IAEA
International Atomic Energy Agency

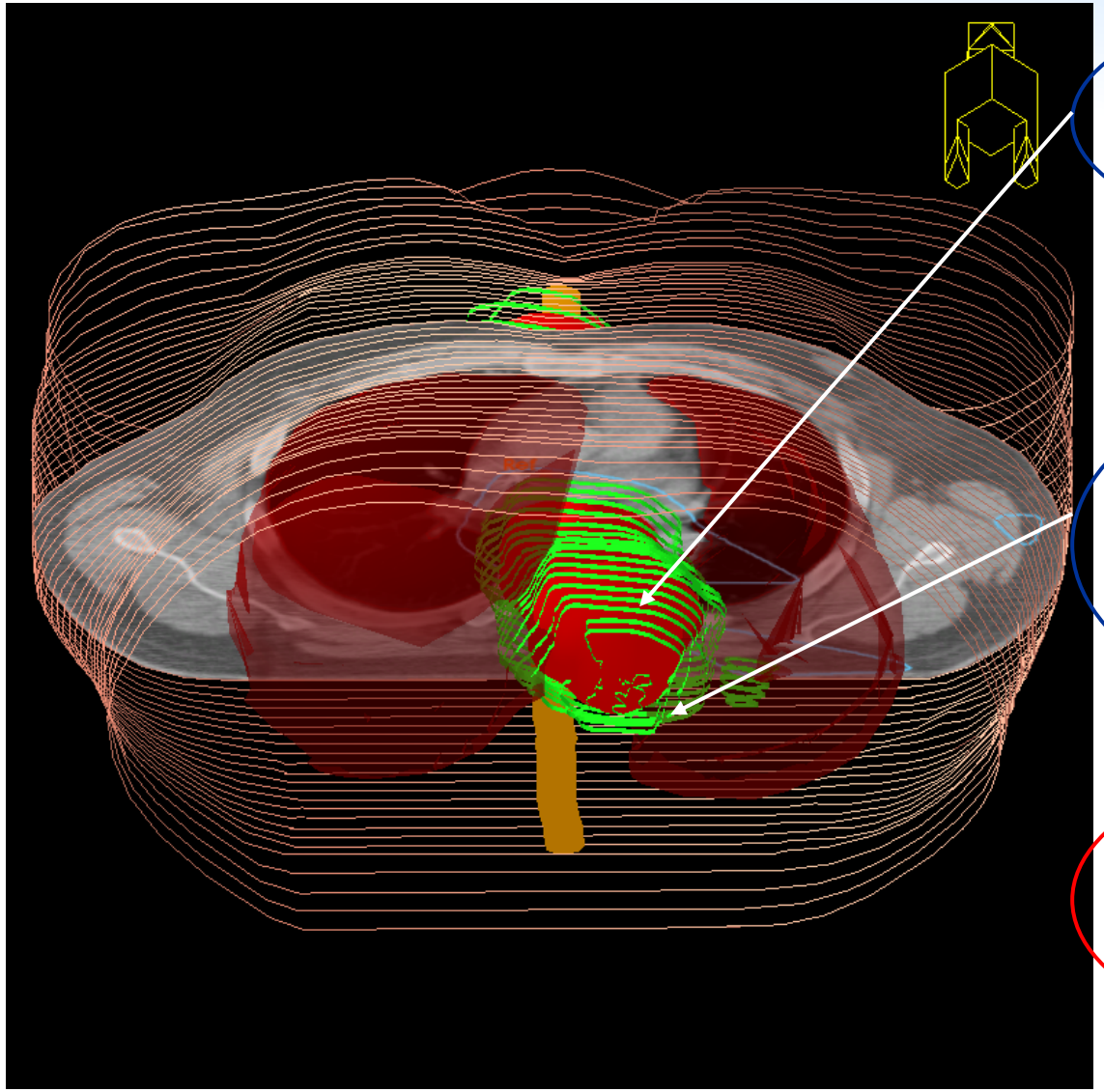
Topical Session on Radiation Induced Second Primary Cancer
Following Radiotherapy and Associated Imaging

Different volumes in radiotherapy

Ola Holmberg
Head, Radiation Protection of Patients Unit (RPOP)
NSRW, IAEA

54th Meeting of the Radiation Safety Standards Committee (RASSC)
Vienna, 13-16 June 2023

Background



Tumour cells contained in the red volume throughout the treatment course

95% or more of the prescribed dose given to everything inside green lines – and lower dose outside green lines

Looks nice as a picture – BUT: How do we ensure that this picture reflects the reality of the treatment?

Background

Problem:

We need common and wise definitions of volumes and dose in radiotherapy. Otherwise: No progress! How is it possible to share experience of radiotherapy if every centre and every physician has a different definition of:

- volume that has been treated

- dose given to this volume

- dose received by organs at risk

Solution:

International recommendations for definitions of dose and volume in RT: International Commission on Radiation Units and Measurements (ICRU)

Volumes in ICRU29 - 1978

“The Target Volume”

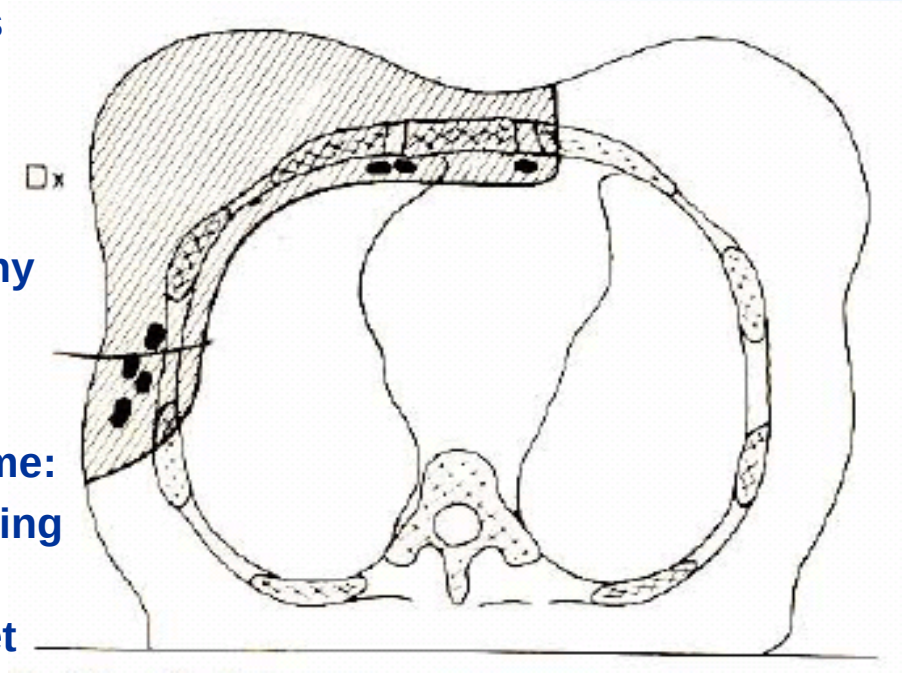
The *target volume* contains those tissues that are to be irradiated to a specified absorbed dose

The *target volume* consists of the demonstrated tumours (if present) and any other tissue with presumed tumour

These parameters should be taken into account when describing the target volume:

- **expected movements of tissues containing the target volume**
- **variations in shape and size of the target volume**
- **variations in treatment set-up**

+ Organs at risk whose presence influence treatment planning



Volumes

1978 ICRU29 **“The Target Volume”** **Organs at risk**

Volumes

1978 ICRU29 **“The Target Volume”** **Organs at risk**

1993 ICRU50 ***… a realization that better tools were needed …***

Volumes in ICRU50 - 1993

Gross Tumour Volume (GTV)

The GTV is the gross demonstrable extent and location of the malignant growth.

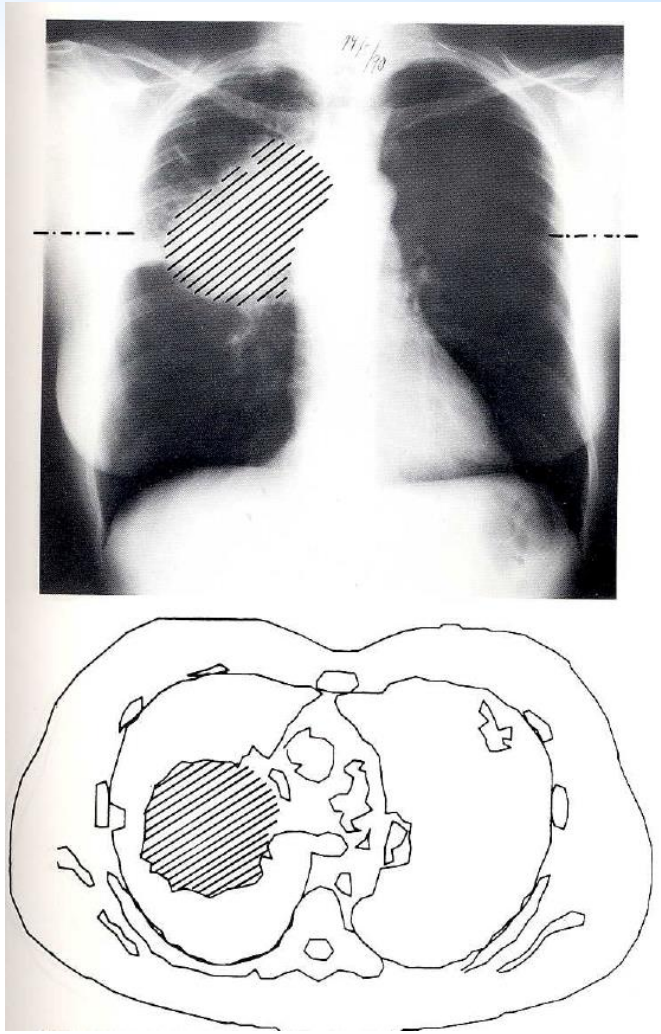
GTV consists of:

primary tumour

metastatic lymphadenopathy

other metastases

An adequate dose must be delivered to the whole GTV to achieve the aim of radical radiotherapy.



The demonstrated tumour in the right hilar region

Volumes in ICRU50 - 1993

Clinical Target Volume (CTV)

The CTV is a tissue volume that contains a demonstrable GTV and/or subclinical, microscopical malignant disease, which must be eliminated.

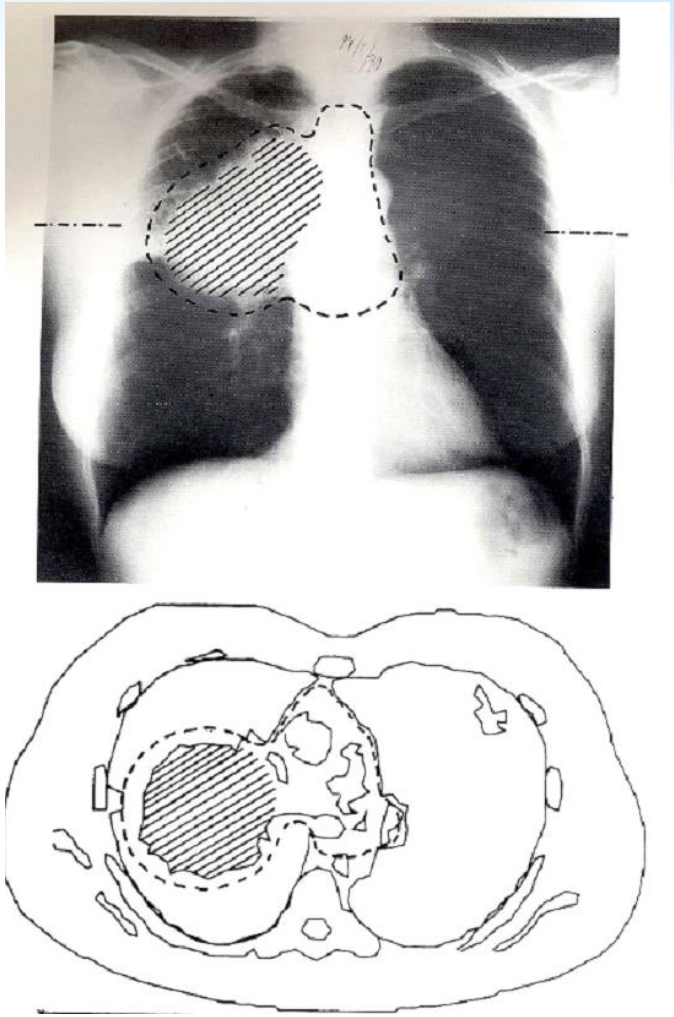
CTV = GTV (if there) + subclinical disease

Subclinical disease consists of:

Suspected disease around the GTV

Suspected lymph nodes

Suspected tissue locations for cancer cells that cannot be detected - “subclinical”. Based on clinical experience. This is the tissue volume that needs to be treated.



CTV I - GTV with margin, and CTV II – mediastinal lymph nodes

Volumes in ICRU50 - 1993

Planning Target Volume (PTV)

The PTV is a geometrical concept … taking into consideration the net effect of all the possible geometrical variations in order to ensure that the prescribed dose is actually ensured in the CTV

PTV = CTV + margin for geometrical variations

Geometrical variations consist of:

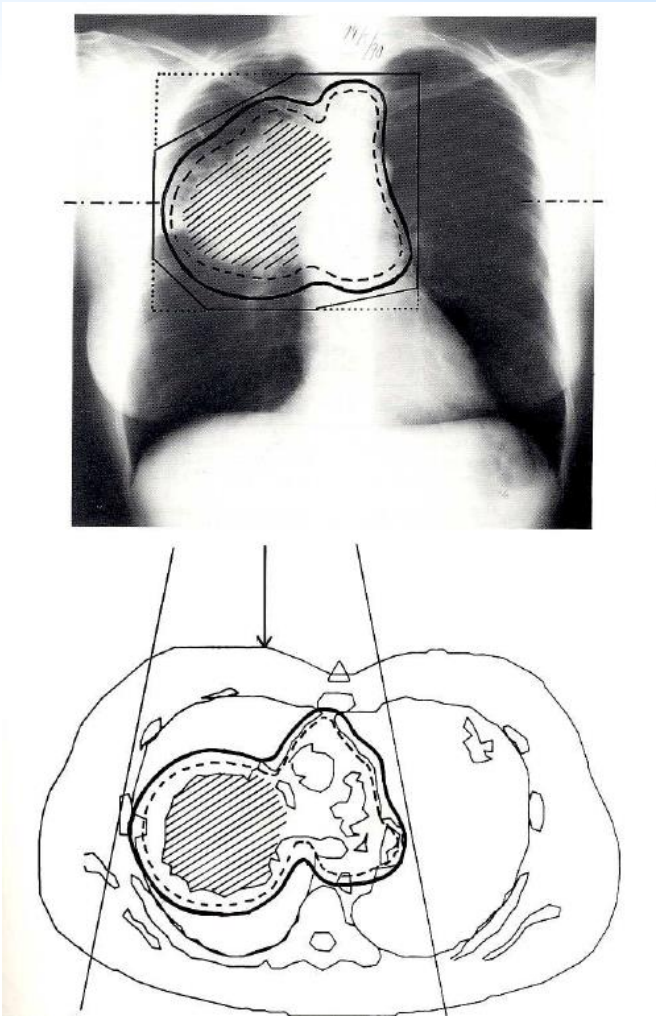
Movements of tissues containing CTV

Movements of patient

Variations in size and shape

Variations in beam geometry characteristics

Aid for treatment planning; dose to PTV representing dose to CTV



CTV with margin forming the PTV

Volumes in ICRU50 - 1993

Organs at risk

The Organs at Risk are normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose

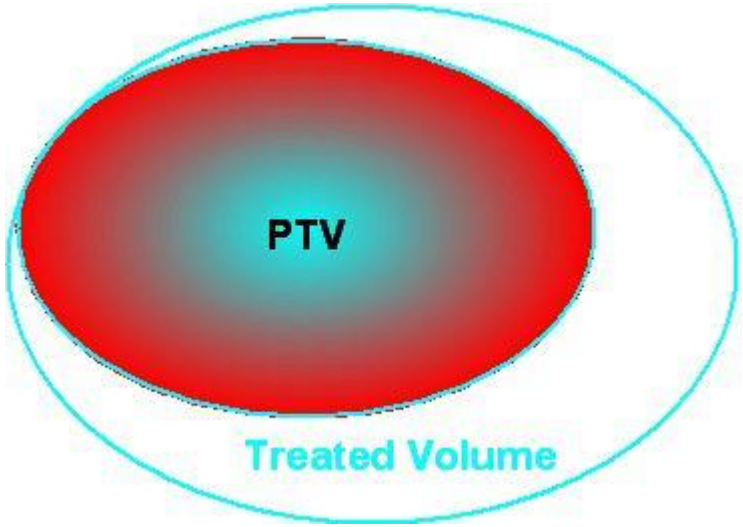
“Any possible movement of the organ at risk during treatment, as well as uncertainties in the set up during the whole treatment course must be considered”



Volumes in ICRU50 - 1993

Treated Volume

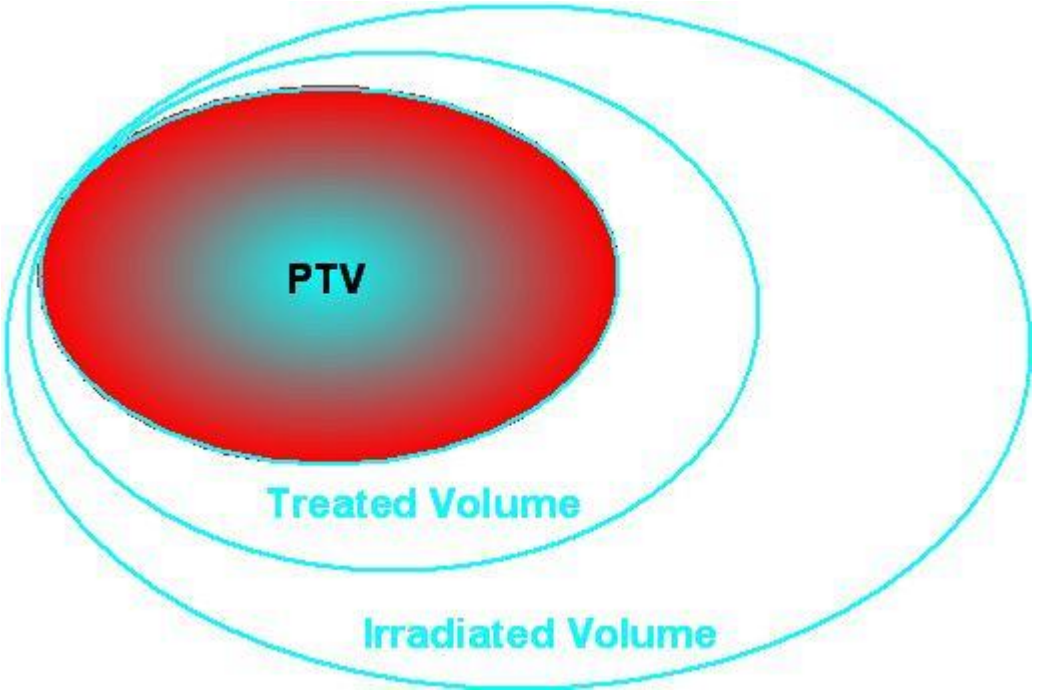
The Treated Volume is the volume which receives at least the dose specified as being appropriate to achieve the purpose of the treatment.



Volumes in ICRU50 - 1993

Irradiated Volume

The Irradiated Volume is the volume which receives a dose that is considered significant in relation to normal tissue tolerance.



Volumes

1978 ICRU29 — **“The Target Volume”** — **Organs at risk**

1993 ICRU50 — **GTV** — **CTV** — **PTV** — **Organs at risk**

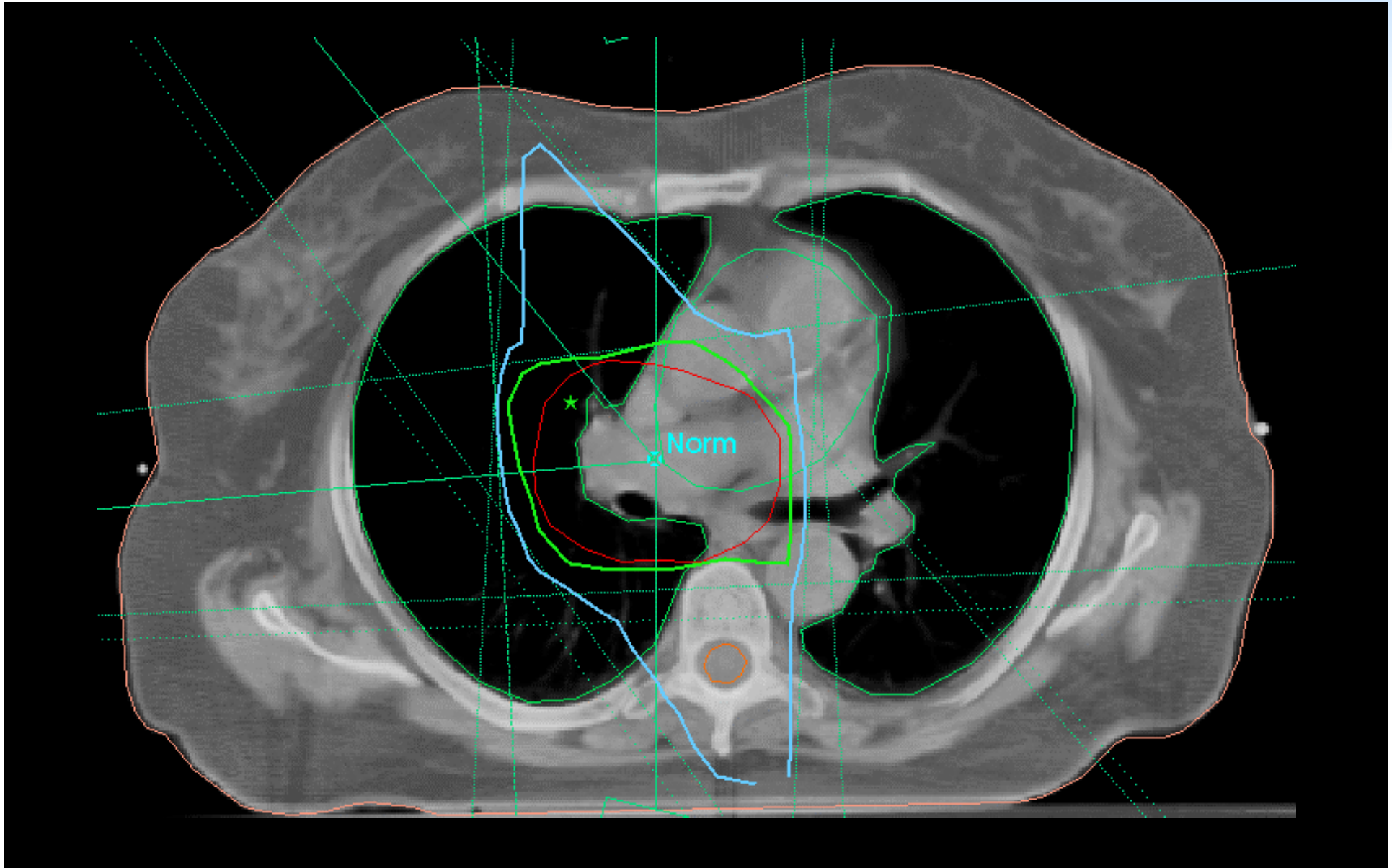
Volumes

1978 ICRU29 **"The Target Volume"** **Organs at risk**

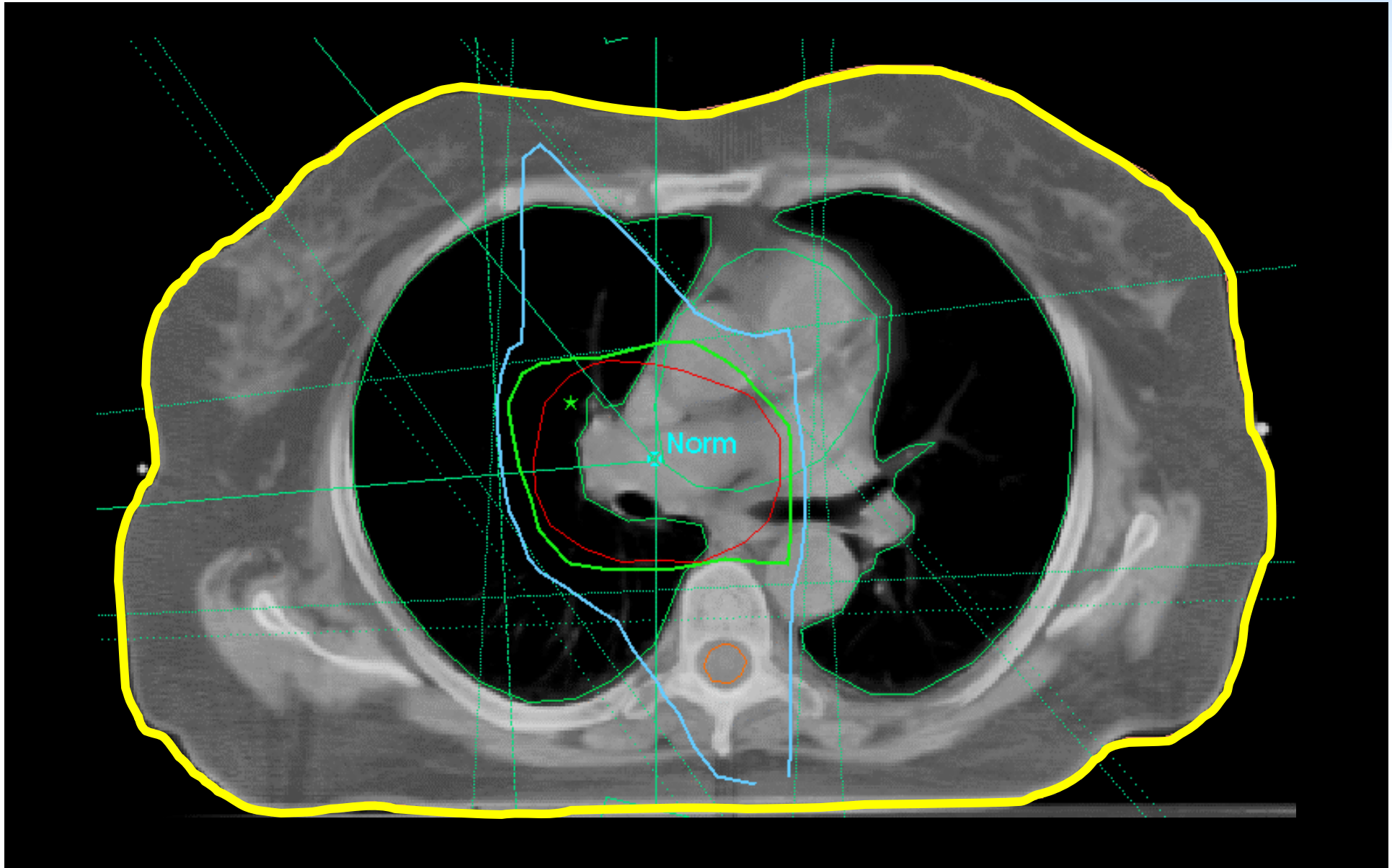
1993 ICRU50 **GTV** **CTV** **PTV** **Organs at risk**

1999 ICRU62 ***… a lot of focus on geometrical variations in this time period…***

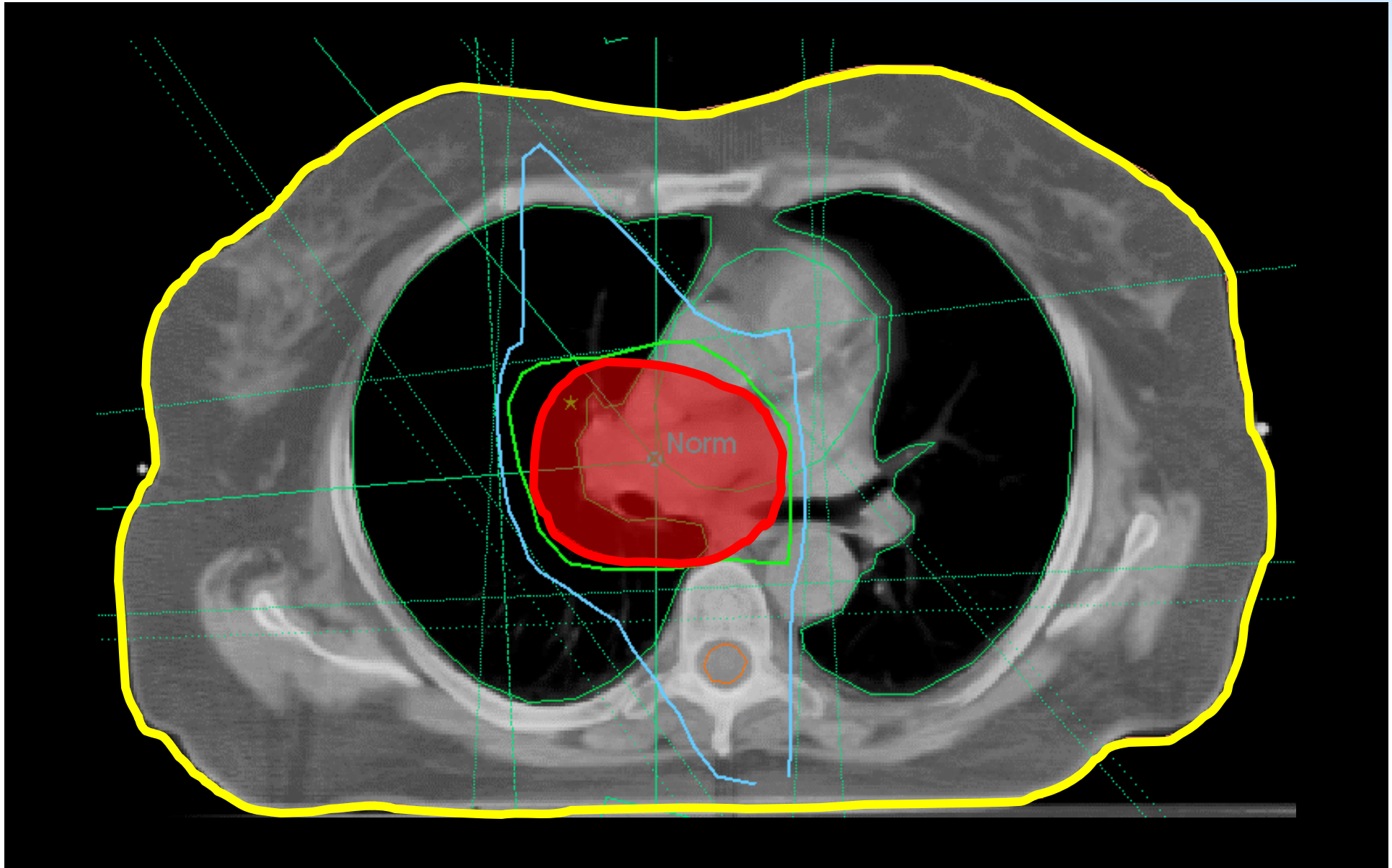
Computerised Tomography (X Ray)



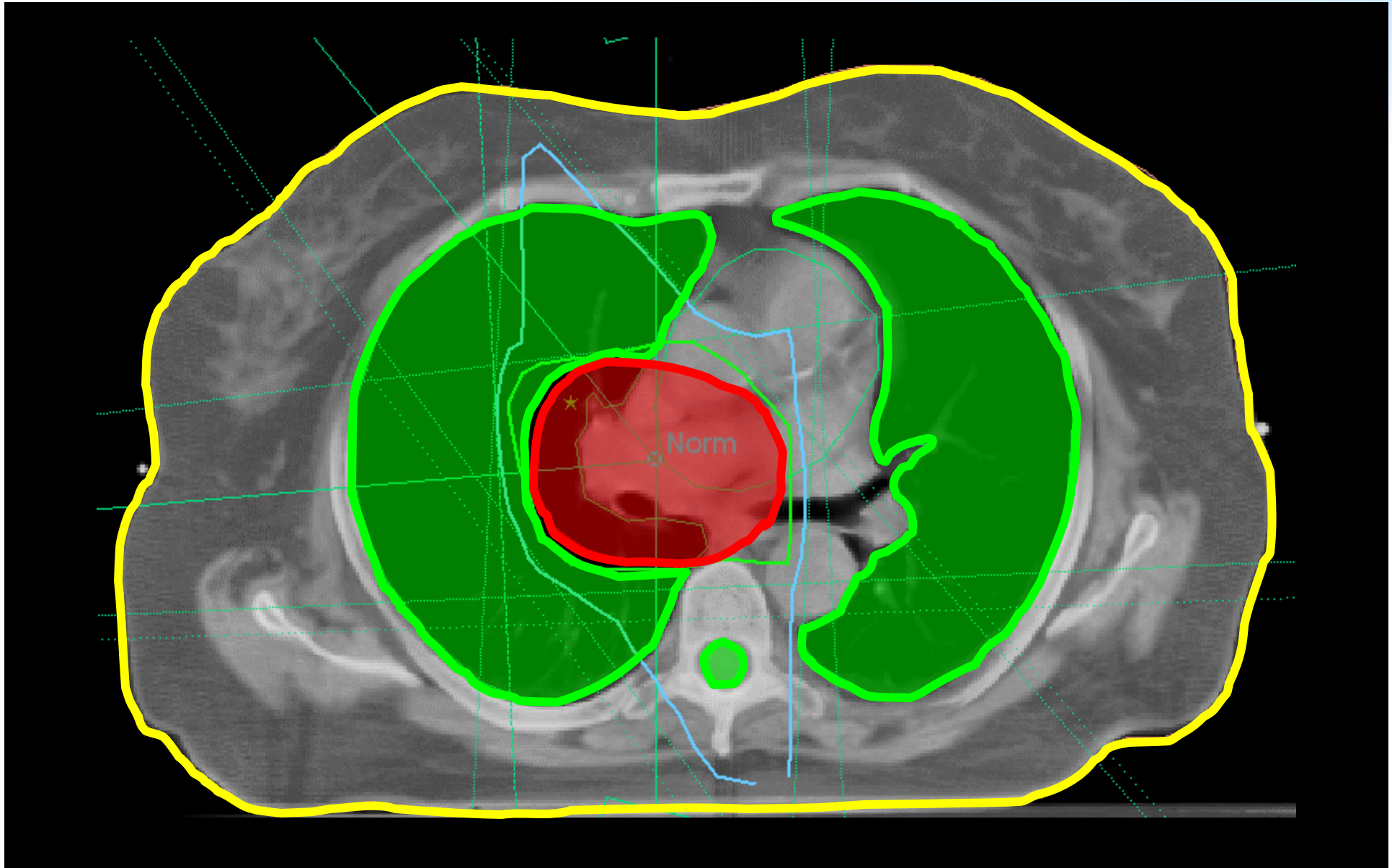
Outline of patient’s body



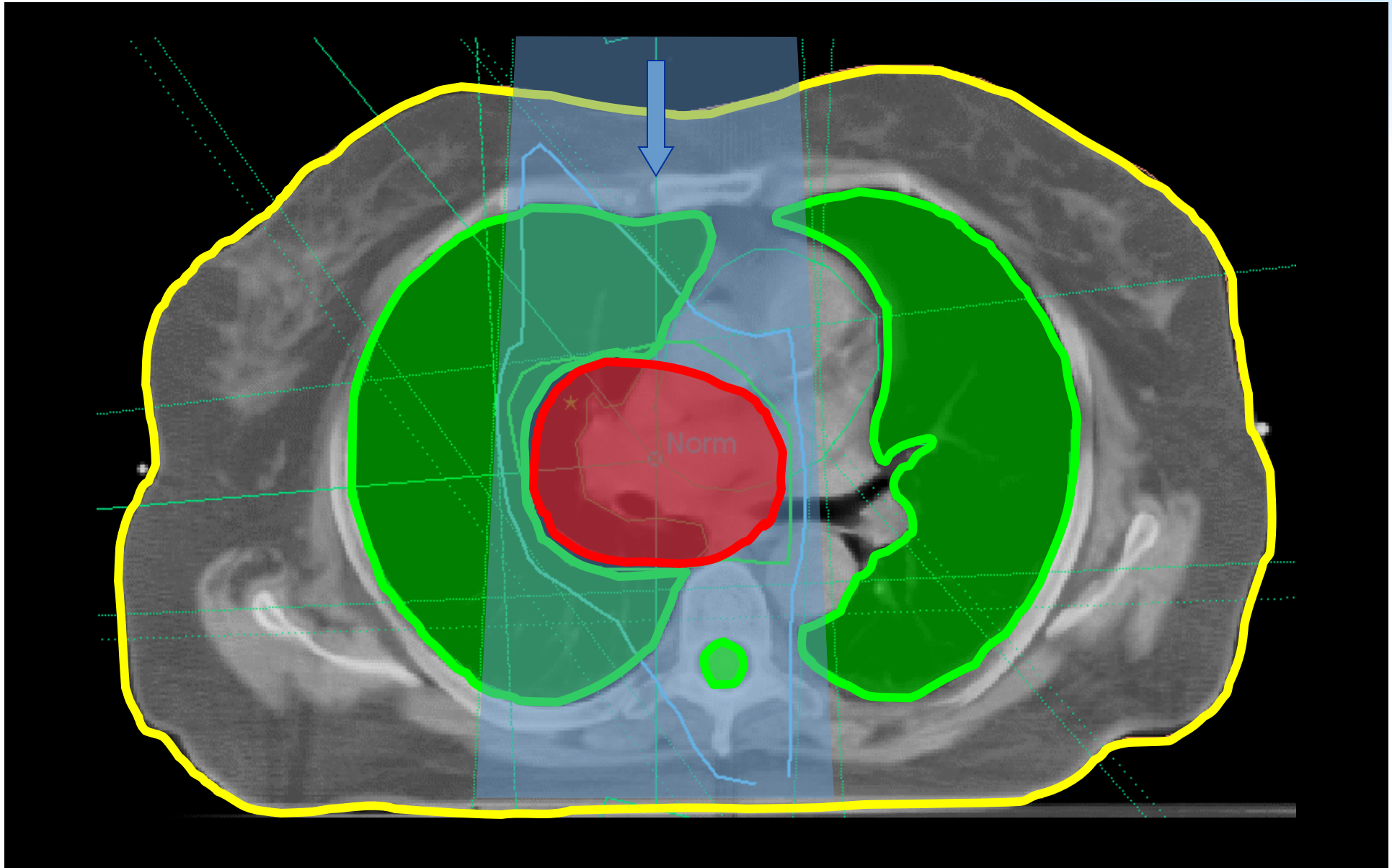
Tumour cells inside patient's body



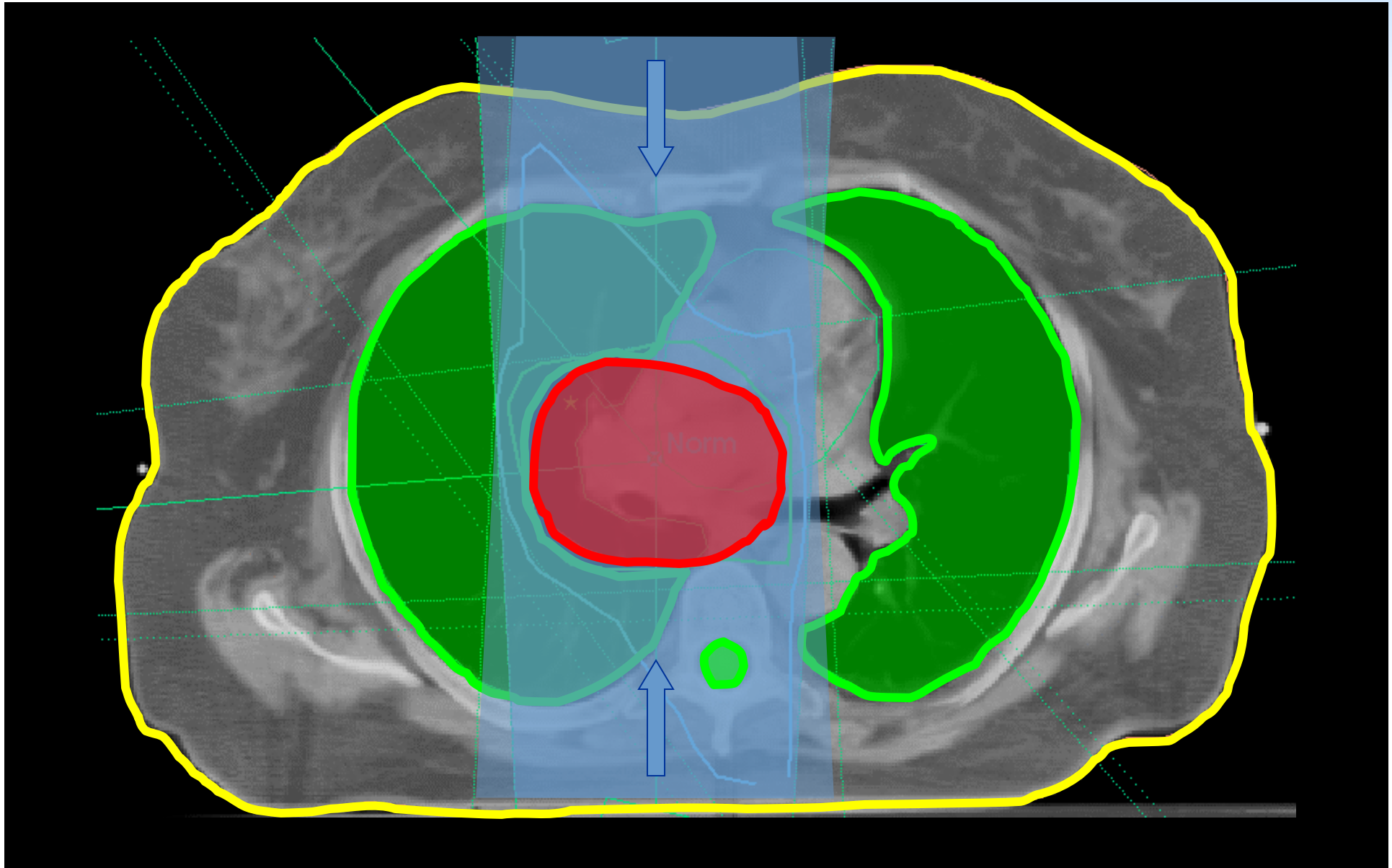
Sensitive organs around tumour cells



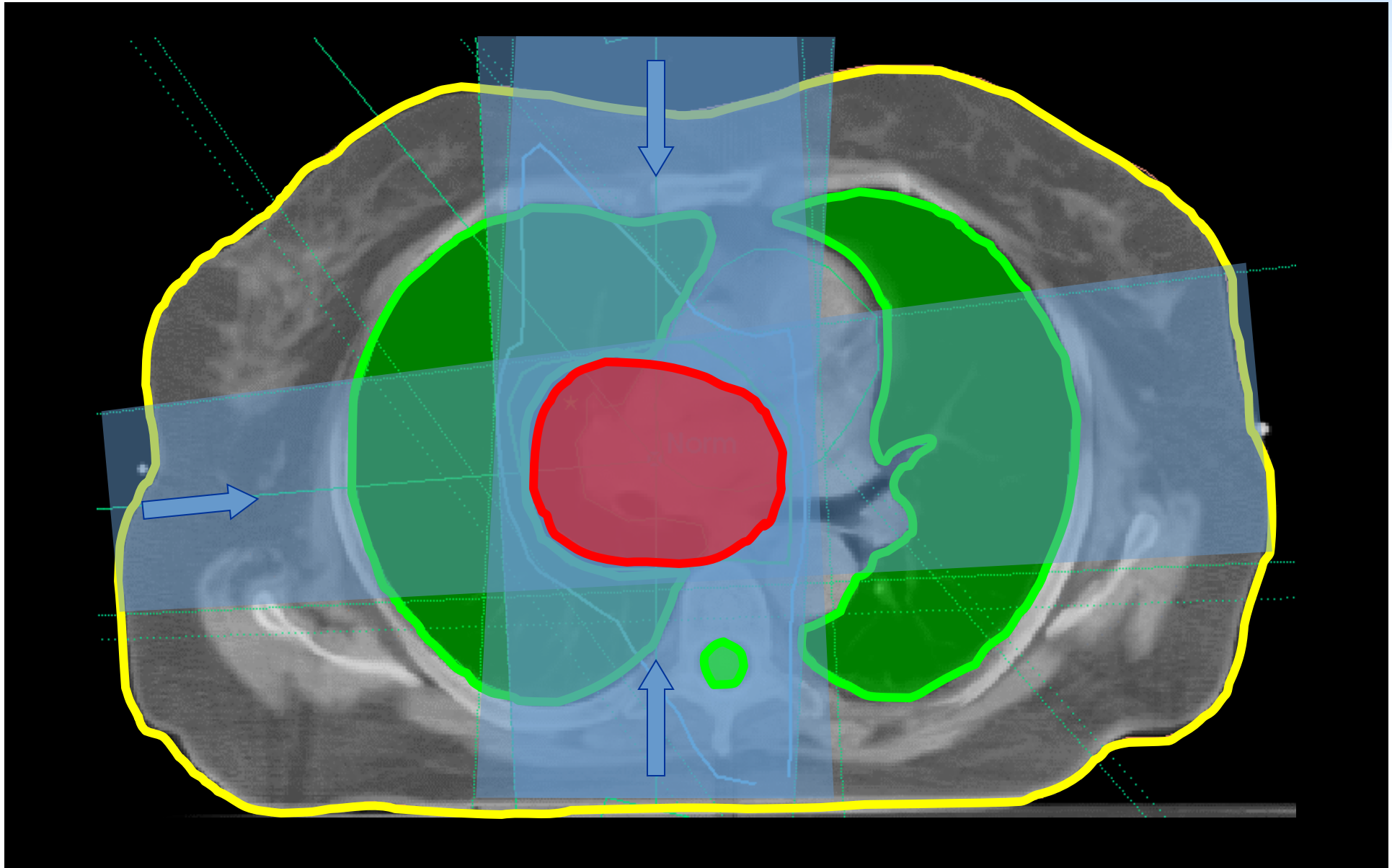
Irradiation of tumour cells



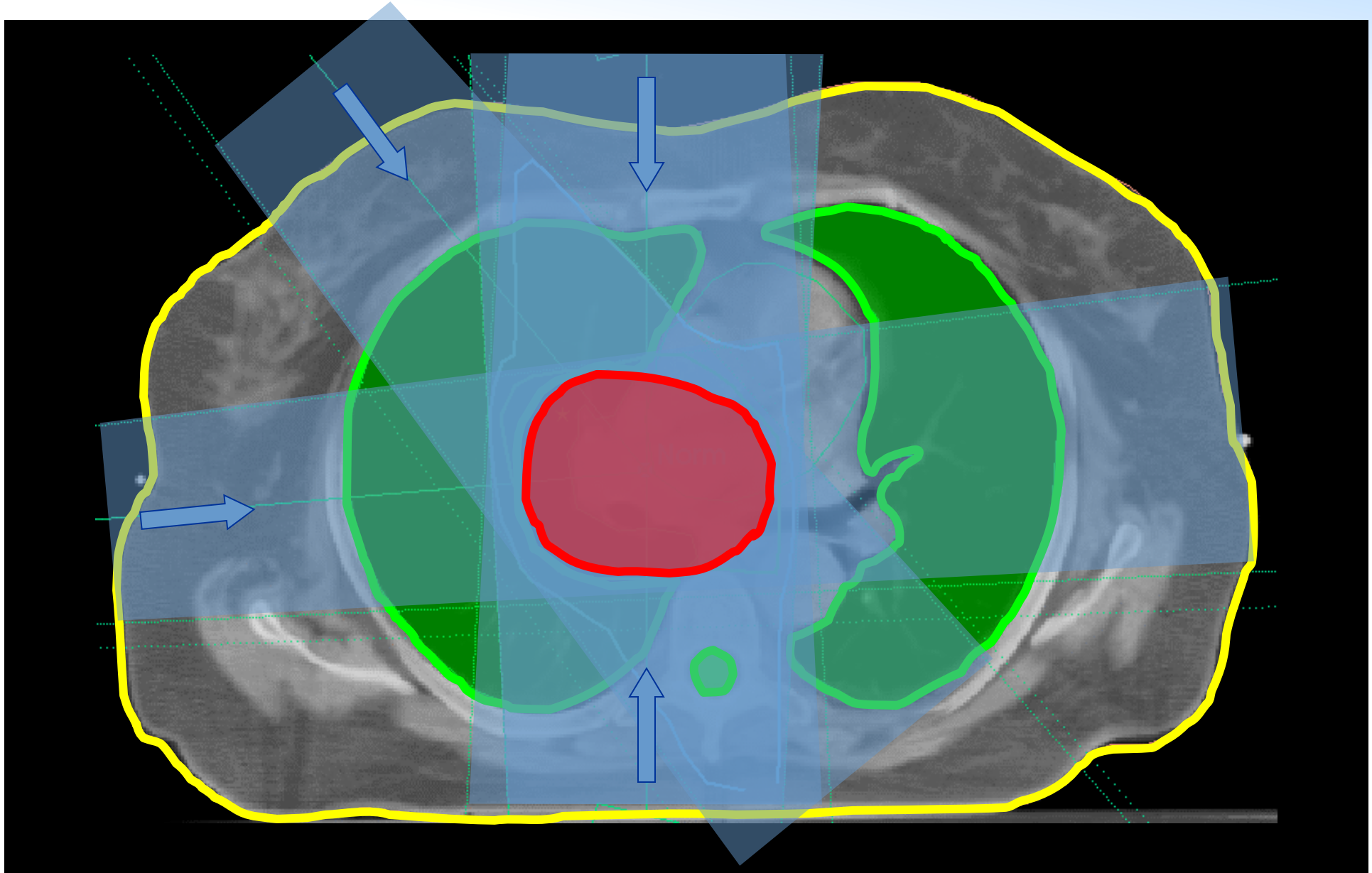
Irradiation of tumour cells



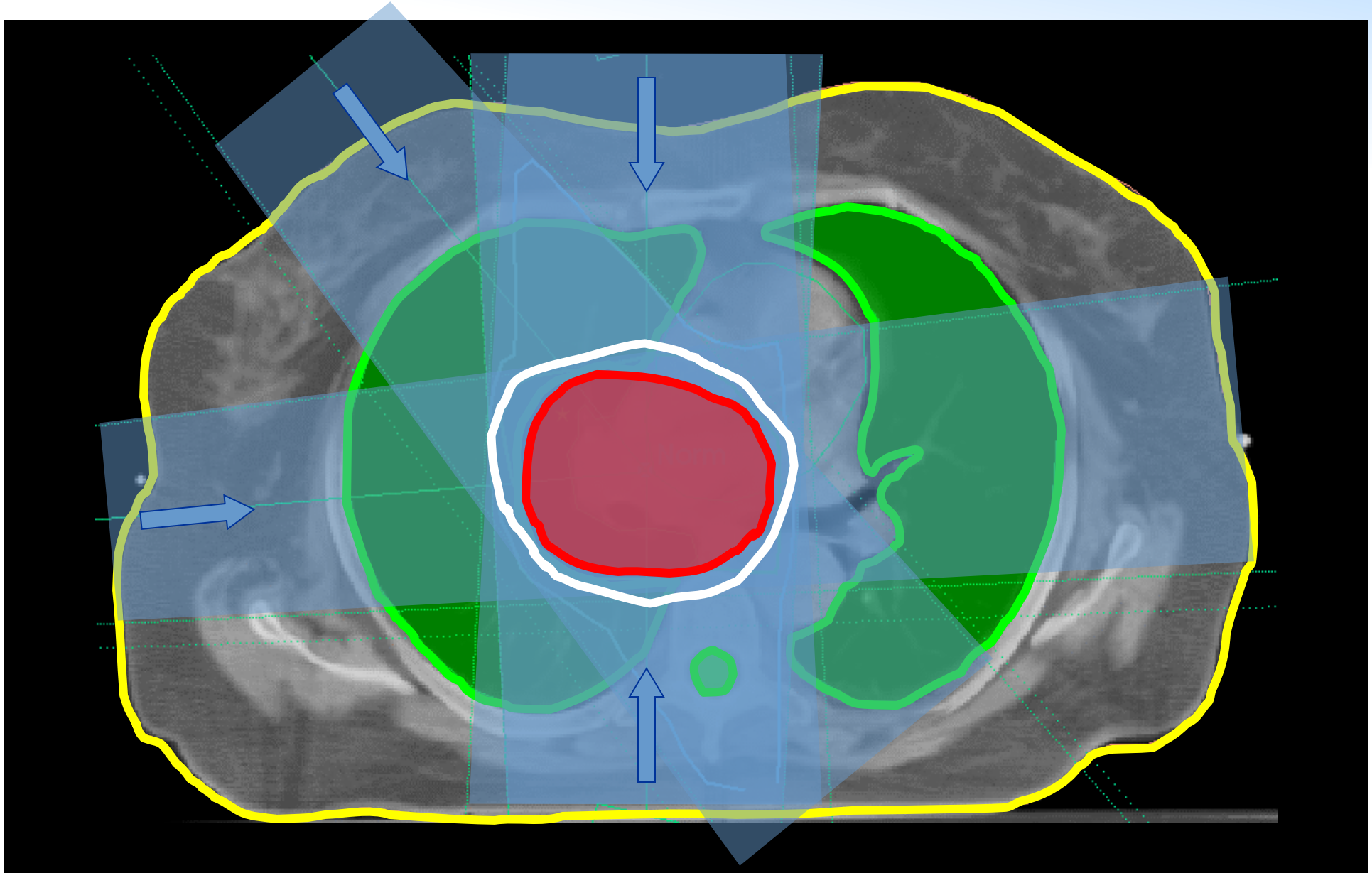
Irradiation of tumour cells



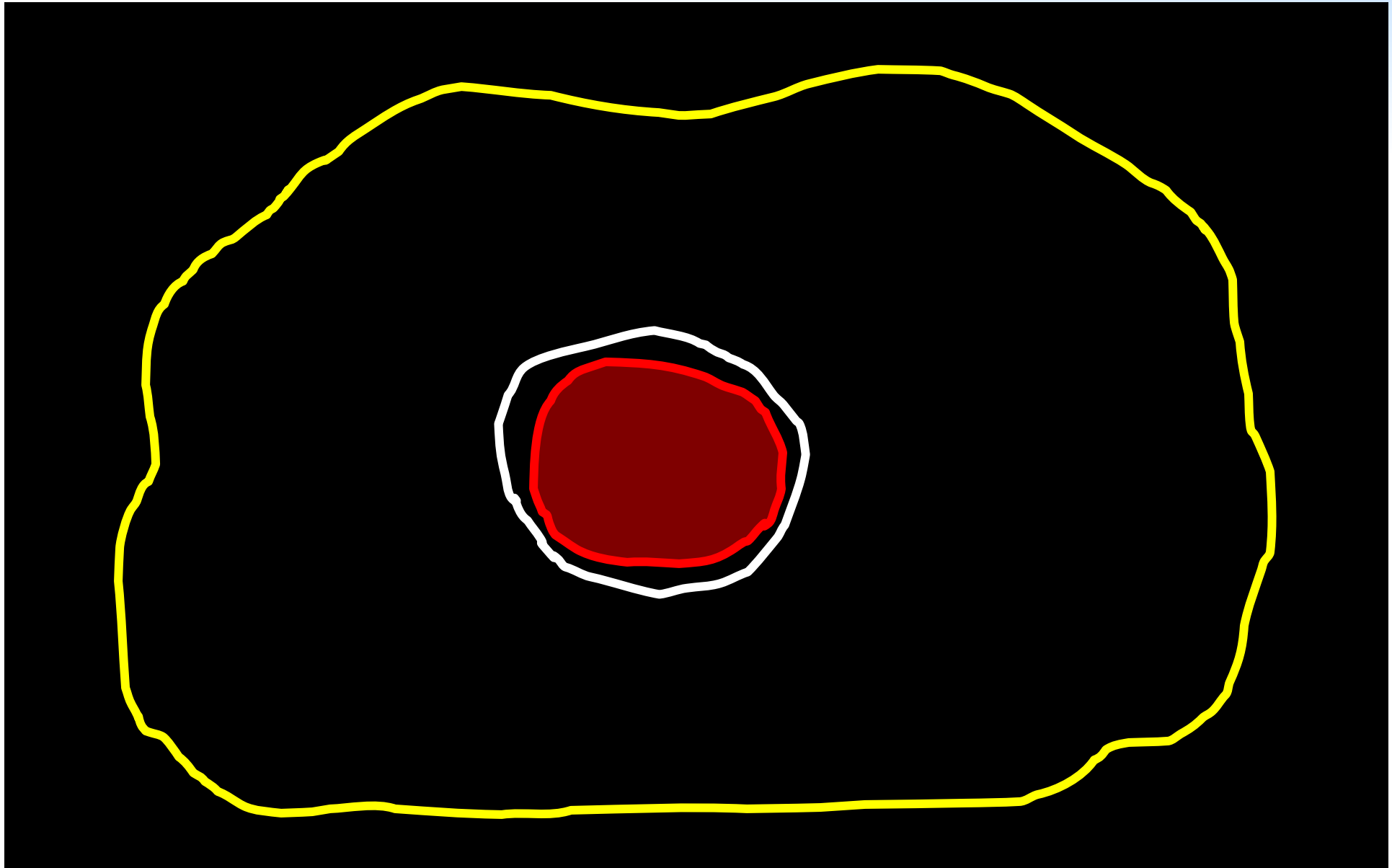
Irradiation of tumour cells



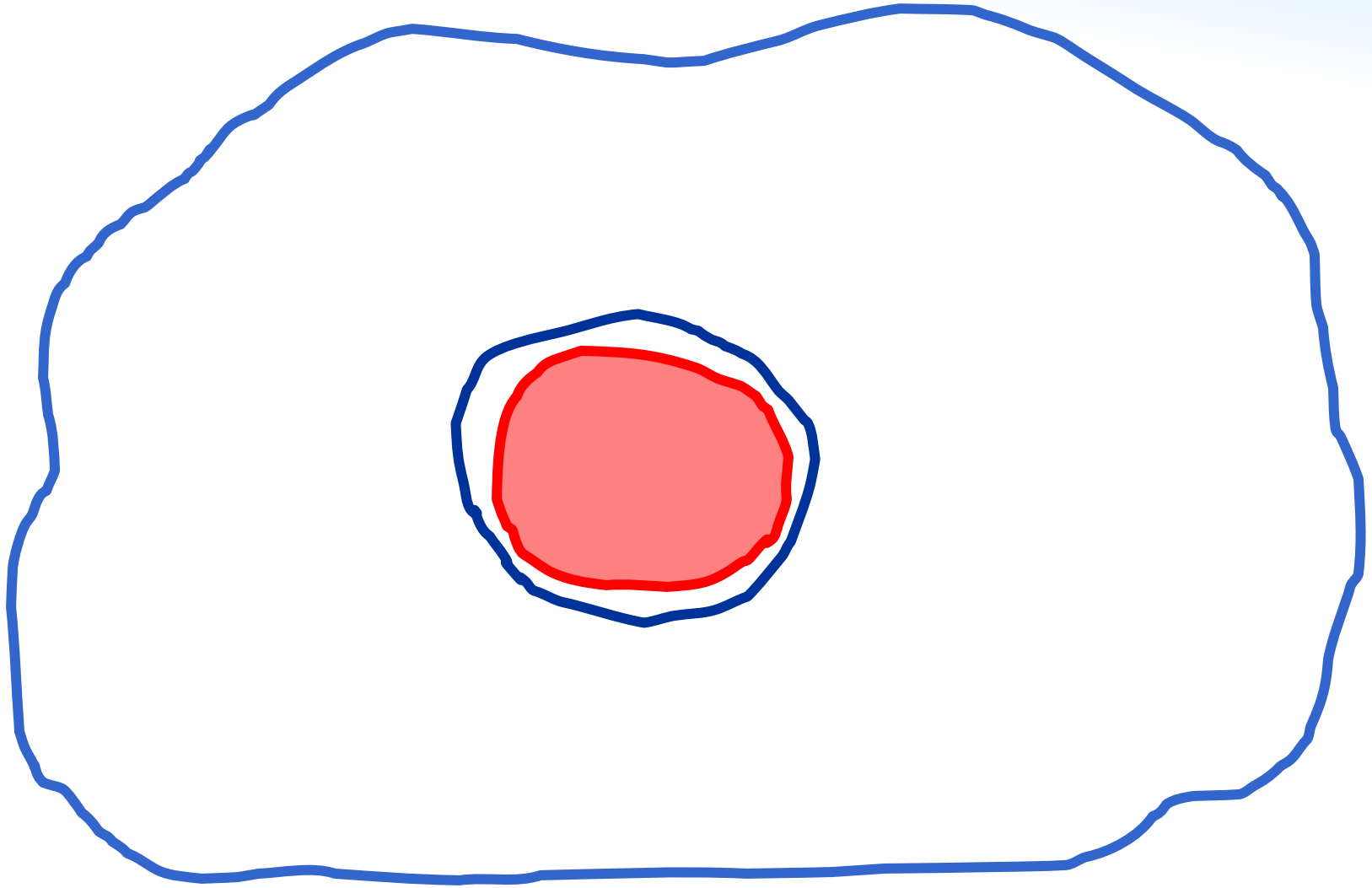
Irradiation of tumour cells



Irradiation of tumour cells



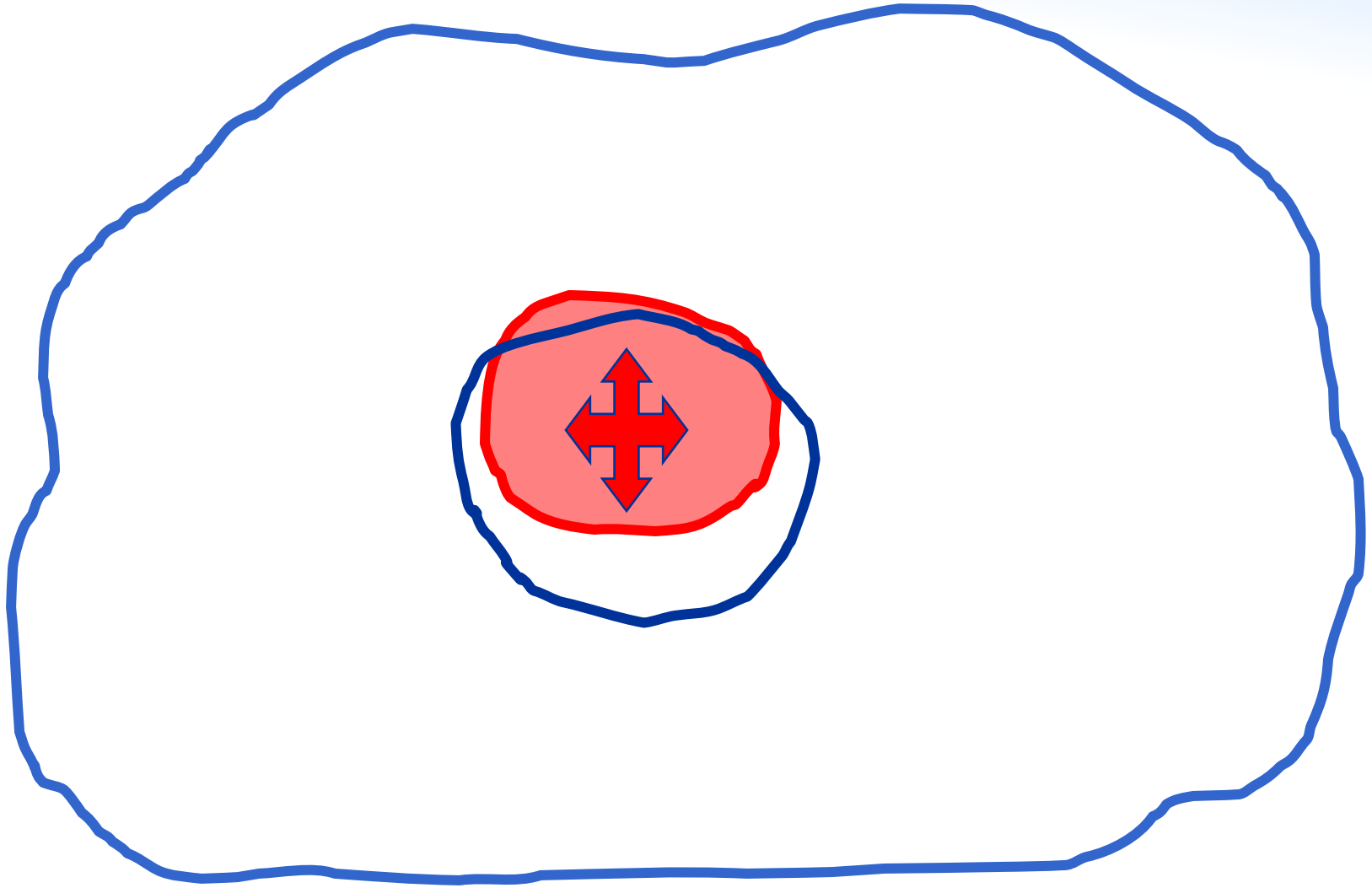
Irradiation of tumour cells



PROBLEM

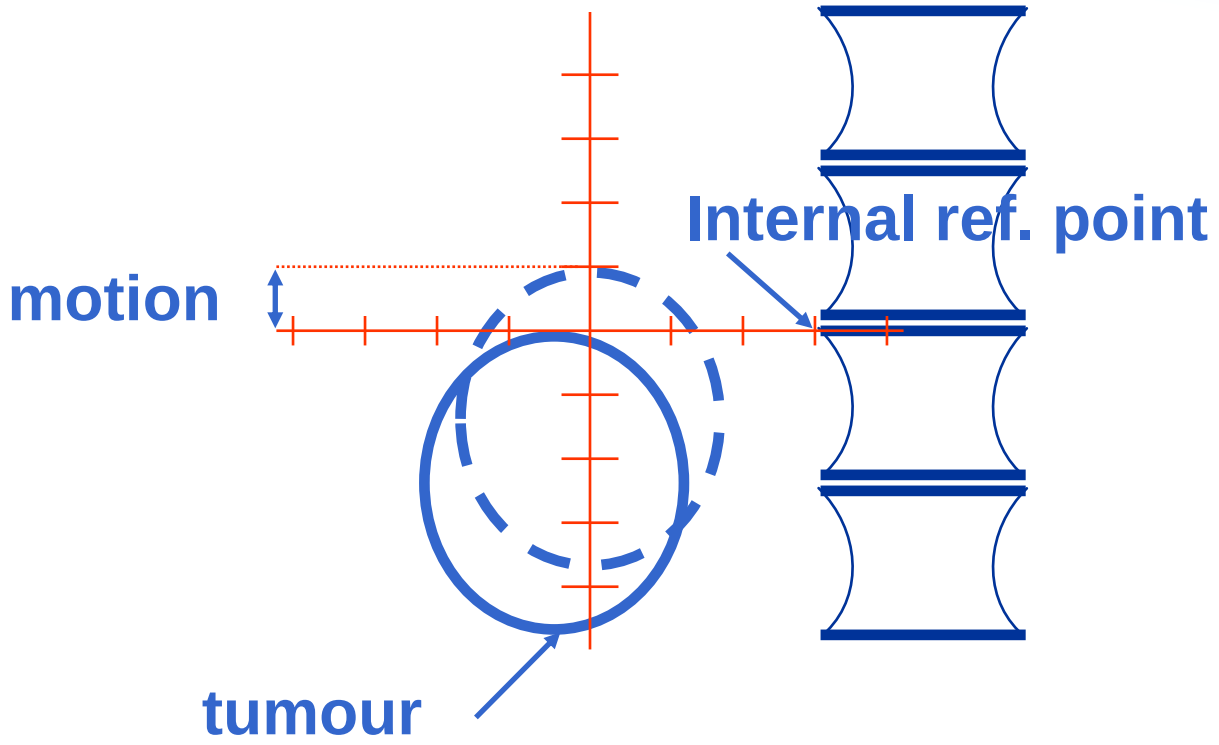
Structures within a body are not static

Tumour cells are moving when the patient is breathing



Breathing positional variations

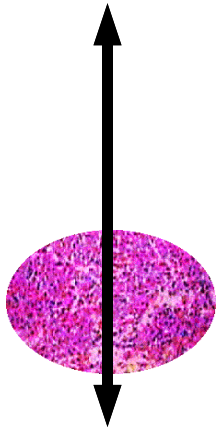
The biological volume goes through positional variations in relation to the irradiation field throughout the treatment course!

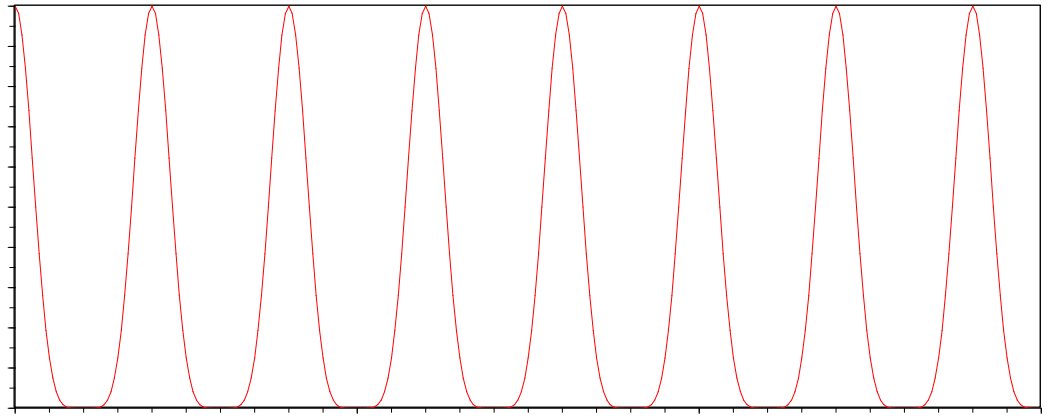


Lung tumour movement

(From L. Ekberg, O. Holmberg, L. Wittgren, G. Bjelkengren, T. Landberg: “What margins should be added to the clinical target volume in radiotherapy treatment planning for lung cancer?” Radiother Oncol 48 (1998) 71–77.

Breathing positional variations





Respiratory cycle (3-5 s): Many complete cycles during a single irradiation fraction

Movement of organs and tumours in the abdomen region. Examples: lung tumours, kidneys, liver, breasts.

Mechanical impact from muscles during respiration (NB diaphragm!)

Diaphragm moves 1 - 4 cm under normal free-breathing conditions. For deep-breathing, the corresponding figure can be 10 cm!

Breathing positional variations

Results of the tumour movement study

	Medio-lateral	Cranio-caudal	Dorso-ventral
Maximum movement	5.0	12.0	5.0
Average movement	2.4	3.9	2.4
Standard deviation	1.4	2.6	1.3

Summary of the lung tumour movements in three dimensions studied with fluoroscopy in 20 patients. All measurements are in mm.

Ekberg *et al.* Radiother Oncol 48: 71-77, 1998: 20 nsclc patients – organ motion measured with fluoroscopy

Mean CTV movement with quiet respiration:

- **2.4 mm (med-lat)**
- **2.4 mm (ant-post)**
- **3.9 mm (sup-inf)**

Range (sup-inf): 0 – 12 mm

Necessary to quantify organ motion individually for “curative” lung cancer patients

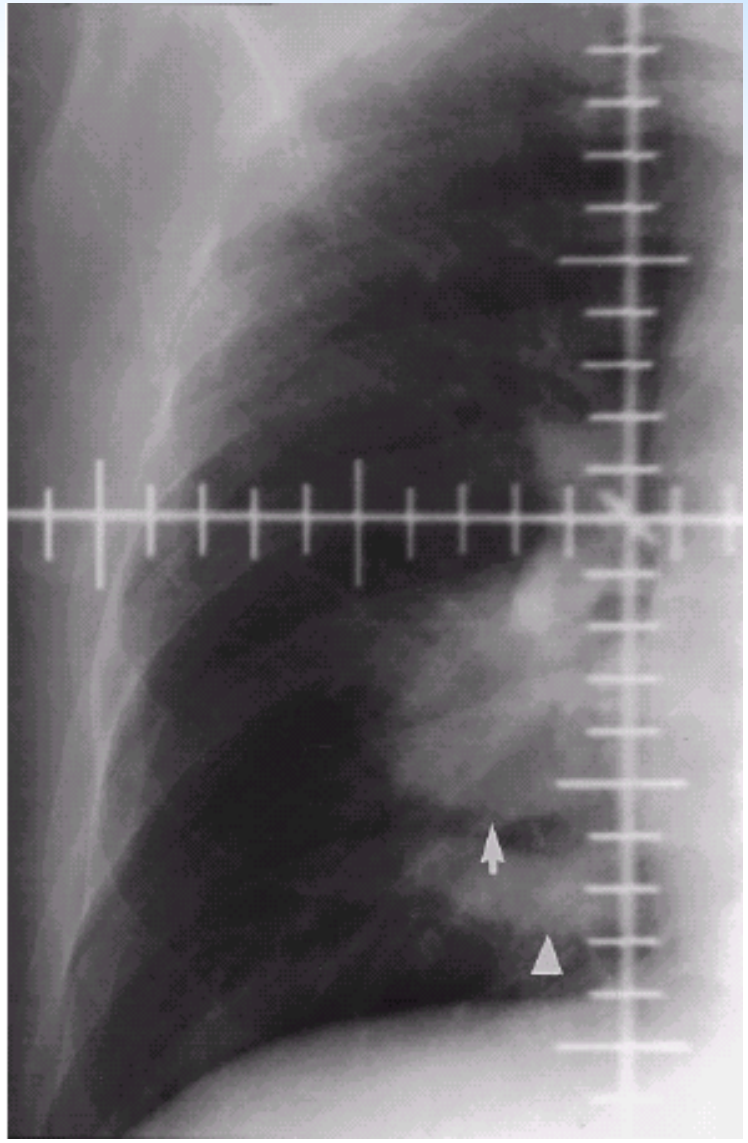
Breathing positional variations

Stevens *et al.* Int J Radiat Oncol Biol Phys 51: 62-68, 2001:

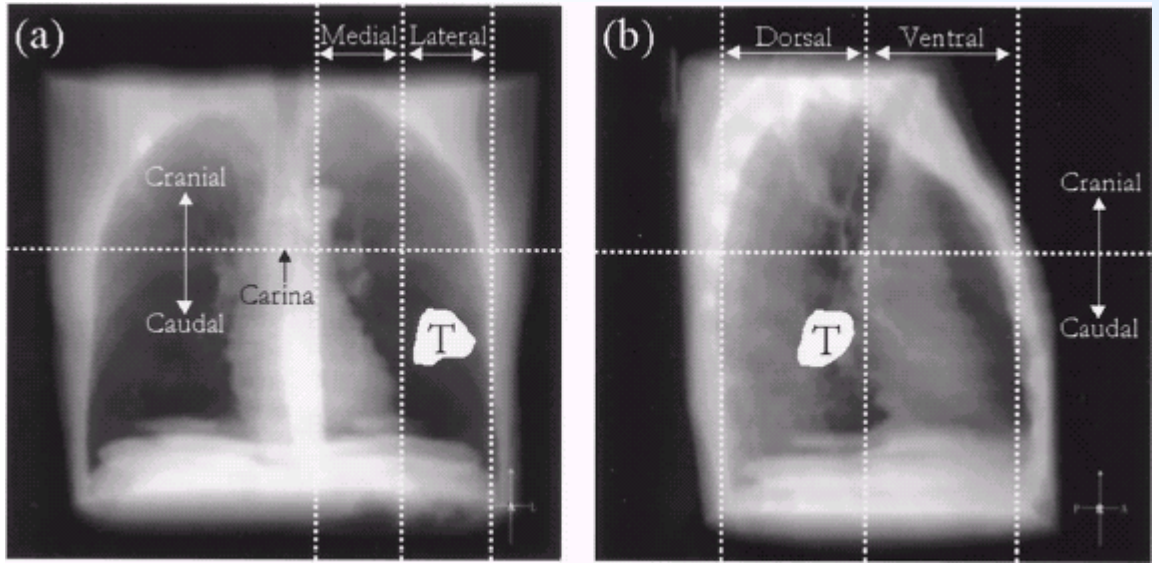
22 lung cancer patients. Sup-inf motion range: 0 – 22 mm

No correlation between movement and tumour size, location or pulmonary function

Individual quantification necessary!



Breathing positional variations

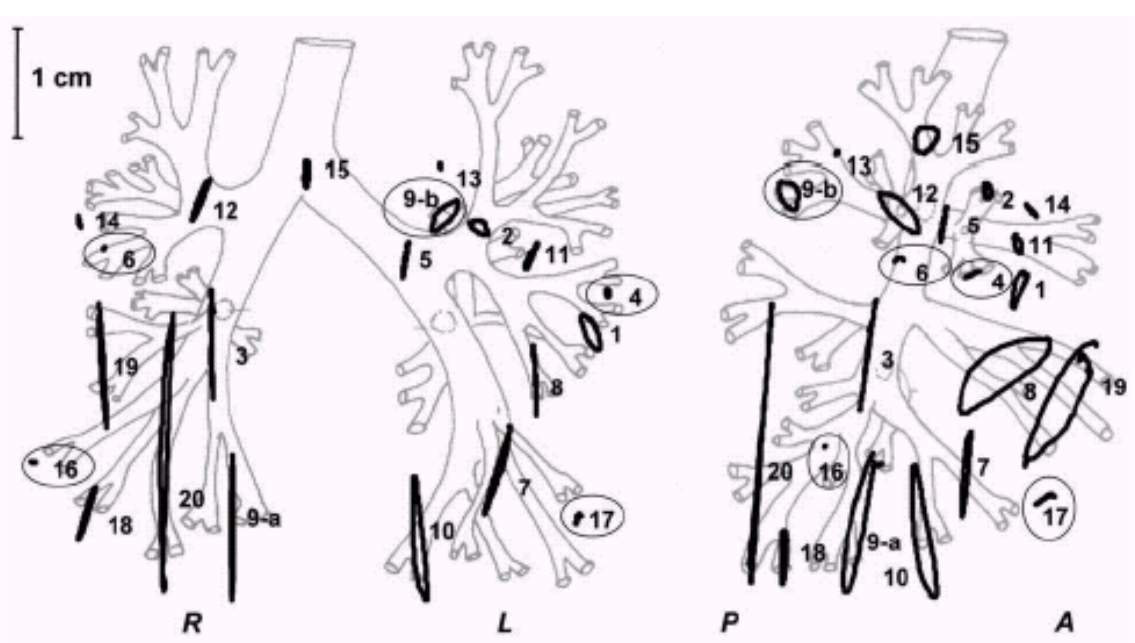


Van Sörnsen de Koste *et al.* Int J Radiat Oncol Biol Phys 56: 348-354, 2003:

29 lung cancer patients. Mean CTV movement 4.3 mm (med-lat), 6.9 mm (ant-post), 6.0 mm (sup-inf).

No correlation with anatomic location.

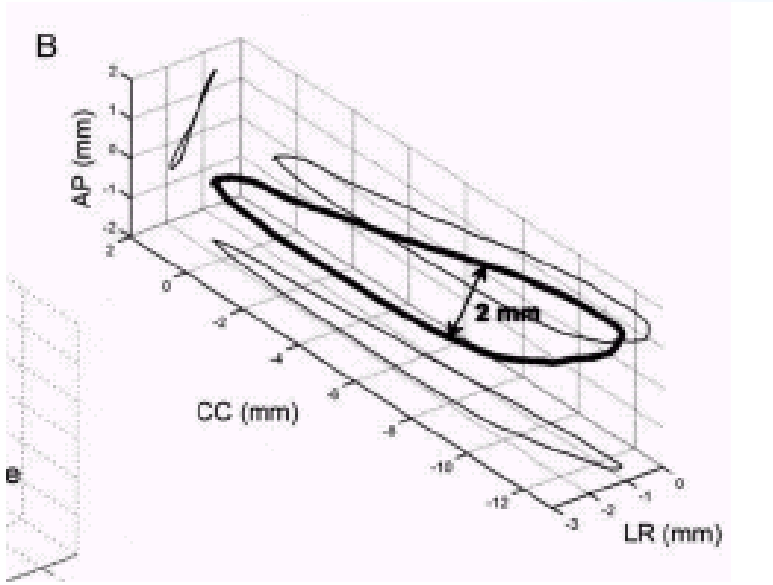
Breathing positional variations



Seppenwoolde *et al.* Int J Radiat Oncol Biol Phys 53: 822-834, 2002:

20 lung cancer patients. Mean amplitude (mm) for all patients ranged from 0.2-2.8 (med-lat), 0.2-8.2 (ant-post), 0.2-24.6 (sup-inf).

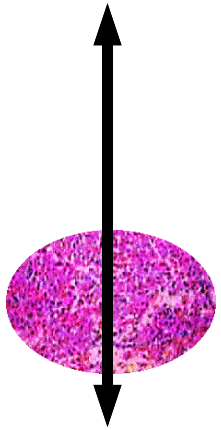
Breathing positional variations

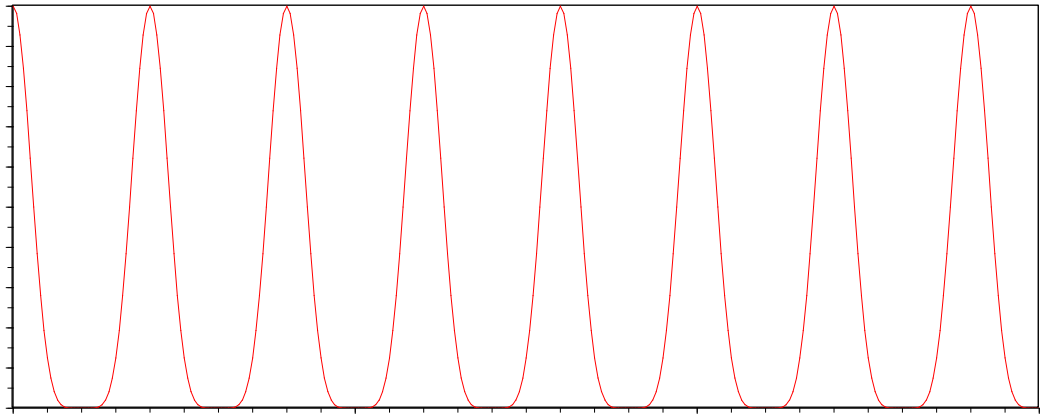


Seppenwoolde *et al.* Int J Radiat Oncol Biol Phys 53: 822-834, 2002:

In ½ of the patients, the tumour took different paths in inhalation versus exhalation (hysteresis).

Other positional variations



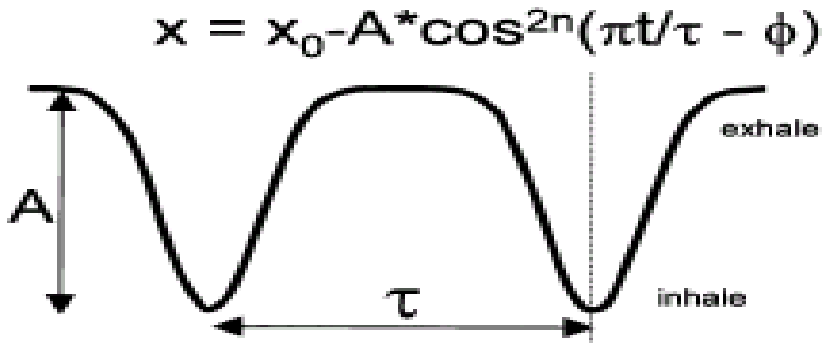


Cardiac cycle (1 s): Even more complete cycles during a single irradiation fraction. Mechanical impact from cardiac contraction and also aortic pulsation.

Seppenwoolde *et al.* Int J Radiat Oncol Biol Phys 53: 822-834, 2002:

In ⅓ of patients, heartbeat caused motion ranging from 1 – 4 mm

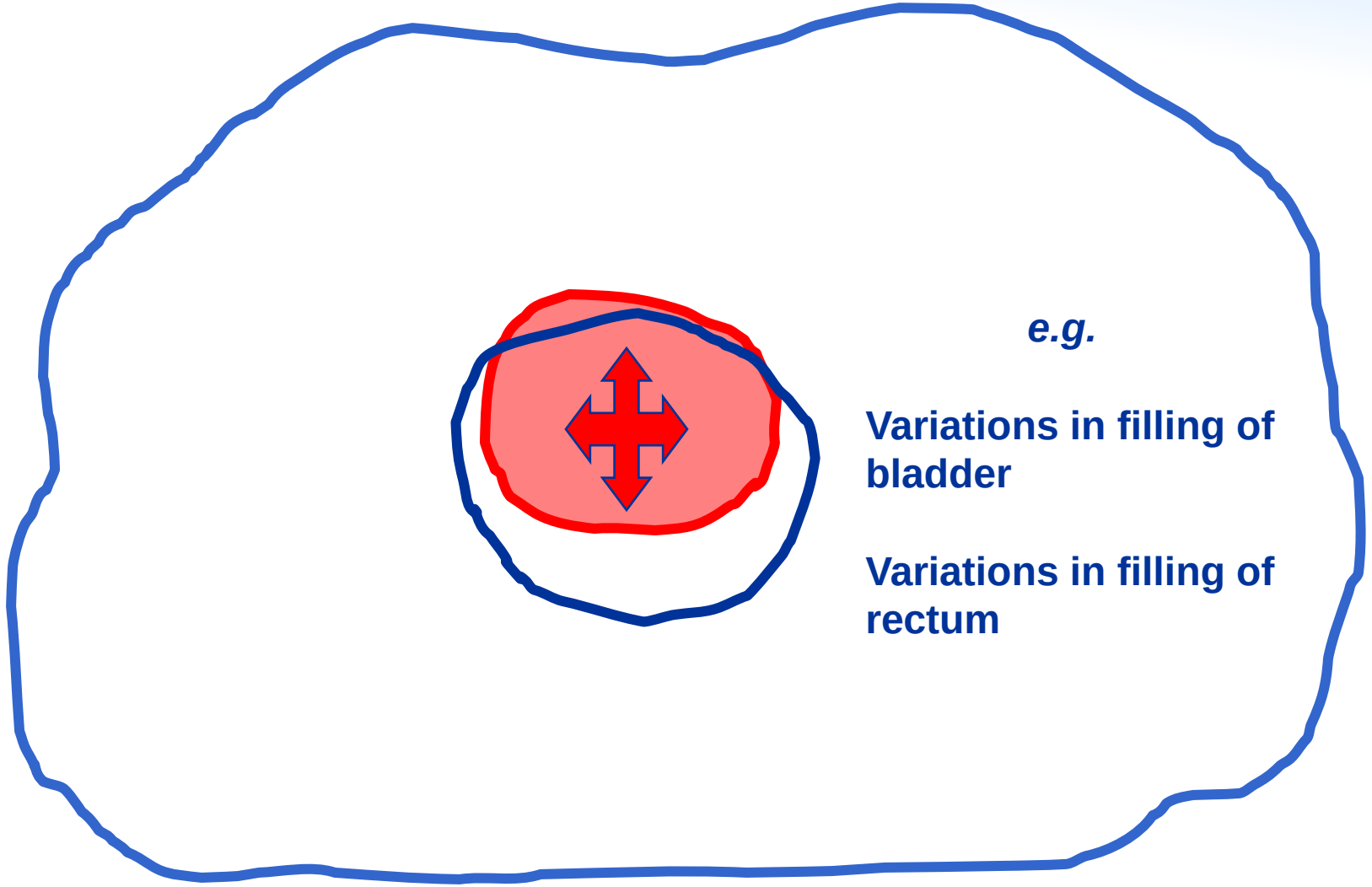
Breathing positional variations



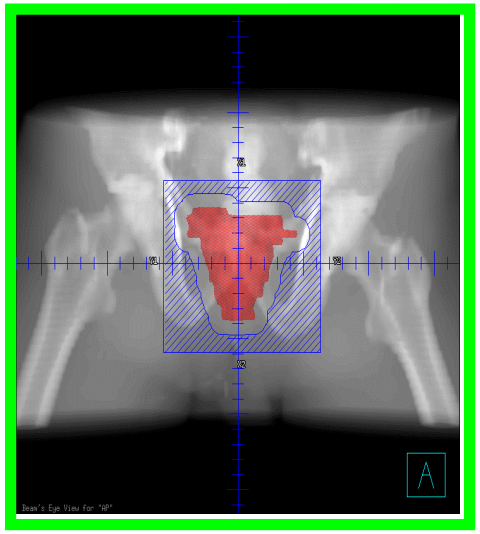
McKenzie Br J Radiol 73: 973-977, 2000:

Probability that CTV oscillating with the respiration cycle is close to its endpoints (and in particular the exhalation endpoint) is higher than that it will be somewhere in between.

Position of tumour cells can also be influenced by other physiological processes



Other organ-positional variations



Organs and tumours in the pelvic region moves mainly due to changes in the digestive system and filling of bladder and rectum from day-to-day. Example: prostate, bladder, rectum, cervix.

Mainly inter-fraction positional variation (different position at different treatment fractions) as opposed to intra-fraction variation of breathing.

Typical values (1 SD) are 3 - 5 mm.

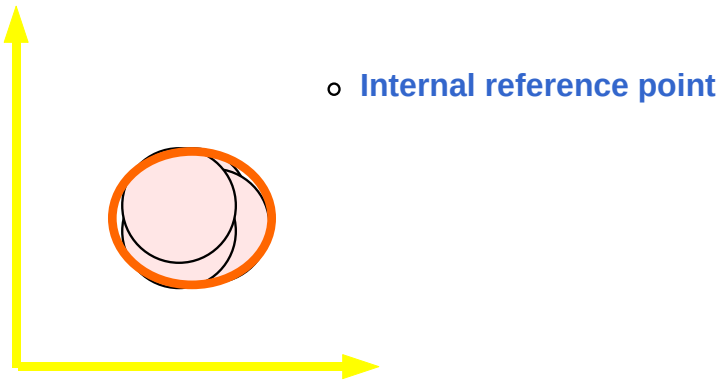
Organ-positional variations

- **These variations in organ position and shape can have a systematic impact on position in relation to original scan (Σ_{motion}) and also a day-to-day impact (σ_{motion}).**

- **Σ_{motion} and σ_{motion} should be known in magnitude and minimised, if possible.**

- **Remaining Σ_{motion} and σ_{motion} should be taken into account.**

Volumes in ICRU62 - 1999



Internal Target Volume (ITV)

CTV with margin added to compensate for expected physiologic movements and variations in size shape and position of CTV in relation to Internal Reference Point.

ITV = CTV + IM (Internal Margin)

Summary of problem

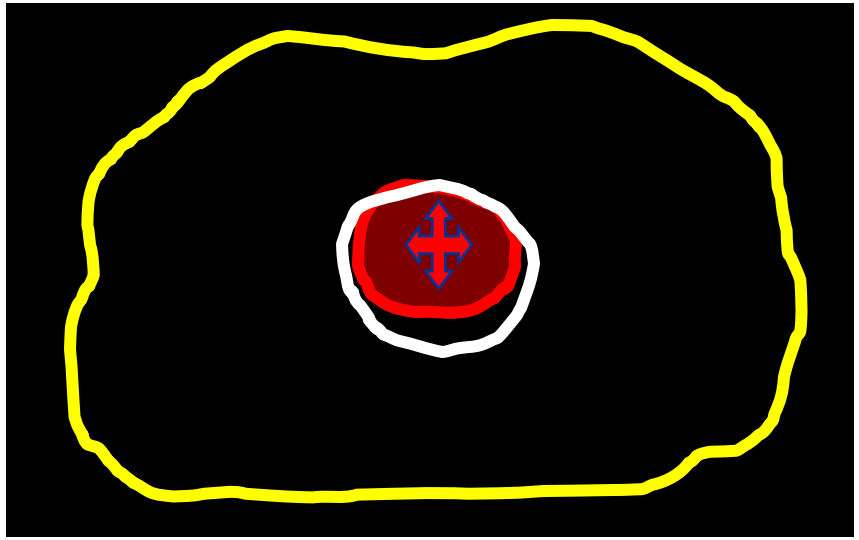
Extent of geometric variations:

- **abdomen target – mm to cm (intra-fx amplitude)**
- **pelvis target – a few mm (1 SD inter-fx)**

Strategies for dealing with geometric variations in practice:

- **breathing control**
- **reproducible filling of bladder and rectum**
- **real-time tumour tracking**

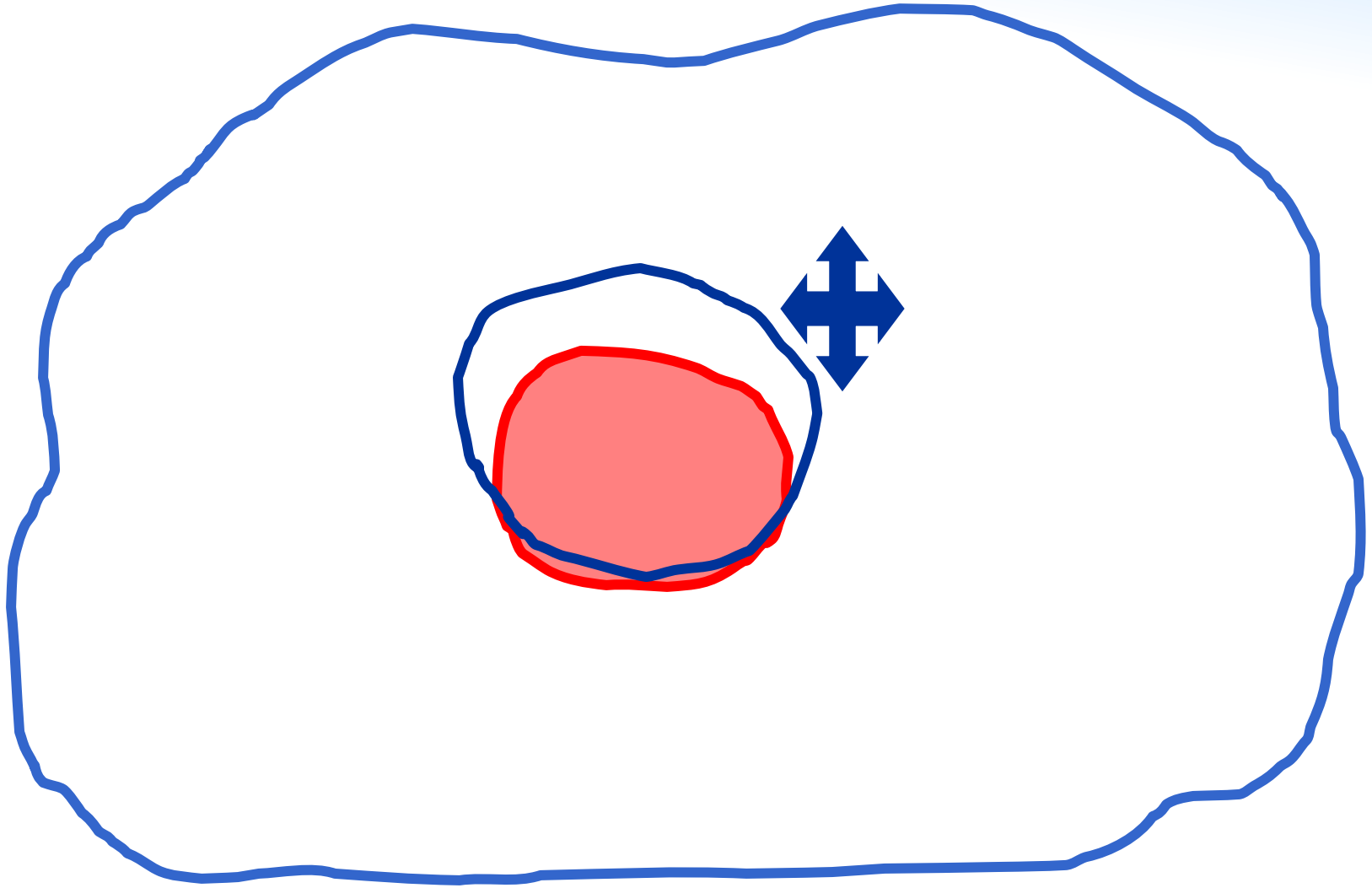
+ internal margin (IM)



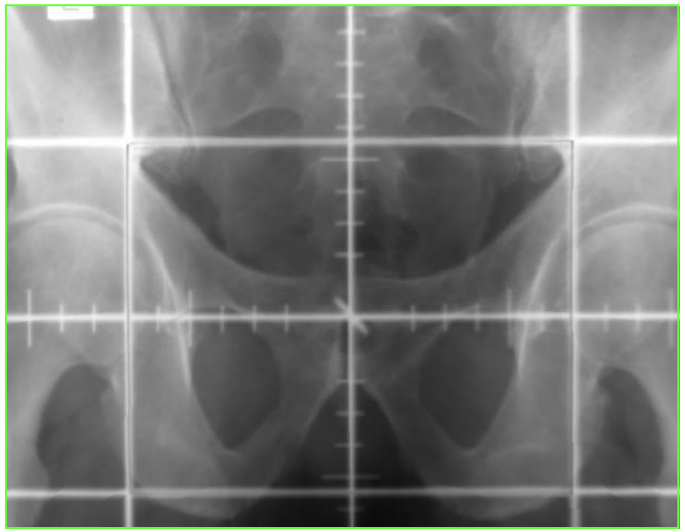
PROBLEM

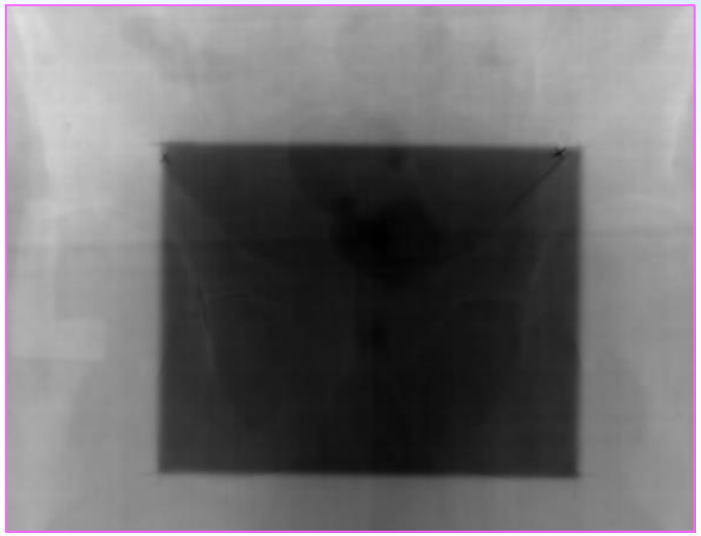
Setting up the patient and the irradiation fields can not be done identically from day-to-day

High dose area is moving when set-up of patient is varying



Set-up variations



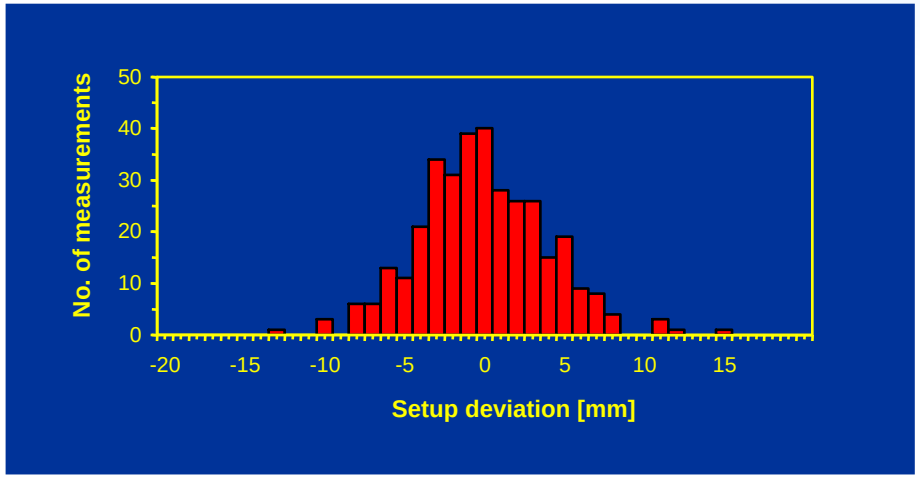


Set-up variations originate in the difficulty of reproducing repeated daily set-up of irradiation fields and patients at the treatment units.

There are many studies of set-up variations for various treatment sites using EPIDs.



Set-up variations

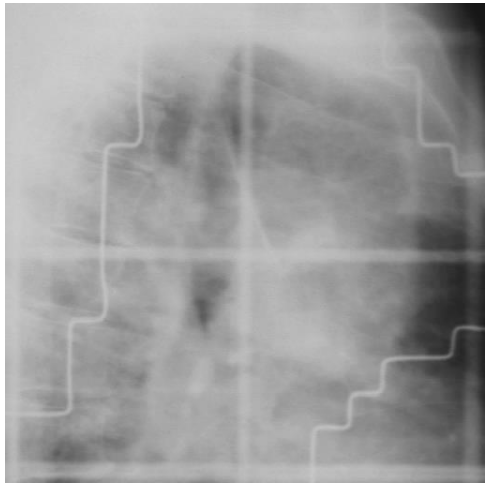


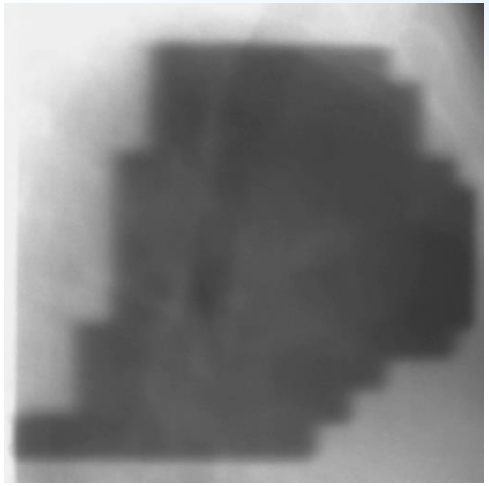
When measuring repeatedly throughout the treatment course for a single patient, there will be a distribution of field placements. The distribution will have a width indicating the variation between the locations of fields within the treatment course for the single patient. This is the *random set-up variation* for the single patient. There is often also a difference between the mean position of this distribution and the intended position. This is the *systematic set-up variation* for the single patient.

Breast irradiation setup

(From O. Holmberg, H. Huizenga, M. Idzes, J. Lebesque, R. Vijlbrief, B. Mijnheer: “In vivo determination of the accuracy of field matching in breast cancer irradiation” Radiother Oncol 33 (1994) 157–166.

Set-up variations



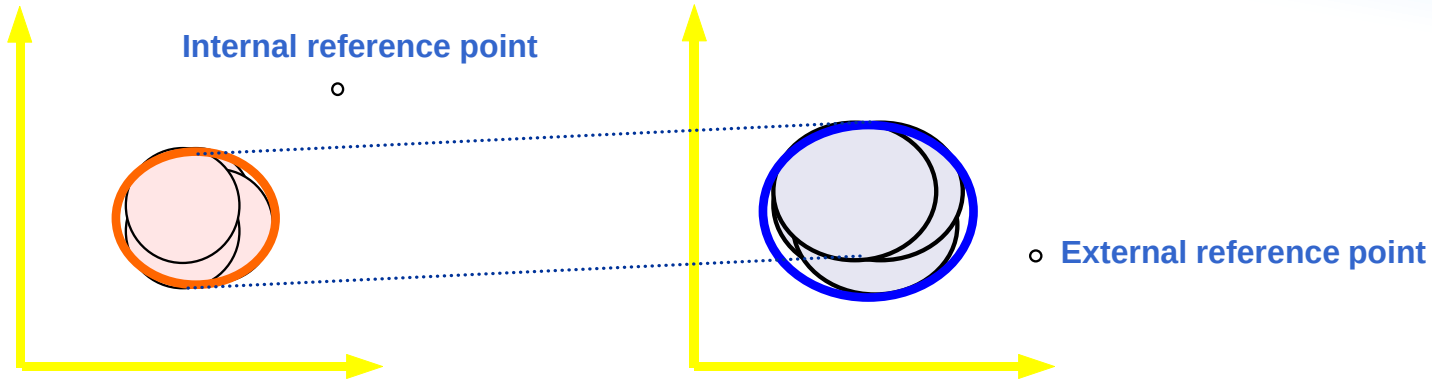


- **We need to know the magnitude of these "set-up variations" ($\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$).**

- **$\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ should be minimised.**

- **Remaining $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ should be taken into account.**

Volumes in ICRU62 - 1999



Planning Target Volume (PTV)

ITV with margin added to compensate for external geometric uncertainties in relation to External Reference Point.

PTV = ITV + SM (Set-up Margin)

Summary of problem

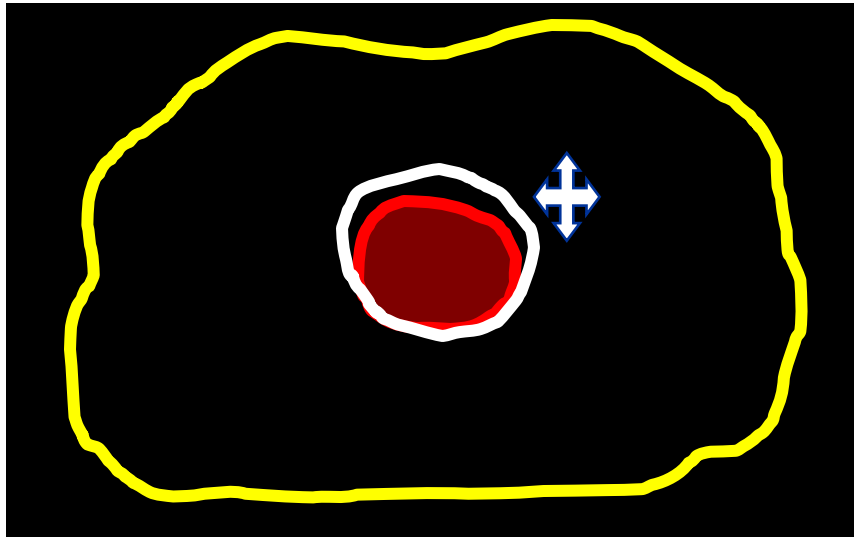
Extent of geometric variations:

- **often a few mm (1 SD inter-fx)**

Strategies for dealing with geometric variations in practice:

- **fixation**
- **off-line portal imaging with decision rule protocols**
- **on-line portal imaging**
- **real-time tumour tracking**

+ set-up margin (SM)



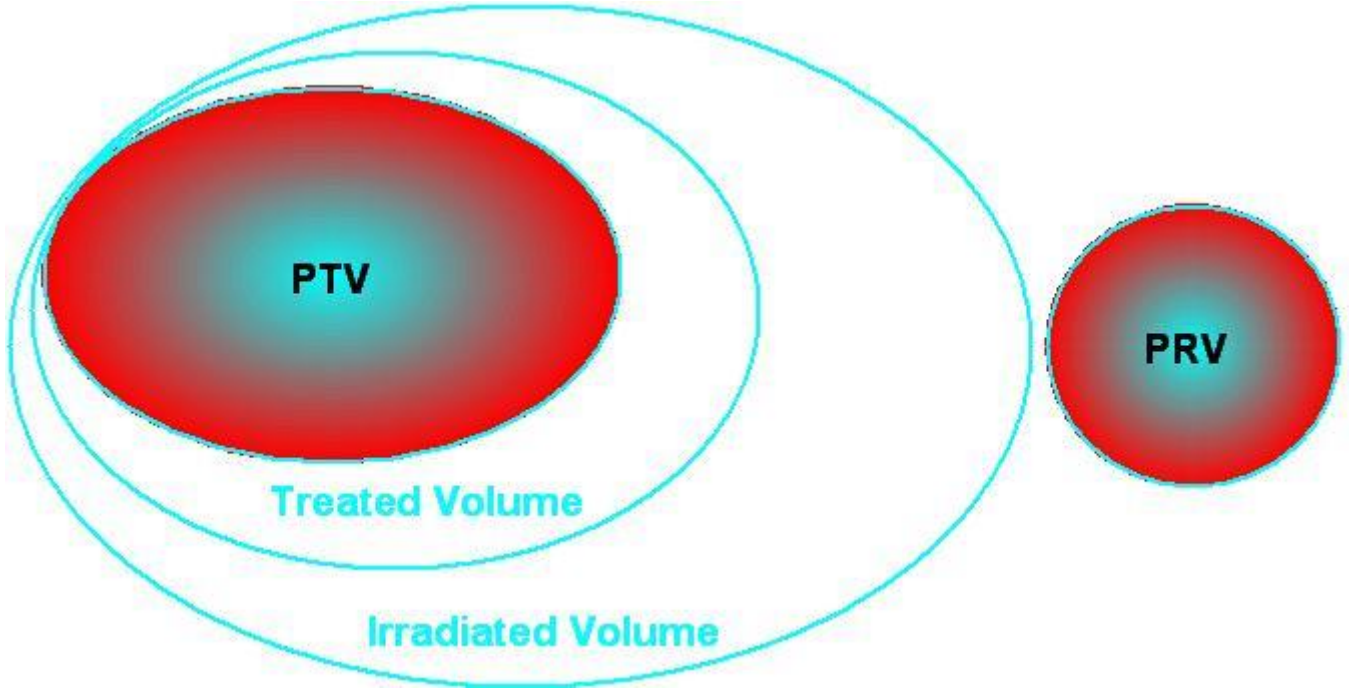
Volumes in ICRU62 - 1999

Organ at Risk (OR)

Organs at Risk are normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose.

Planning Organ at Risk Volume (PRV)

The PRV is the OR with an integrated geometric margin added, in analogue with the CTV-to-PTV expansion.



Volumes


1978 ICRU29
"The Target Volume"
Organs at risk
1993 ICRU50
GTV
CTV
PTV
Organs at risk
1999 ICRU62
GTV
CTV
ITV
PTV
OR
PRV

Volumes


1978 ICRU29
"The Target Volume"
Organs at risk
1993 ICRU50
GTV
CTV
PTV
Organs at risk
1999 ICRU62
GTV
CTV
ITV
PTV
OR
PRV
2004 ICRU71

Volumes in ICRU71 - 2004

Gross Tumour Volume (GTV)

The GTV is the gross demonstrable extent and location of the malignant growth.

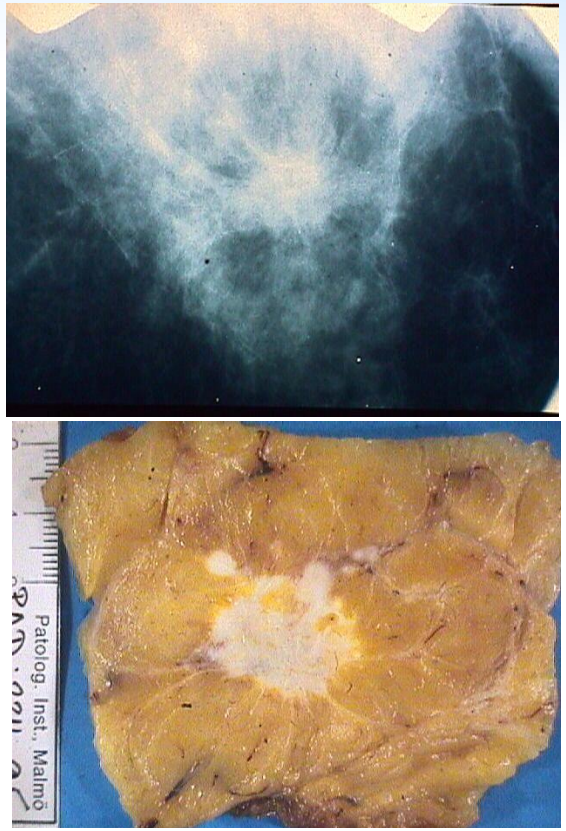
GTV consists of:

primary tumour – (GTV-T)

metastatic lymphadenopathy – (GTV-N)

other metastases – (GTV-M)

Those parts of the malignant growth where the tumour cell density is the highest ($\geq 10^6/mm^3$).



Tubulo-ductal breast cancer
Mammography (above)
Surgical specimen (below)

Volumes in ICRU71 - 2004

Clinical Target Volume (CTV)

The CTV is a tissue volume that contains a demonstrable GTV and/or subclinical, microscopical malignant disease, which must be eliminated.

CTV = GTV (if there) + subclinical disease

(CTV-T, CTV-N, CTV-M)

Also combinations, e.g. CTV-TN

Planning Target Volume (PTV)

As above: PTV-T, PTV-N, PTV-M





Thyroid cancers

Encapsulated (above)

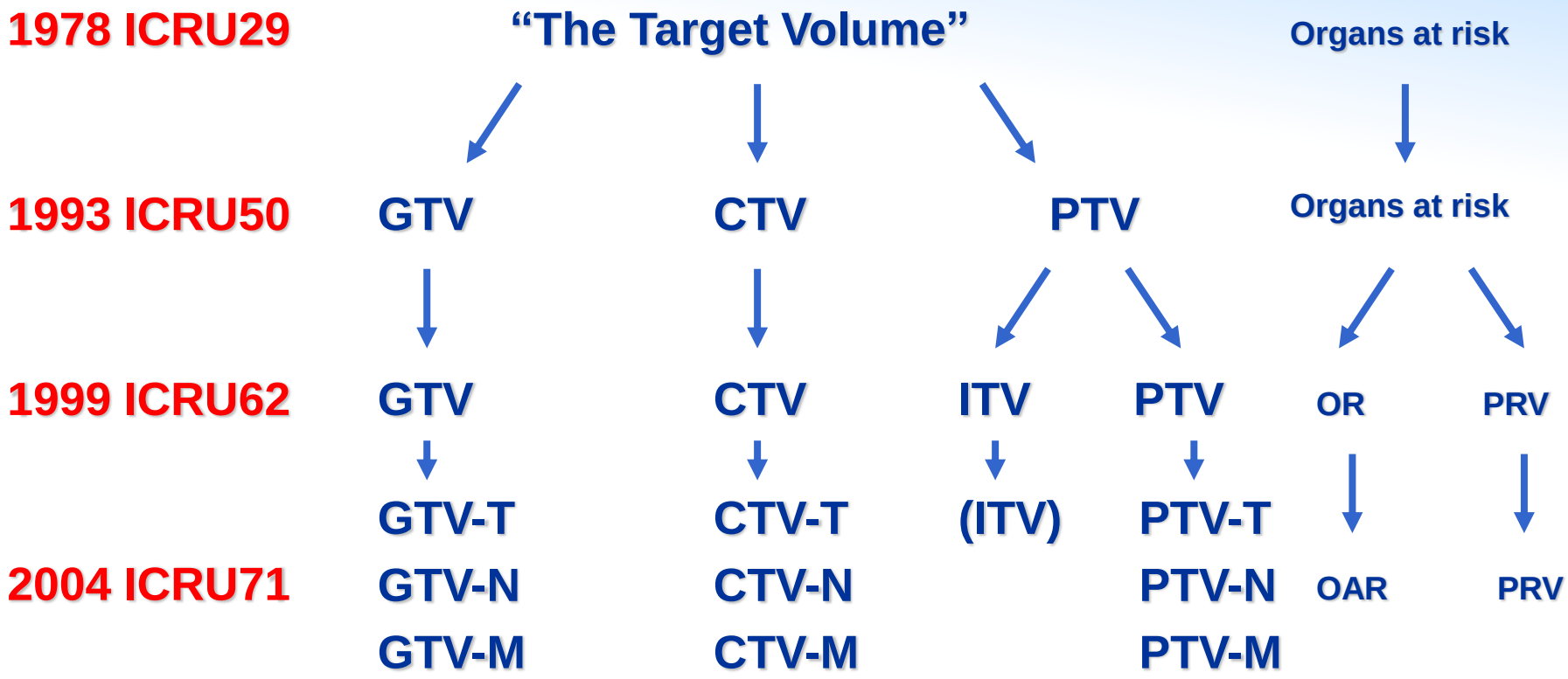
Un-encapsulated (below)

(From Malmö Univ. Hospital)

Volumes


1978 ICRU29
"The Target Volume"
Organs at risk
1993 ICRU50
GTV
CTV
PTV
Organs at risk
1999 ICRU62
GTV
CTV
ITV
PTV
OR
PRV
GTV-T
CTV-T
(ITV)
PTV-T
2004 ICRU71
GTV-N
CTV-N
PTV-N
OAR
PRV
GTV-M
CTV-M
PTV-M

Volumes



2008 ICRU

… variations in delineation …

… a lot of work on imaging …

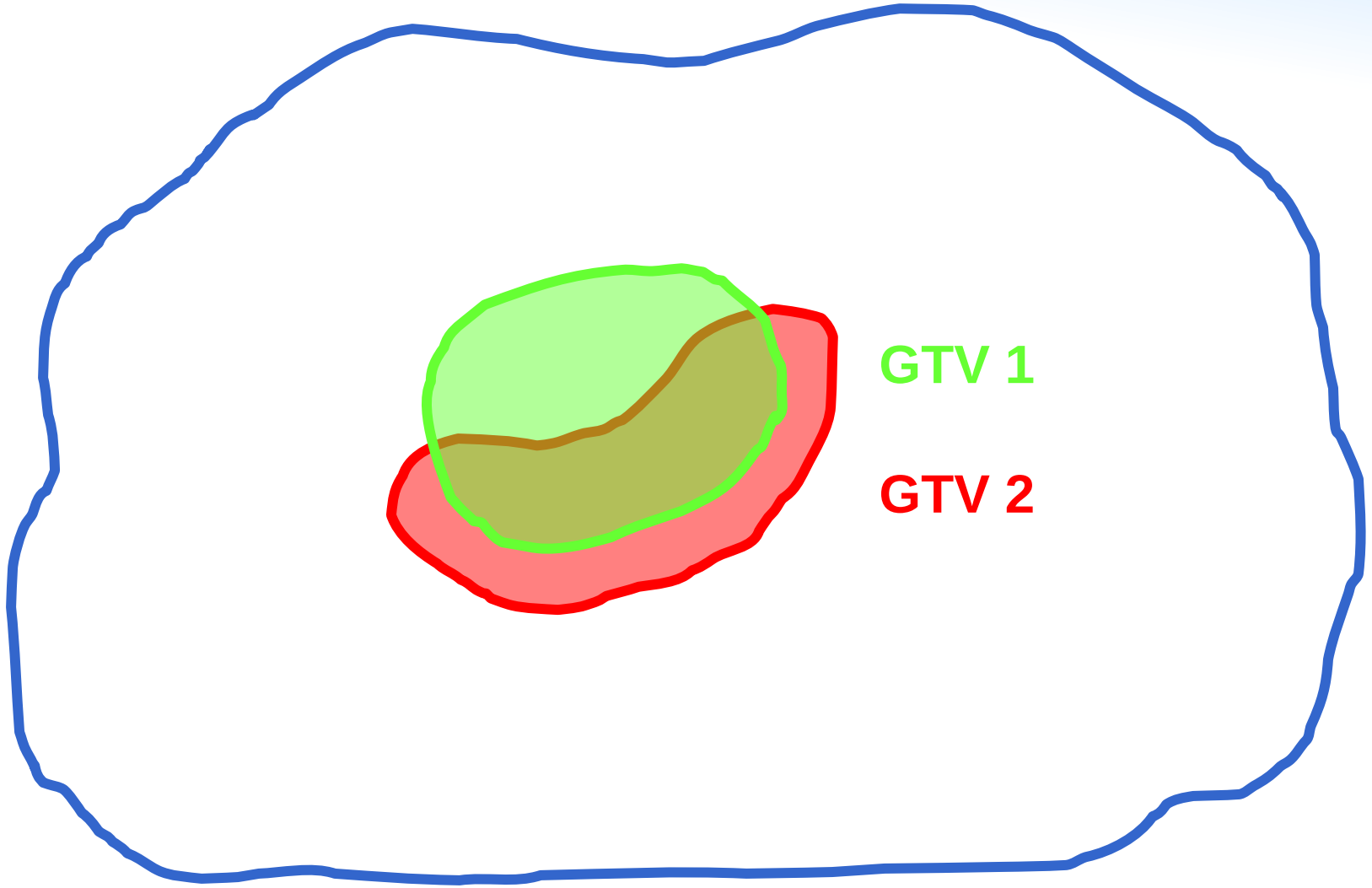
… "dose sculpting" is more readily done …

… the "dose-bath" might be a problem …

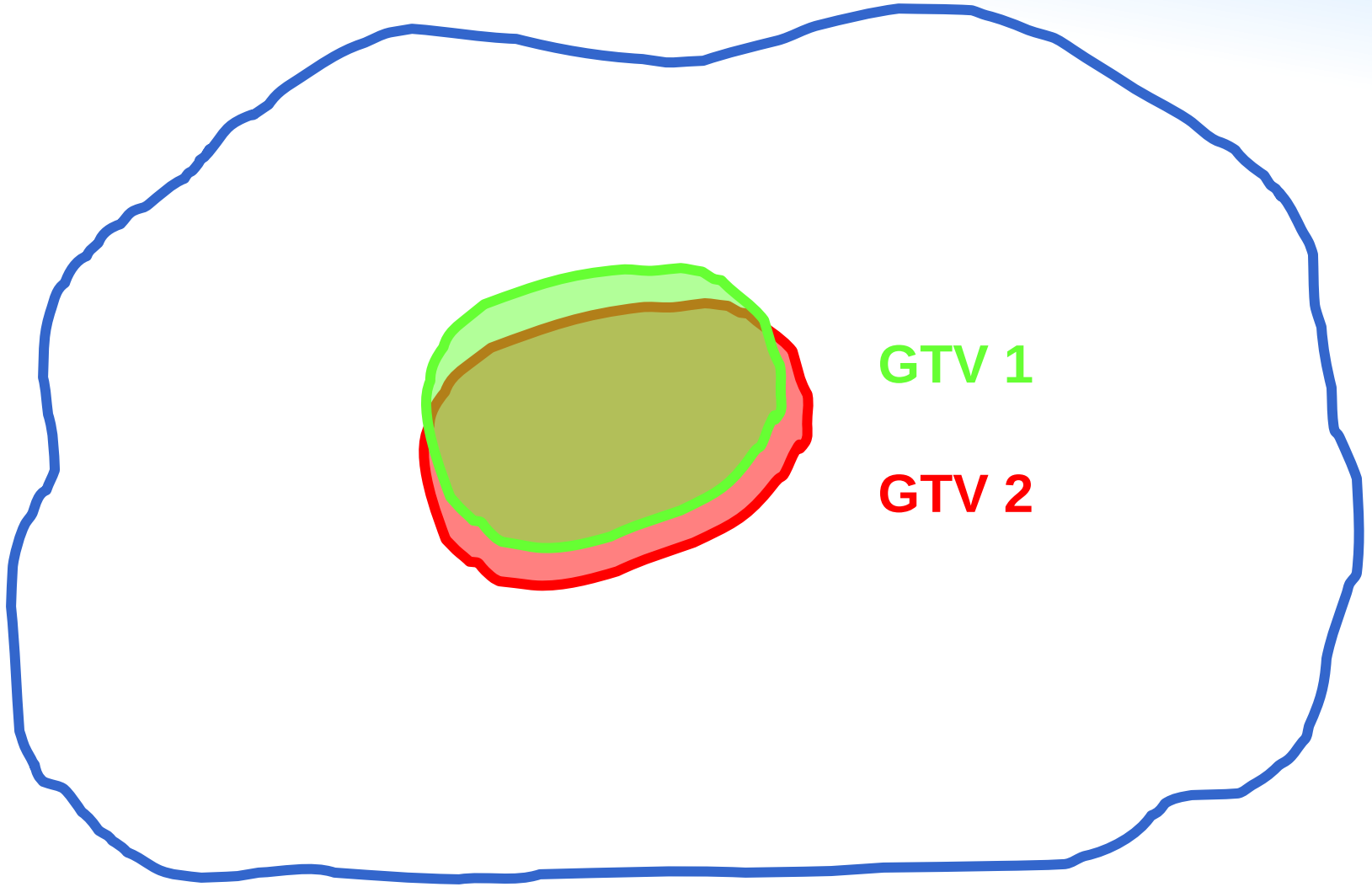
PROBLEM

Target-location might shift, depending on who is delineating it

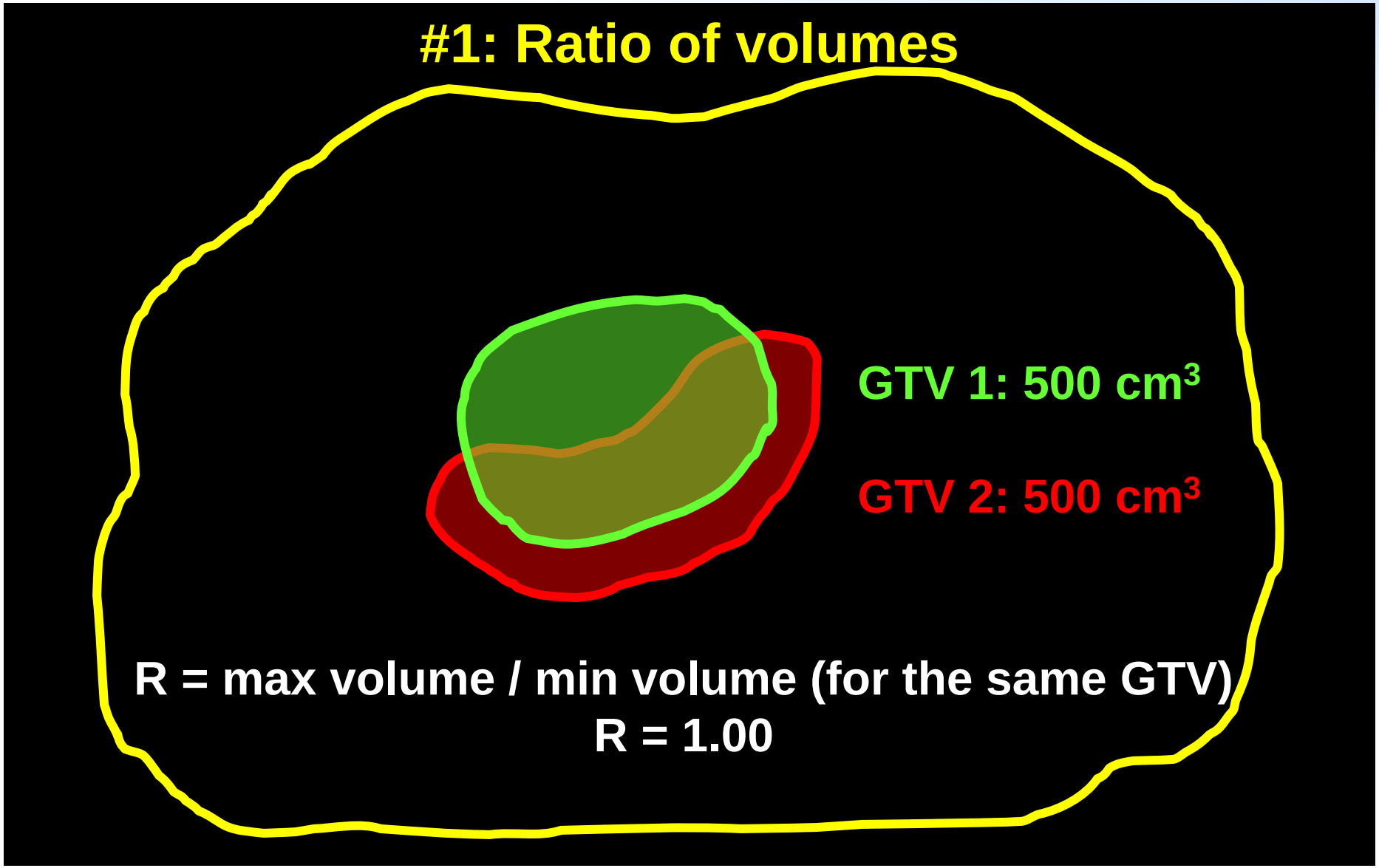
Target-location might shift, depending on who is delineating it



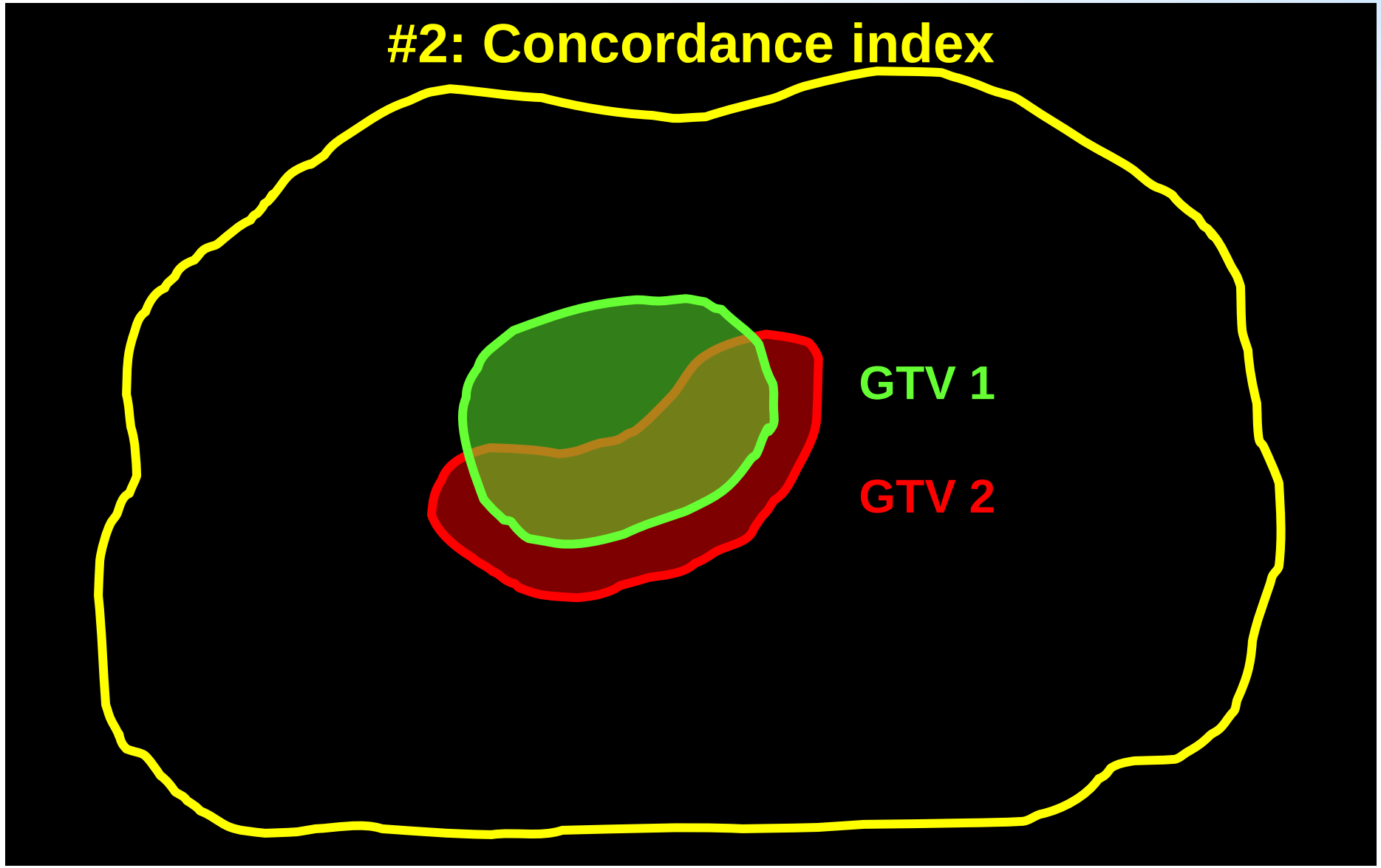
It is a big challenge to minimize this variation!



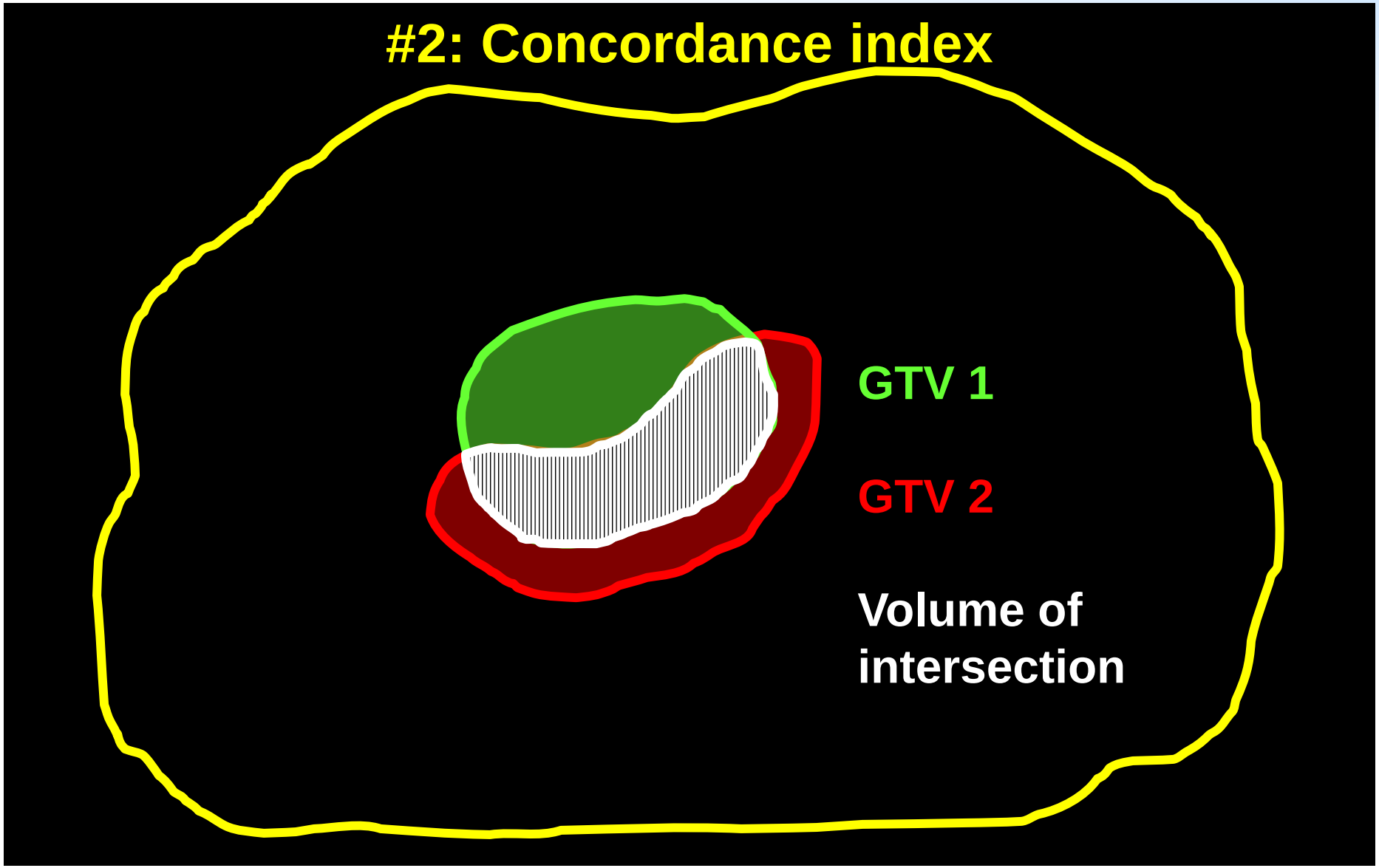
Measuring delineation variation



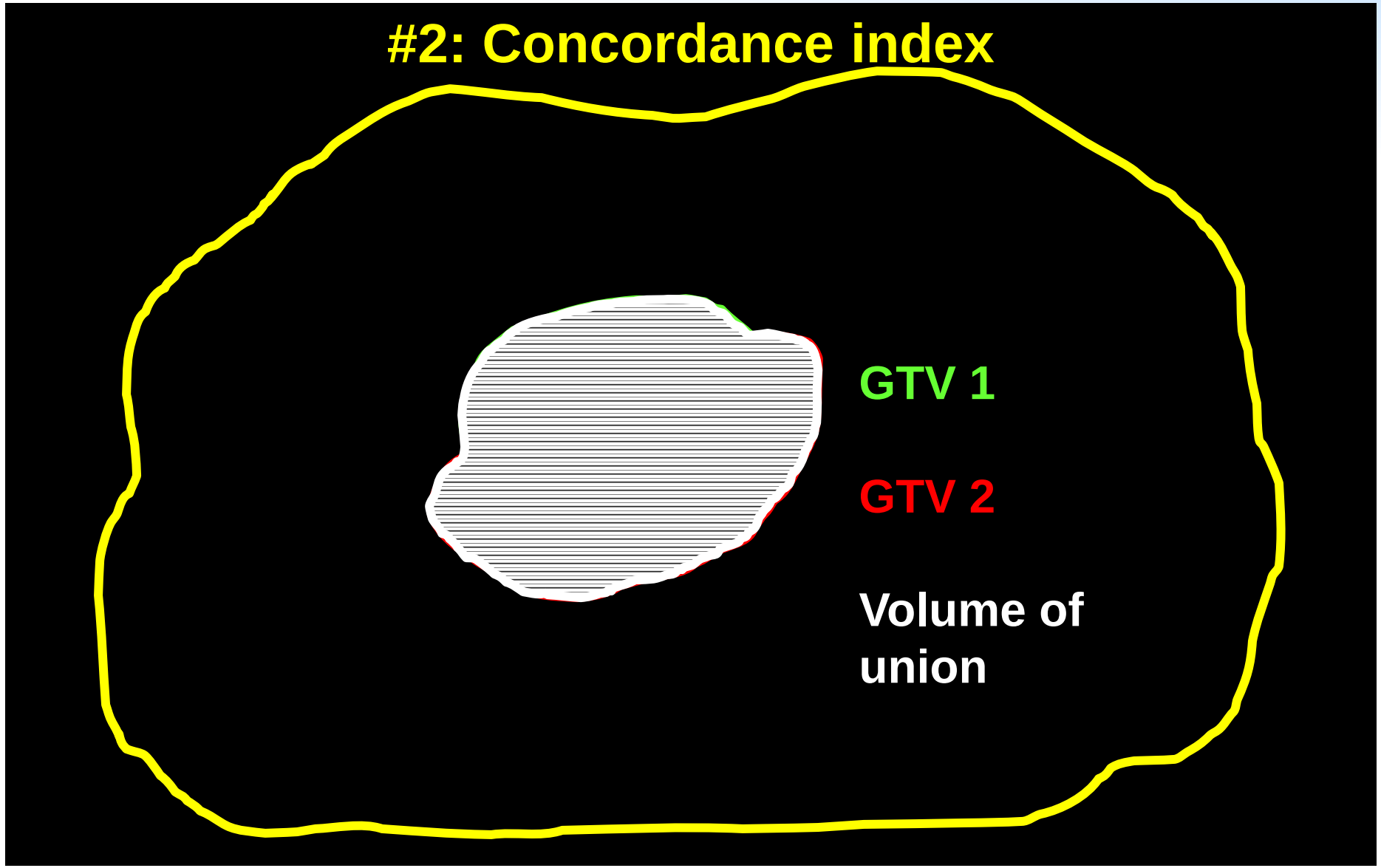
Measuring delineation variation



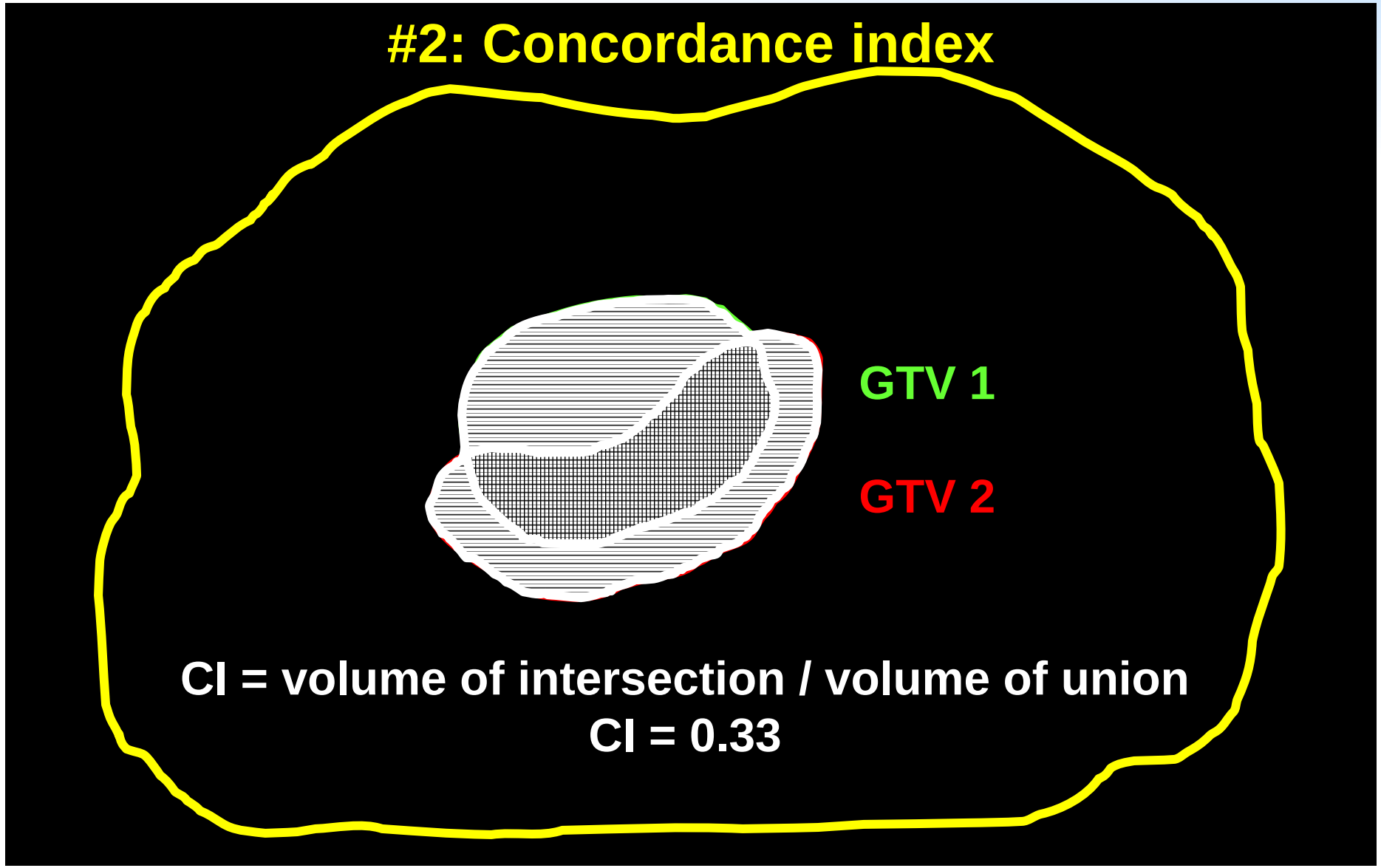
Measuring delineation variation



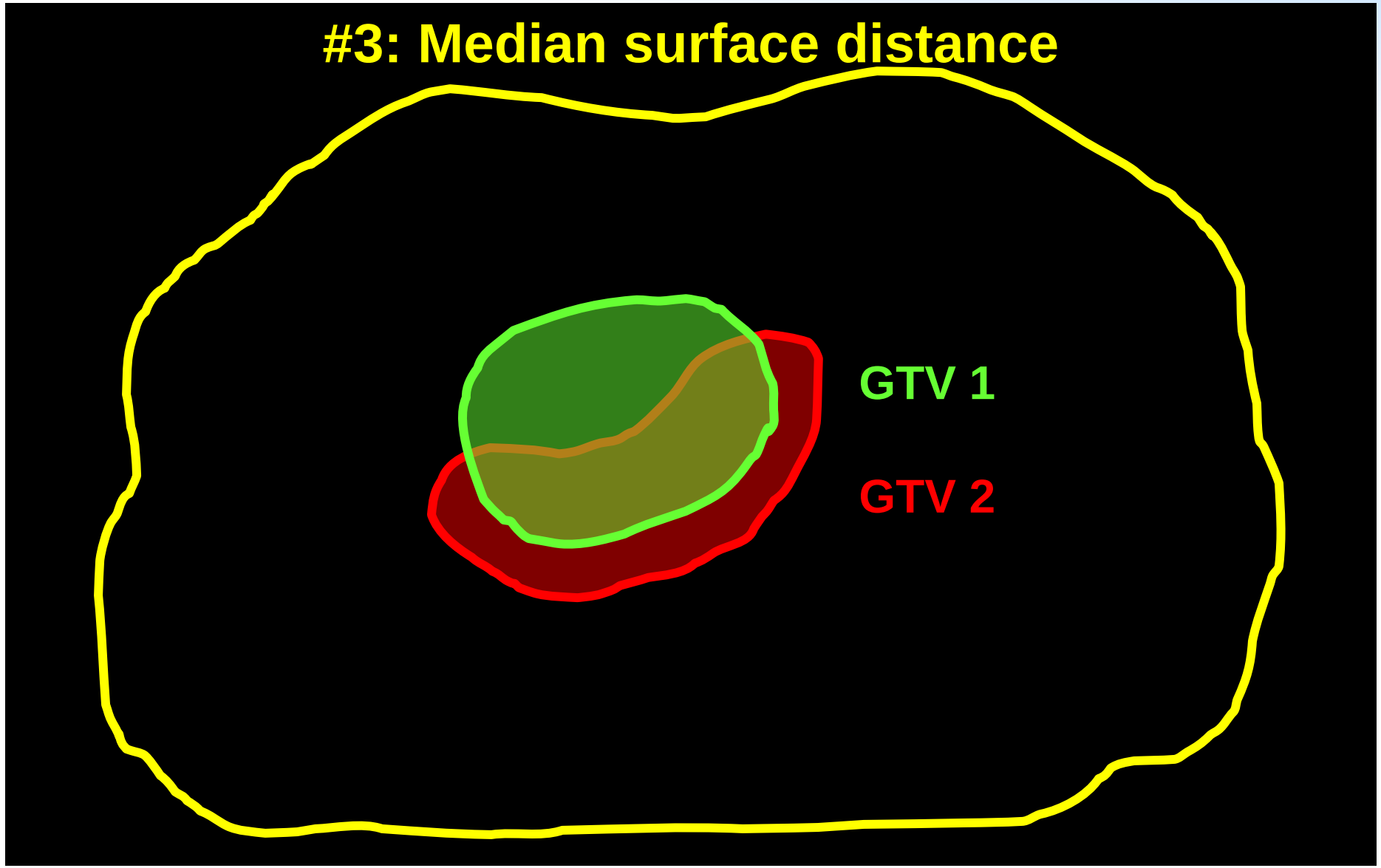
Measuring delineation variation



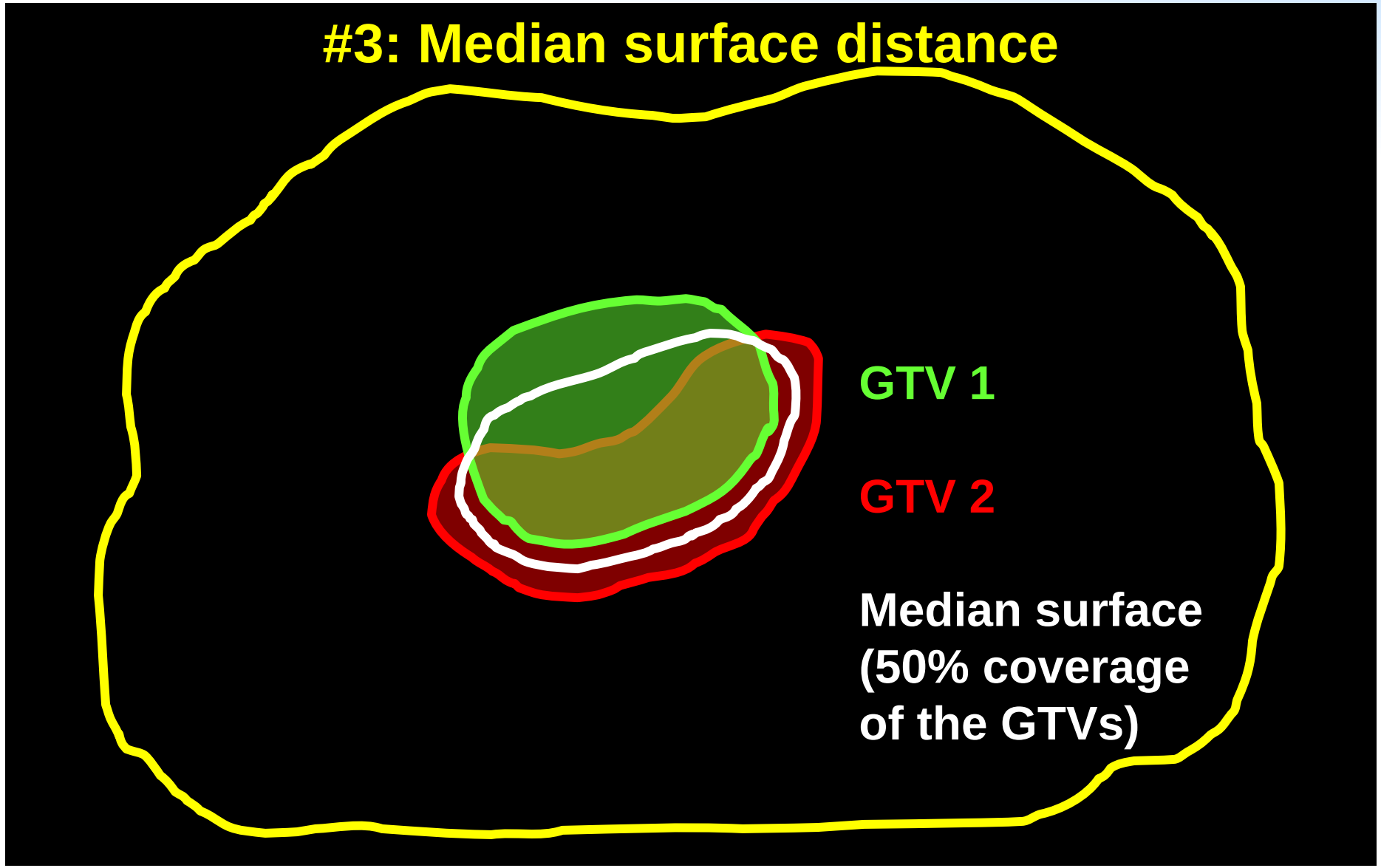
Measuring delineation variation



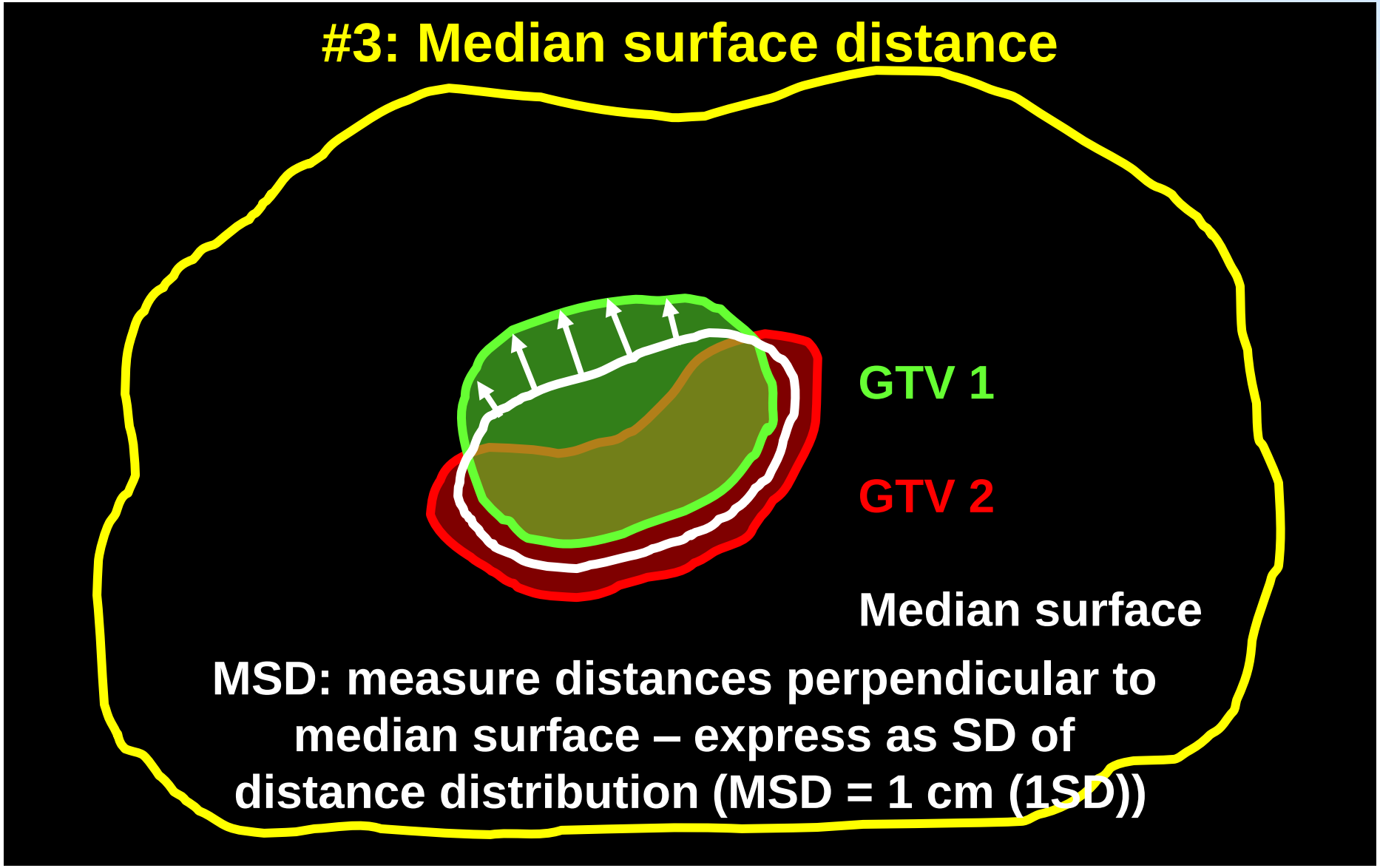
Measuring delineation variation



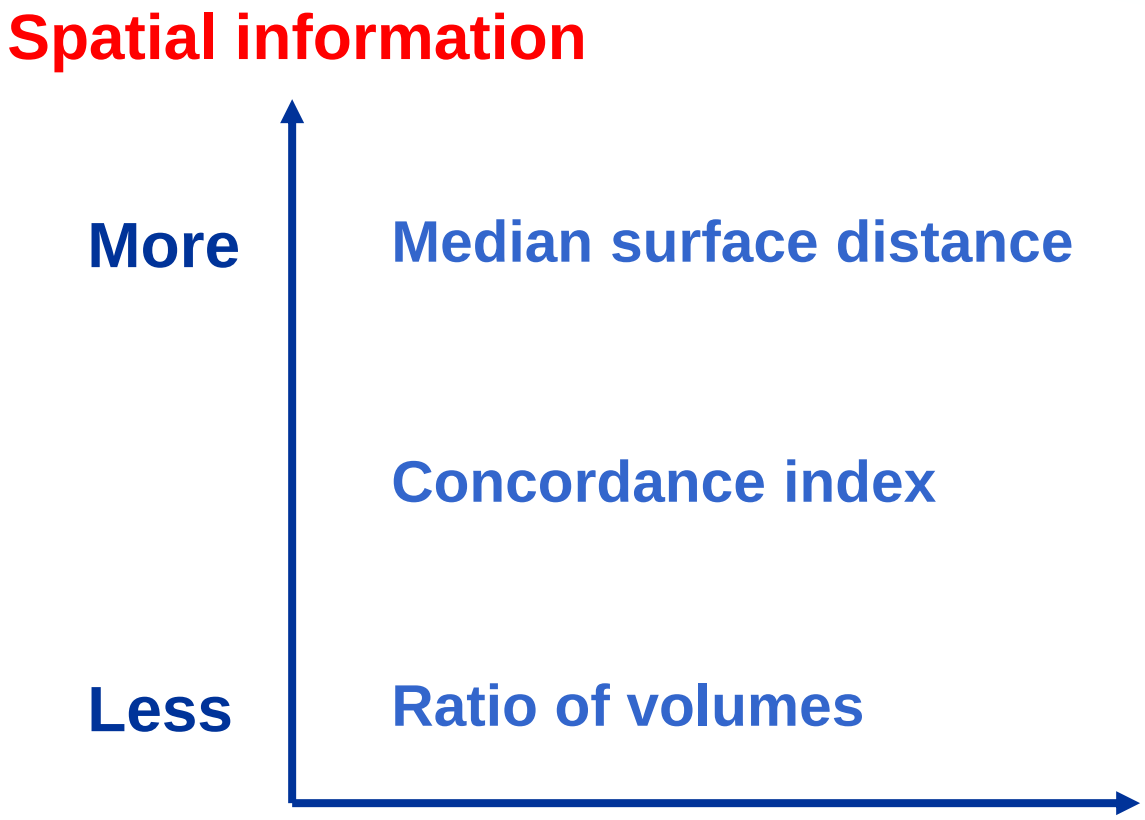
Measuring delineation variation



Measuring delineation variation



Measuring delineation variation



Minimizing delineation variation

Reference	Patients	Clinicians	Parameter
1. Logue et al 1998 IJROBP	4 bladder ca	8 rad onc 3 radiol	R = 1.2 - 3.7 R = 1.1 - 1.7
2. Giraud et al 2002 RO	10 lung ca	8 rad onc 9 radiol	CI = 0.06 CI = 0.10

→ **Take into account the expertise of radiologists in interpretation of images when delineating a GTV.**

Minimizing delineation variation

Reference	Patients	Clinicians Image-aid	Parameter
1. Weltens et al 2001 RO	5 brain ca	9 clinicians CT+MRI	R = 1.7 - 2.8 R = 1.5 - 2.7 aided
2. Caldwell et al 2001 IJROBP	30 lung ca	9 clinicians CT+FDG-PET	R = 2.3 R = 1.6 aided

→ **Other imaging modalities could be of value to aid delineation in CT-scan (depending on site and modality).**

Minimizing delineation variation

Reference	Patients	Clinicians Image-aid	Parameter
1. McGibney et al work-in-progress	10 lung ca	8 clinicians IV-contrast	MSD= 9 mm (1SD) 9 mm (aided)

However, IVC brought down variation in delineation significantly in certain regions systematically (which can be analysed with this particular method).

→ **Contrast can aid for sub-group of patients.**

It might be necessary to be very systematic in analysis to minimise variation

Summary of problem

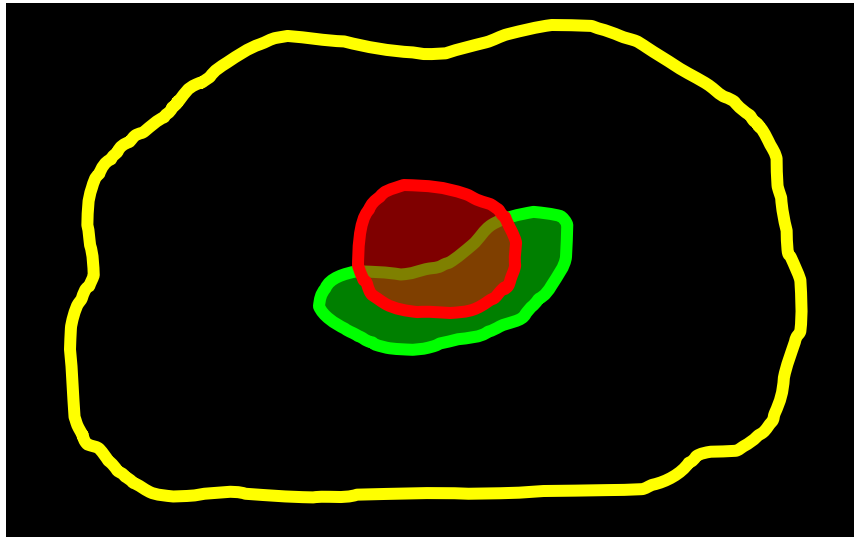
Extent of geometric variations:

- **Delineation variation the largest geometrical variation in radiotherapy – often cm**

Strategies for dealing with geometric variations in practice:

- **radiologists input in GTV delineation**
- **use optimal imaging modalities**
- **e.g. contrast**

ICRU: "The uncertainty in the delineation *(of GTV and CTV)* should be included in margin considerations"



ICRU

With new techniques, carcinogenesis needs to be monitored; there might also be unsuspected regions of high dose within the patient

ICRU: "… The volume within the patient excluding any delineated OAR and the CTV(s) should be identified as the "remaining volume at risk" (RVR)"


HEADQUARTERS
INTERNATIONAL ATOMIC ENERGY AGENCY
Thank You!