Resolution [mm]:	3.00
<input type="checkbox"/>	penalty3	Volume [cc]:	44	Points:	2270	Resolution [mm]:	1.70

Add Upper Objective

Add Lower Objective

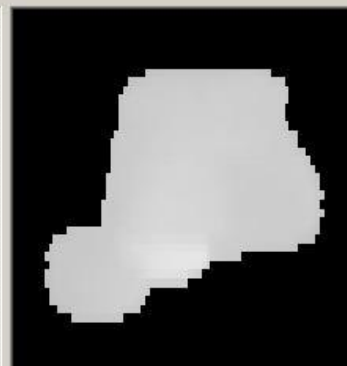
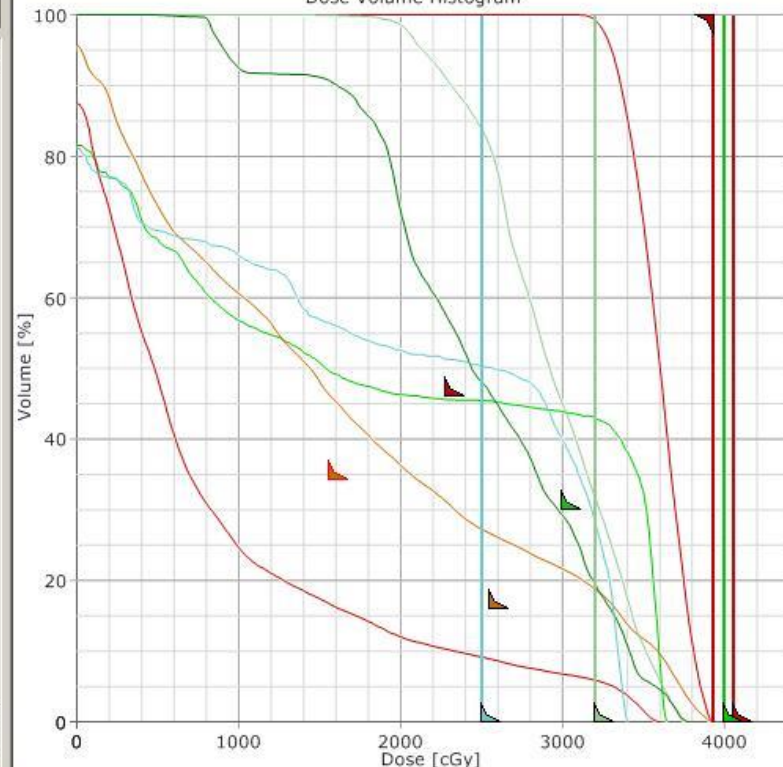
Delete

Base dose plan:

Select...

	MLC	Method	X Smooth	Y Smooth	Minimize Dose	Fixed Jaws	Field Weight
Field 1	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 2	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 3	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 4	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 5	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 6	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 7	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 8	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 9	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000

Dose Volume Histogram

Max time (min): Max iterations: 0h 0m 39s  
1

Continue

☐ View with interpolation☐ Use color

OK

Cancel

Apply



## Structures and Objectives

☐ Use Normal Tissue ObjectivePriority: 

Normal Tissue Objective Parameters...

<input checked="" type="checkbox"/>	PTV_40	Volume [cc]:	646	Points:	21517	Resolution [mm]:	3.00
	Upper	Volume [%]:	0.0	Dose [cGy]:	4060.0	Priority:	100
	Lower	Volume [%]:	100.0	Dose [cGy]:	3940.0	Priority:	100
<input type="checkbox"/>	PTV_66	Volume [cc]:	237	Points:	7893	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-1	Volume [cc]:	19	Points:	2000	Resolution [mm]:	2.06
<input type="checkbox"/>	SPECT7-2	Volume [cc]:	99	Points:	3302	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-3	Volume [cc]:	212	Points:	7055	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-4	Volume [cc]:	304	Points:	10119	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-5	Volume [cc]:	331	Points:	11020	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-6	Volume [cc]:	346	Points:	11517	Resolution [mm]:	3.00
<input type="checkbox"/>	SPECT7-7	Volume [cc]:	495	Points:	16487	Resolution [mm]:	3.00
<input type="checkbox"/>	body	Volume [cc]:	22497	Points:	222191	Resolution [mm]:	4.50
	Upper	Volume [%]:	0.0	Dose [cGy]:	4000.0	Priority:	250
<input checked="" type="checkbox"/>	esophagus	Volume [cc]:	30	Points:	2000	Resolution [mm]:	2.38
	Upper	Volume [%]:	30.0	Dose [cGy]:	3000.0	Priority:	80
	Upper	Volume [%]:	0.0	Dose [cGy]:	4000.0	Priority:	80
<input checked="" type="checkbox"/>	heart	Volume [cc]:	530	Points:	17651	Resolution [mm]:	3.00
	Upper	Volume [%]:	46.0	Dose [cGy]:	2281.2	Priority:	80
<input checked="" type="checkbox"/>	lung	Volume [cc]:	1702	Points:	56732	Resolution [mm]:	3.00
	Upper	Volume [%]:	34.2	Dose [cGy]:	1561.9	Priority:	90
	Upper	Volume [%]:	16.0	Dose [cGy]:	2553.3	Priority:	90
<input type="checkbox"/>	penalty	Volume [cc]:	462	Points:	15398	Resolution [mm]:	3.00
	Upper	Volume [%]:	0.0	Dose [cGy]:	3200.0	Priority:	90
<input checked="" type="checkbox"/>	penalty2	Volume [cc]:	131	Points:	4365	Resolution [mm]:	3.00
<input type="checkbox"/>	penalty3	Volume [cc]:	44	Points:	2276	Resolution [mm]:	1.76

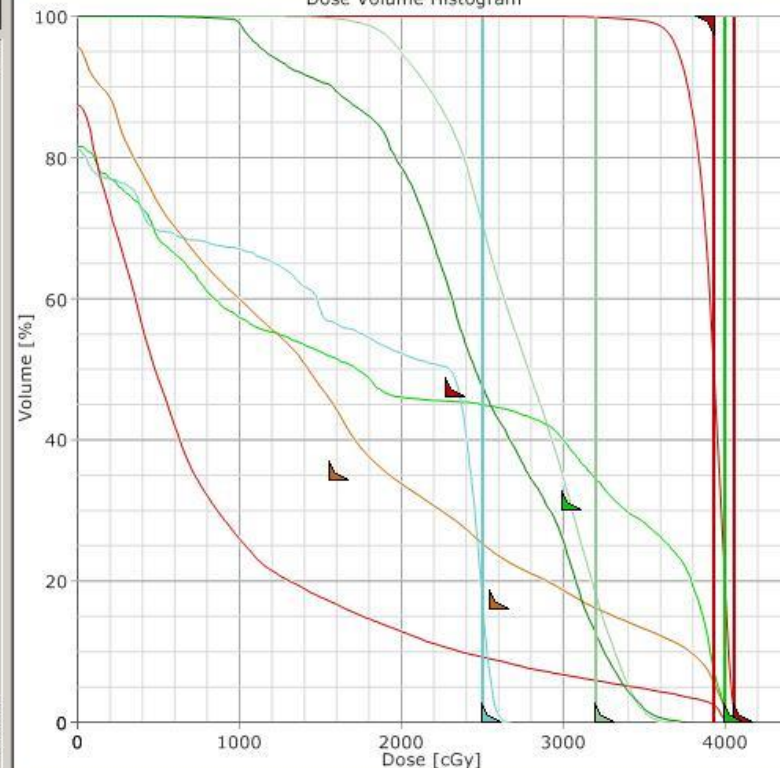
Add Upper Objective

Add Lower Objective

Delete

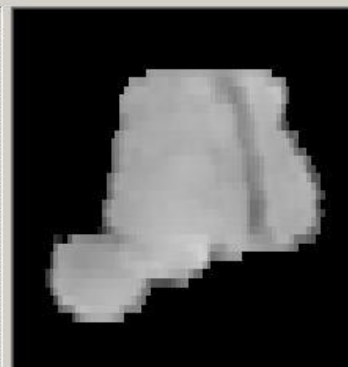
	MLC	Method	X Smooth	Y Smooth	Minimize Dose	Fixed Jaws	Field Weight
Field 1	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 2	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 3	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 4	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 5	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 6	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 7	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 8	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000
Field 9	Millennium_1...	Beamlet	40	30	0	<input type="checkbox"/>	1.000

Dose Volume Histogram



Base dose plan:

Select...

Max time (min): Max iterations: 0h 1m 40s  
13

Continue

- ☐ View with interpolation  
☐ Use color

OK

Cancel

Apply

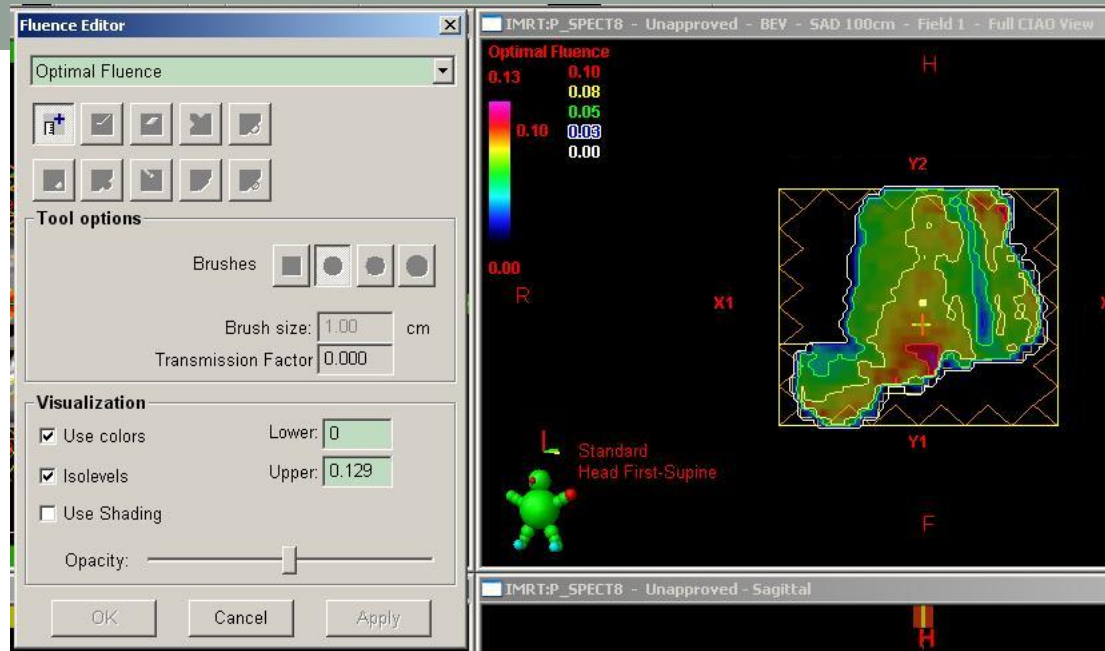
**Leaf Motion Calculation Options** [X]

	Delivery Method	Intensity Levels	Fixed Jaws
Field 1	Sliding Window		<input type="checkbox"/>
Field 2	Sliding Window		<input type="checkbox"/>
Field 3	Sliding Window		<input type="checkbox"/>
Field 4	Sliding Window		<input type="checkbox"/>
Field 5	Sliding Window		<input type="checkbox"/>
Field 6	Sliding Window		<input type="checkbox"/>
Field 7	Sliding Window		<input type="checkbox"/>

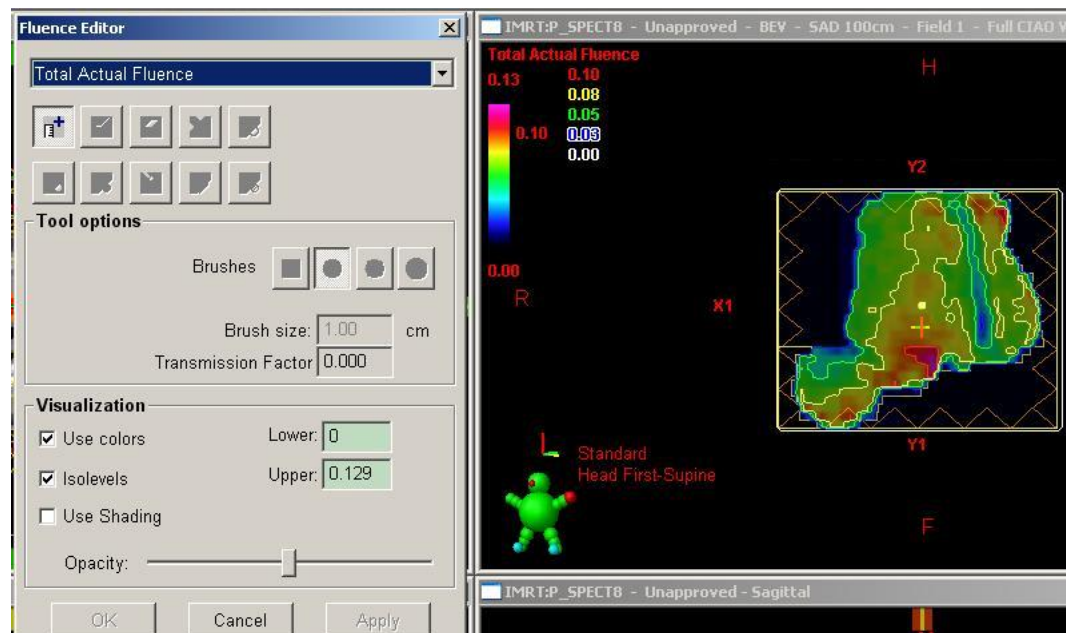
OK Cancel

Sliding window = dynamic delivery; Step and shoot = static delivery

# Optimal Fluence

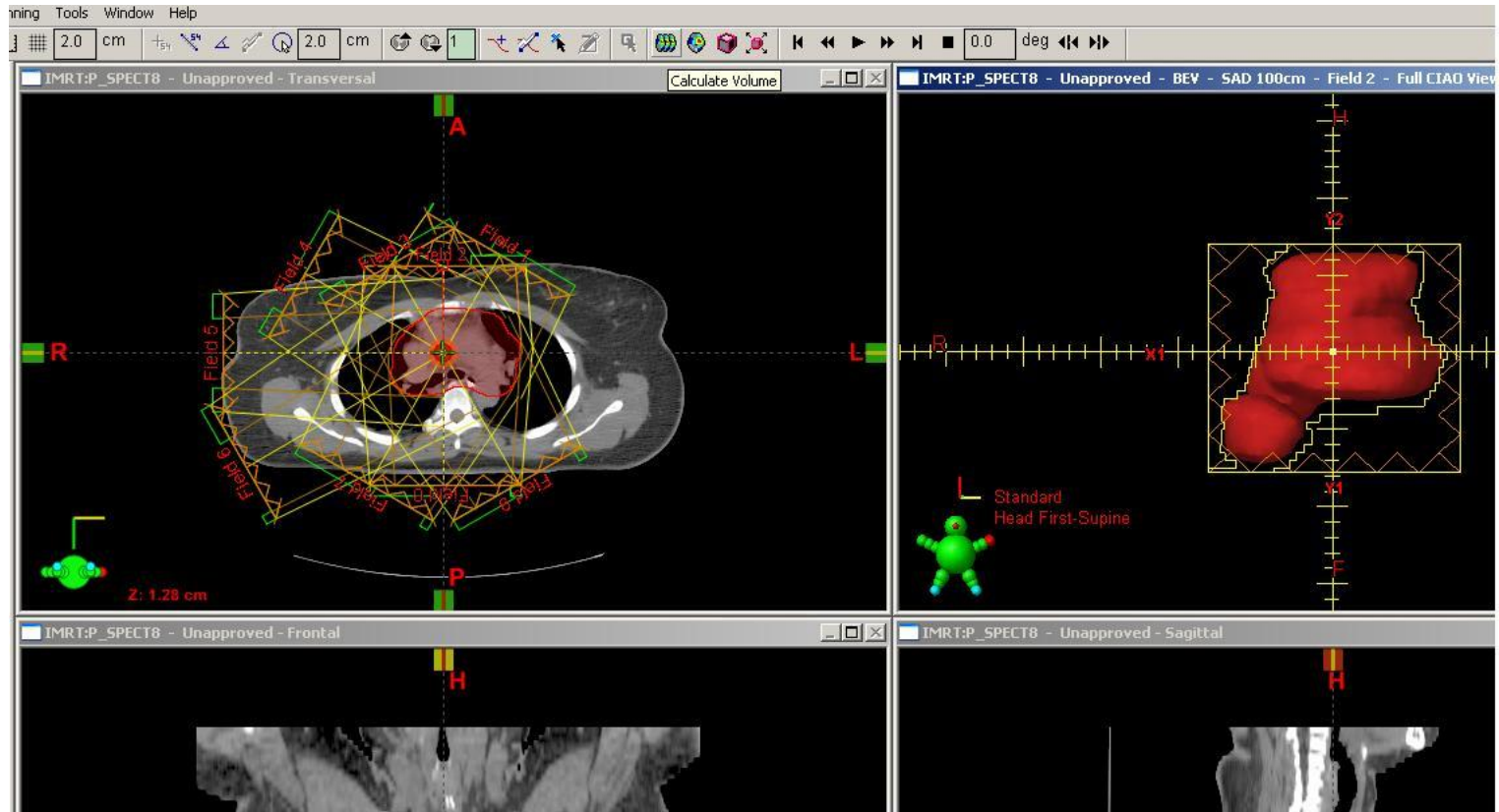


# Actual Fluence





# Calculate dose in 3D volume



## IMRT Optimization: Mathematical Basis

Two different ways of formulating the optimization problem:

Unconstrained optimization problem: Formulate a quantitative objective (goal) function to be minimized. The objective function is a measure of violation of the target (PTV) and critical structure constraints.

Constrained optimization problem: Formulate a quantitative objective (goal) function to be minimized. The objective function is a measure of violation of the target (PTV) constraints. Use explicit constraints for the critical structures.

We will talk about unconstrained optimization, which is usually faster than constrained optimization and less likely to get “stuck” in local minima.

## Specifications required to formulate objective function

Minimum target dose (  $d_{\min}^{\text{target}}$  ) and associated weight (  $w_{\min}^{\text{target}}$  )

Maximum target dose (  $d_{\max}^{\text{target}}$  ) and associated weight (  $w_{\max}^{\text{target}}$  )

Critical structure constraints:

Critical structure #1, constraint #1: dose (  $d_{\text{con}\#1}^{\text{cs}\#1}$  ), volume (  $V_{\text{con}\#1}^{\text{cs}\#1}$  ), weight (  $w_{\text{con}\#1}^{\text{cs}\#1}$  )

Critical structure #1, constraint #2: dose (  $d_{\text{con}\#2}^{\text{cs}\#1}$  ), volume (  $V_{\text{con}\#2}^{\text{cs}\#1}$  ), weight (  $w_{\text{con}\#2}^{\text{cs}\#1}$  )

.....

For all critical structures

Objective function to be minimized is sum of components from target and each of the critical structures. ***It is a function of the fluences (f).***

$$\Omega(f) = \Omega^{\text{target}} + \sum_j \Omega^{\text{cs}\#j}$$

$$\Omega = \Omega^{\text{target}} + \sum_j \Omega^{cs\#j}$$

$$\Omega^{\text{target}} =$$

$$w_{\text{max}}^{\text{target}} \times \frac{\sum_{i \in \text{target}} \max(d_i^{\text{target}} - d_{\text{max}}^{\text{target}}, 0)^2}{N_{\text{target}}} + w_{\text{min}}^{\text{target}} \times \frac{\sum_{i \in \text{target}} \max(d_{\text{min}}^{\text{target}} - d_i^{\text{target}}, 0)^2}{N_{\text{target}}}$$

point/voxel number in target

For each critical structure, sum over all constraints:

$$\Omega^{cs\#j} = \sum_k \Omega_{con\#k}^{cs\#j}$$

Assume, for the moment, that our critical structure constraints are maximum dose constraints, i.e., dose-volume constraints where constraint volume = 0.

$$\Omega_{con\#k}^{cs\#j} = w_{con\#k}^{cs\#j} \times \frac{\sum_{m \in cs\#j} \max(d_m^{cs\#j} - d_{con\#k}^{cs\#j}, 0)^2}{N_{cs\#j}}$$

point/voxel number in critical structure # j

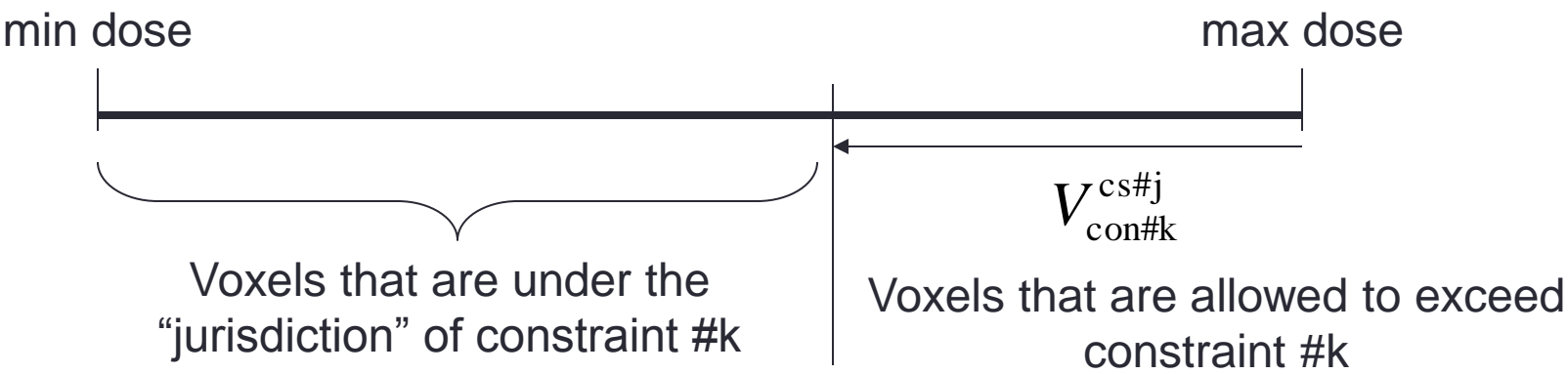
Let's go one step further with the critical structure constraints: general dose-volume constraints.

We can still use the previous formulation for critical structures, with a simple extension.

Imagine that we are looking at critical structure #j and constraint #k.....

First sort the dose in critical structure #j from minimum to maximum

$$sorted\ cs\#j\ dose = \times \quad \times \quad \times \quad \times \quad ..... \times \quad \times \quad \times \quad \times$$



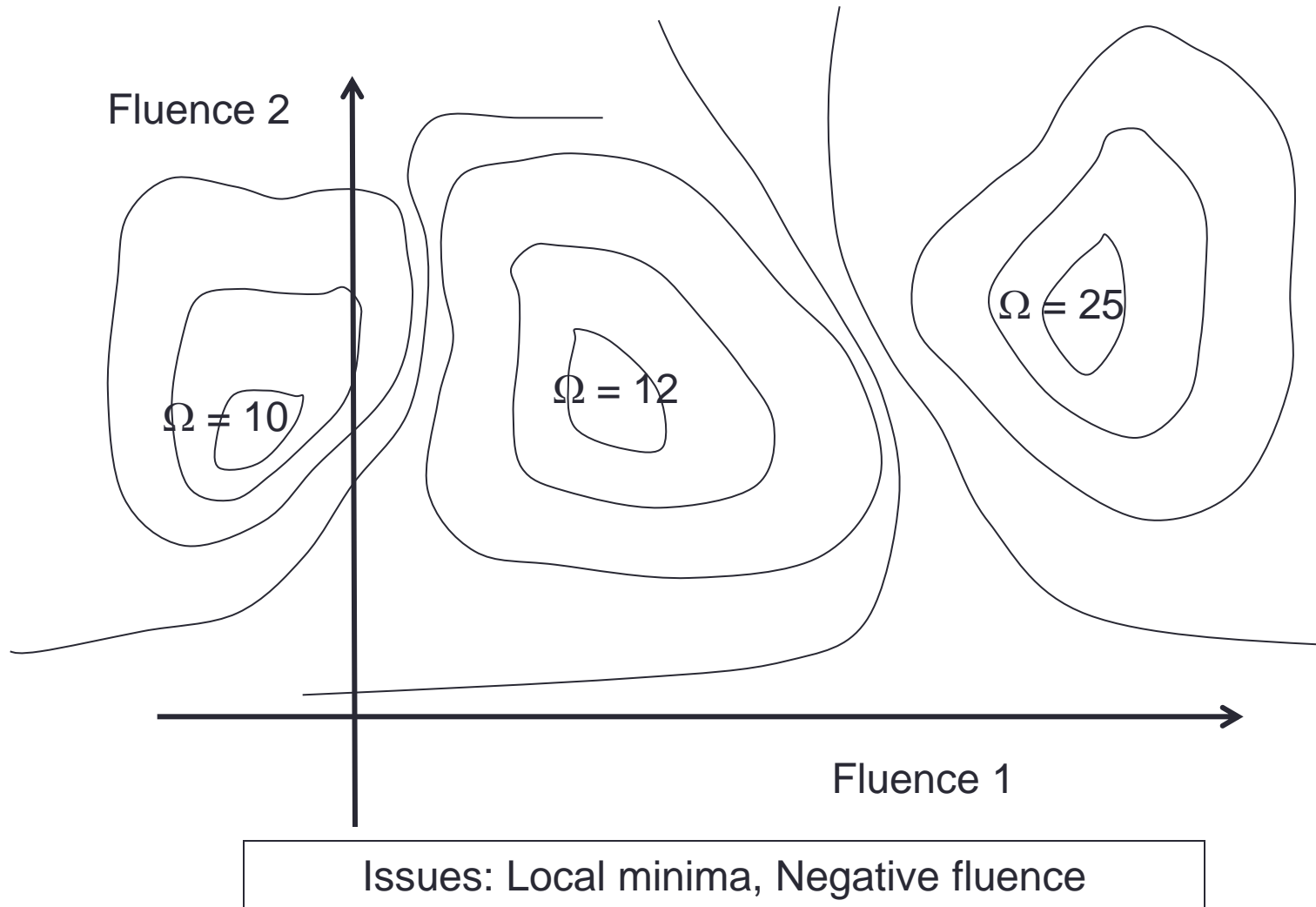
For  
constraint k  
of critical  
structure j

$$\Omega_{con\#k}^{cs\#j} = w_{con\#k}^{cs\#j} \times \frac{\sum_{\substack{m \in cs\#j \\ m \in con\#k}} \max(d_m^{cs\#j} - d_{con\#k}^{cs\#j}, 0)^2}{N_{con\#k}^{cs\#j}}$$

Summation  
only for  
voxels in  
jurisdiction!

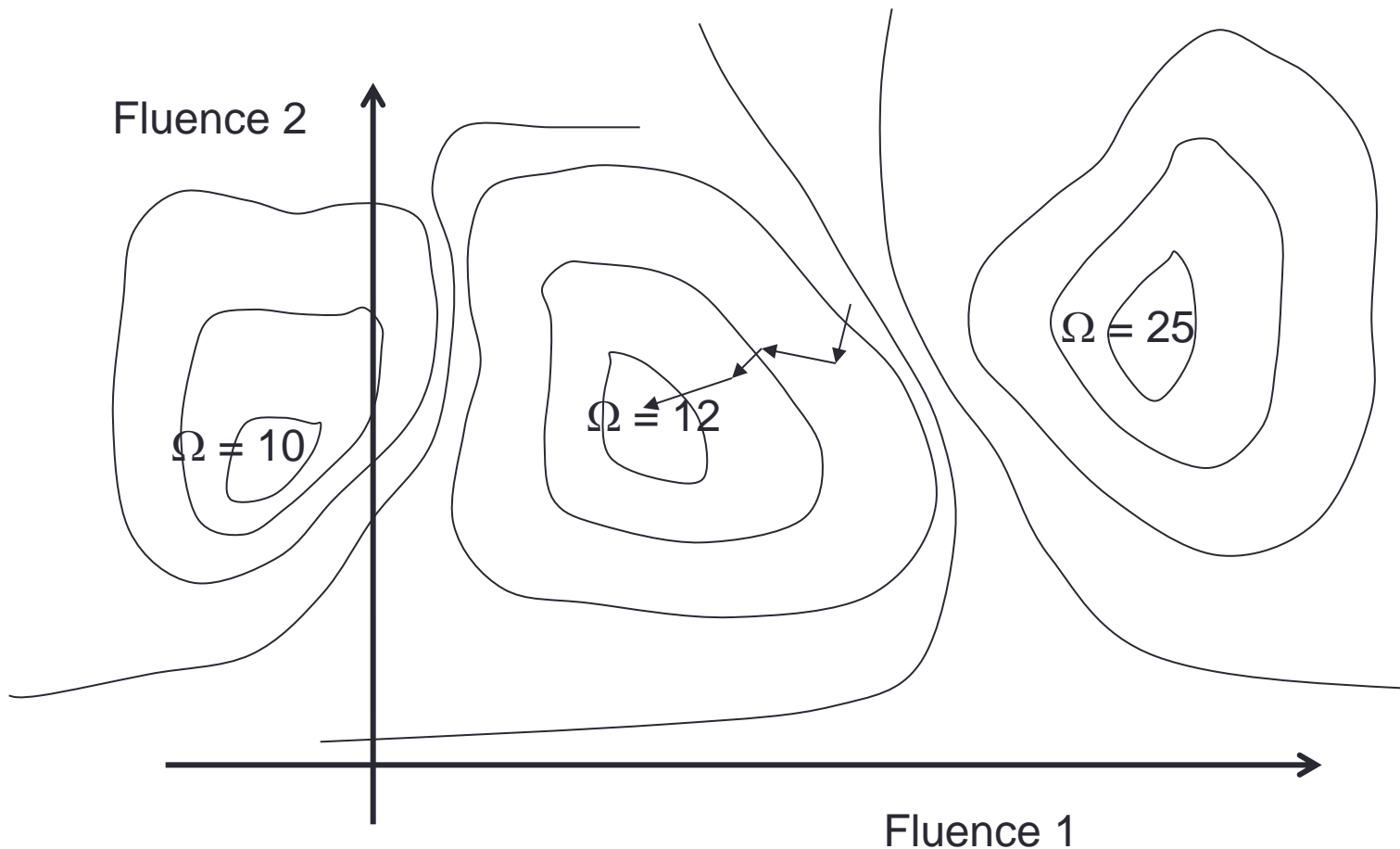
How do we optimize the fluences?

Assume there are only two fluences, for which the plot below shows iso-contours of  $\Omega$ .



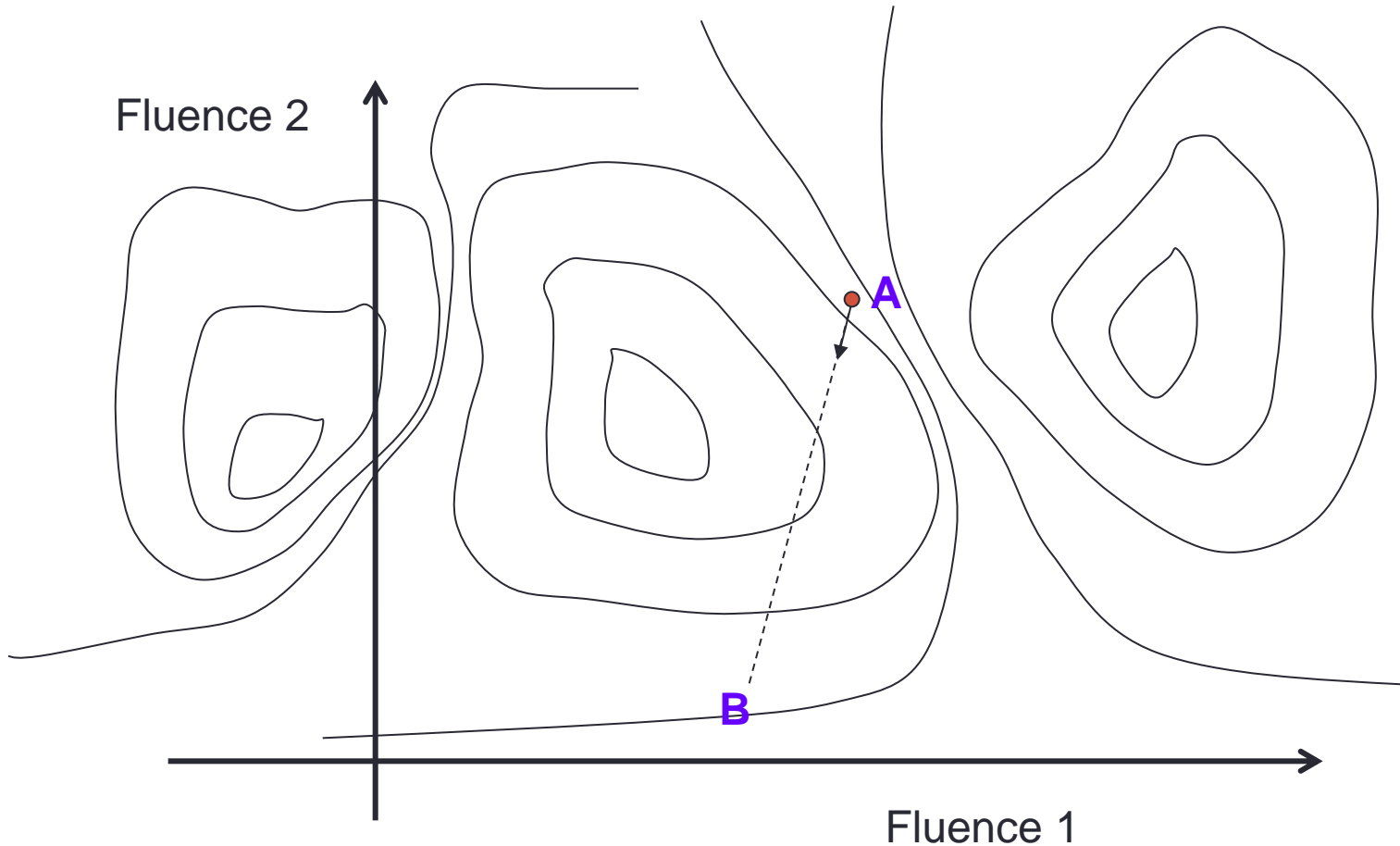
**Let's just consider the simplest form of gradient-descent optimization:**  
**Steepest-descent optimization.**

The optimization proceeds down the steepest path – not the best strategy, but easy to implement.



## Steepest-descent optimization

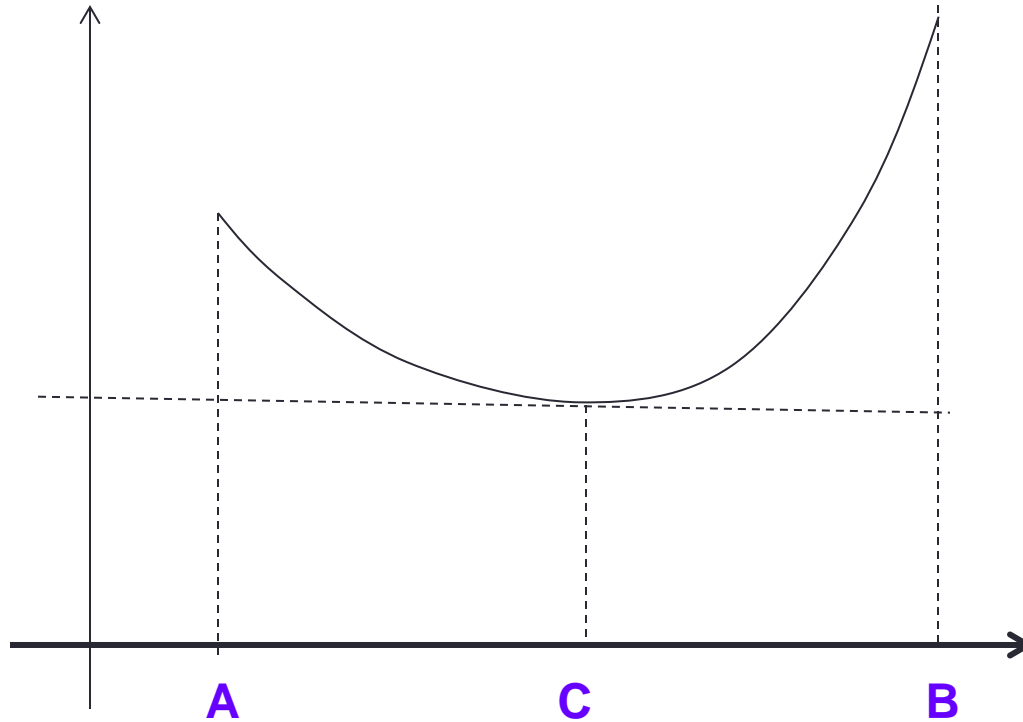
For each steepest-descent direction, how far to move along the vector?

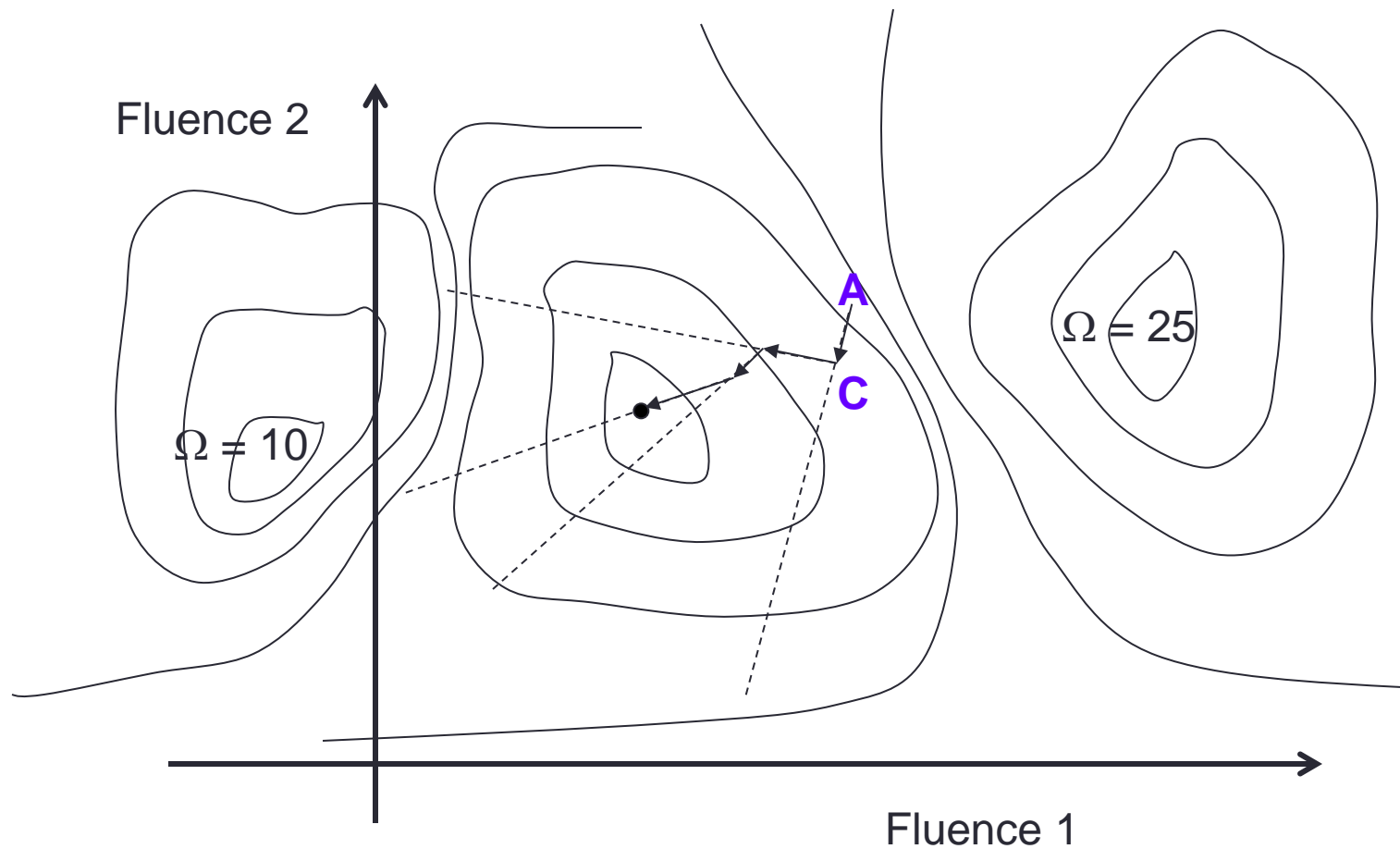


Along the steepest-descent direction conduct a “line search”



## Line Search





At point C, compute steepest-descent direction and initiate new line search, until convergence to optimal fluence values.

# **Volumetric Modulated Arc Therapy (VMAT)**





**RAPID ARC VIDEO CLIP**

### **VMAT characteristics**

- Dose rate varies as a function of angle.
- Gantry speed can vary as a function of angle.
- Leaves move back-and-forth (not just right to left, as in IMRT).
- Much lower delivery time.

However, VMAT can not always achieve the extent of sparing provided by IMRT, especially in complicated cases.

The optimization methodology is basically an extension of static field IMRT.

# Leaf Motion Calculation



## Static step-and-shoot technique (areal step-and-shoot, powers of 2)

Block off everything at level below  $2^{k-1}$ , where  $k = \log_2(\text{max intensity})$  rounded up.

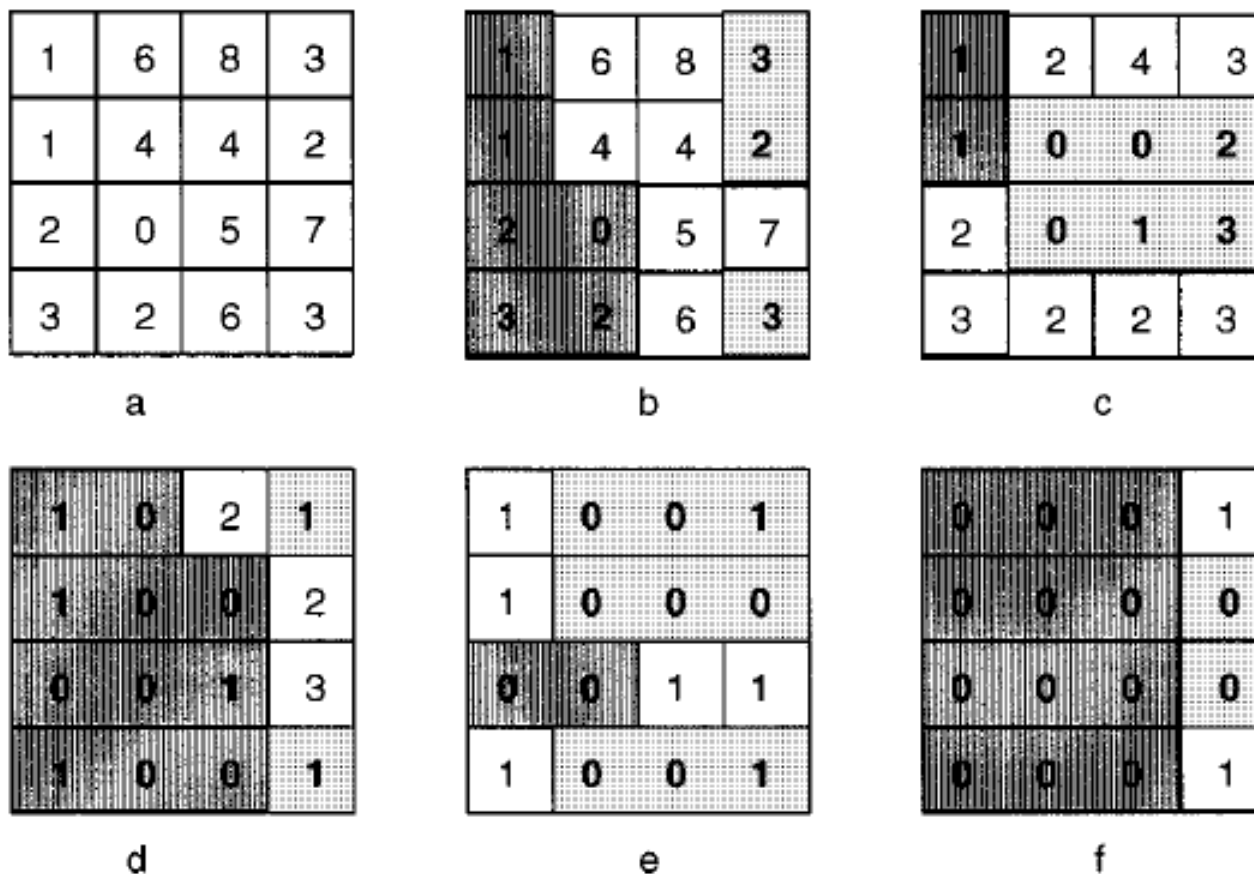
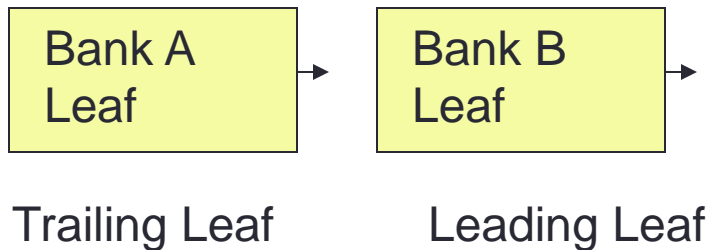
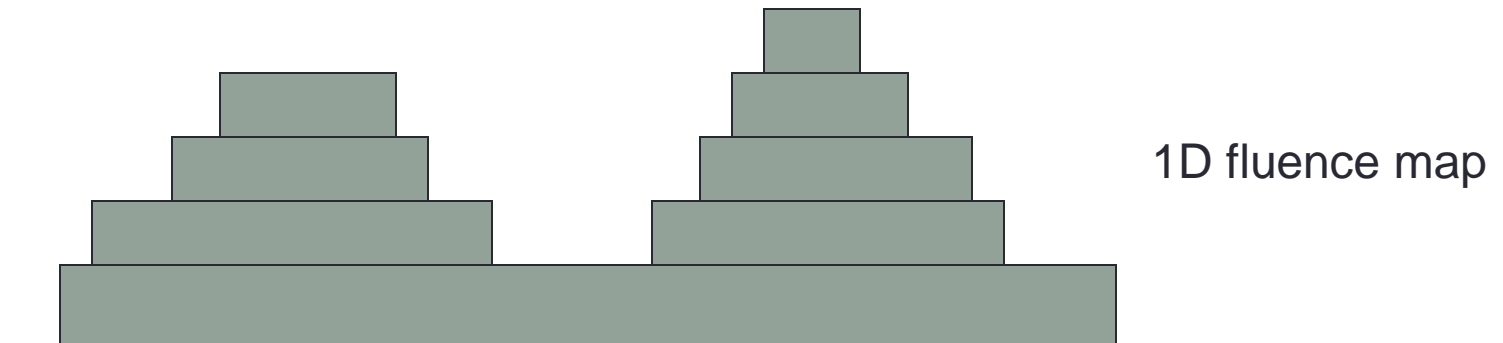


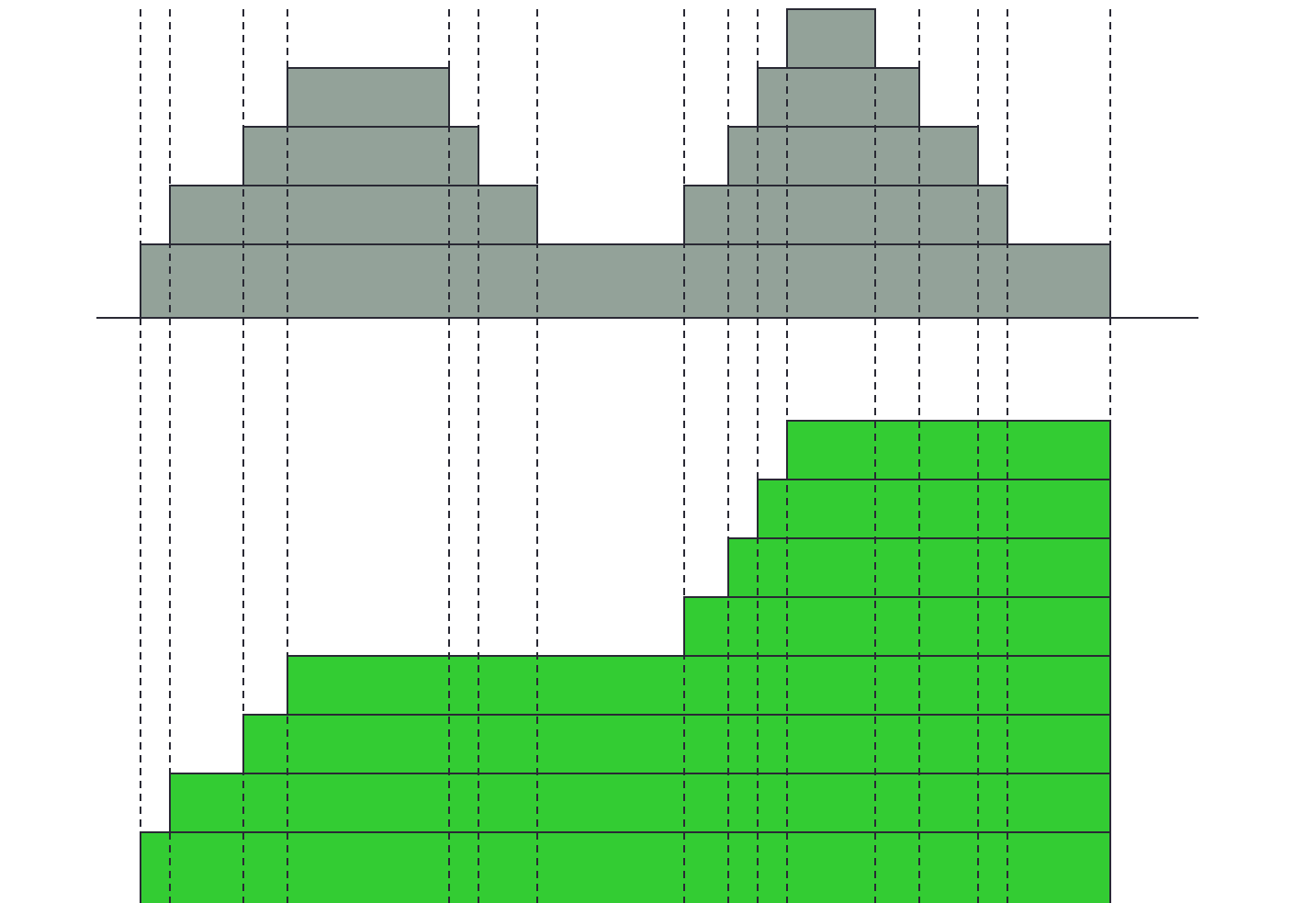
FIG. 5. (a) The same intensity matrix as Fig. 4(a), delivered by reducing level technique with intensity sequence of  $\{4,2,2,1,1,\}$ ; (b)–(f) are the MLC shapes and their corresponding intensity matrix before delivery.

## Dynamic dose delivery

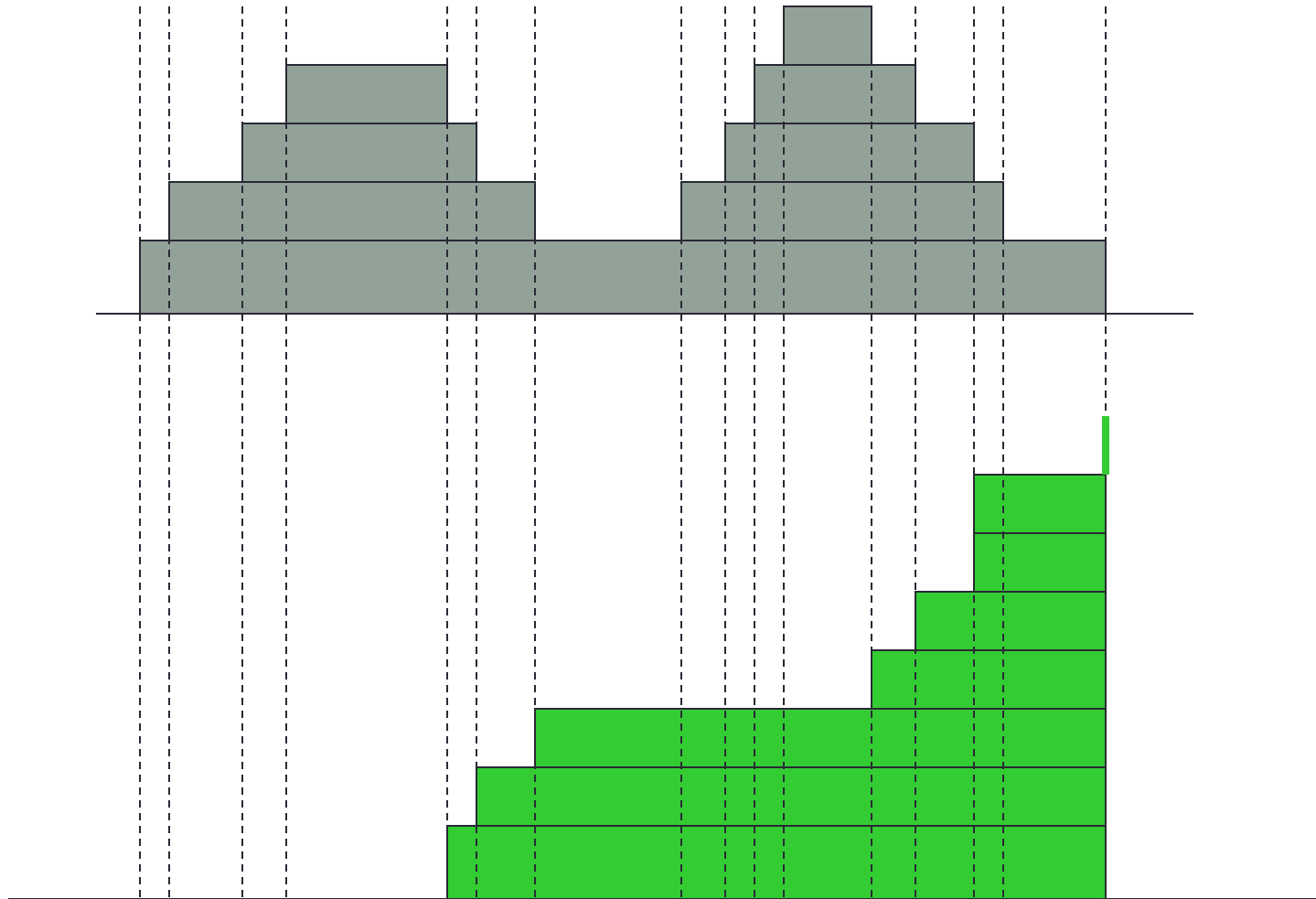
**An optimized leaf-setting algorithm for beam intensity modulation using dynamic multileaf collimators** Lijun Ma, Arthur L Boyer, L Xing and C-M Ma  
Phys. Med. Biol. **43** (1998) 1629–1643.



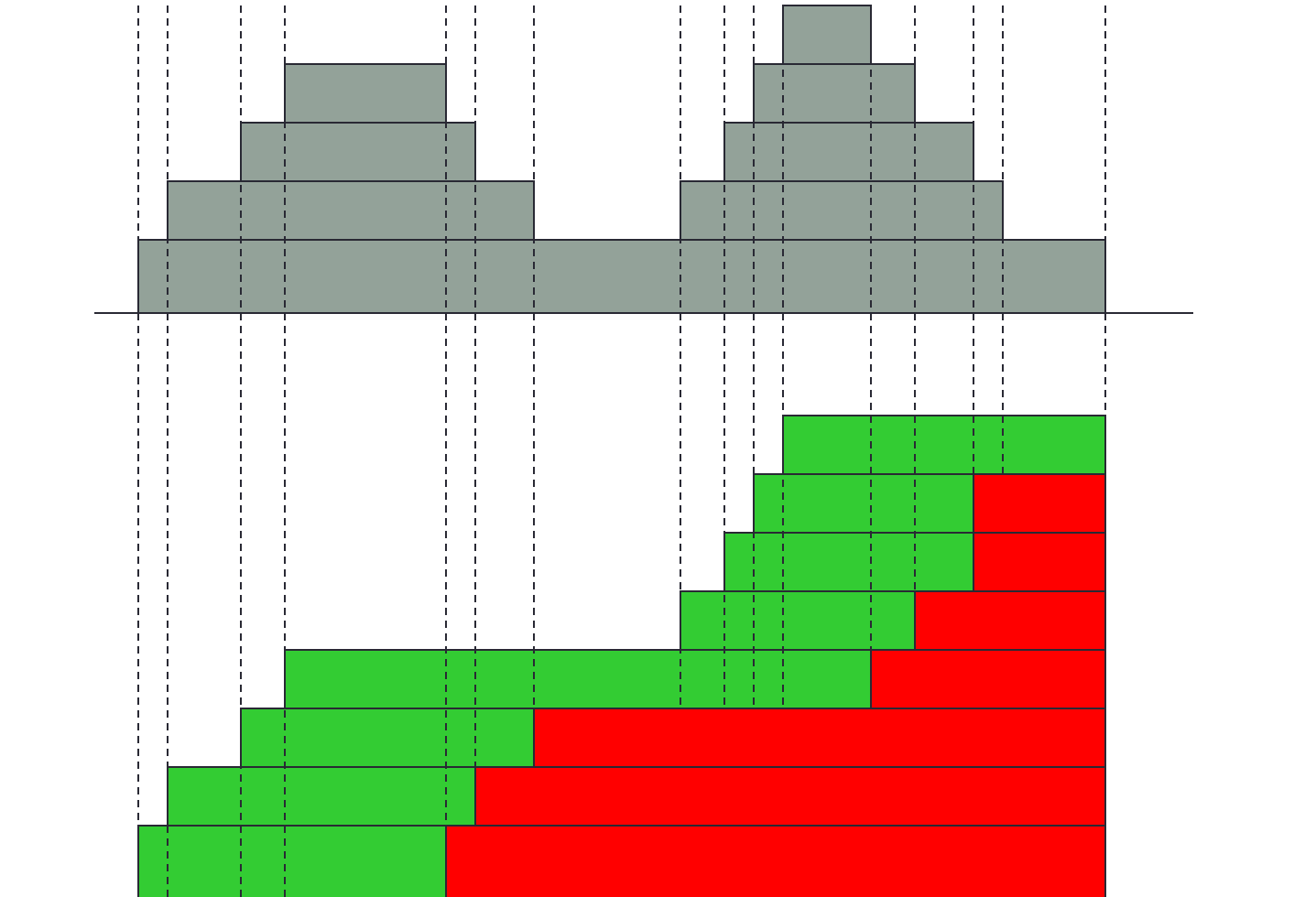
## Generate trailing leaf pattern



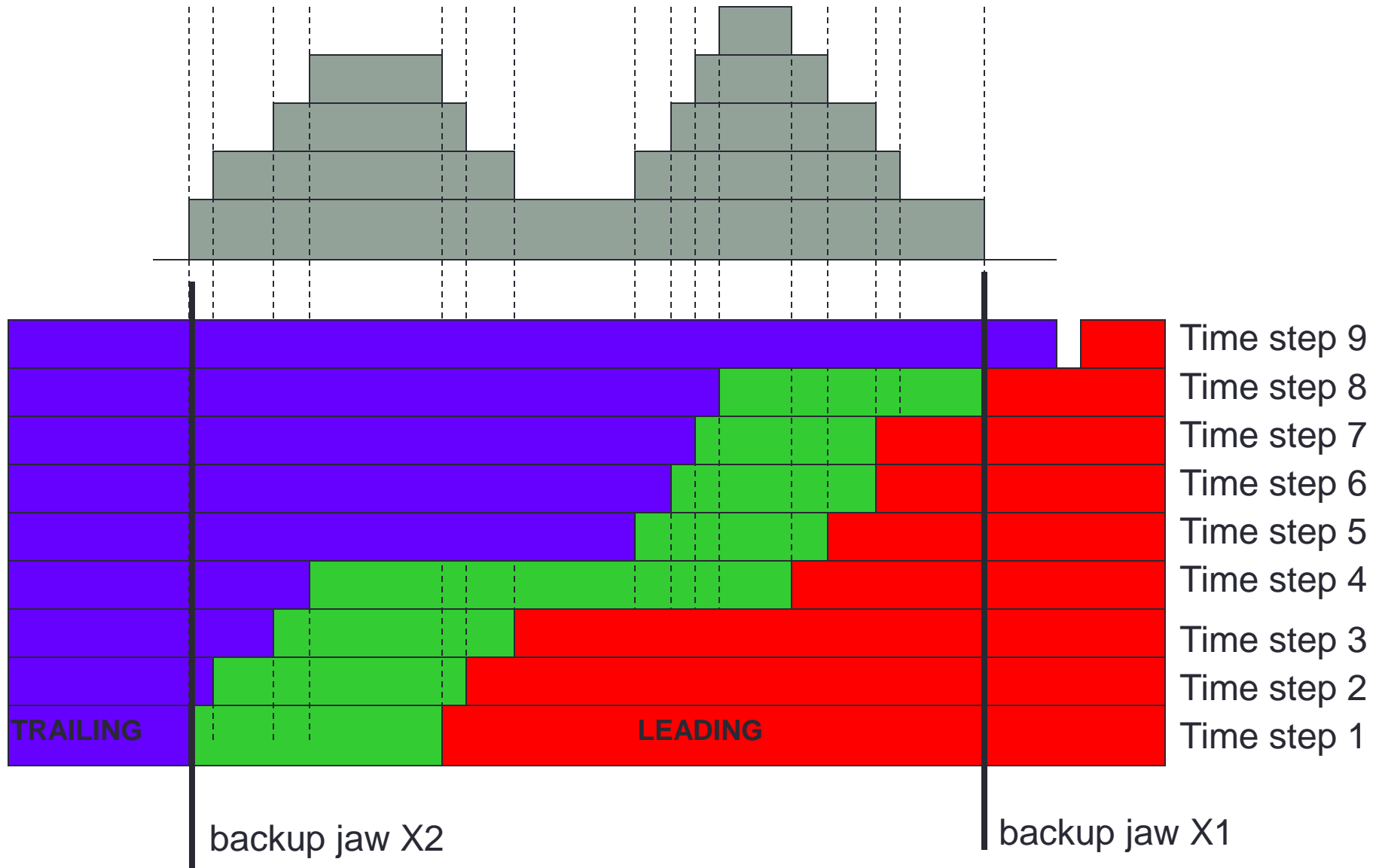
## Generate leading leaf pattern



Combine to obtain positive and negative fluence pattern

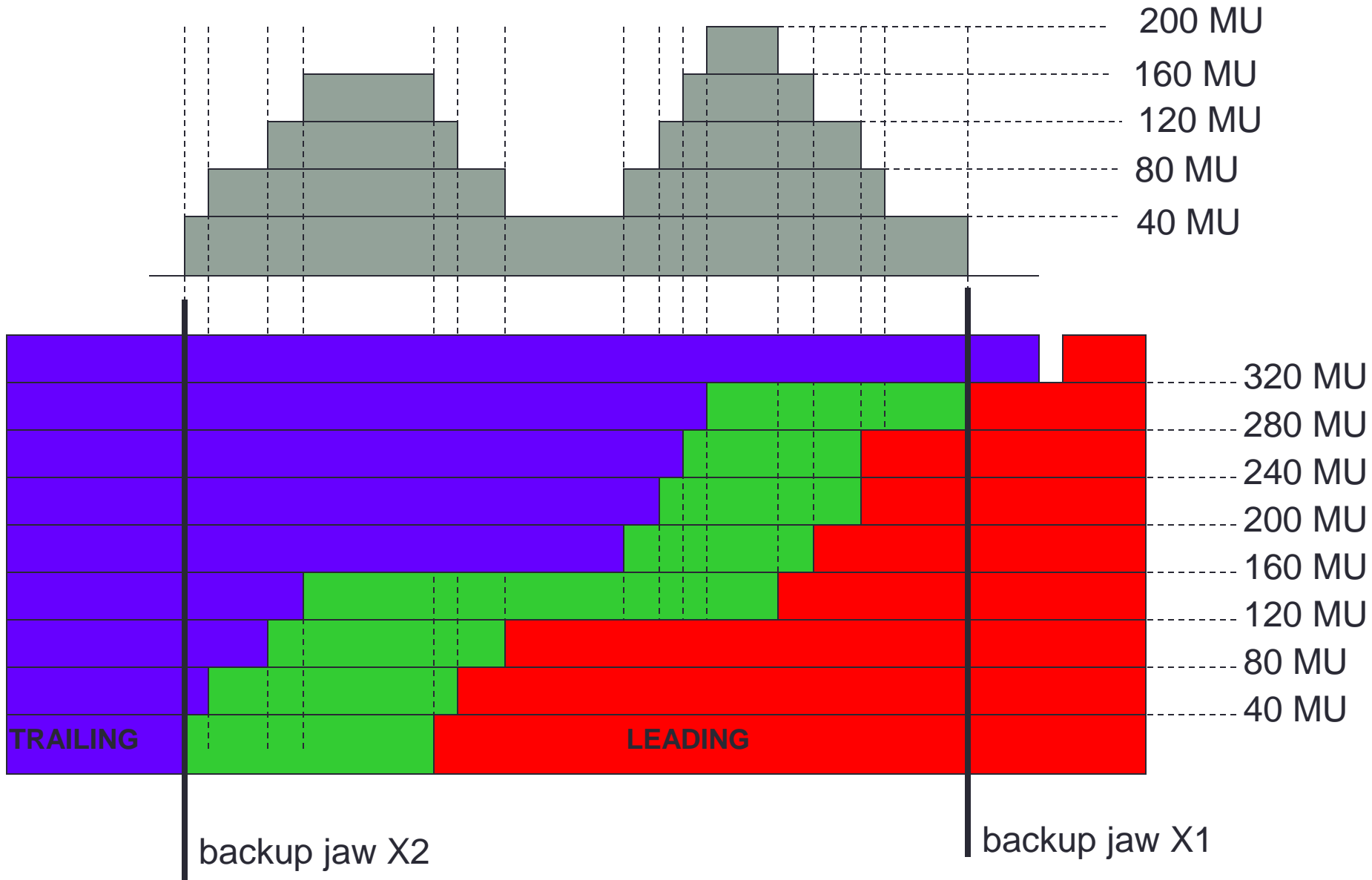


Combine to obtain complete dynamic leaf motion

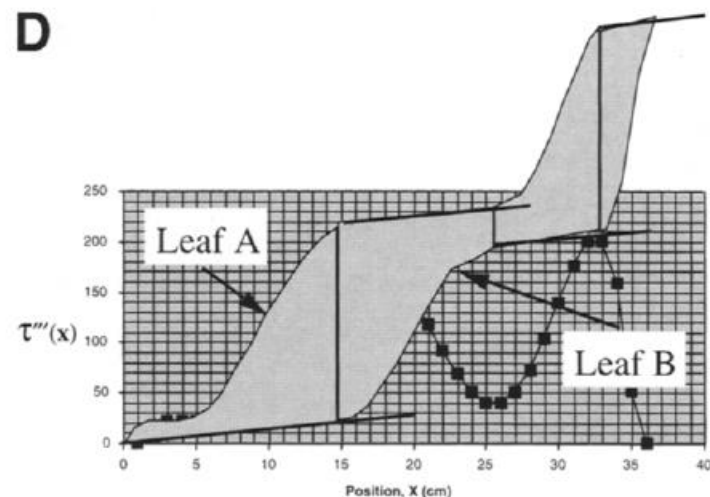
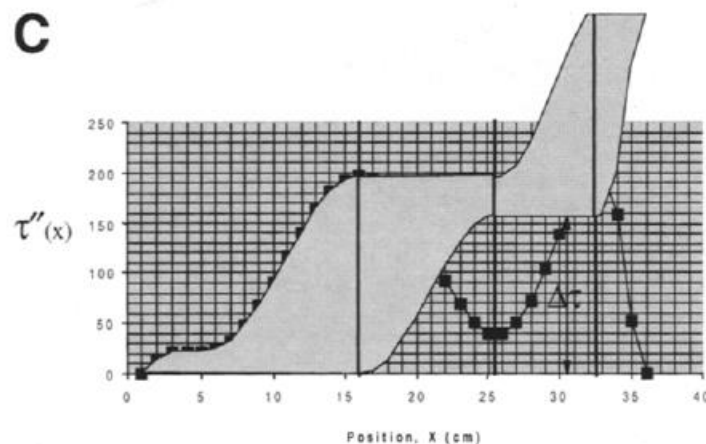
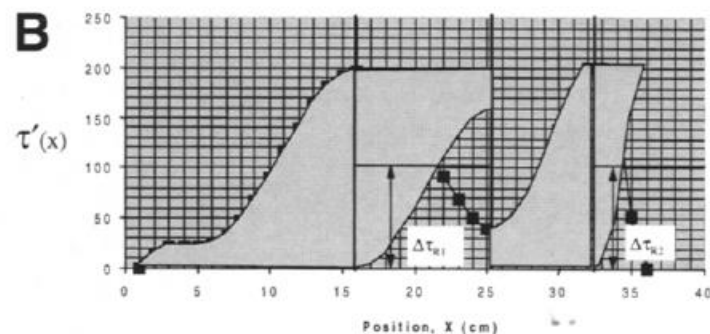
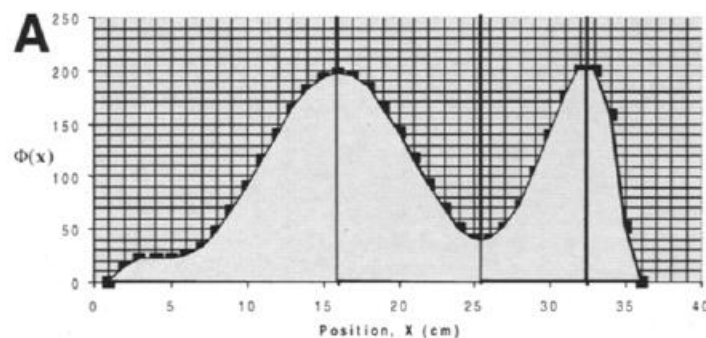


## To convert time steps to actual monitor units

First, convert (scale) the energy fluence to open field monitor units



Since our leaves have a finite maximum speed .....



**INFINITE SPEED MOTION**

**FINITE SPEED "SHEARED" MOTION**

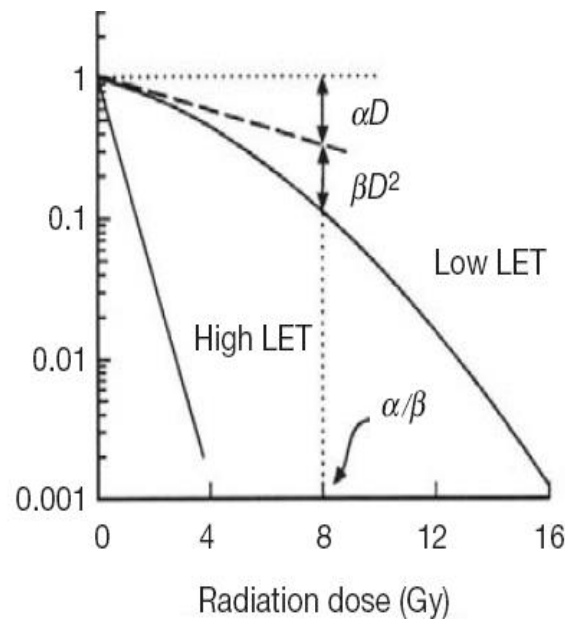
**Figure 1.** (A) An arbitrary fluence profile  $\Phi(x)$ . The positive and negative gradient regions are separated by vertical lines on the continuous profile. (B) Time reversals removed with the reflection operation on negative gradient regions.  $\Delta\tau_{R1}$  is the average value of the portion of the profile having a negative gradient within the R1 gradient region, and  $\Delta\tau_{R2}$  is the average value of the portion of the profile having a negative gradient within the R2 gradient region. (C) Time reversals removed with the reflection operation on negative gradient regions with a translation operation. (D) Infinite velocities removed with shear operation on the continuous profile.



**Calculation of  
Tumor Control Probability (TCP)  
and  
Normal Tissue Complication Probability (NTCP)**

## Cell survival curves: Linear-Quadratic model (LQ model)

$$S = e^{-(\alpha d + \beta d^2)}$$



Higher fractional dose  $\Rightarrow$  disproportionately greater damage

For  $f$  fractions:

$$S = e^{-f(\alpha d + \beta d^2)}$$

This is equivalent to the probability  $p$  of a tumor “clonogen” surviving the course of radiation.

## Tumor control probability (TCP)

If  $p$  is small, binomial distribution can be approximated by a Poisson arrival process.

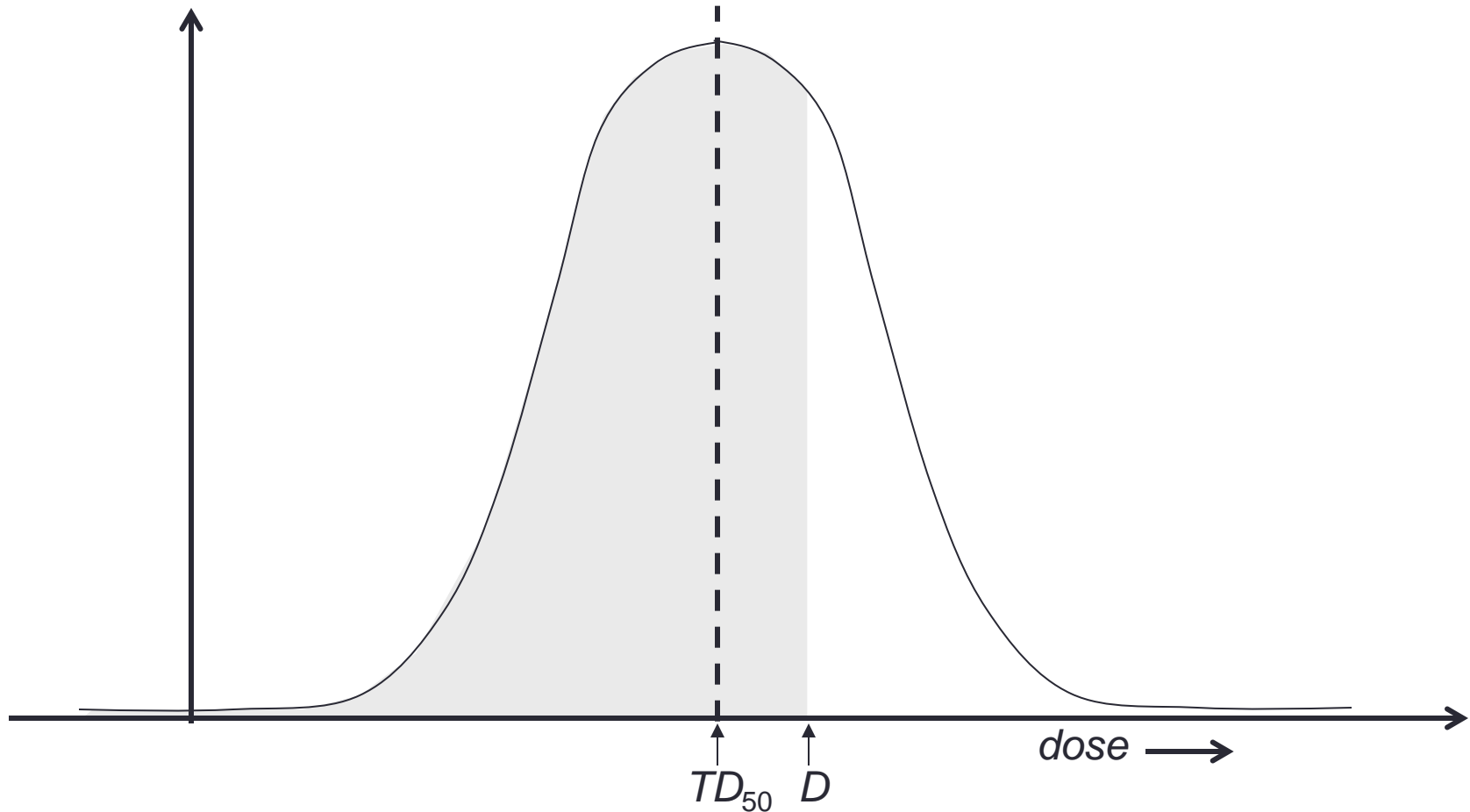
$$\text{Probability of } k \text{ clonogens surviving} = \frac{(Np)^k e^{-Np}}{k!}$$

$Np$  is the mean number of surviving clonogens

$$\text{TCP} = \text{Probability of no clonogens surviving } (k=0) = e^{-Np}$$

## Normal Tissue Complication Probability (NTCP): Lyman model

For the moment, assume a uniform dose in the organ.

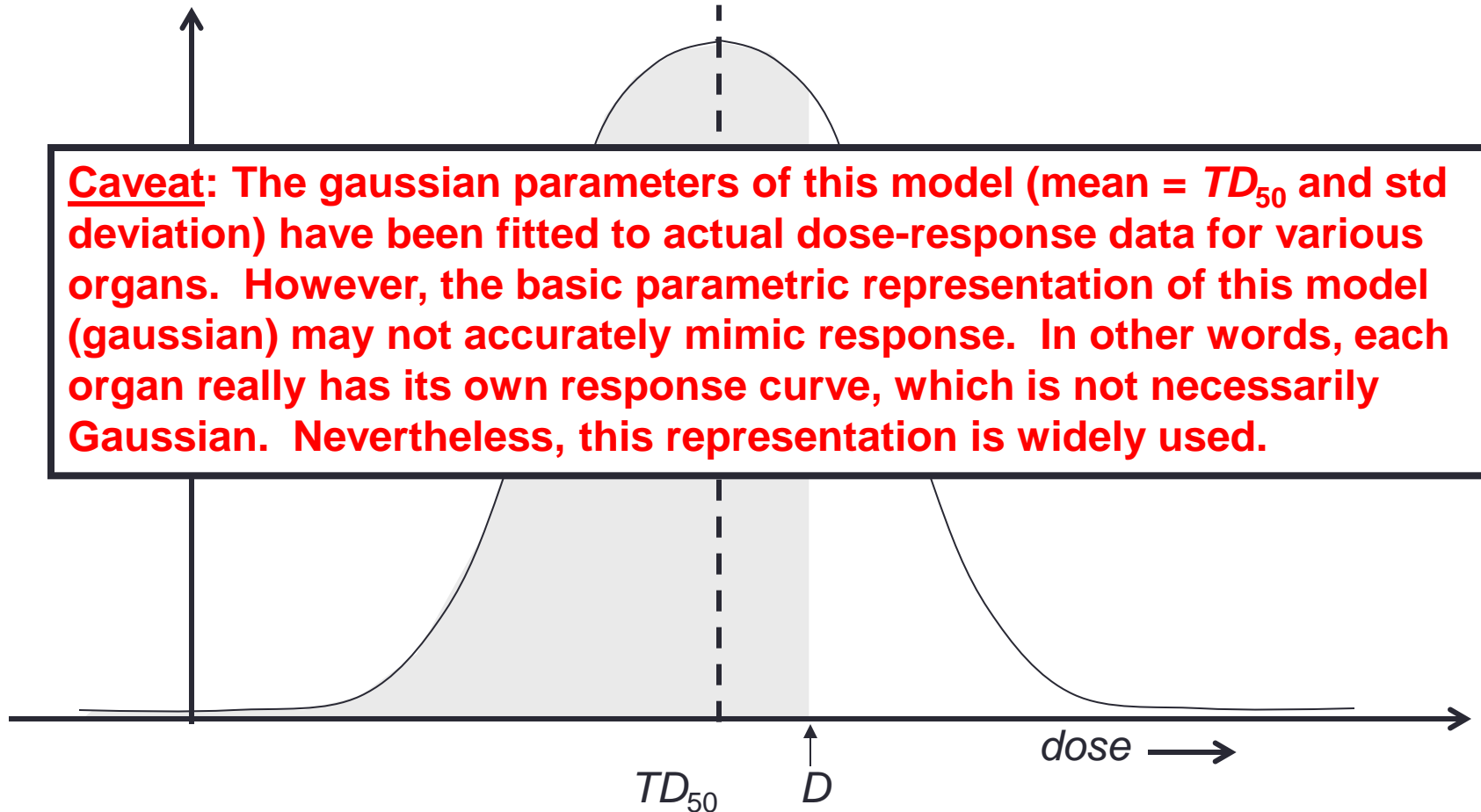


$TD_{50}$  = tolerance dose for 50% probability of injury

To compute probability of injury for dose  $D$  in organ, integrate gaussian probability function from  $-\infty$  to  $D$ .

## Normal Tissue Complication Probability (NTCP): Lyman-Kutcher-Burman model

For the moment, assume a uniform dose in the organ.



## Normal Tissue Complication Probability (NTCP): Lyman model

Probability of complication for a uniform dose  $D$  to organ

$$p(D) = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^D e^{-\left(\frac{(x-TD_{50})^2}{2\sigma^2}\right)} dx$$

Notationally, you will find that the standard deviation ( $\sigma$ ) is frequently denoted as:

$$\sigma = mTD_{50}$$

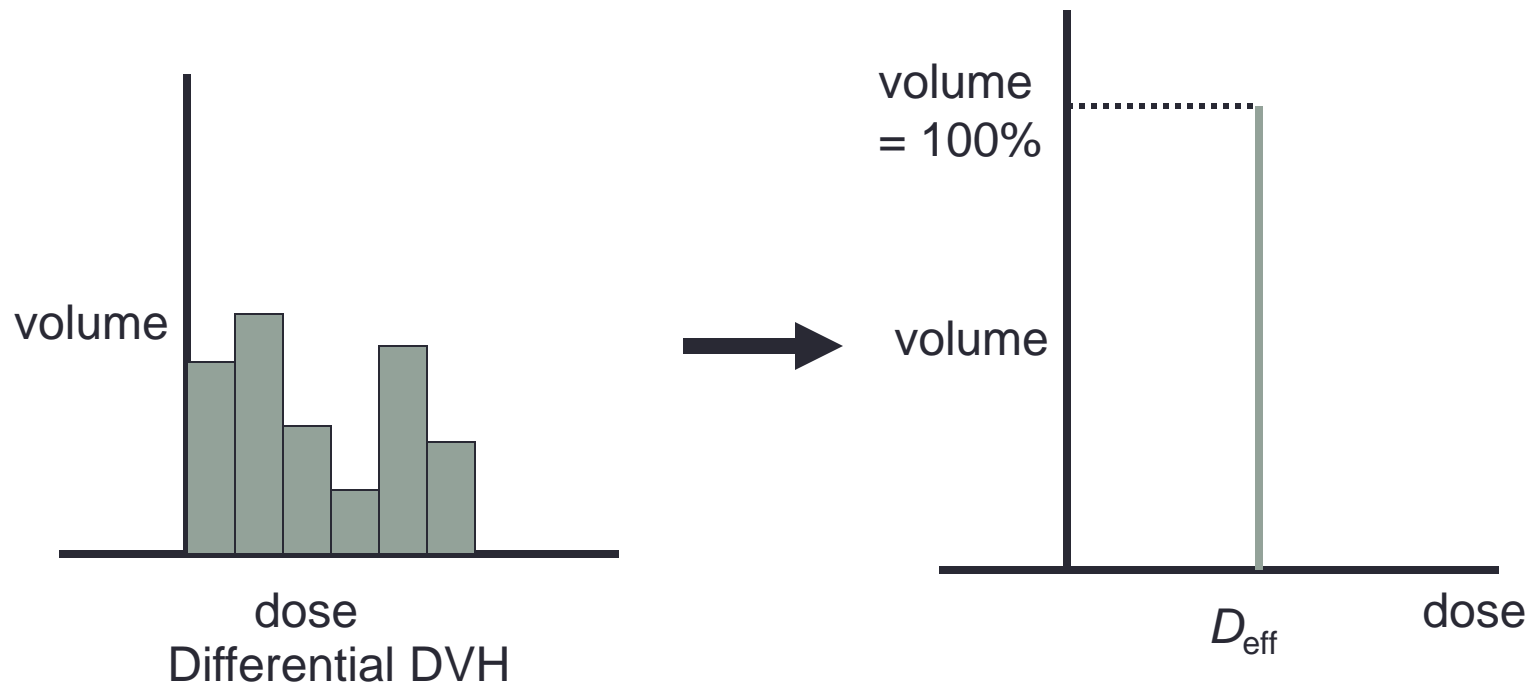
where parameter  $m$  can be found in literature (previously fitted to the dose-response of a specific organ).

For example, if  $m = 0.11$  and  $TD_{50} = 80$  Gy:  $\sigma = 0.11 \times 80 = 8.8$  Gy .

## Normal Tissue Complication Probability (NTCP): Lyman model

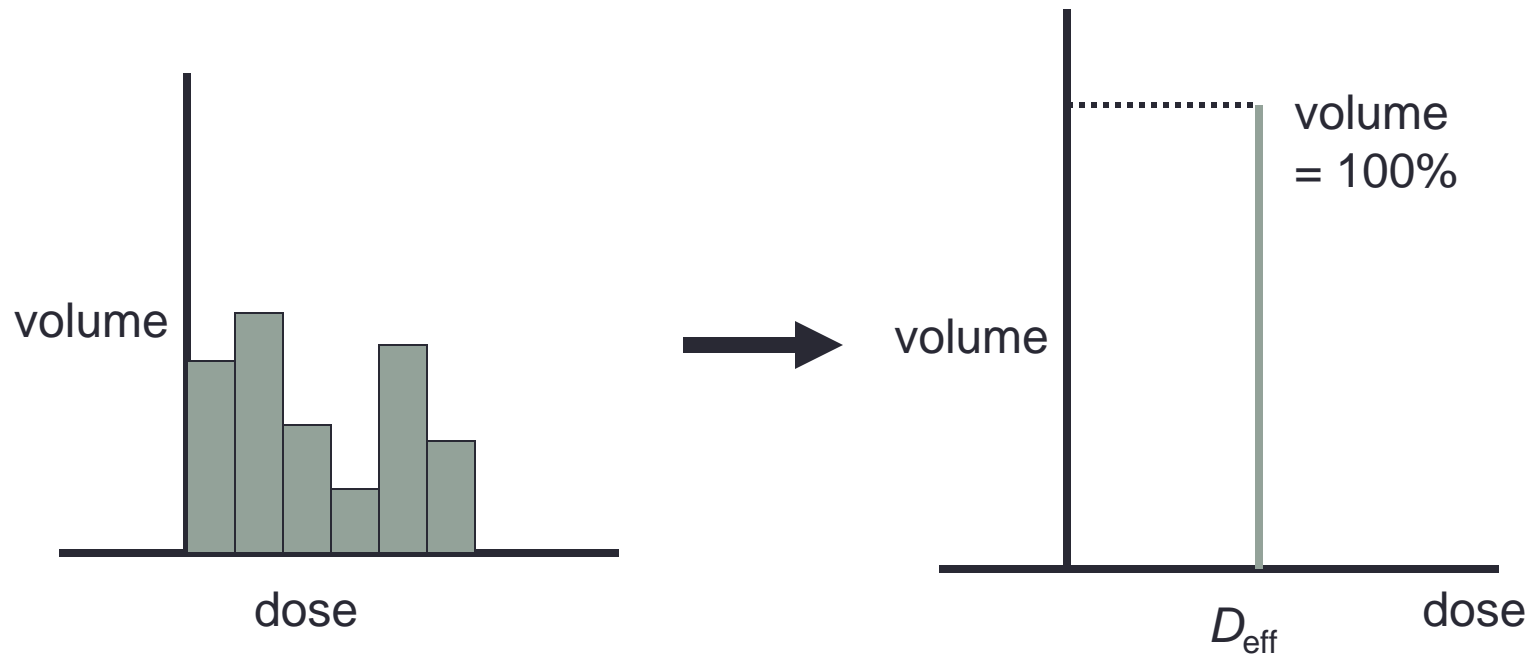
But, in fact, the dose distribution in an organ is non-uniform. How do we account for dose nonuniformity?

Convert the nonuniform dose to an “effective” uniform dose and then use the LKB NTCP equation.



## Normal Tissue Complication Probability (NTCP): Lyman model

Convert the nonuniform dose to an “effective” uniform dose and then use the LKB NTCP equation.



You can think of effective uniform dose as the dose that most closely correlates to a “bad” response from the organ.

For example, in lung, a higher mean lung dose is a good indicator of pneumonitis.

In spinal cord, the maximum dose is what matters in creating complications.



## Normal Tissue Complication Probability (NTCP): Lyman model

“Generalized equivalent uniform dose” or “Equivalent uniform dose”

$$EUD = \left( \frac{\sum_i V_i D_i^{1/n}}{\sum_i V_i} \right)^n$$

Sometimes, you will see  $1/n$  replaced by parameter  $a$ .

Where  $V_i$  is the volume at dose  $D_i$  (obtained from the differential DVH), and parameter  $n$  can be found in literature (previously fitted to the dose-response of a specific organ).

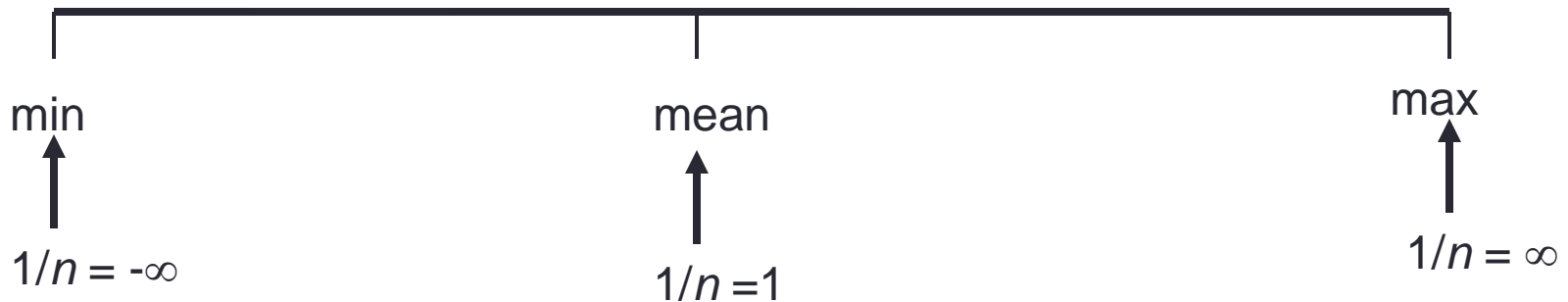
$$p(EUD) = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{EUD} e^{-\left(\frac{(x-TD_{50})^2}{2\sigma^2}\right)} dx$$

## Normal Tissue Complication Probability (NTCP): Lyman model

How can we interpret the  $n$  value in the EUD formalism?

$$EUD = \left( \frac{\sum_i V_i D_i^{1/n}}{\sum_i V_i} \right)^n$$

Imagine a bar with doses in the organ sorted from min to max



$1/n$  is essentially the slider on the bar that selects the appropriate EUD value.

## Normal Tissue Complication Probability (NTCP): Lyman model

1. Use the value of  $n$ ,  $m$ ,  $TD_{50}$  for the appropriate organ.
2. Compute the differential dose-volume histogram for the organ.
3. Compute the equivalent uniform dose for organ.

$$EUD = \left( \frac{\sum_i V_i D_i^{1/n}}{\sum_i V_i} \right)^n$$

4. Compute the standard deviation for the probability equation.

$$\sigma = mTD_{50}$$

5. Compute the NTCP

$$p(EUD) = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{EUD} e^{-\left(\frac{(x-TD_{50})^2}{2\sigma^2}\right)} dx$$

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	$n$	$m$	$TD_{50}$ (Gy)
bladder	0.5	0.11	80
rectum	0.12	0.15	80
femoral heads	0.25	0.12	65
small intestine	0.15	0.16	55
colon	0.17	0.11	55