IMRT,IGRT,SBRT

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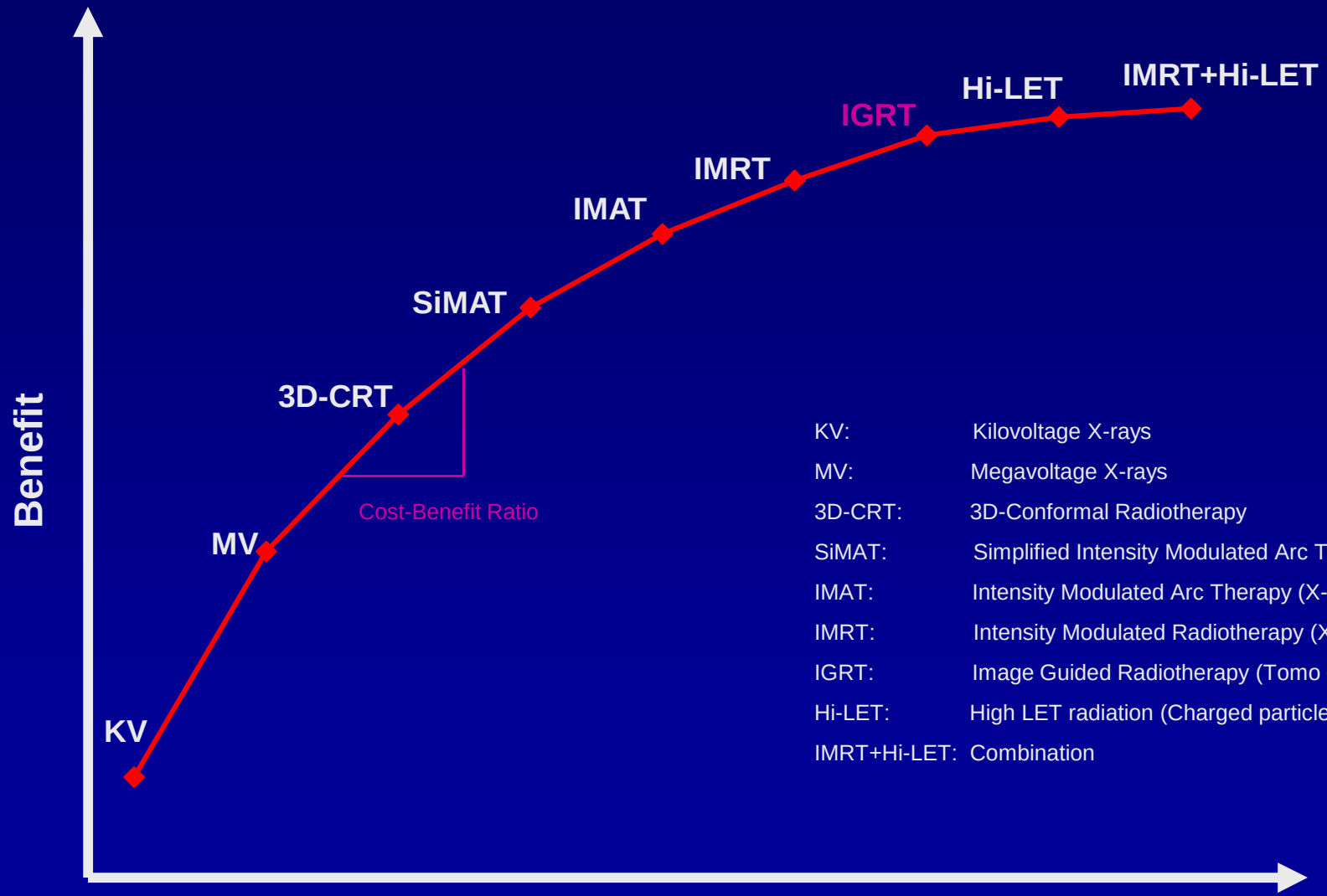
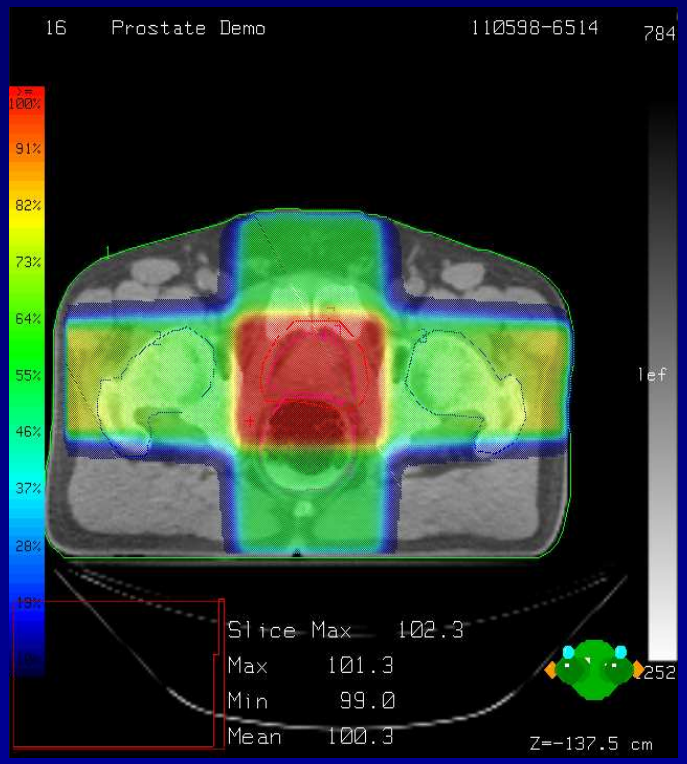
CUTTACK

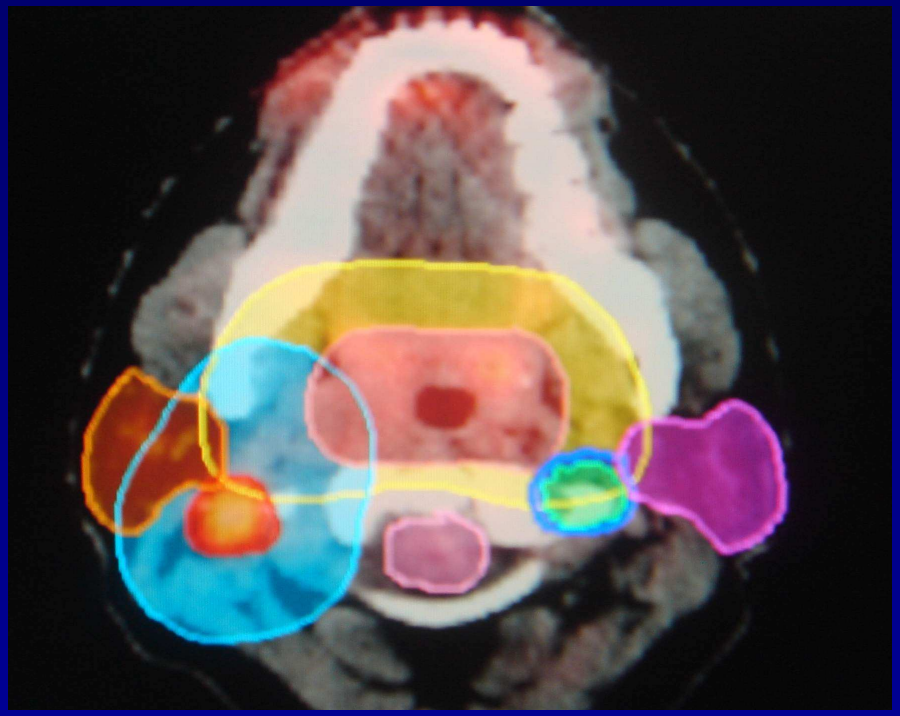
High-cost Technology in Radiation Oncology: A value judgment



KV:	Kilovoltage X-rays
MV:	Megavoltage X-rays
3D-CRT:	3D-Conformal Radiotherapy
SiMAT:	Simplified Intensity Modulated Arc Therapy
IMAT:	Intensity Modulated Arc Therapy (X-rays)
IMRT:	Intensity Modulated Radiotherapy (X-rays)
IGRT:	Image Guided Radiotherapy (Tomo etc.)
Hi-LET:	High LET radiation (Charged particles)
IMRT+Hi-LET:	Combination

CONVENTIONAL RADIATION





Conventional RT Beam

Uniform Beam Intensity

squares / rectangles

THERAPEUTIC RATIO

CURE CANCER WITHOUT INCURRING SIDE EFFECT

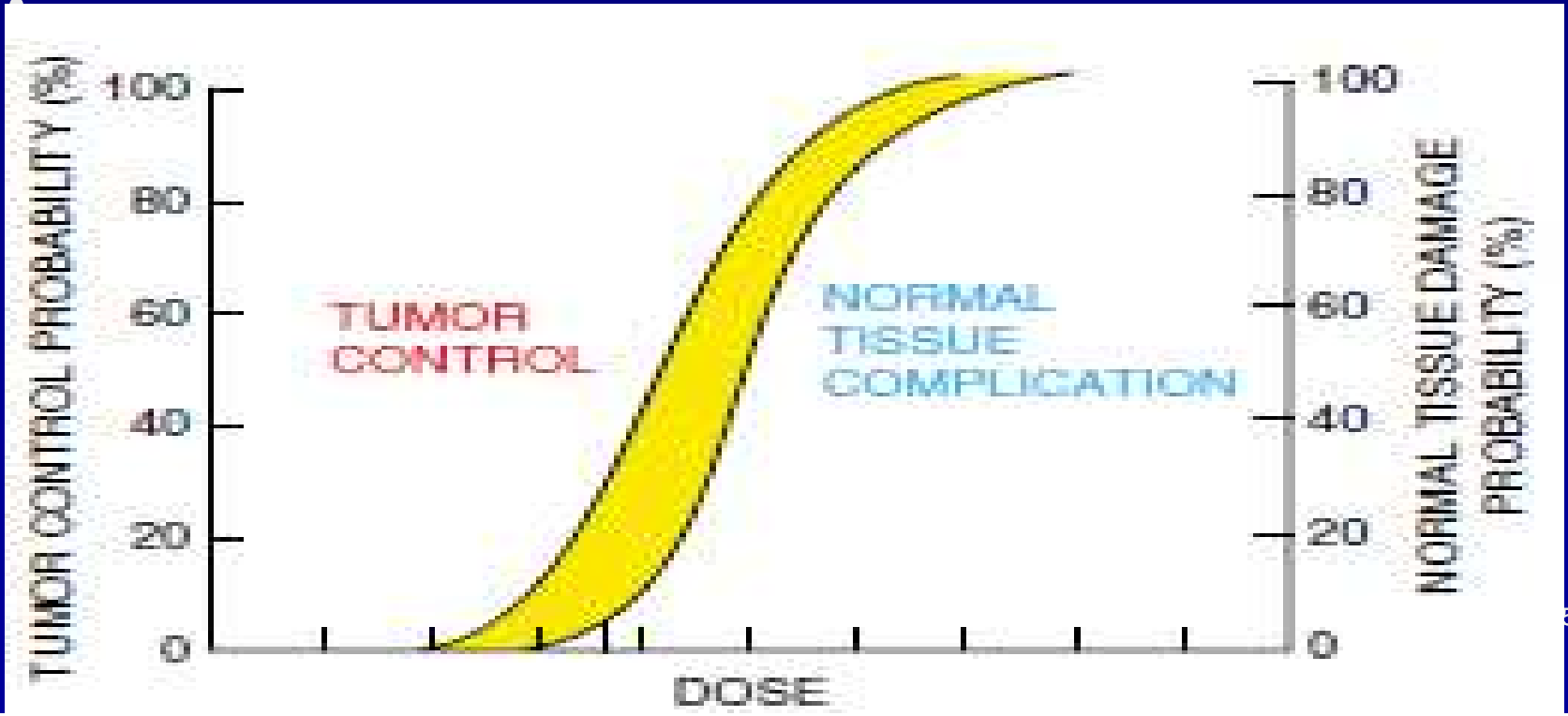
TUMOR CONTROL PROBABILITY

NORMAL TISSUE TOXICITY

$$\frac{\text{TUMOR CONTROL PROBABILITY}}{\text{NORMAL TISSUE TOXICITY}} > 1$$

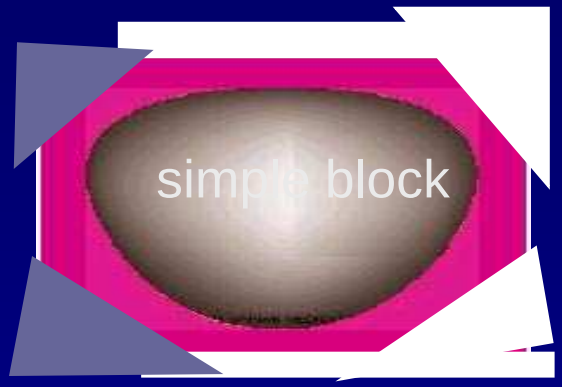
TCP,NTCP

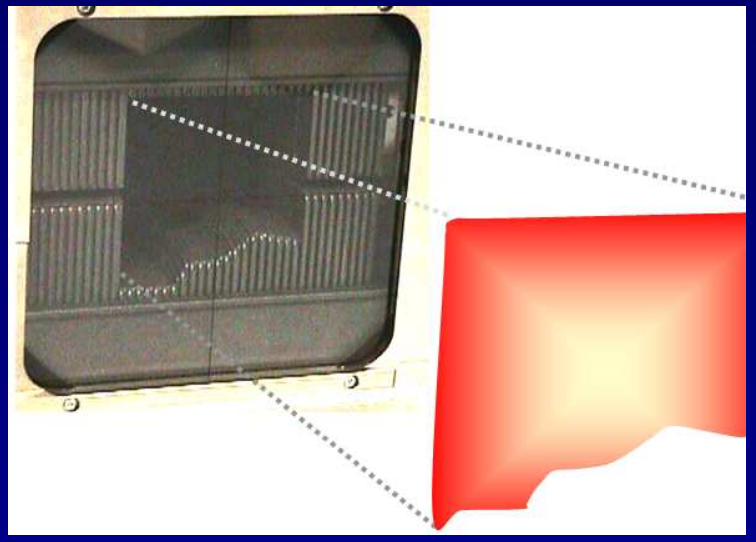
TCP and NTCP curves are sigmoid in shape. The purpose of treatment is to move the TCP curve to the left and the NTCP curve to the right.The therapeutic index (= therapeutic window increases if the region the between two curves becomes large, and the expected benefit from treatment increases

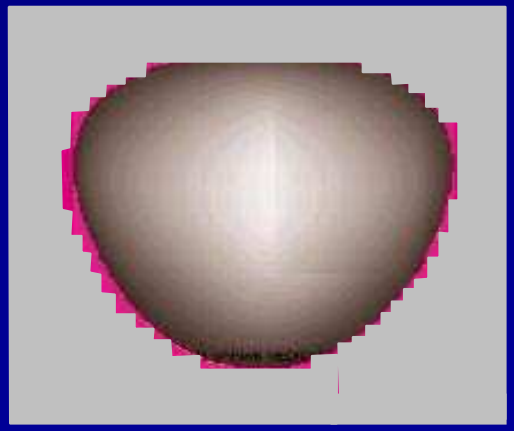


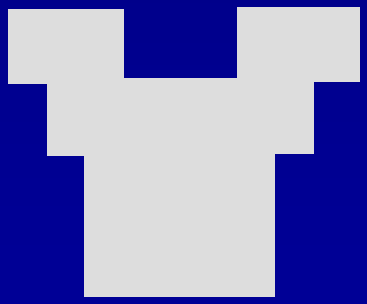
CONFORMAL RADIATION

Conventional open field









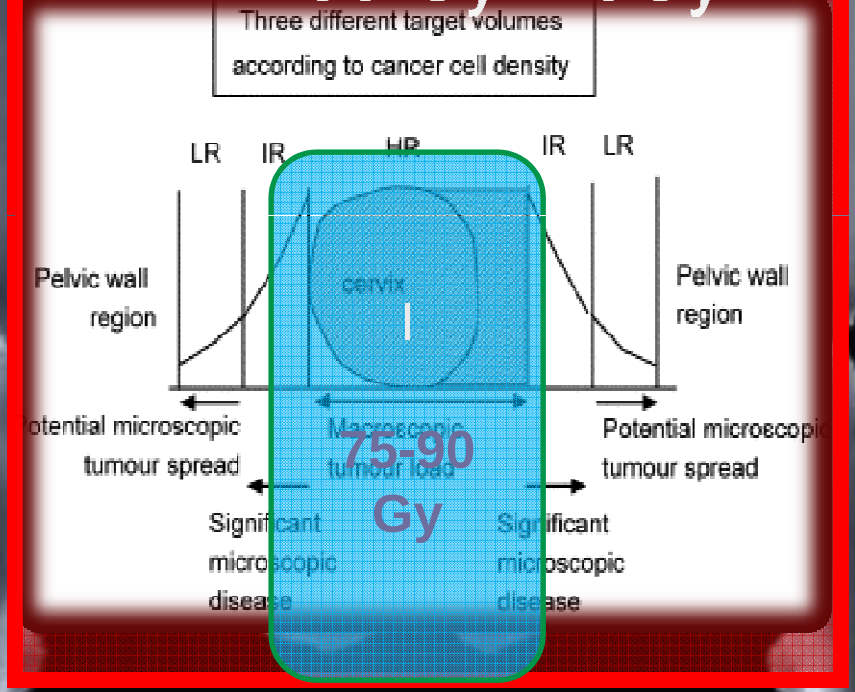
3 D CRT with MLC

Uniform Beam Intensity

45-50 Gy+
5-10Gy III

II

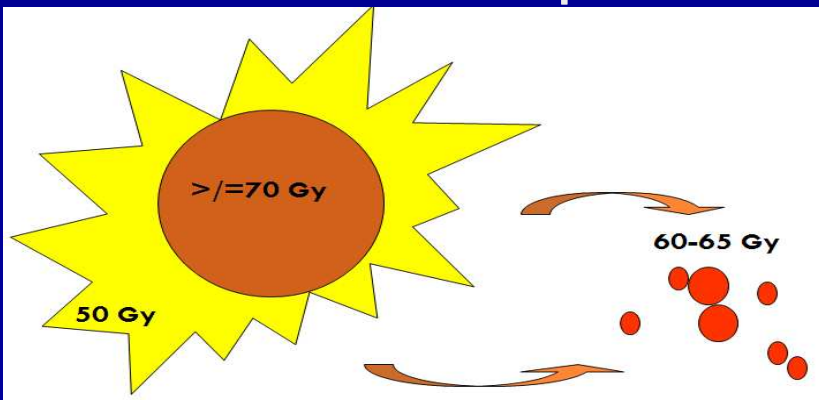
50 Gy+10Gy

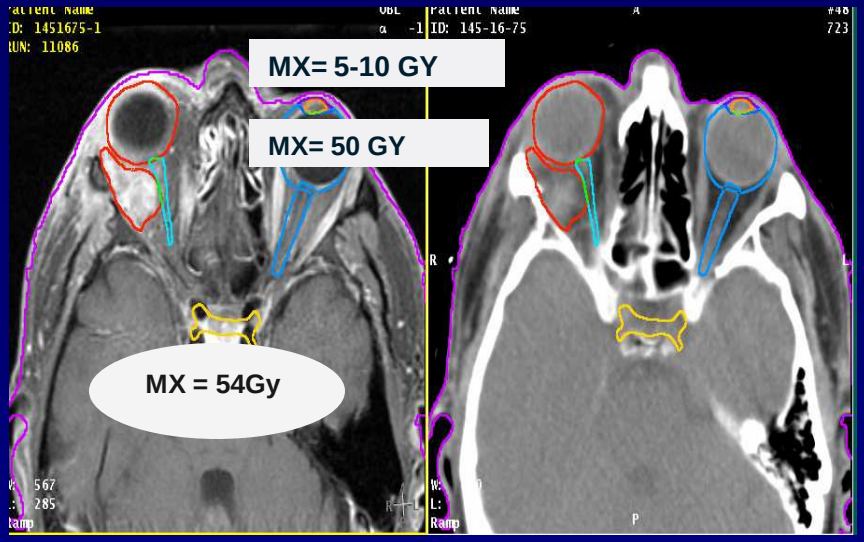


Pelvis

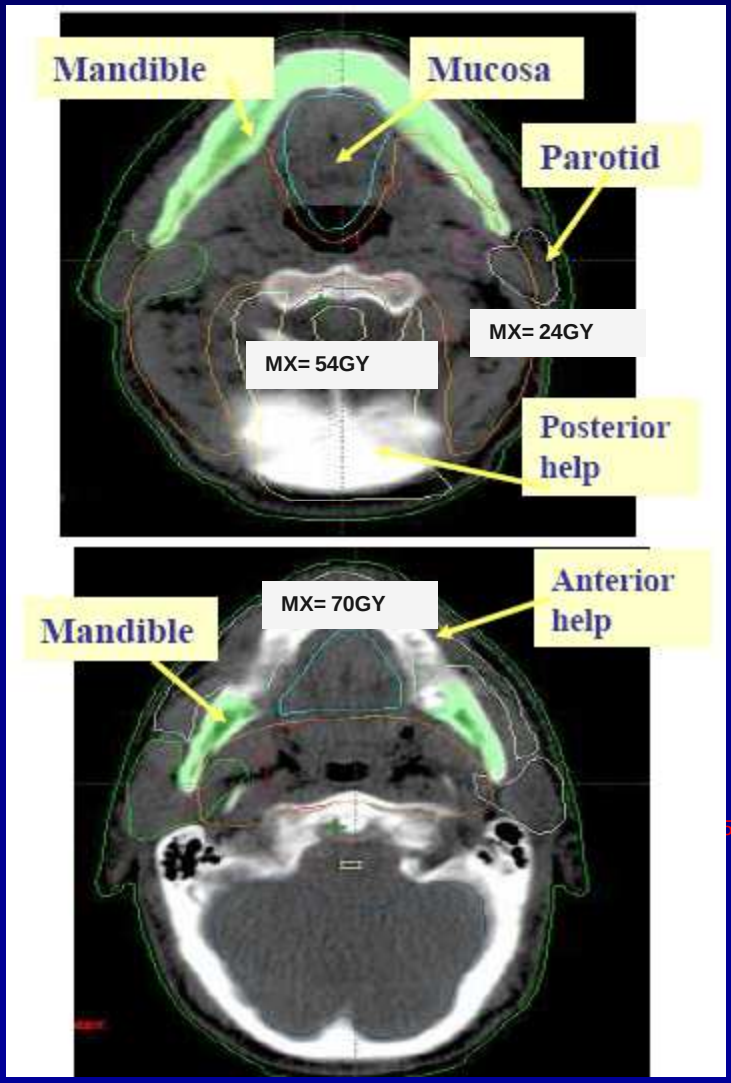
CTV Delineation

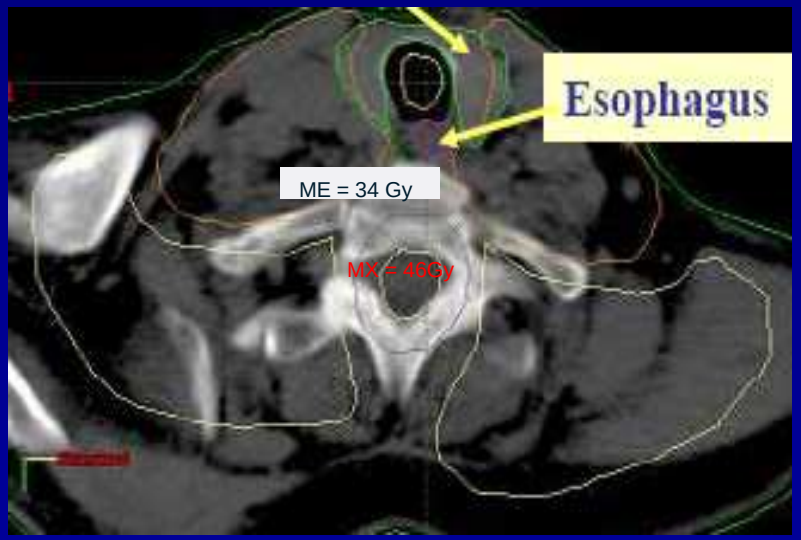
- **Low Risk CTV**: Consists volume at risk of potential microscopic disease spread at the time of diagnosis. Typically treated to a dose of 50 -55 Gy.
- **Intermediate Risk CTV**: Major risk of local recurrence in areas that correspond to significant macroscopic extent of disease. which corresponds to a dose of at least 60 Gy.
- **High Risk CTV**: Gross Disease.Dose to be delivered as high as possible (>/=70 Gy) and appropriate to eradicate all residual macroscopic tumour.

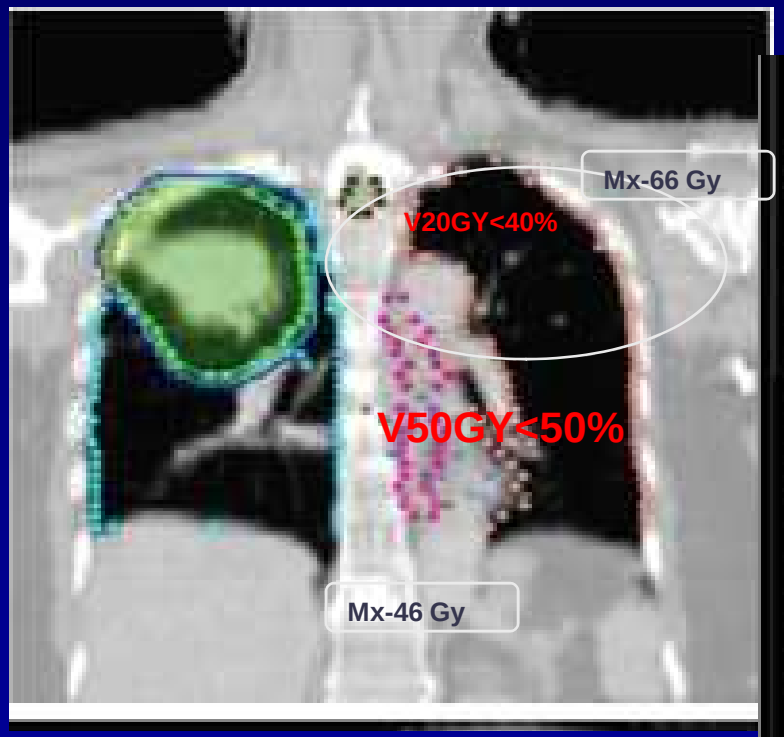


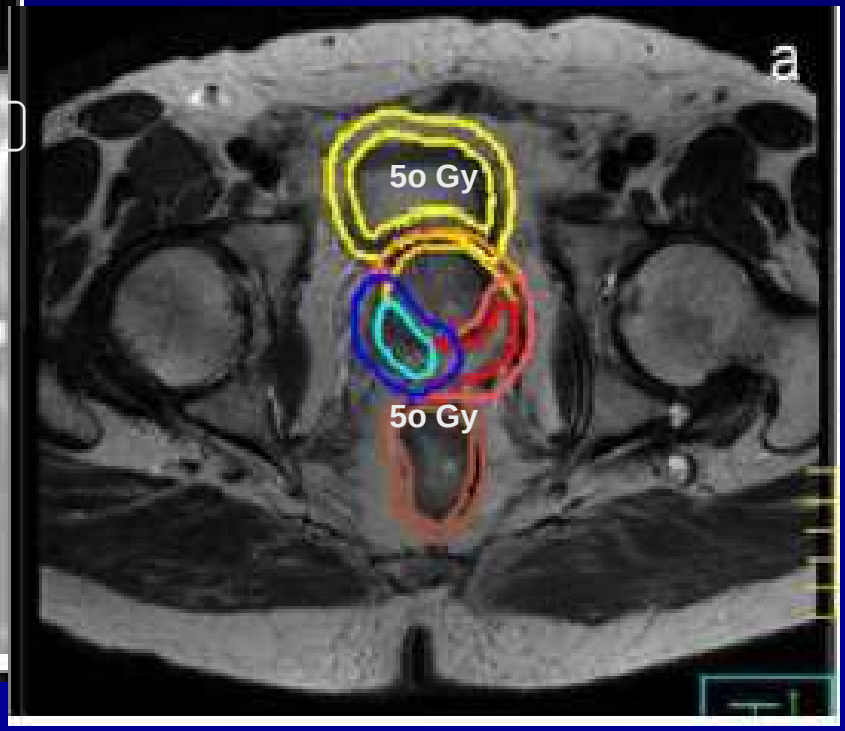


ME = 45-48 Gy
MX = 50Gy



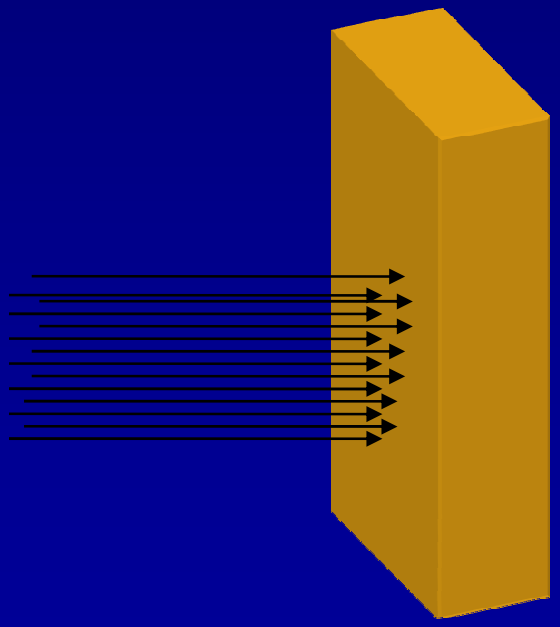



Mx-66 Gy
V20GY<40%
V50GY<50%
Mx-46 Gy


a
5o Gy
5o Gy

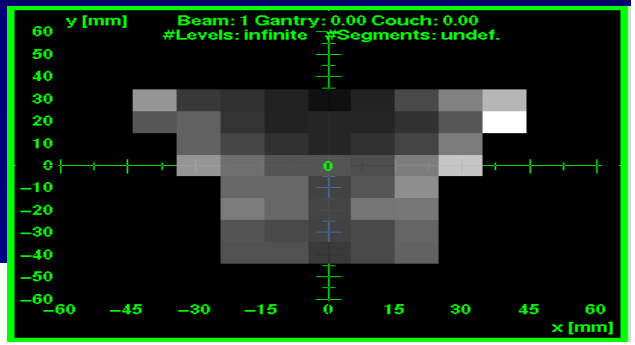
FLUENCE

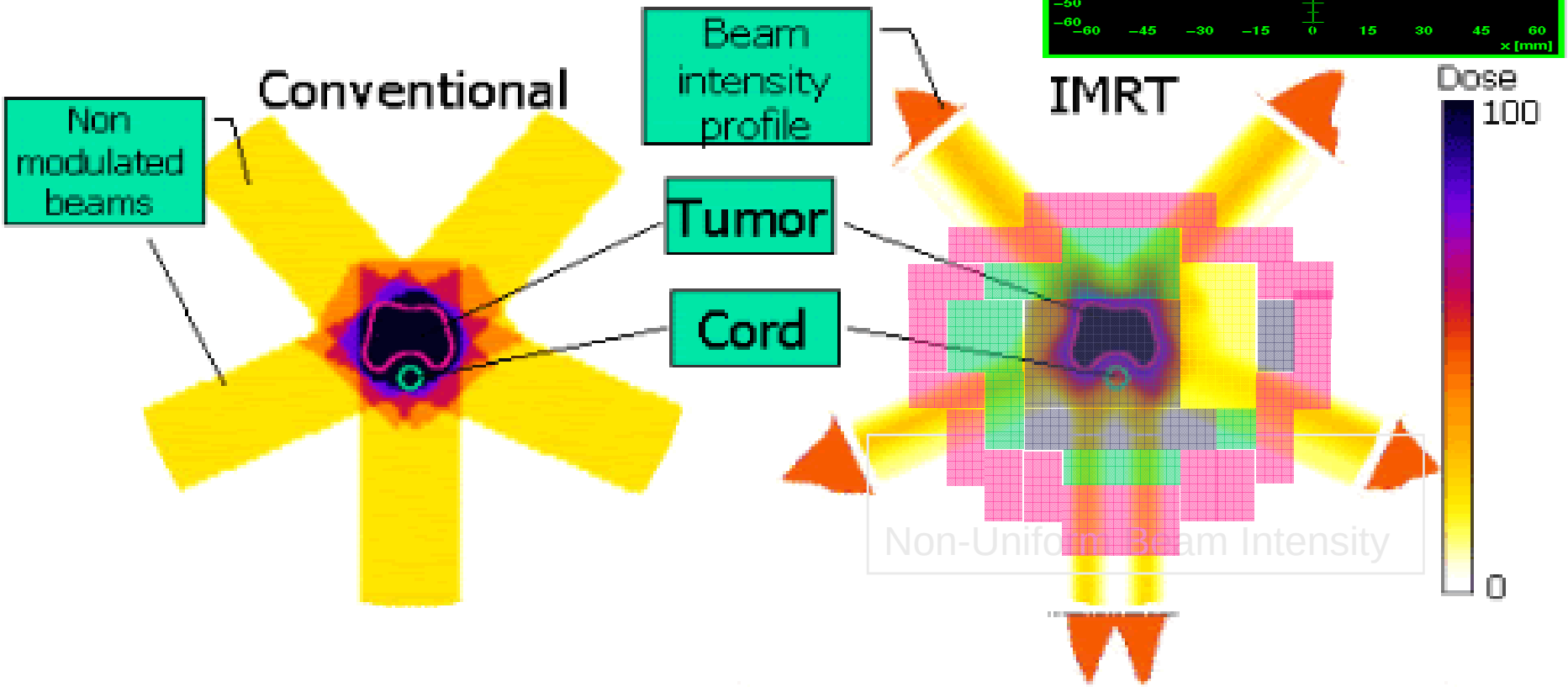
- Fluence referes to the **number** of "particles" incident on an **unit area** (m^{-2})



What exactly *is* IMRT?

A TYPE OF PRECISSION RADIOTHERAPY WHERE BEAM INTENSITY MODULATED TO ACHIEVE A HIGHLY CONFORMAL DOSE DISTRIBUTION IN THE TARGET VOLUME



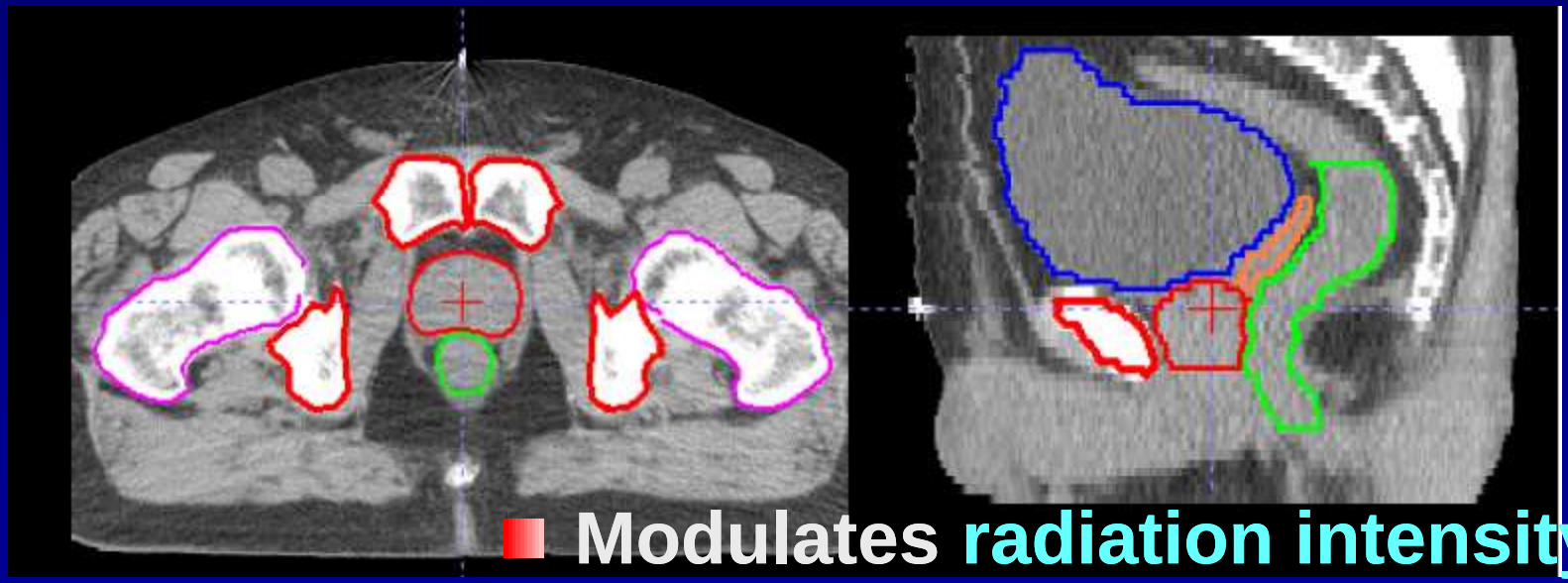


COMMON RADIATION MODALITIES

- CONVENTIONAL RADIOTHERAPY
- GEOMETRIC FIELD SHAPING:-3DCRT
- GEOMETRIC FIELD SHAPING+MODULATION OF THE INTENSITY OF THE FLUENCE:- IMRT
- GEOMETRIC FIELD SHAPING+MODULATION OF THE INTENSITY OF THE FLUENCE+IMAGE GUIDANCE:-IGRT

IMRT FACTS

Better normal tissue sparing



- **Modulates radiation intensity.**

Dose escalation

Better conformality

STEPS IN IMRT

Patient positioning and Immobilization

Volumetric Data acqusition

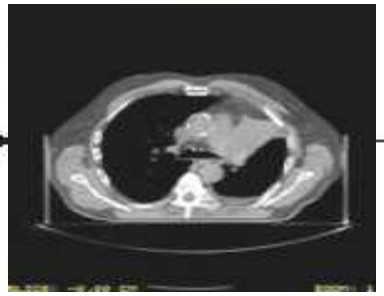


Image Transfer to the TPS

Target Volume Delineation

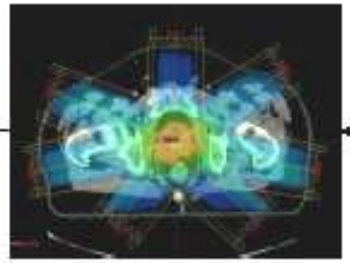
Treatment QA

Treatment Delivery

3D Model generation

Forward Planning

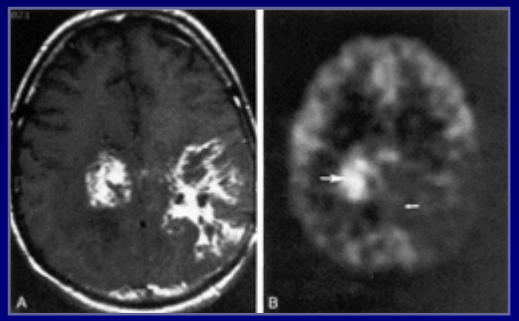
Inverse Planning

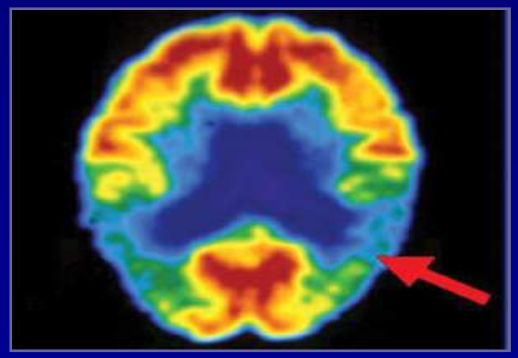


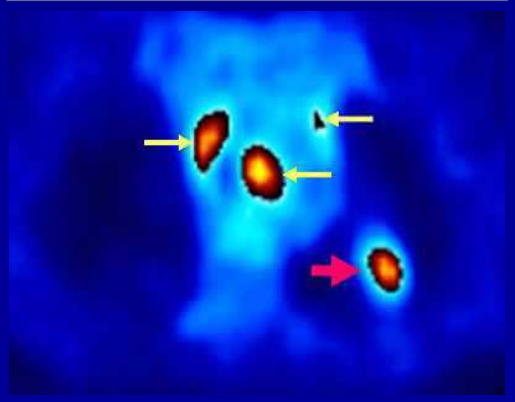
Dose distribution Analysis

PT
POSITIOING,IMMOBILIZATION

IMAGE ACQUISITION





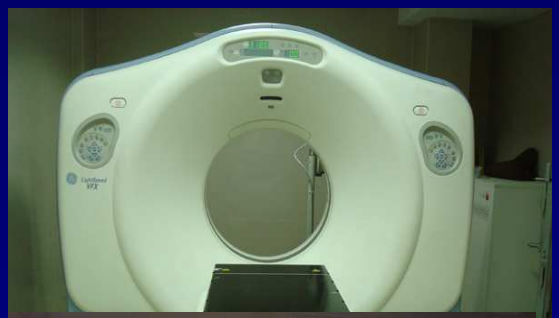


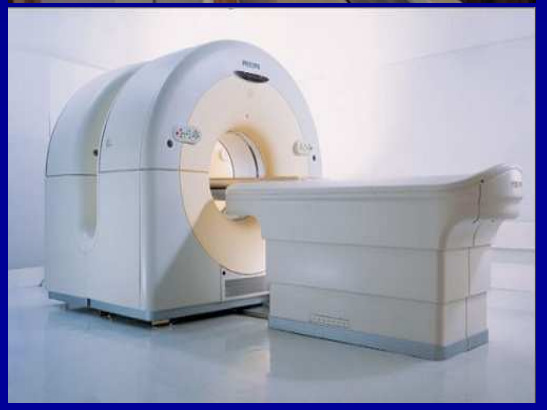
KNOW THE EXTENT

RADIATION PLANNING

IGRT

RESPONSE EVALUATION





CT SIMULATOR

- WIDE BORE(75-85cm)
- FLAT COUCH
- LASER SYSTEM(Intrnal as well as externalnlaser)
- WORK STATION

IMAGE ACQUISITION

- MOSTLY BY CT SIMULATION
- PT IS IN TREATMENT POSITION
- USE IMMOBILIZATION.
- PUT FIDUCIAL AT PRESUMED ISOCENTRE(needed for cordinate Transformation for image registration)
- GENERATE TOPOGRAM:-For patient allignment,area to be scanned.
- FOV is selected to permit visualization of the external contour
- IMAGE ACQUIZITION:-3 TO 5 MM CUTS.
- IMAGE & DATA TRANSFER TO TPS

TREATMENT PLANNING SYSTEM

- IMAGE REGISTRATION
- IMAGE SEGMENTATION
- VIRTUAL SIMULATION
- DOSE CALCULATION
- PLAN EVALUATION
- DATA STORAGE
- DATA TRANSFER TO CONSOLE
- TREATMENT CERIFICATION

WHY IMAGE REGISTRATION

- TO DEFINE THE TARGET VOLUME
- FUSION:- BETTER ASSESS THE ANATOMY AS WELL AS PHYSIOLOGY
- ORGAN MOTION STUDY
- 3D CT+ ORGAN MOTION= 4D CT
- ANALYSIS OF DOSE DISTRIBUTION

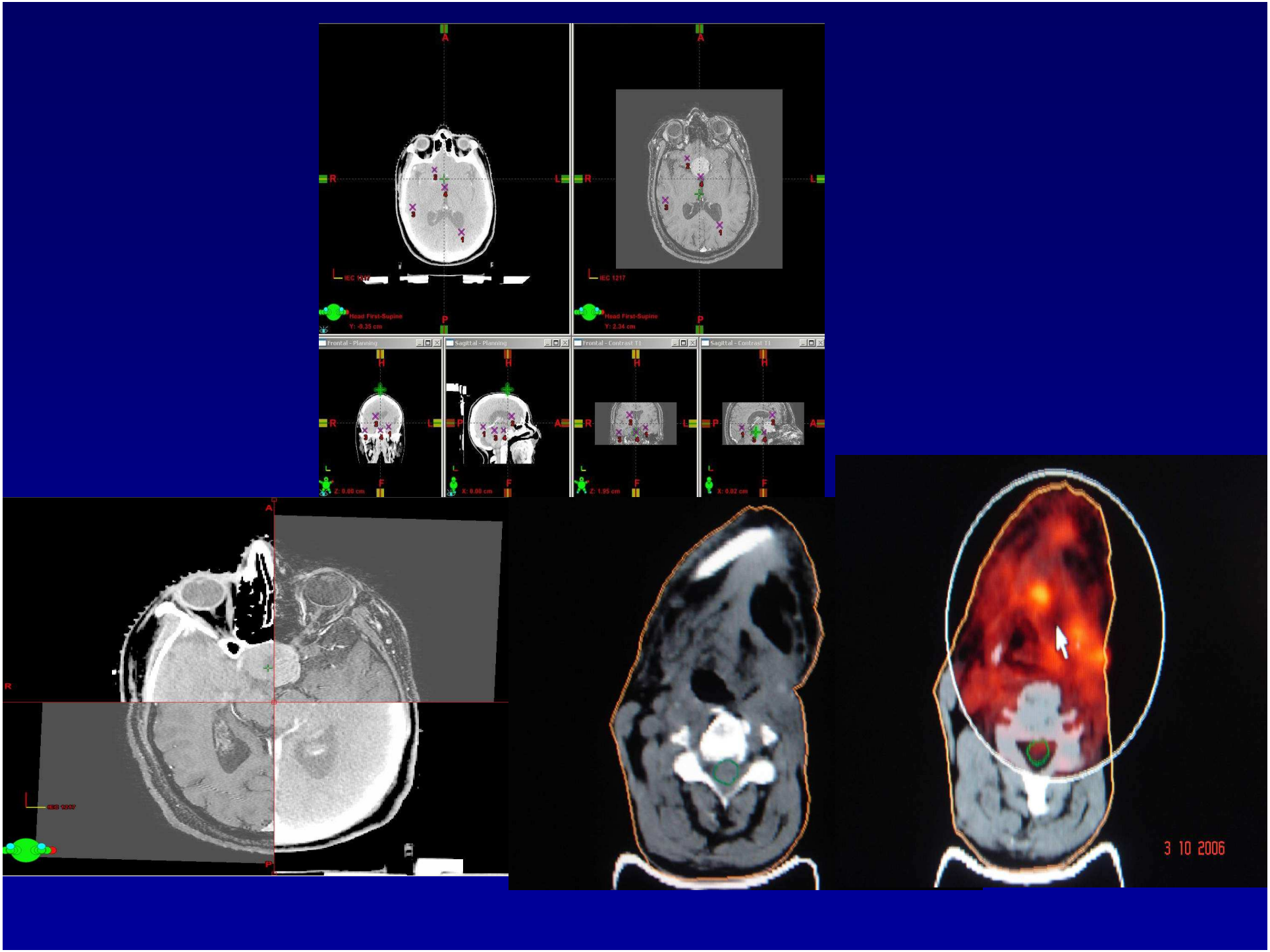
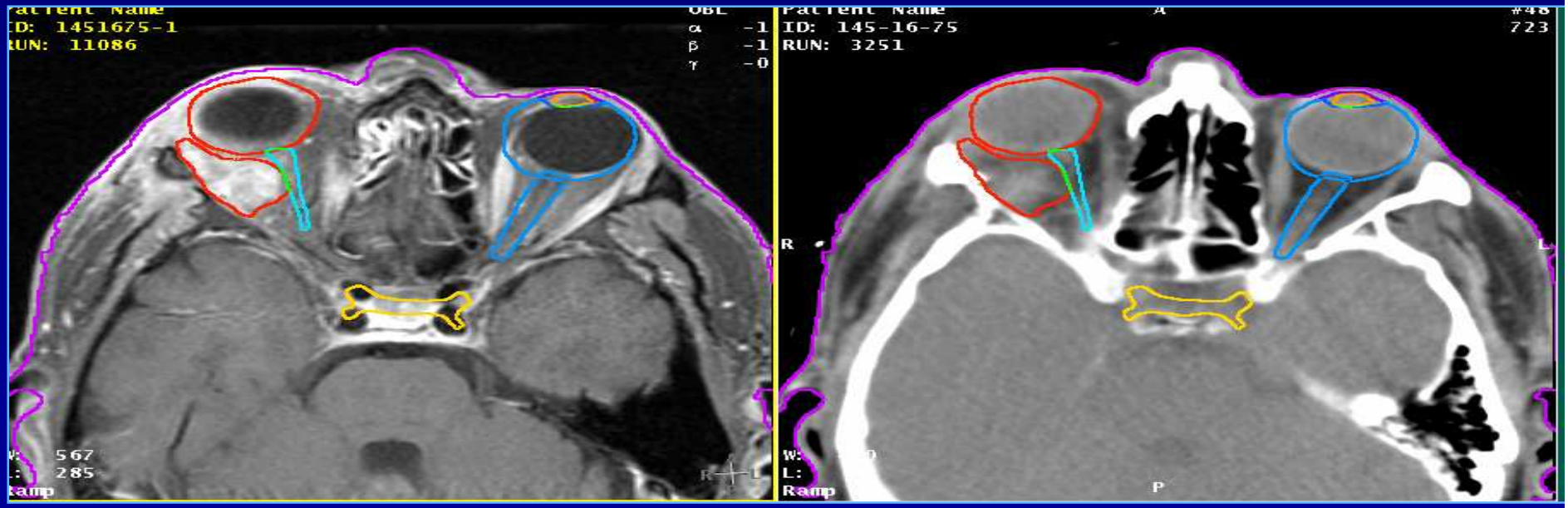
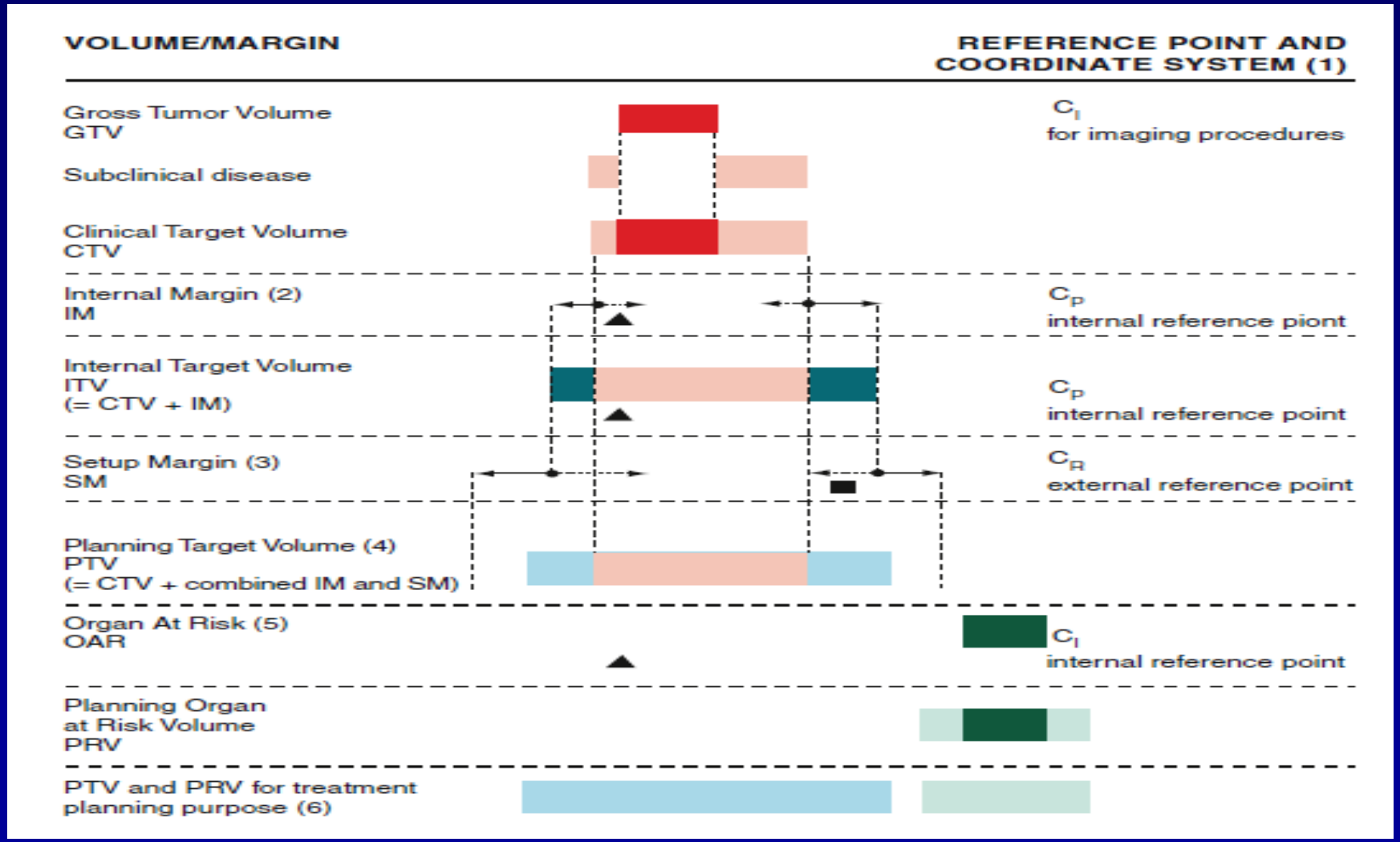

Head First-Supine
Y: -9.35 cm
Head First-Supine
Y: 2.34 cm
Frontal - Planning
Sagittal - Planning
Frontal - Contrast T1
Sagittal - Contrast T1
3 10 2006

IMAGE SEGMENTATION

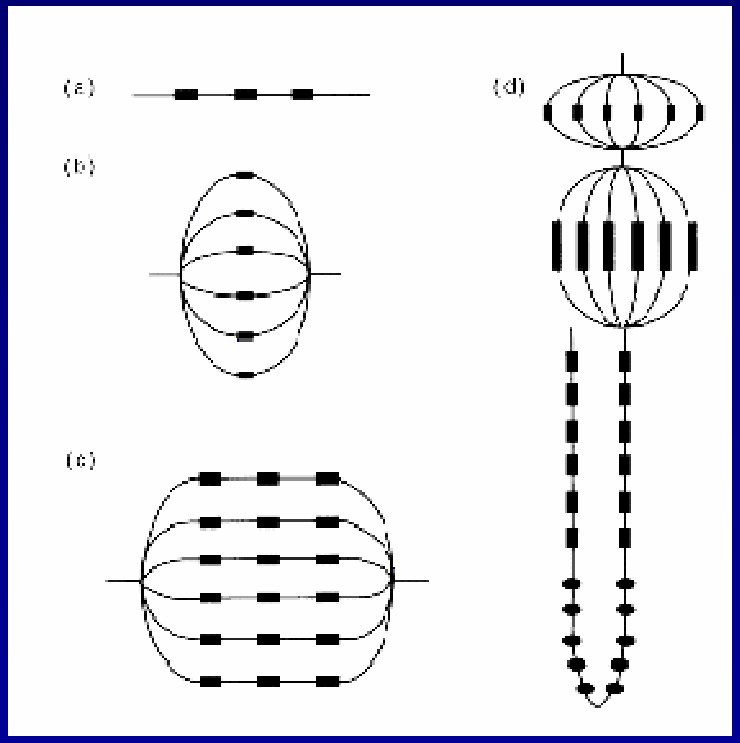
An image segmentation is the partition of an image into a set of regions whose union is the entire image.



TARGET VOLUME



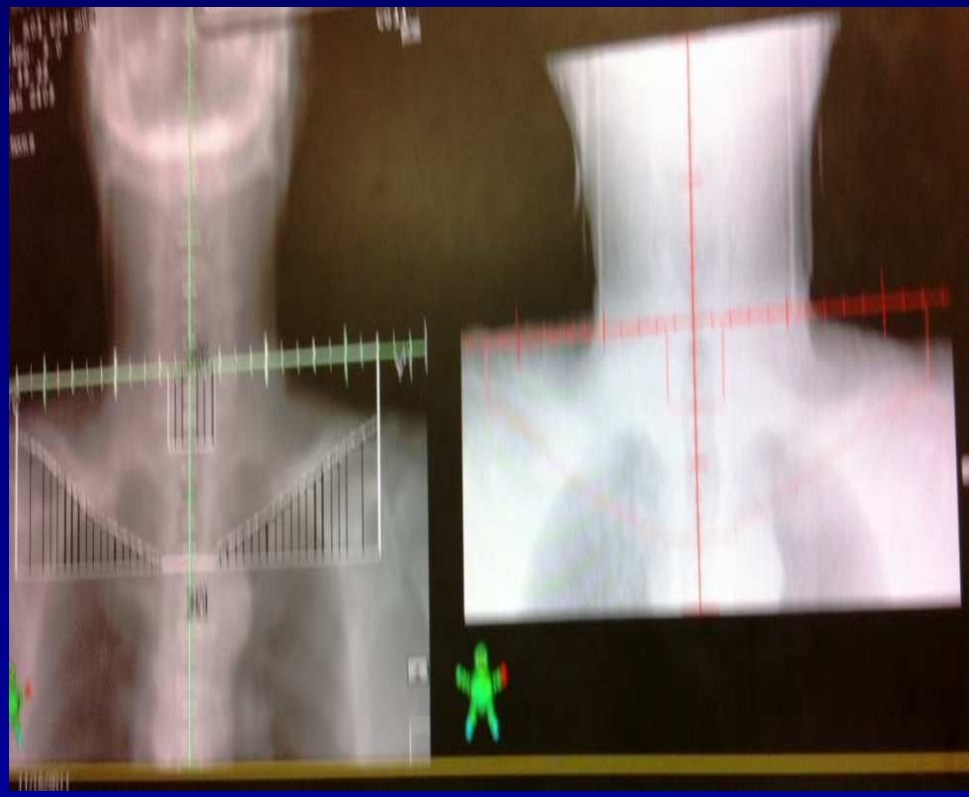
Organ at Risk (ICRU 62)



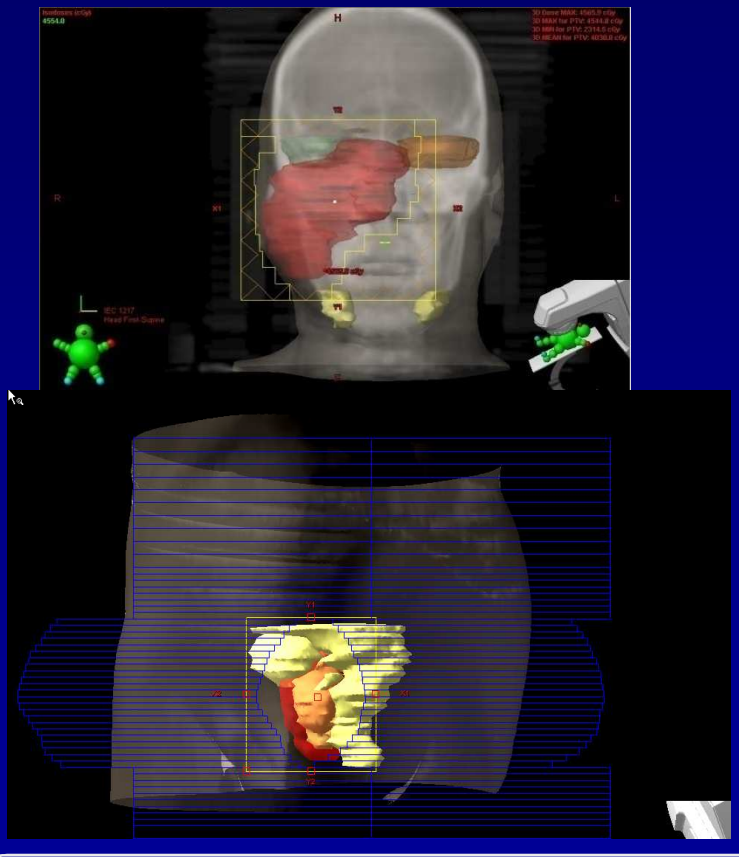
- Normal critical structures whose radiation sensitivity may **significantly** influence treatment planning and/or prescribed dose.
- Each organ is made up of a functional subunit (**FSU**)

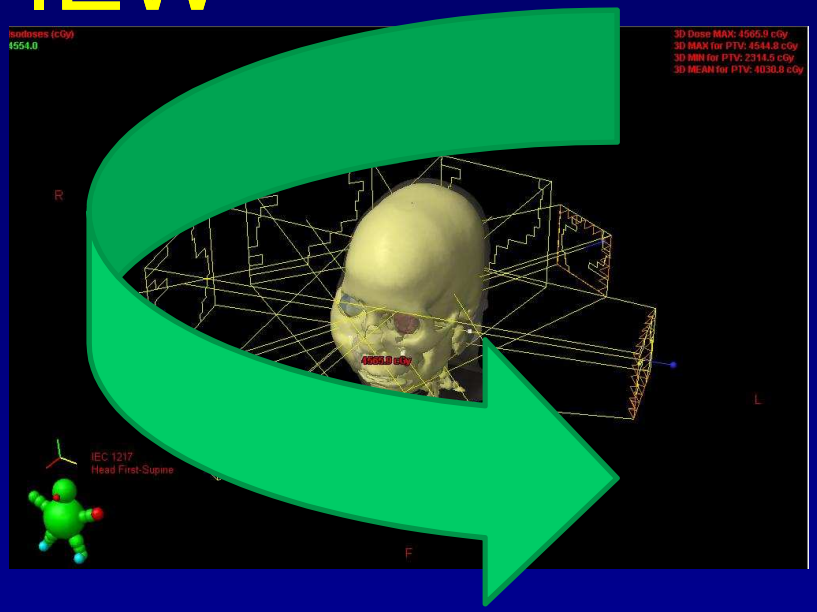
DRR

- DRR IS THE ARTIFICIAL VERSION OF AN X-RAY IMAGE .COMPUTED FROM CT DATA
- TWO DIMENSIONAL IMAGE SIMULATING NORMAL X-RAY/FLUOROSCOPIC IMAGE.
- USE TO DESIGN TREATMENT PORTAL
- VERIFICATION OF TREATMENT PORTAL



BEAMS EYE VIEW,ROOM EYE VIEW





VIEW THE GEOMETRIC COVERAGE OF TARGET VOLUME
IDENTIFY MOST SUITABLE GANTRYCOLLIMATOR,COUCH ANGLE
DESIGN OF SHIELDING,MLC

UNDERSTAND THE OVERALL TREATMENT GEOMETRY

Planning

Forward Planning

From field definition
to dose distribution

T/t parameters

↓

Dose calculation

↓

Dose distribution

↓

Dose delivery with
uniform radiation intensity

Inverse Planning

From dose distribution
to field definition

Dose delivery with
nonuniform radiation intensity

↑

leaf sequence generation

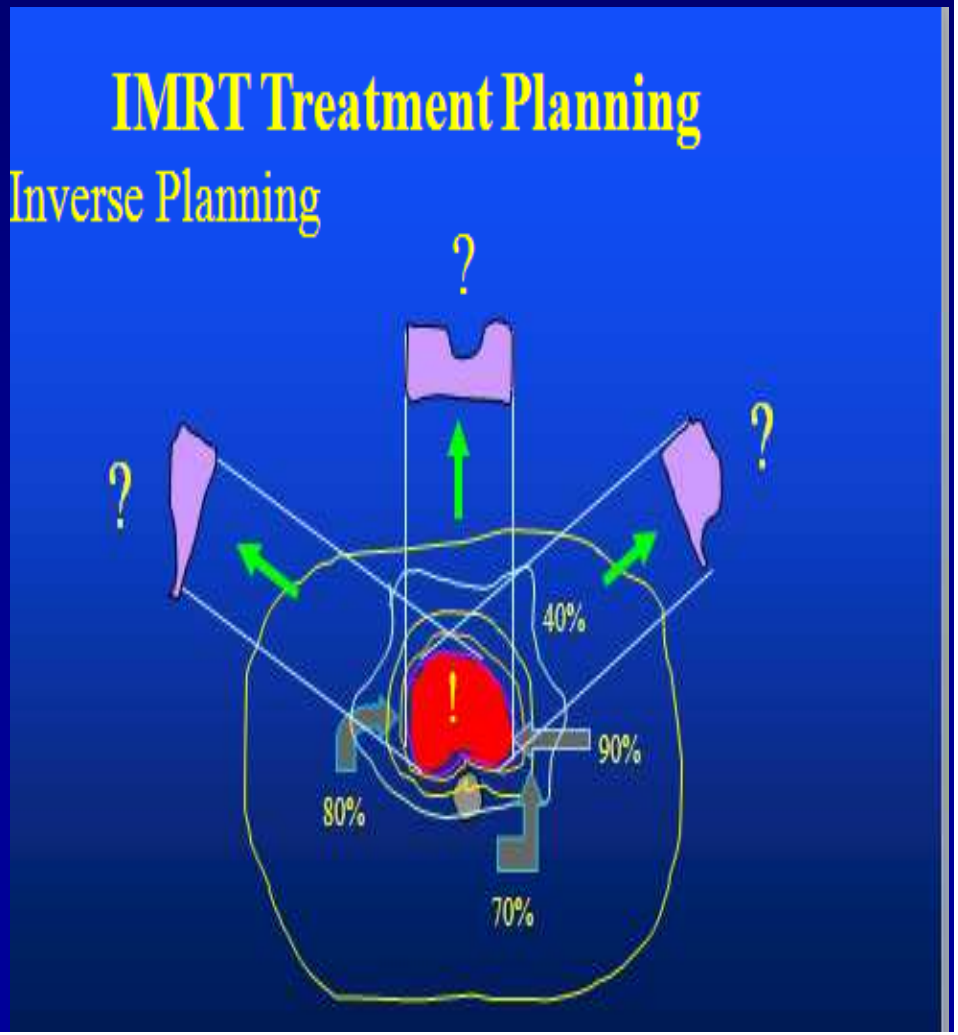
↑

optimization

↑

T/t goals
(objective function)

FORWARD Vs INVERSE PLANNING



OPTIMISZATION

Refers to the technique of finding the best physical and technically possible treatment plan to fulfill the specified physical and clinical criteria

- **Physical Optimization Criteria:**
- Based on physical dose coverage

- **Biological Optimization Criteria**: Based on TCP and NTCP calculation

A total objective function (**score**) is then derived from these criteria

PLAN EVALUATION

TOOLS USED TO EVALUATE THE PLAN

2D DISPLAY

DOSE DISTRIBUTION STATISTICS

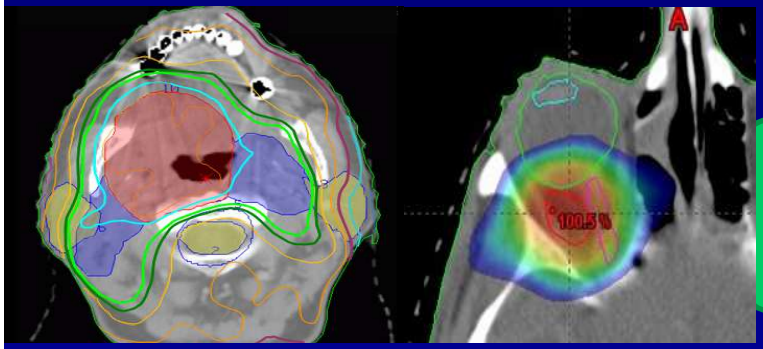
ISODOSE LINES

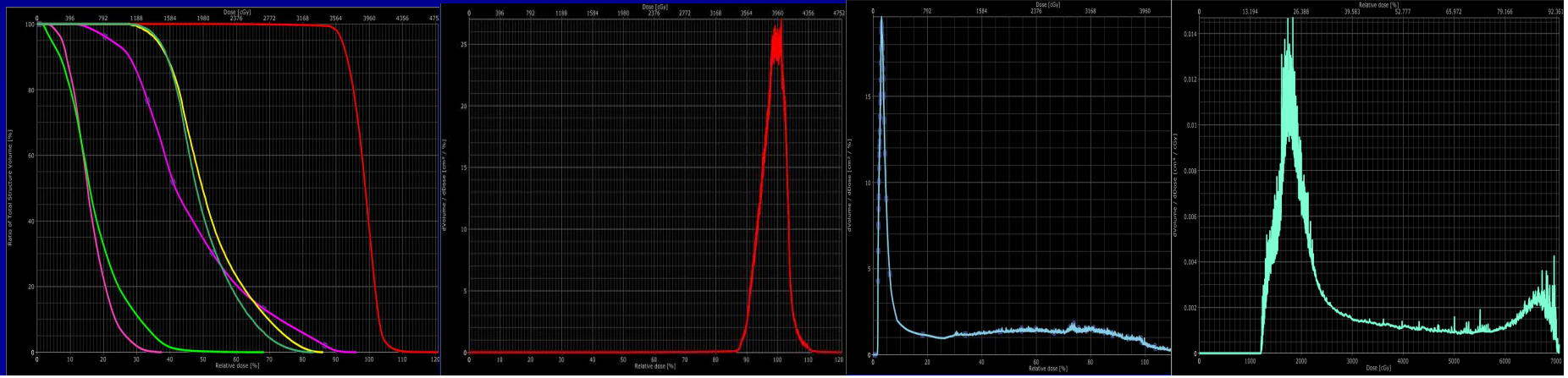
COLOUR WASH

DVH

CUMULATIVE DVH

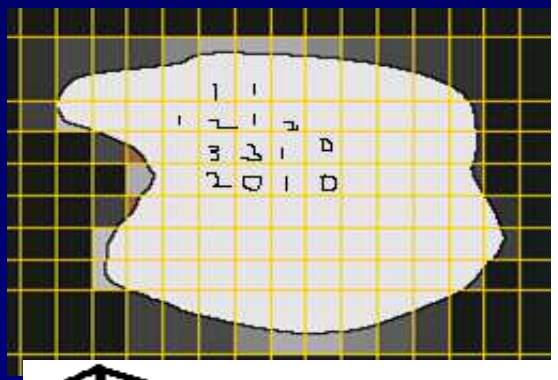
DIFFERENTIAL DVH

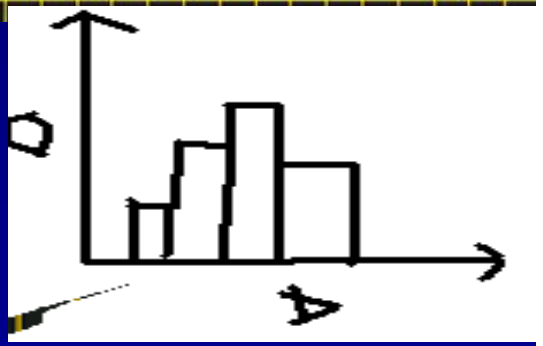


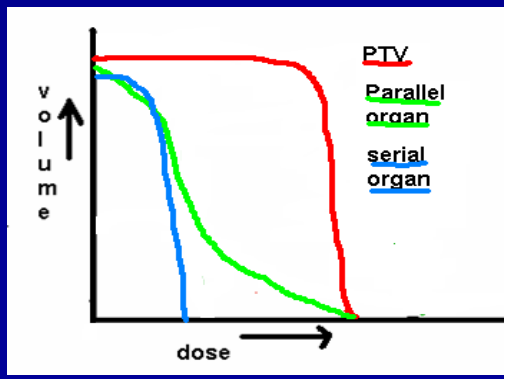


DVH

- Differential DVH
  - Represents exact volume of tissue receiving that particular dose.
  - Histogram of frequency with which each dose occurs.
- Cumulative DVH:
  - Plot of entire volume of anatomical structure specified dose or higher dose.
  - More useful and commonly used.

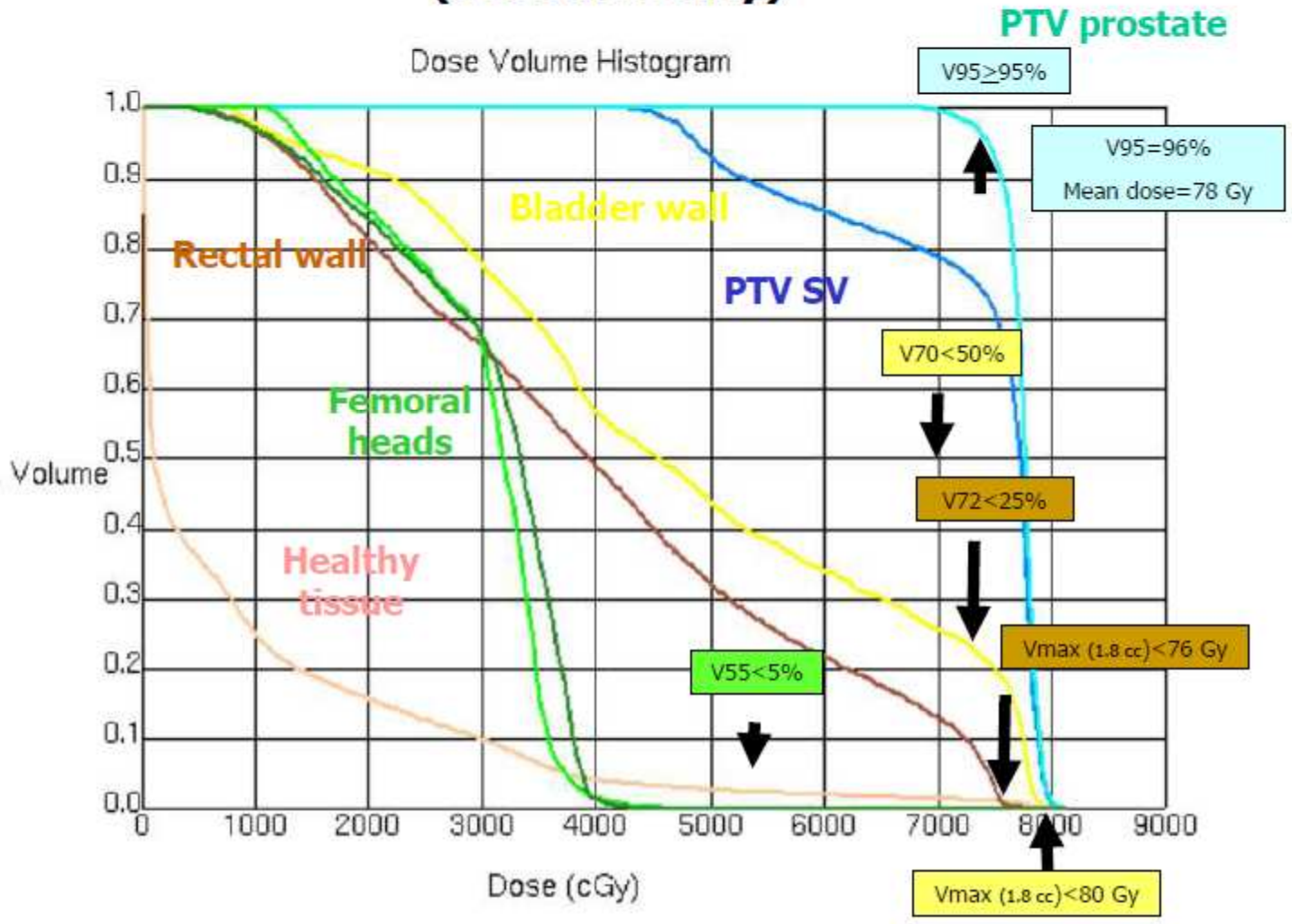






DVH 78 Gy

(Prostate only)



PLAN EVALUATION

CI is employed when the PTV is completely enclosed by the Treated volume.

Quotient of treated volume and PTV.

Absorbed dose distribution

Homogenous dose distribution through out the PTV is desirable.

Inhomogeneity should be within + 7 % and - 5 % of the prescription dose

Maximum dose (Dmax):

Maximum dose to the PTV and to the tissues outside the PTV and to OAR should be identified.

A volume is considered significant only if its minimum diameter exceeds 15mm

Hot spots:

Volume outside the PTV receiving dose higher than 100% of the specified PTV dose.A volume is considered significant only if its minimum diameter exceeds 15mm

PLAN IMPLEMENTATION

- BEAM PARAMETERS
- MLC PARAMETERS
- DRR GENERATION
- TRANSFER DATA

PLAN VERIFICATION

IMRT DELIVERY TECHNIQUE

- Physical compensator & conformal blocks
- MLC based system
  - segmented MLC (SMLC) – step & shoot
  - dynamic MLC (DMLC) – sliding window
- IMAT – Intensity modulated arc therapy
- Tomotherapy
- IMRT with robotic arm

Revolution Continues

Varian *Trilogy*

IMRT

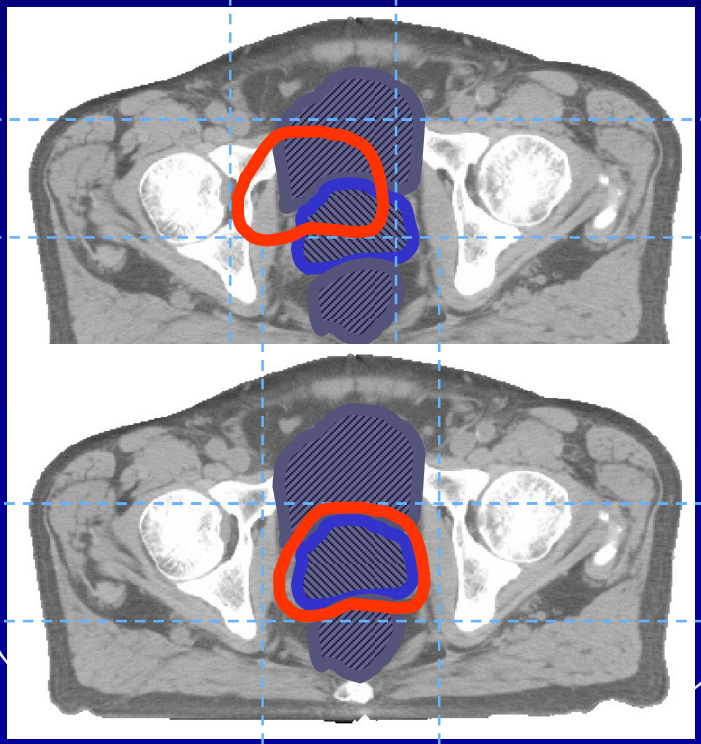
↓

Image Guided IMRT

IGRT

TIGHT MARGIN

GEOGRAPHICAL MISS



INTER AND INTRA FRACTION ORGAN MOTION

PERIODIC PHYSICAL MOMENT

BREATHING,CARDIAC MOTION

RANDOM PHYSIOLOGICAL MOVEMENT

SWALLOWING,COUGH

PT SET UP ERROR

PATIENT MOTION
WEIGHT LOSS

Image Guided Radiotherapy (IGRT)

Organ Motion

- **Interfraction**
  - motion occurs between fractions and primarily is related to ***changes in patient localization***
- **Intrafraction**
  - motion occurs during fractions and ***primarily is related to respiration***

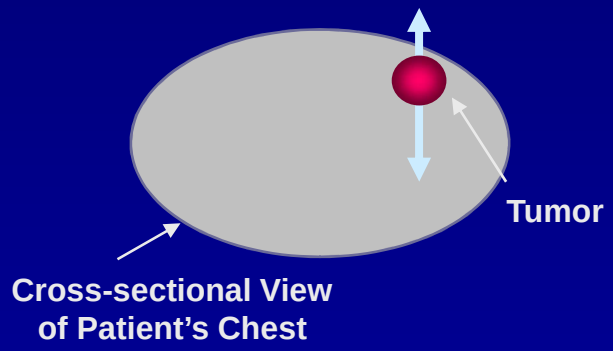
Table 1 Anatomic "Motions" and the Timescale at Which They Occur

Day to day	Skin motion	Nonpredictable
Hour to hour	Prostate motion	Nonpredictable
Minute to minute	Bladder filling	Predictable
	Neck flex	Nonpredictable
Second to second	Respiration	Predictable
	Heartbeat	Predictable
	Peristalsis	Nonpredictable

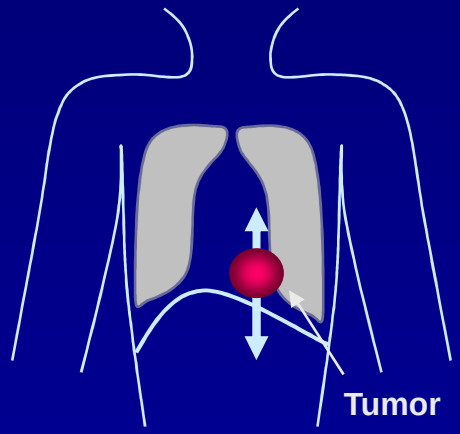
Van Herk M. Semin Radiat Oncol 2007; 17: 258-267

Tumor Motion During Respiration

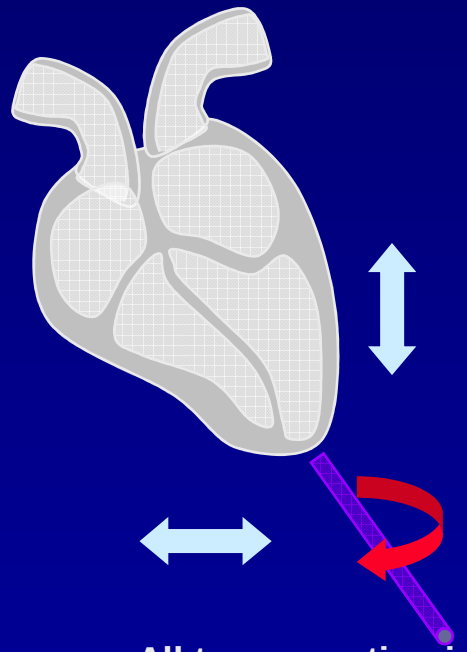
- All tumor motion is complex



Some motion is mostly
Anterior / Posterior



Some motion is mostly
Superior / Inferior



All tumor motion is
Complex

IGRT

TIGHT MARGIN

GEOGRAPHIC AL MISS

- Planar X ray based
  - EPID
  - Cyber knife
- Volumetric
  - CT on rails
  - Tomotherapy
  - MV cone beam CT
  - KV cone beam CT
- Video based
  - Real Time video guided IMRT
- Ultrasound based
  - BAT

INTER & INTRA FRACTION ORGAN MOTION

PT SETUP ERROR

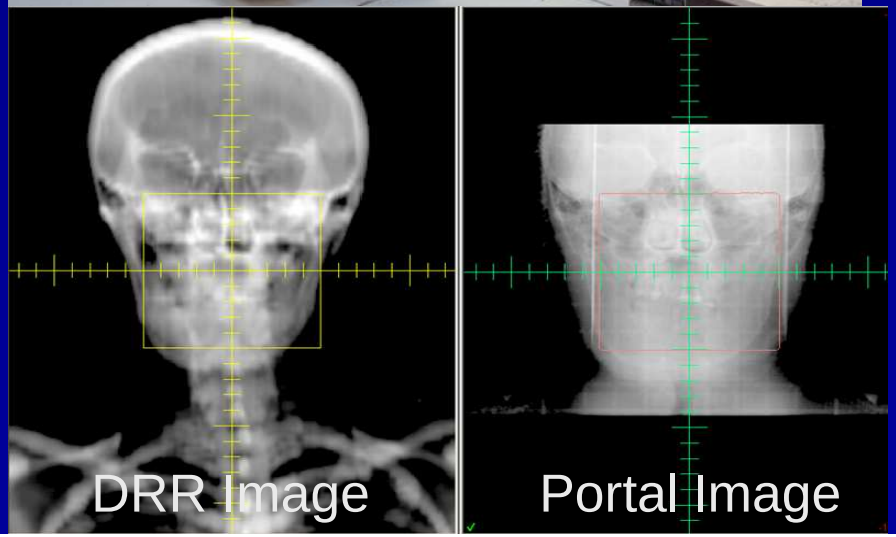
Electronic portal imaging (EPID)

Verification of patient setup

Uses 6 MV beam to acquire image.

Take one AP and one LAT field for setup verification

The position error is determined using a daily treatment radiographic image and a reference radiographic image digital reconstructed radiographic (DRR) image created in treatment planning



2D KV imaging: on-board imagers

- Two arms with kV x-ray tube, flat-panel imager
- Plain radiographs/fluoroscopic
- kV contrast is superior to MV imaging
- Orthogonal portal images – can be acquired without gantry rotation for AP and Lat online patient setup or KV/KV image pair

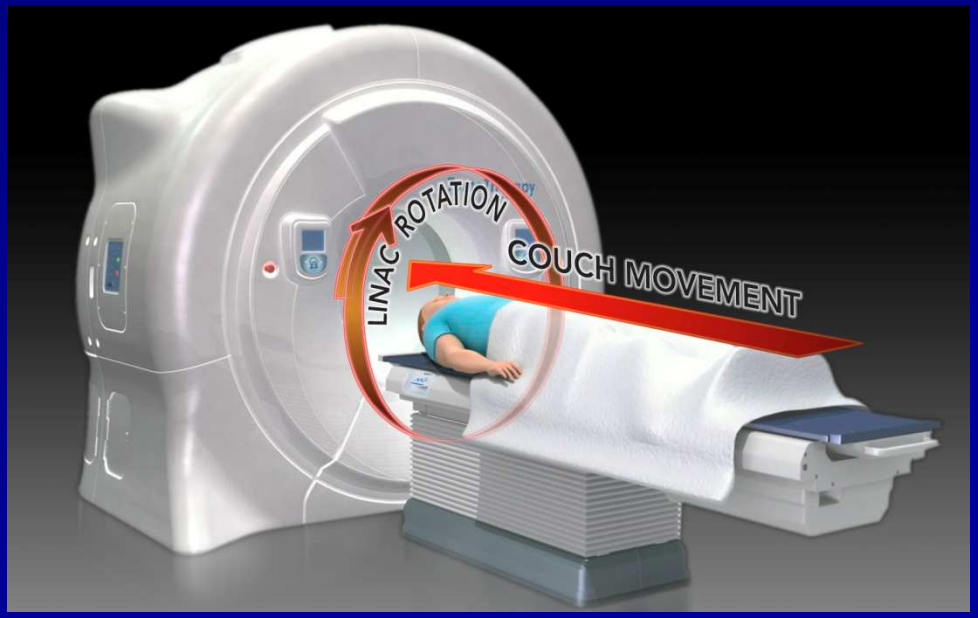
In-room kV 2D x-ray imaging:

- Diagnostic x-ray tube on the axis of source rotation, but at an angle of 30° to 45° from the MV source
- Dual x-ray sources and fluoroscopic image intensifiers mounted in the floor and ceiling
- These systems use surrogate markers for actual tissue anatomy

kV CT: In-room conventional CT or CT-on-Rails

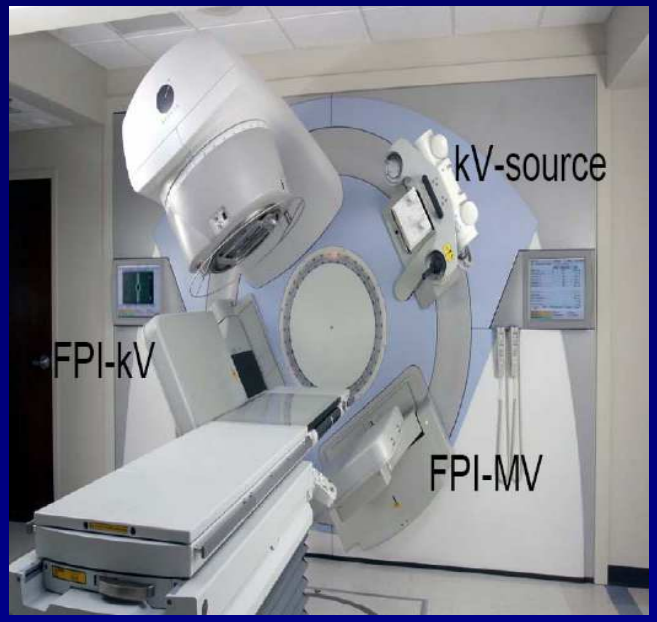
- CT scanner is mounted at the end of the linac couch and a 180-degree couch rotation, with the patient on couch, is then required before treatment

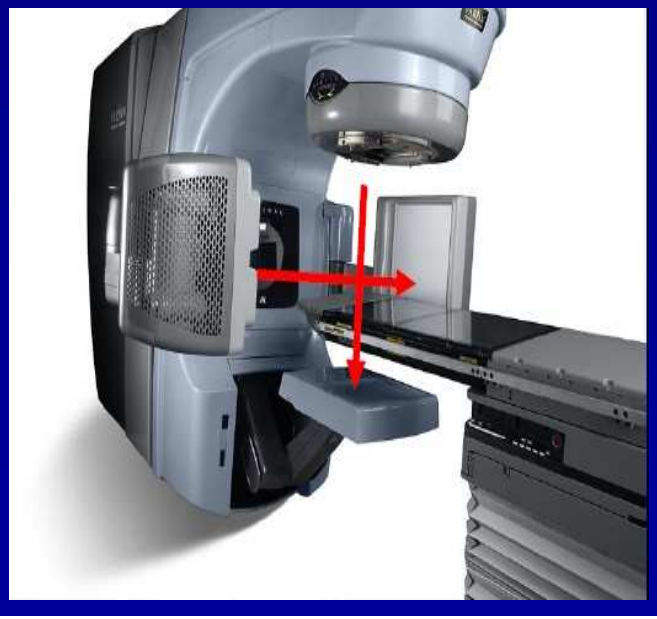
Tomotherapy : Helical MVCT



kV-CB CT On-board imager

- Radiography, fluoroscopy, and CBCT
- Large flat-panel imager
- kV x-ray tube mounted on a retractable arm at 90 degrees to the treatment beam line
- Cone-beam CT reconstruction acquiring multiple kV radiographs as the gantry rotates through at least 180 degrees



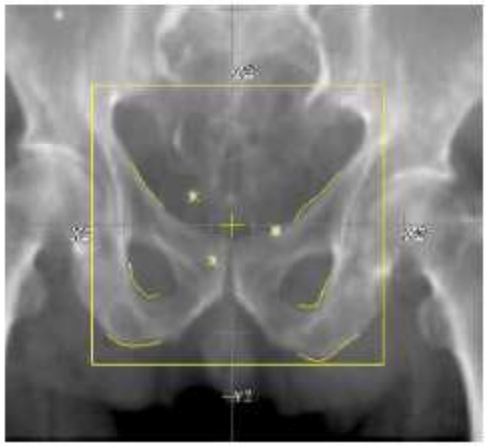


Fiducial Tracking

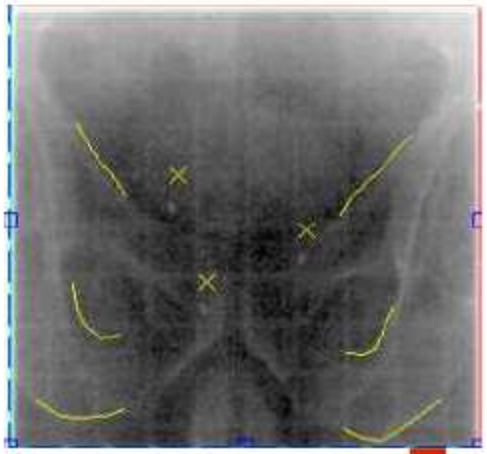
Gold seeds

5.0 mm x 0.9-1.2 mm

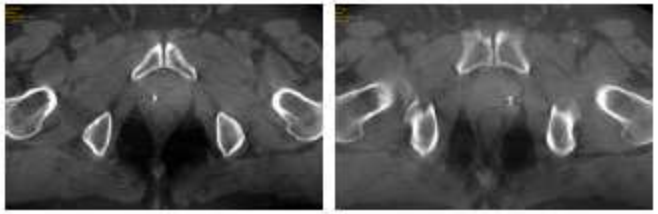
IGRT: with fiducials or CBCT



DRR + fiducials

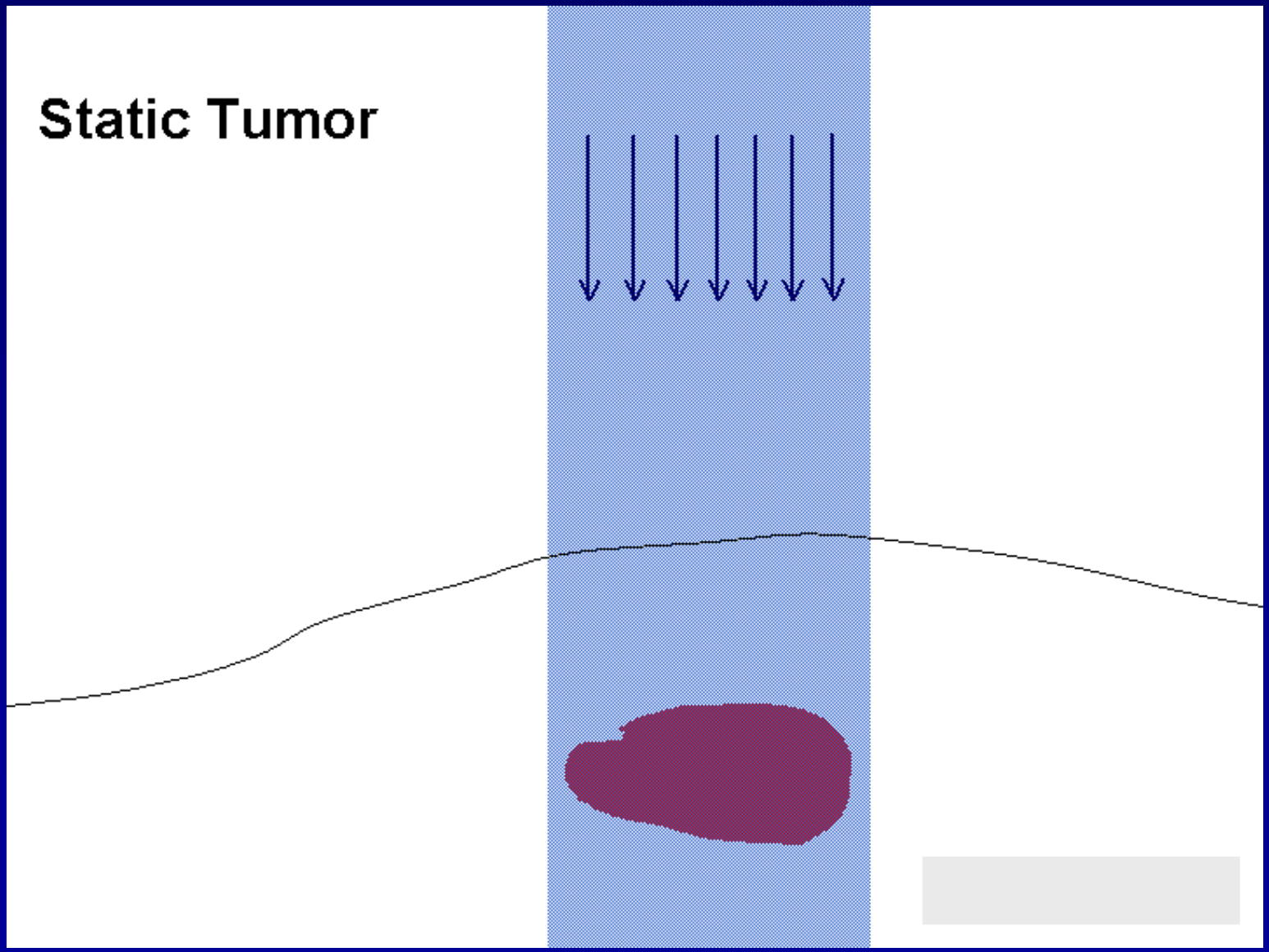


Portal (or kV imaging) + fiducials

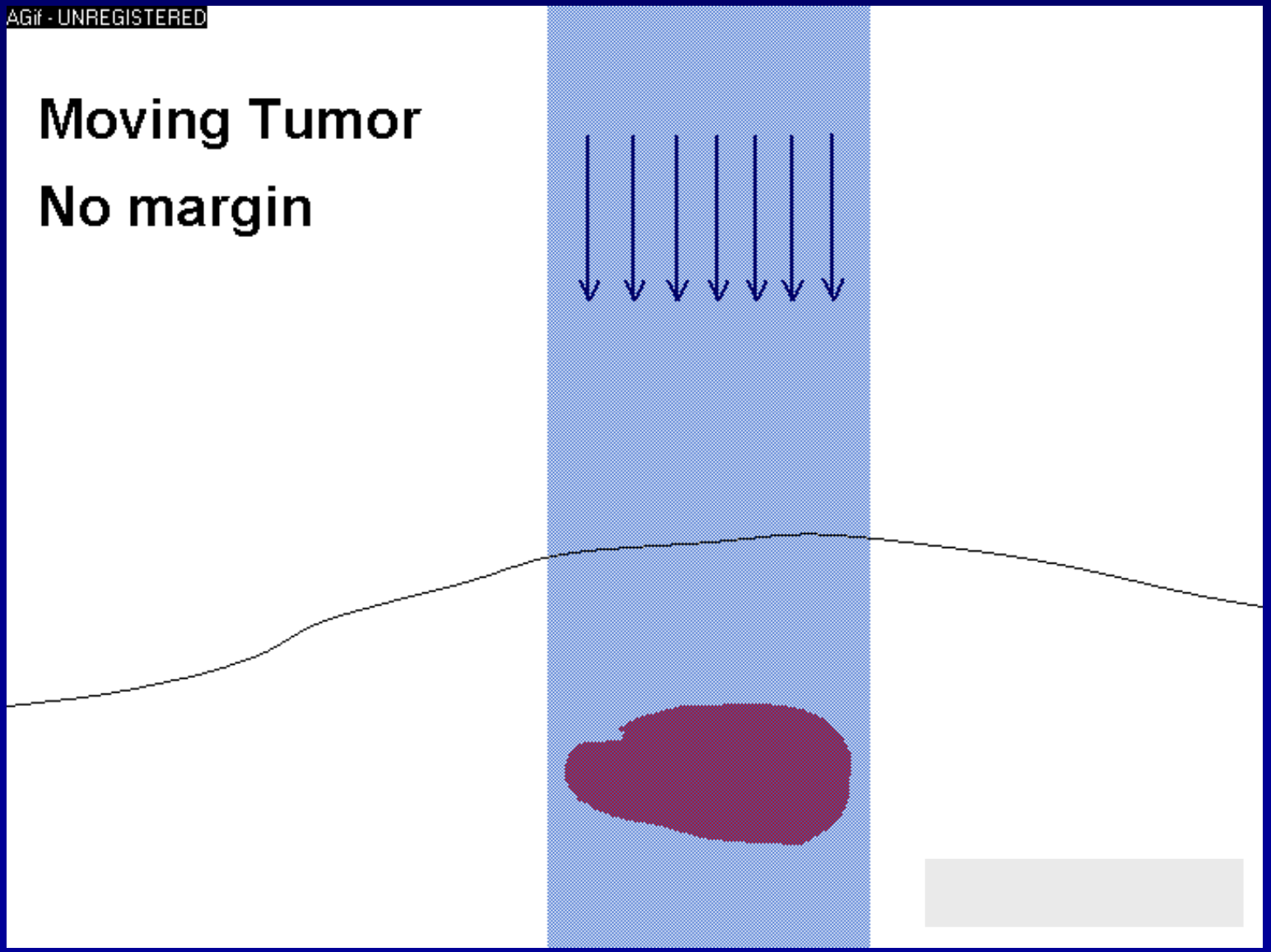


Respiratory Tracking System

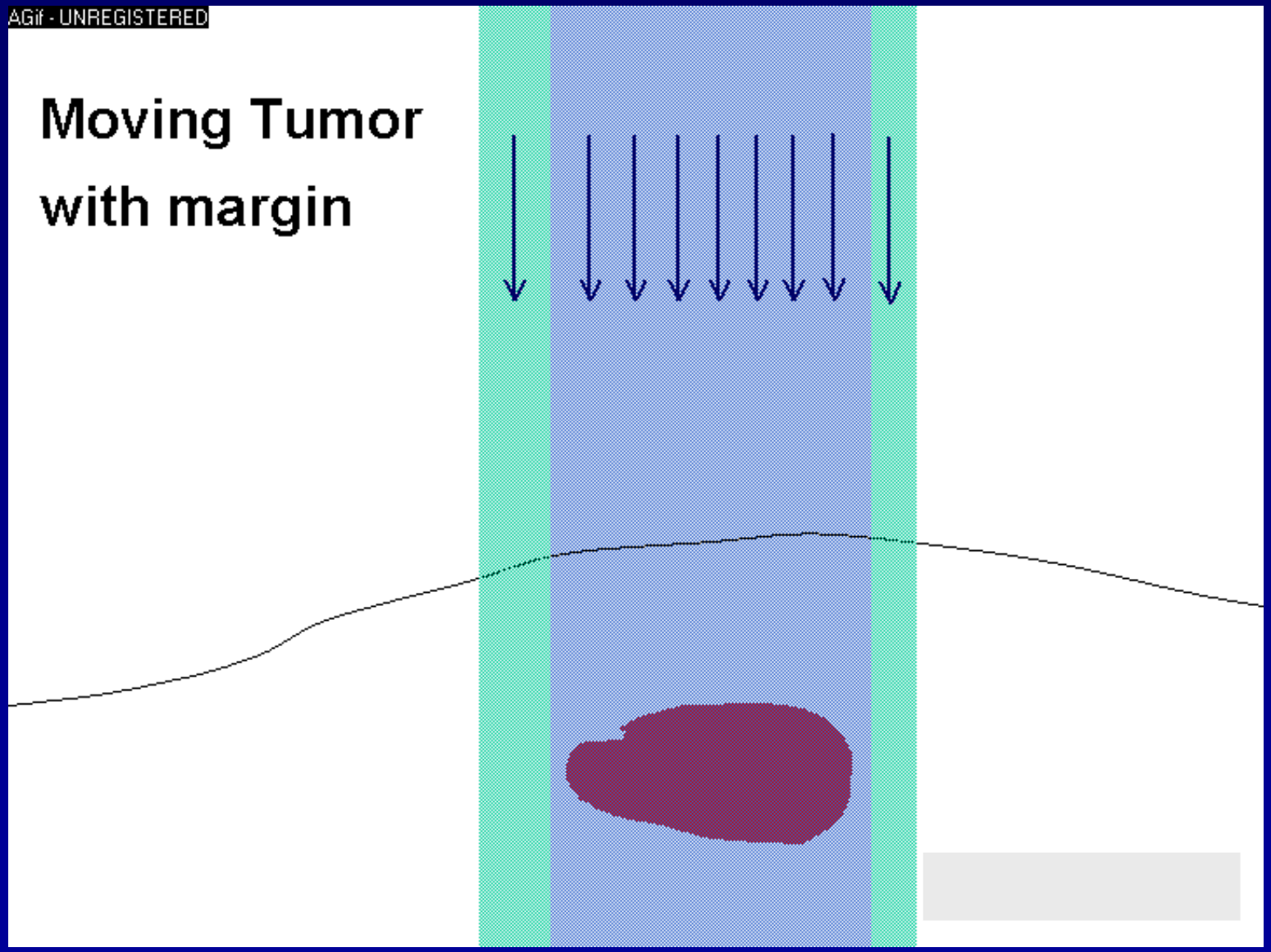
Techniques to treat mobile tumors



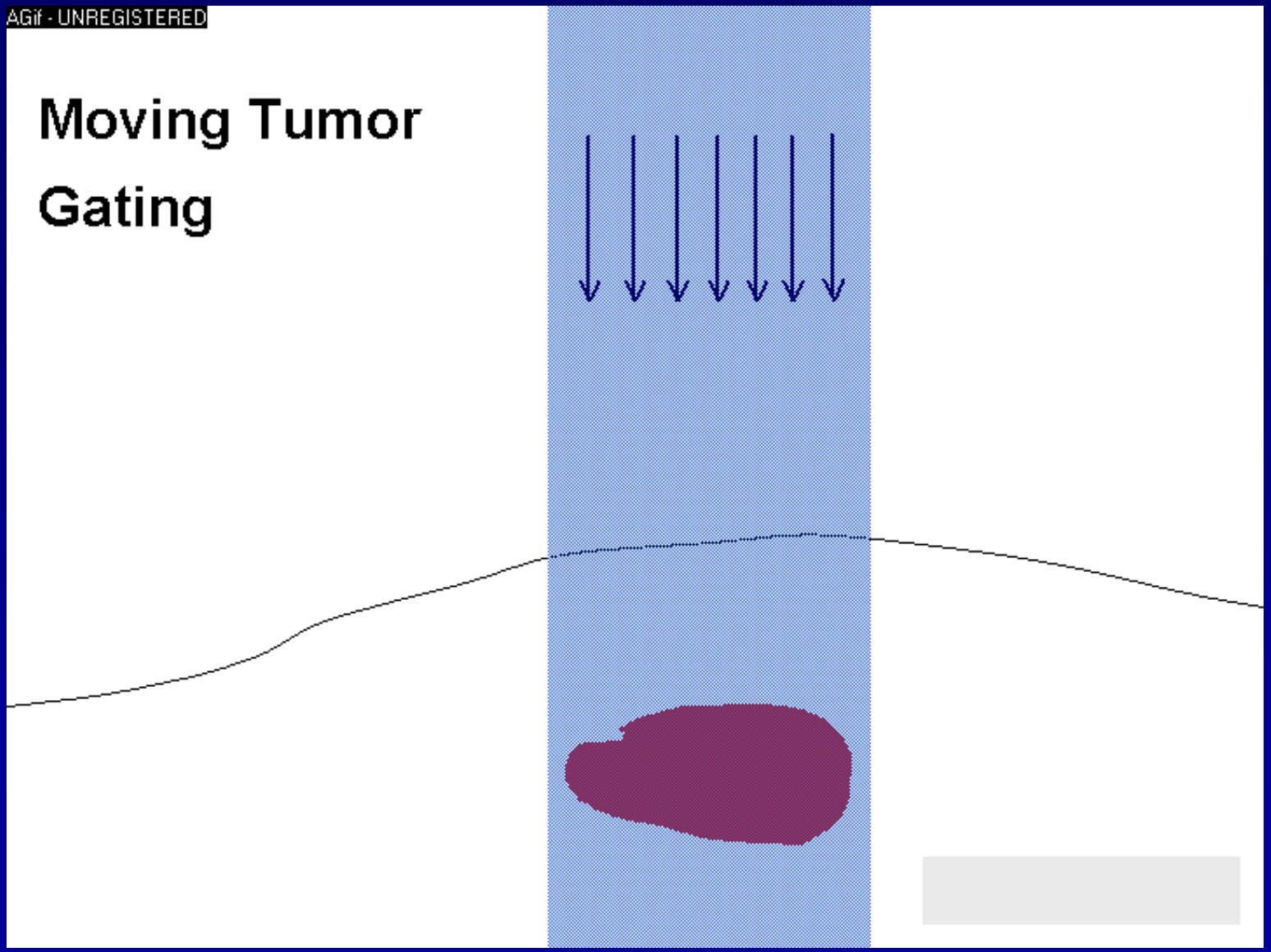
Techniques to treat mobile tumors



Techniques to treat mobile tumors



Techniques to treat mobile tumors

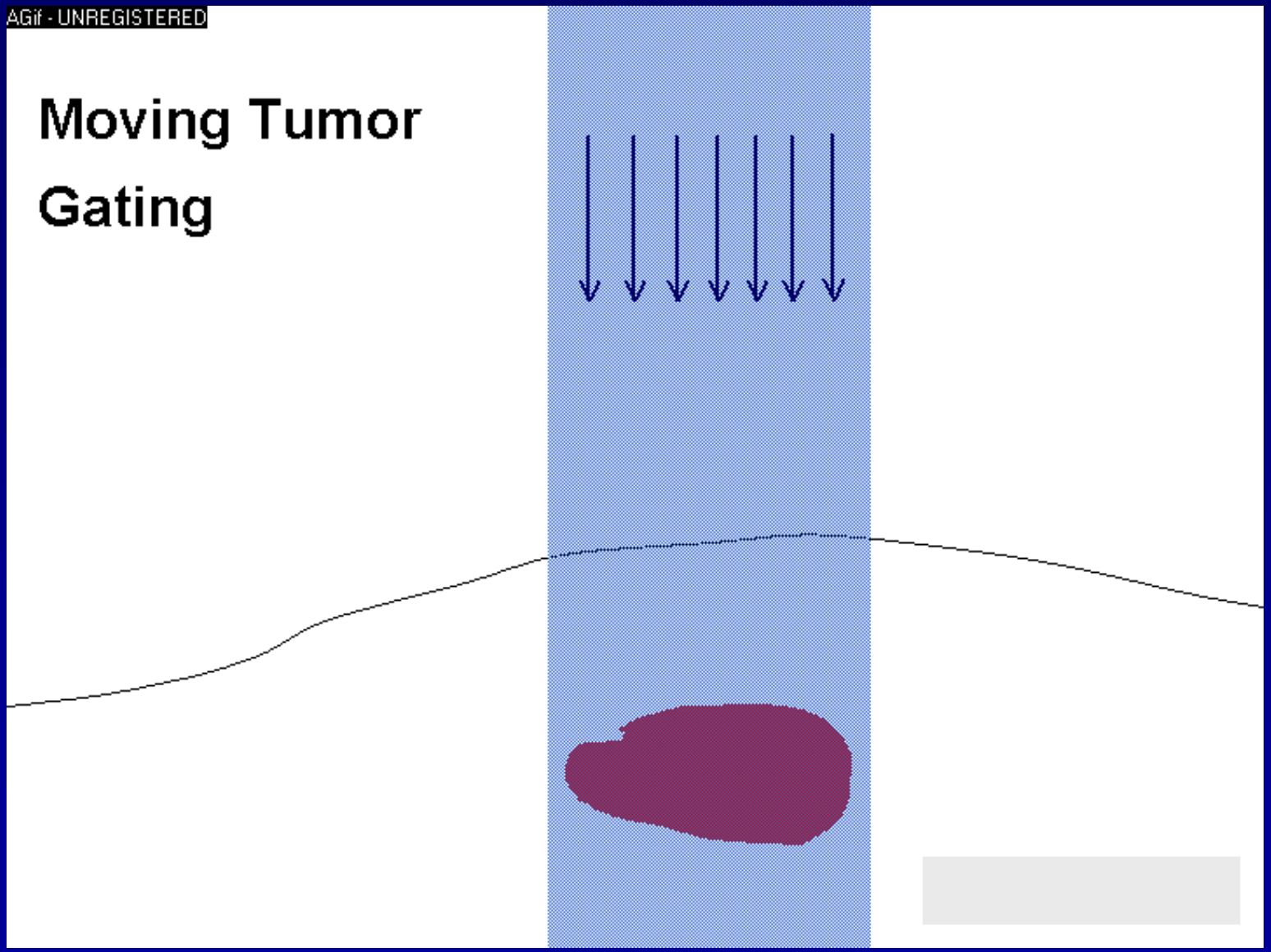


Accounting for Intrafraction Motion

- Respiratory gating techniques
- Active breathing control (ABC)
- Dynamic tumor tracking/4D radiotherapy
- Abdominal compression?

RESPIRATORY GATING

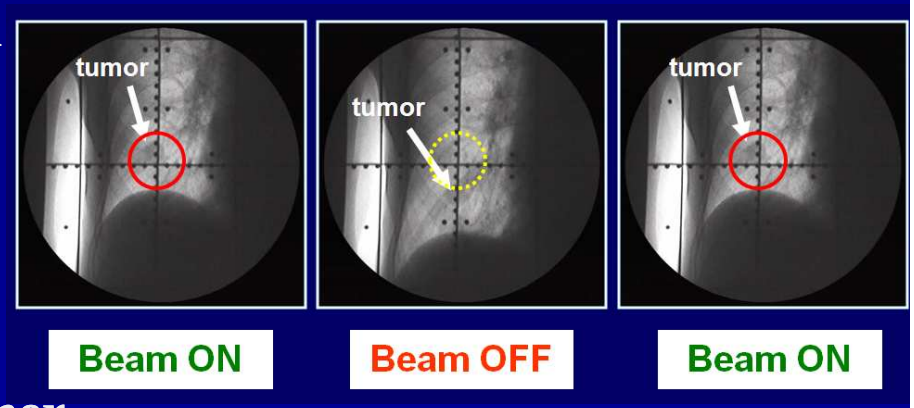
Techniques to treat mobile tumors



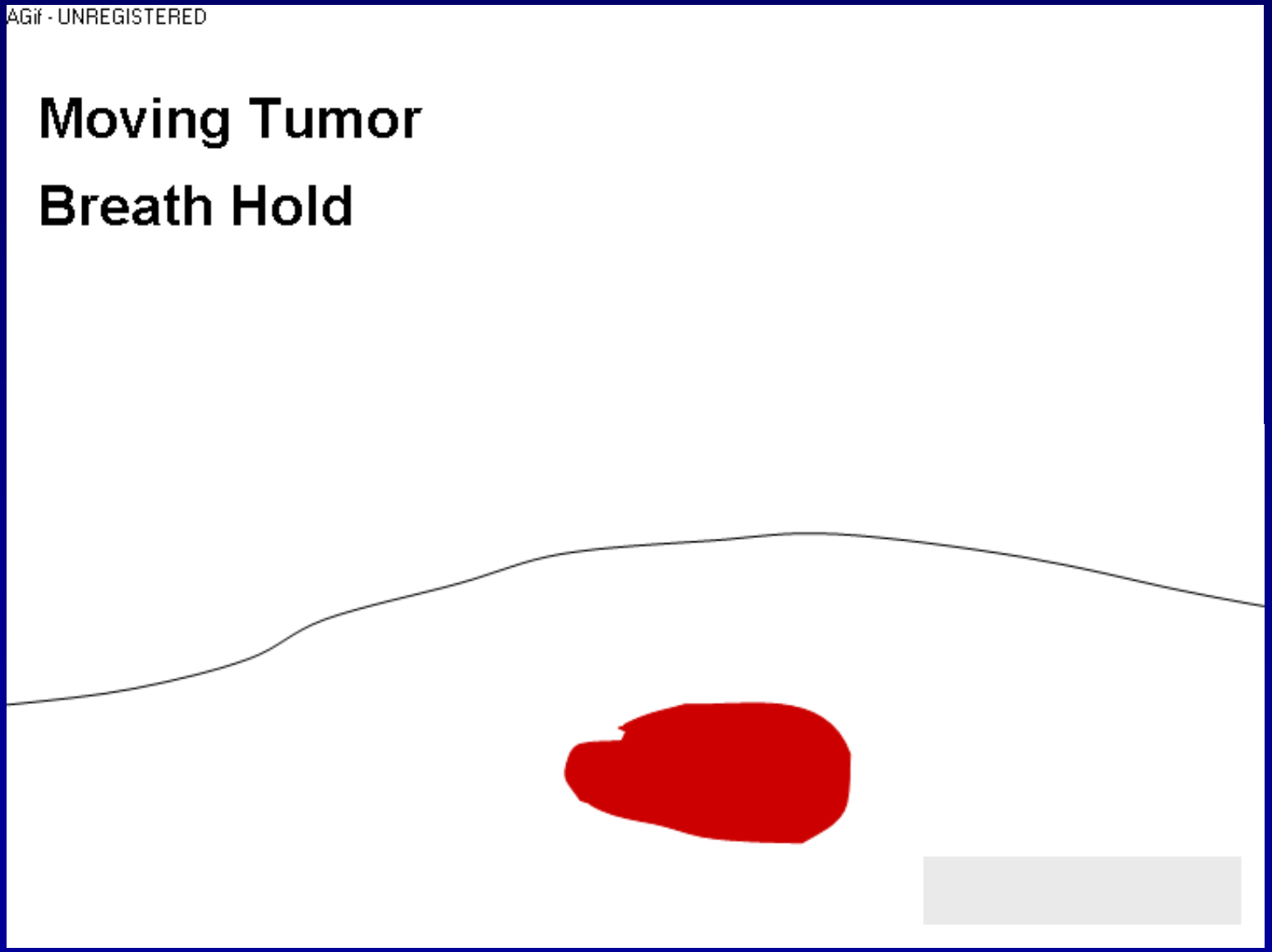
Respiration Gating with RPM

- RPM is a external gating system
- System consists of an infra-red camera that is mounted to the foot of the CT
- Markers block containing 2 reflectors.
- The marker block was placed on the patient's skin in the abdominal region
- Surrogate signal = abdominal surface motion correlation to tumor motion
- The x-ray on signal from the CT scanner was recorded synchronously with the respiration signal

Real-time position Management system (RPM)



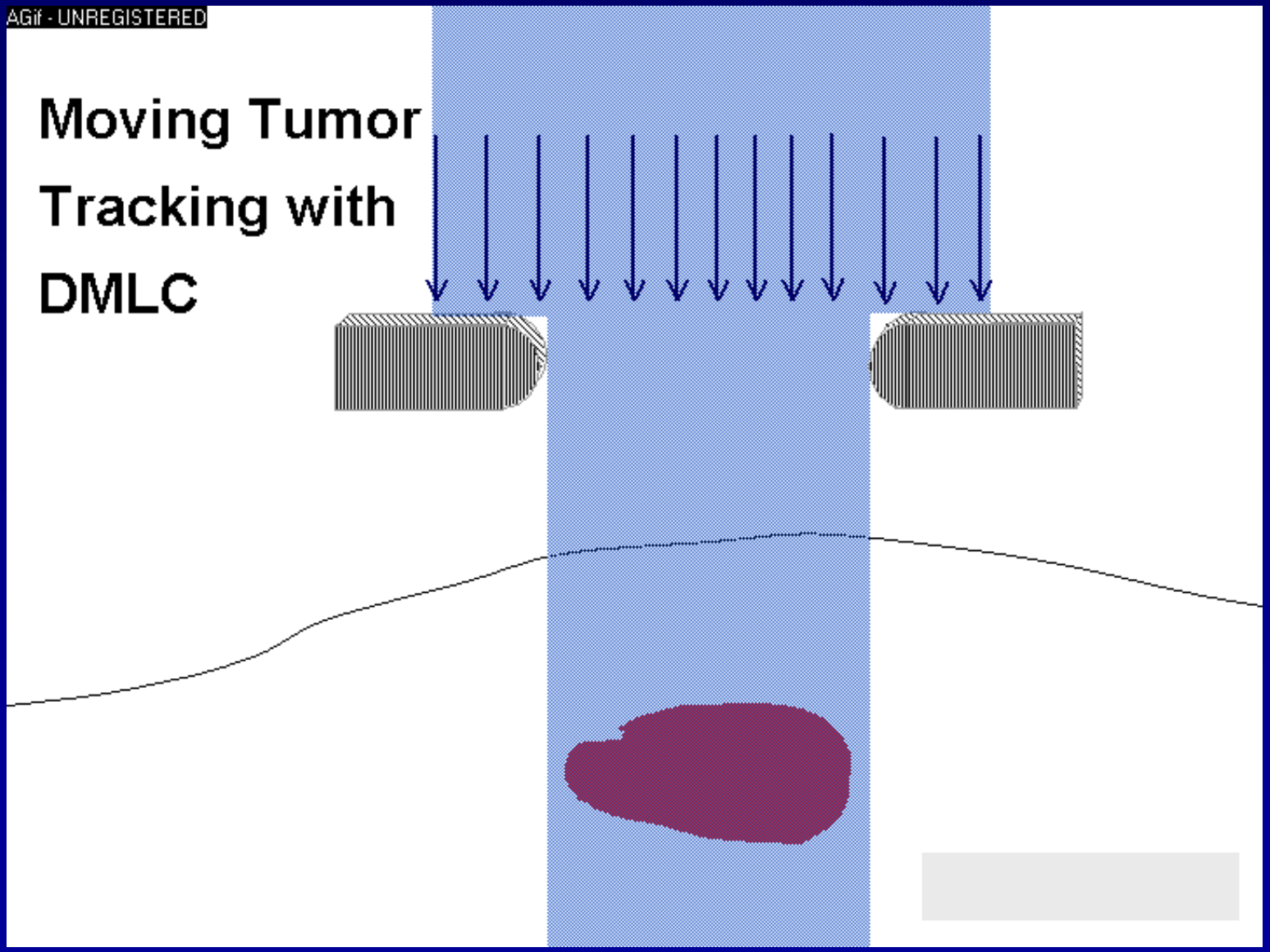
Techniques to treat mobile tumors



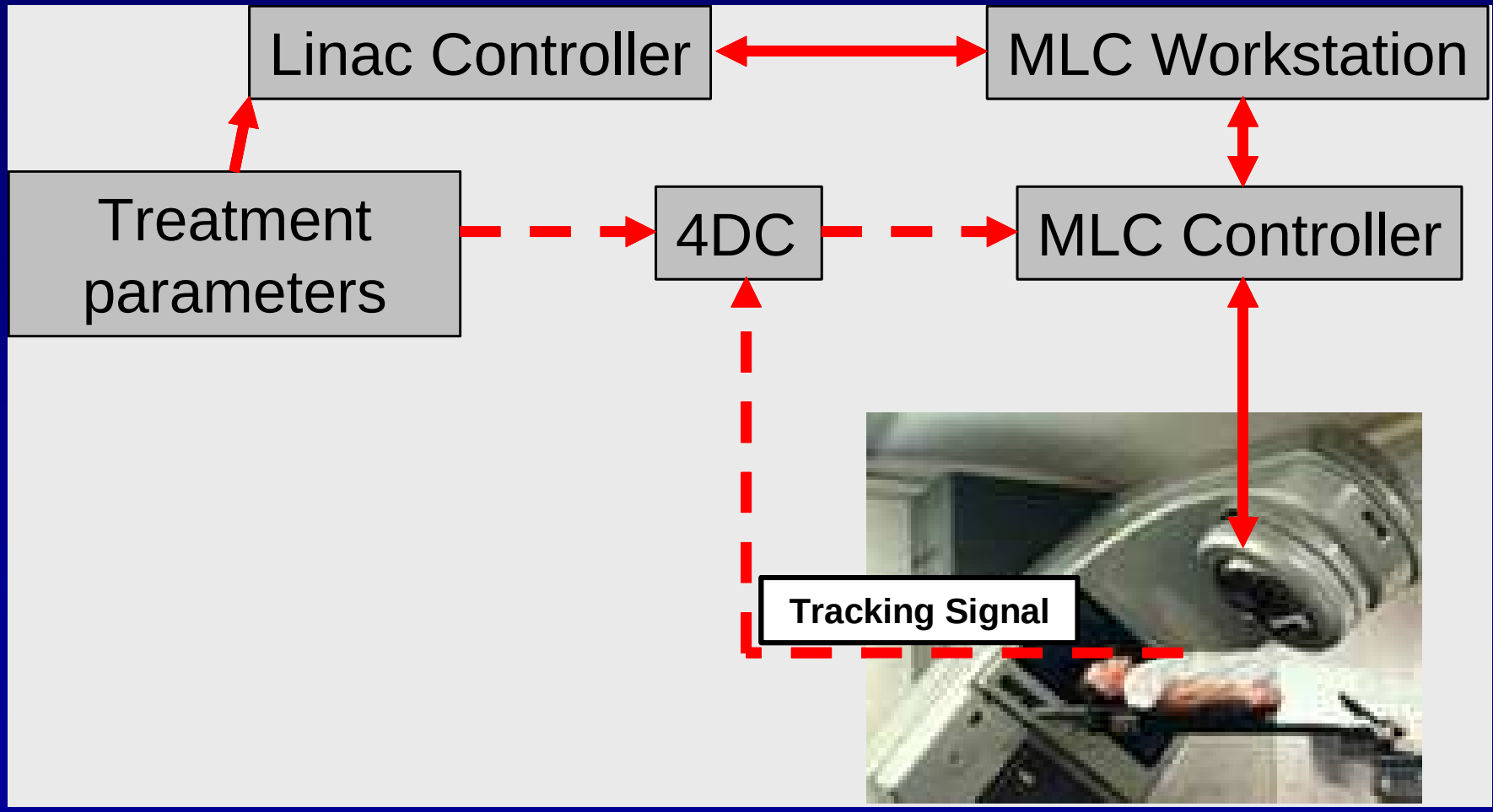
ACTIVE BREATHING COORDINATOR (ABC)

- Temporarily immobilizes patient's breathing
- The inspiration and expiration paths of airflow are closed at a predetermined flow direction

Techniques to treat mobile tumors

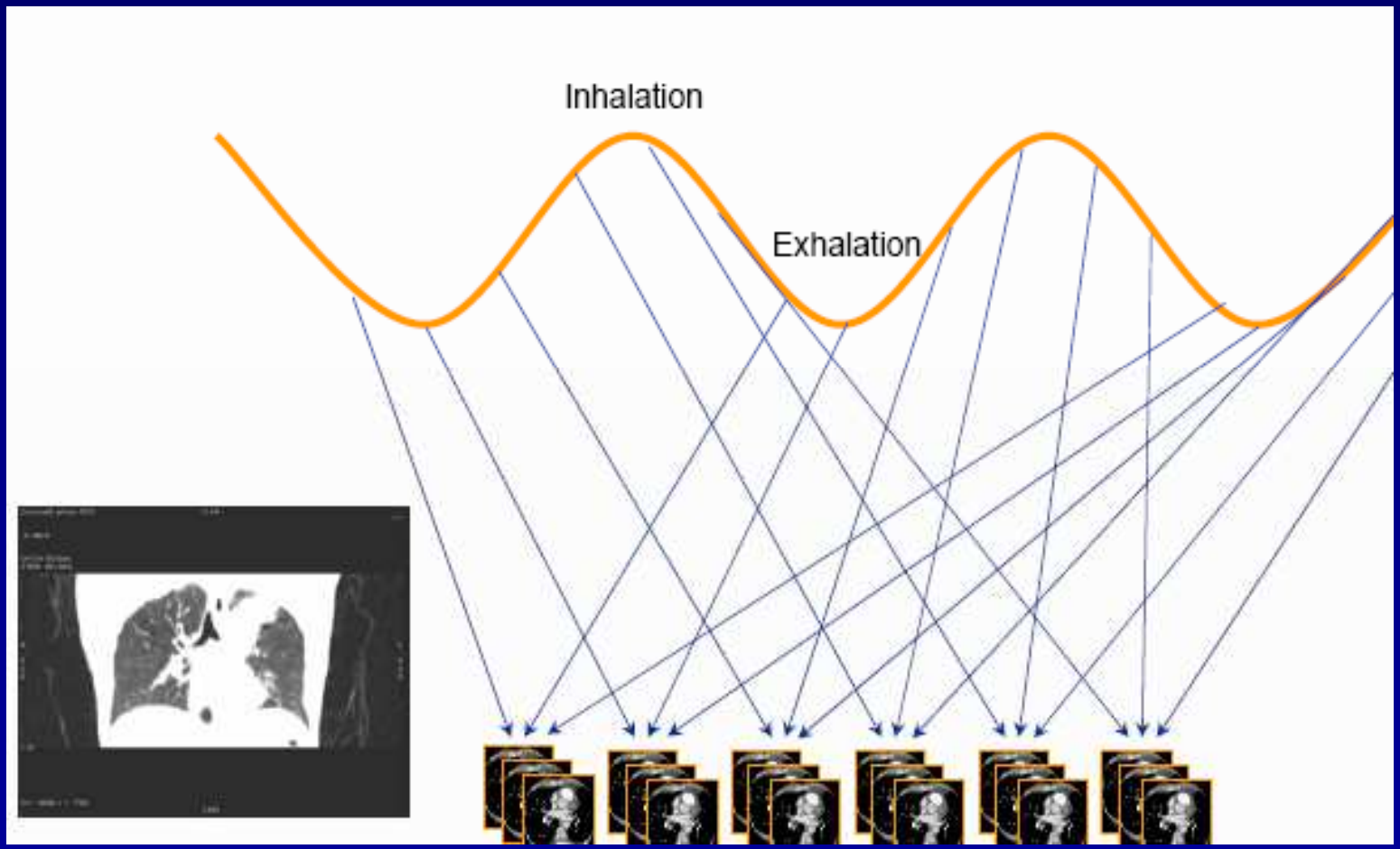


4D Radiotherapy Delivery

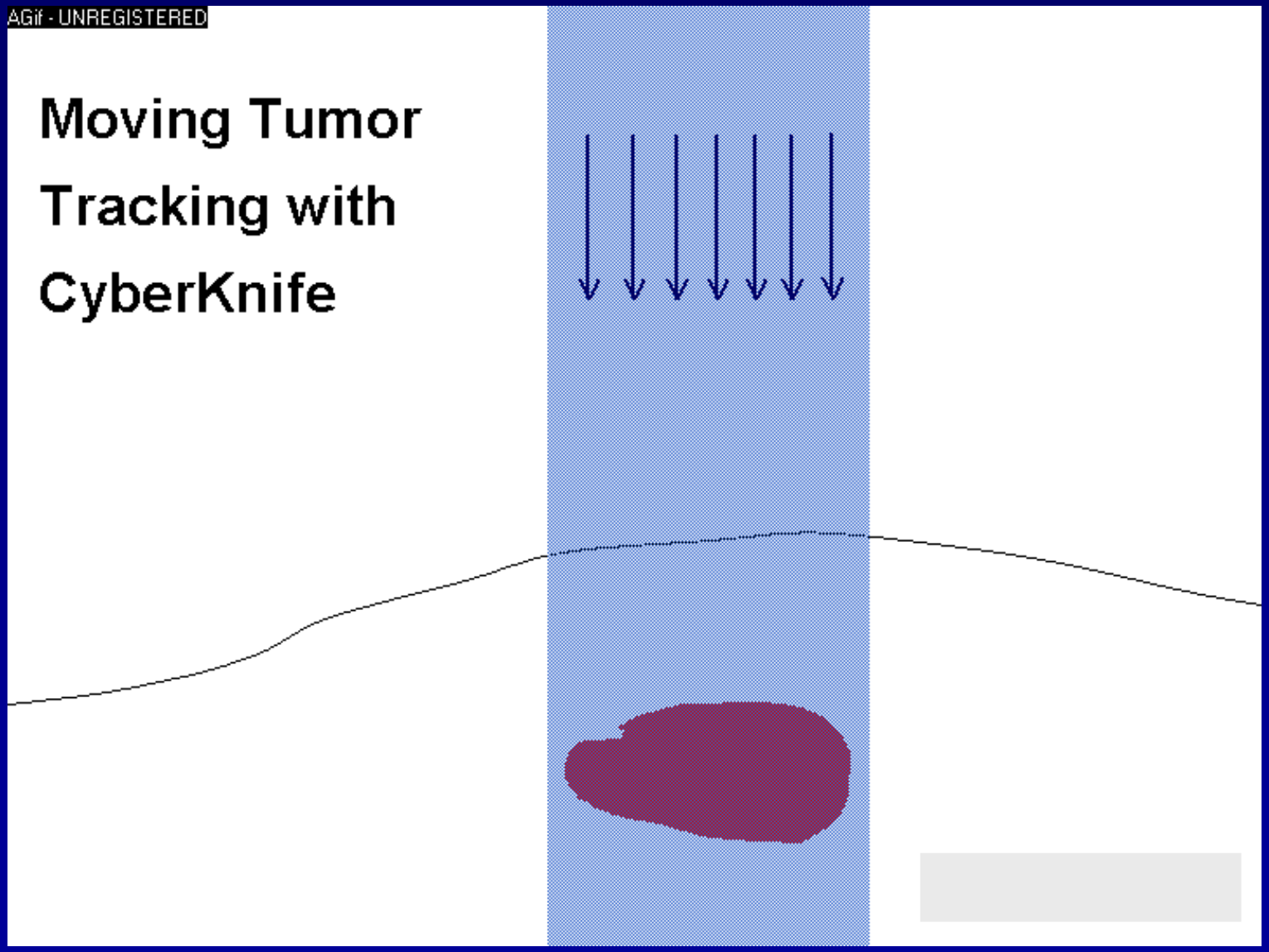


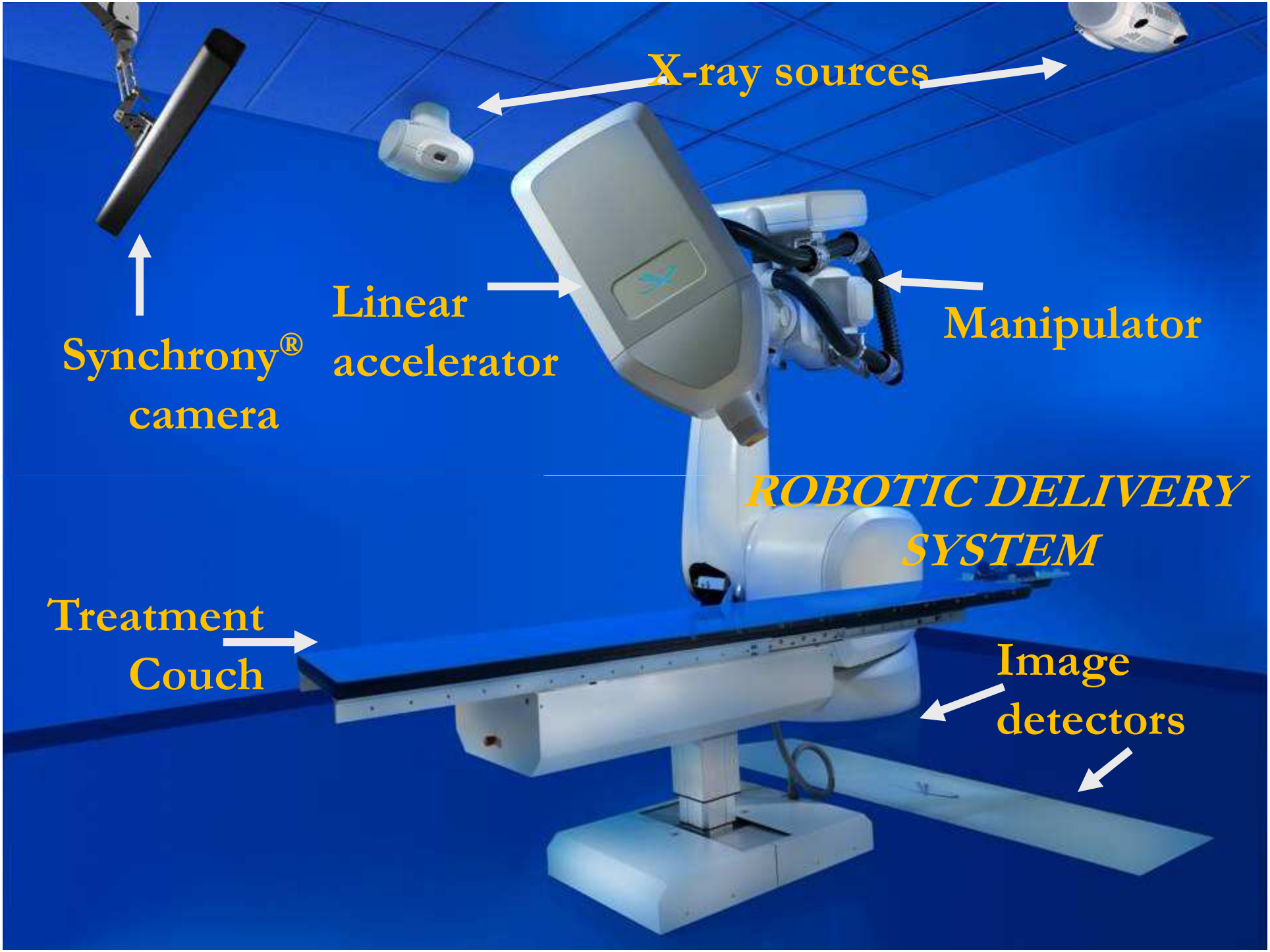
MCV setup for 4D Radiotherapy

Principle of 4D scanning



Techniques to treat mobile tumors




X-ray sources
Synchrony®
camera
Linear
accelerator
Manipulator
ROBOTIC DELIVERY
SYSTEM
Treatment
Couch
Image
detectors

Synchrony™ Respiratory Tracking System

- Synchrony camera
- Synchrony tracking markers
- Fiber optic sensing technology
- Tracks patient's respiratory motion

HEAD AND NECK CANCER

Rationale of IMRT in H & N Cancer

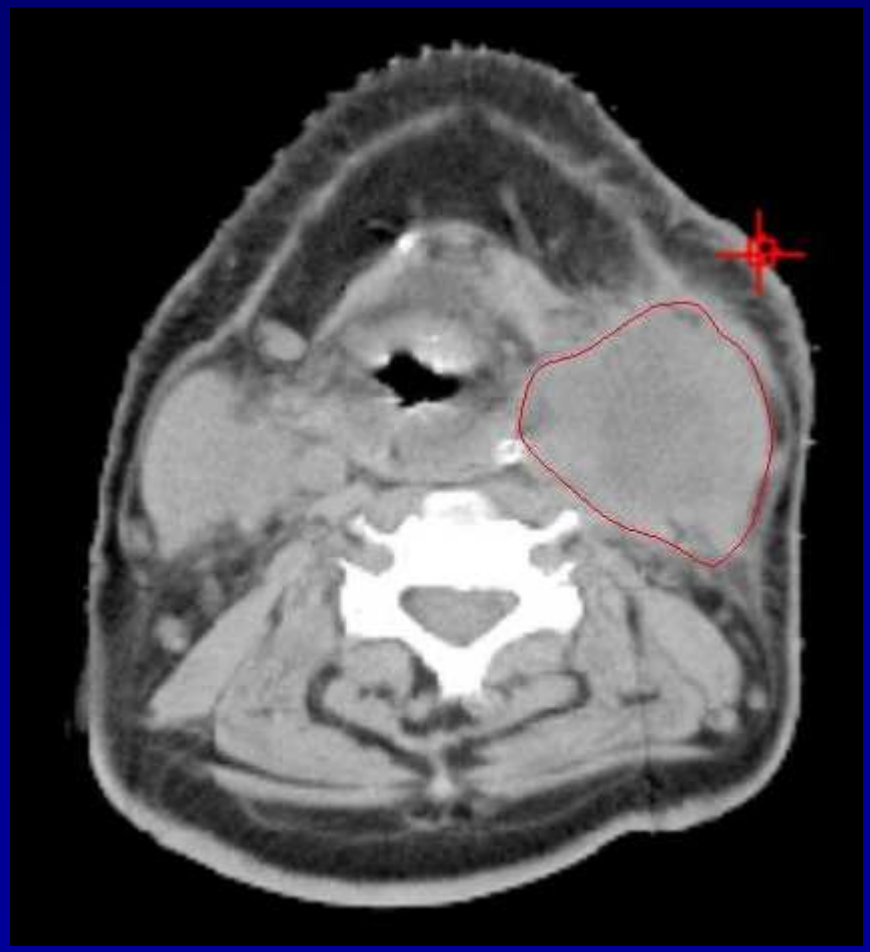
- **Anatomically complex H&N region - *an ideal option - IMRT.***
- **Lack of organ motion in the H&N region - *an ideal region for IMRT.***
- **Allows for dose escalation - *concomitant boost – ideal for H&N***

Impact of PET-CT in H & N Cancer

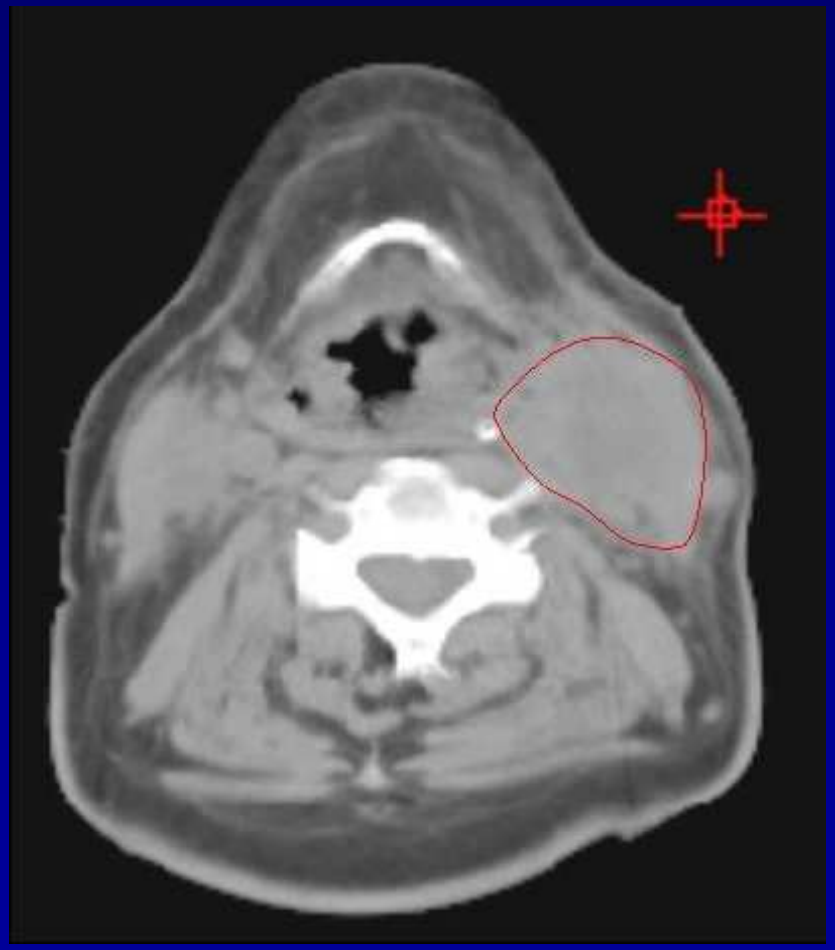
Author	Patients using PET	Change of GTV	Increase in GTV	Decrease in GTV	Remarks
Rahn, 1998	22(prim)	41%	41%	0%	No image fusion
	12(recur)	58%	58%	0%	
Nishioka, 2002 fusion	21	71%	0%	71%	PET/CT/MRI
Ciernik, 2003	12	50%	17%	33%	Integrated PET-CT
Daisne, 2004	29	93%	18%	75%	CT-PET image fusion
Paulino, 2005 image fusion	40	100%	-	-	PET/CT/MRI and surgical specimen

Changes in Anatomy during course of Rx

Planning CT



Three Weeks into RT



Barker et al. *IJROBP* 59:960, 2004 & Lei Dong et al. (MDACC)

Anatomical modifications during radiotherapy

Author	No. of Patients	Per-Treatment Imaging	Image Registration	Volume Analysis	Shape and Positional Analysis
Barker et al (2004)[6]	14	In-room CT-on-rail 3 times/wk; no iv contrast	Rigid	Reduction of: • GTV: 1.8% per treatment day • PGs: 0.6%/treatment day	• GTV: COM displacement: 3.3 mm (asymmetric shrinkage) • PG: COM shift medially by 3.1 mm
Geets et al (2007)[50]	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Rigid	After a mean dose of 45 Gy: • GTV_T: mean decrease of 65.5% • High dose CTV_T: mean decrease of 50.9% • High dose PTV_T: mean decrease of 47.9%	NA
Han et al (2008)[43]	5	Daily helical MVCT	Rigid	At the end of treatment: PGs had decreased from 20.5 to 13.2 cm^3, ie, an average decrease of 0.21 cm^3/treatment day or 1.1%/treatment day	NA
Vasquez Osorio et al (2008)[51]	10	CT scan at 46 Gy; iv contrast	Deformable	Reduction after 46 Gy: • GTV: 25 15% • Homolat PG: 17 7% • Heterolat PG: 5 4% • Homolat SMG: 20 10% • Heterolat SMG: 11 7%	After 46 Gy: • Lateral and inferior regions of homolat PG: medial and posterior shift (3 mm) • Homolat SMG: medial, cranial, and posterior shift (4 mm)
Hansen et al (2006)[52]	13	CT scan after a mean dose of 38 Gy	Rigid	Reduction: • GTV: no change • Right PG: 15.6% • Left PG: 21.5%	NA
Robar et al (2007)[53]	15	Weekly CT scans; no iv constrast	Rigid	Reduction of supercial regions of both PGs: 4.9%/wk	Supercial regions show medial translation of: left PGs: medial shift of 0.91 0.9 mm/wk right PGs: medial shift of 0.78 0.13 mm/wk
Castadot et al (2008)	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Deformable	Reduction of • GTV_T: 3.2%/treatment day • GTV_N: 2.1%/treatment day • Homolateral PG: 0.9%/treatment day • Heterolat PG: 1.0%/treatment day • Low dose homolat CTV_N: 0.5%/treatment day • low dose heterolat CTV_N: 0.4%/treatment day	After 5 treatment wks: • Homolat PG: medial shift of 3.4 mm • GTV_T: lateral shift of 1.3 mm • GTV_N: medial shift of 0.9 mm • Low dose homolat CTV_N: medial shift of 1.8 mm No shift for the heterolat PG and heterolat low dose CTV_N.

CT, computerized tomography; GTV, gross tumor volume; CTV, clinical target volume; PTV, planning target volume; PG, parotid gland; COM,

Dosimetric effect of Anotomical modifications during radiation therapy

Author	No. of Patients	Per-Treatment Imaging	Image Registration	Results	Comments
O'Daniel et al (2007)[44]	11	In-room CT-on-rail scans twice/wk; no iv contrast	Deformable	Cumulative PG dose greater than planned; median dose increase: 1 Gy No impact on tumor dose coverage	If no image-guidance for daily setup error correction, cumulative PG dose greater than planned; median dose increase: 3 Gy for homolat PG and 1 Gy for heterolat PG
Hansen et al (2006)[52]	13	CT scan after a mean dose of 38 Gy	Rigid	• High dose PTV D_{99}, D_{95}, $V_{93\%}$ decreased by 12.1, 12.2 Gy, and 7%, respectively • Low dose PTV D_{99}, D_{95}, $V_{93\%}$ decreased by 12.6, 11.3 Gy, and 8.2%, respectively • Right PG V_{26Gy} increased by 10.9% • Mandible V_{60Gy} increased by 7.2%	If replanning; signicant improvement of: • Low and high dose PTVs D_{99} D_{95} and $V_{93\%}$ • Spinal cord D_{max}, D_{1cc} • Brainstem D_{max} • Right parotid PG D_{mean}, D_{50}, and V_{26Gy} • Mandible D_{max} and V_{60Gy}
Robar et al (2007)[53]	15	Weekly CT scan; no iv contrast	NA	Left PG D_{mean} increased by 2.6 ± 4.3%, V_{26Gy} increased by 3.5 ± 5.2% Right PG D_{mean} increased by 0.2 ± 4.0%, V_{26Gy} increased by 0.3 ± 4.7%	
Han et al (2008)[43]	5	Daily helical MVCT	Rigid	PG D_{median} increased from 0.83 to 1.42 Gy with an average increase rate of 0.17 Gy/treatment day corresponding to an average increase of 2.2%/treatment day	Strong correlation between the volume and the median parotid dose during the treatment (correlation coefcient, − 0.95)
Lee et al (2008)[56]	10	Daily helical MVCT	Deformable	• PG daily D_{mean} differed from the planned dose by an average of 15% • PG cumulative D_{mean}: planned: 29.7 Gy actual: 32.7 Gy (110% of planned dose)	• Changes in the distance between the COMs of the left and right PGs correlated strongly with the mean parotid dose changes (R^2= 0.88) • Correlation between the relative weight loss and higher parotid mean doses (R^2 0.58)
Castadot et al (2009)	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Deformable	• PGs D_{mean}: planned: 17.9 Gy, actual 18.7 Gy • SMGs D_{mean}: planned 51.9 Gy, actual: 52.8 Gy • OC D_{mean}: planned 26.0 Gy, actual 26.7 Gy • SC D_2: planned 40.1 Gy, actual: 41.0 Gy • Skin V_{60}: planned 17.2 Gy, actual 18.3 Gy • No difference in PTV or CTV coverage	

OC, oral cavity; SC, spinal cord; D_x, dose to x% of the volume; D_{max}, maximum dose; D_{1cc}, dose to 1 cc.; D_{mean}, mean dose; D_{median}, dose to 50% of the volume; V_x, volume receiving a dose of x Gy or x% of the prescribed dose.

Table 1. Locoregional Control After IMRT for Head and Neck Cancer

Study	No. of Patients	Primary Site	RT		Follow-Up (months)		Control		
			Definitive	Postoperative	Median	Range	Local (%)	Regional (%)	Interval (years)
Chao et al[19]	126	Various	52	74	26	12-55		85	2
Lee et al[5]	67	NPX	67	0	31	7-72		98	4
Chao et al[20]	74	OPX	31	43	33	9-60		87	4
Eisbruch et al*[21]	133	Various, non-NPX	60	73	32	6-107		82	3
Kam et al[33]	63	NPX	63	0	29	8-45	92	98	3
Kwong et al[34]	33	NPX	33	0	29	11-42	100	92	3

Abbreviations: IMRT, intensity-modulated radiotherapy; RT, radiotherapy; NPX, nasopharynx; OPX, oropharynx.

*Patients treated from 1994 to 2002; three-dimensional conformal radiotherapy was used before 1996, and IMRT thereafter.

JCO, 2006

IMRT Vs. Conventional RT in Head & Neck Cancer

Lee NY , 2006 Comparative Trial

Patients – 112

Disease Control

CVRT		- 71		85%
IMRT		- 41		95%

Toxicity

Died of toxicity	CVRT	- 3 ,	IMRT	– None
Gastrostomy	CVRT	- 21%,	IMRT	– 4%

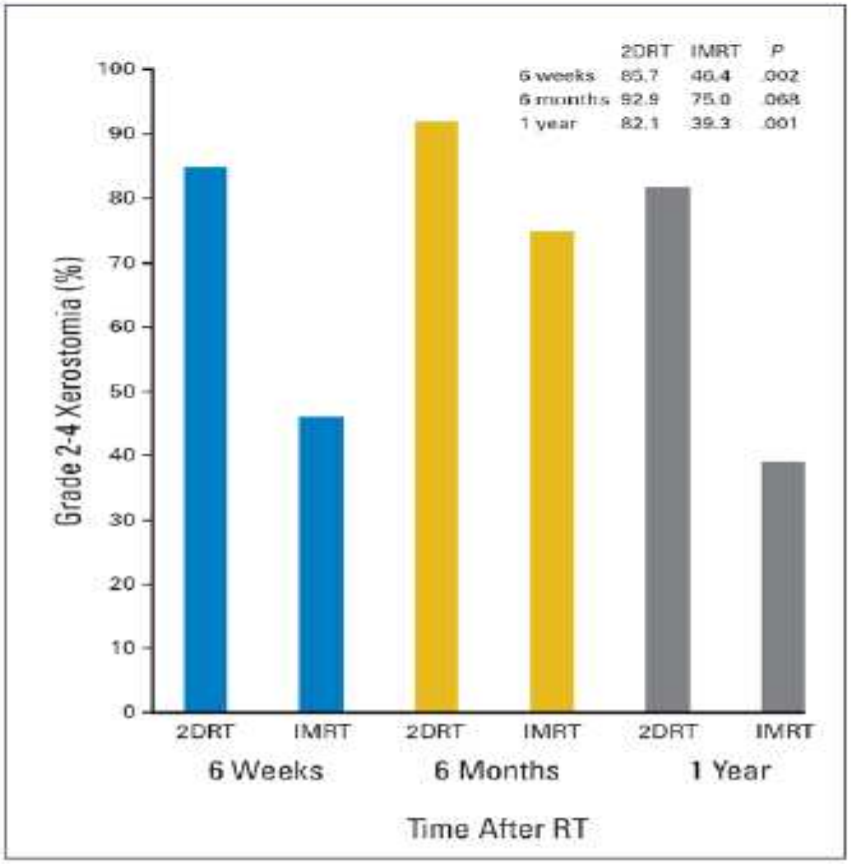
Survival

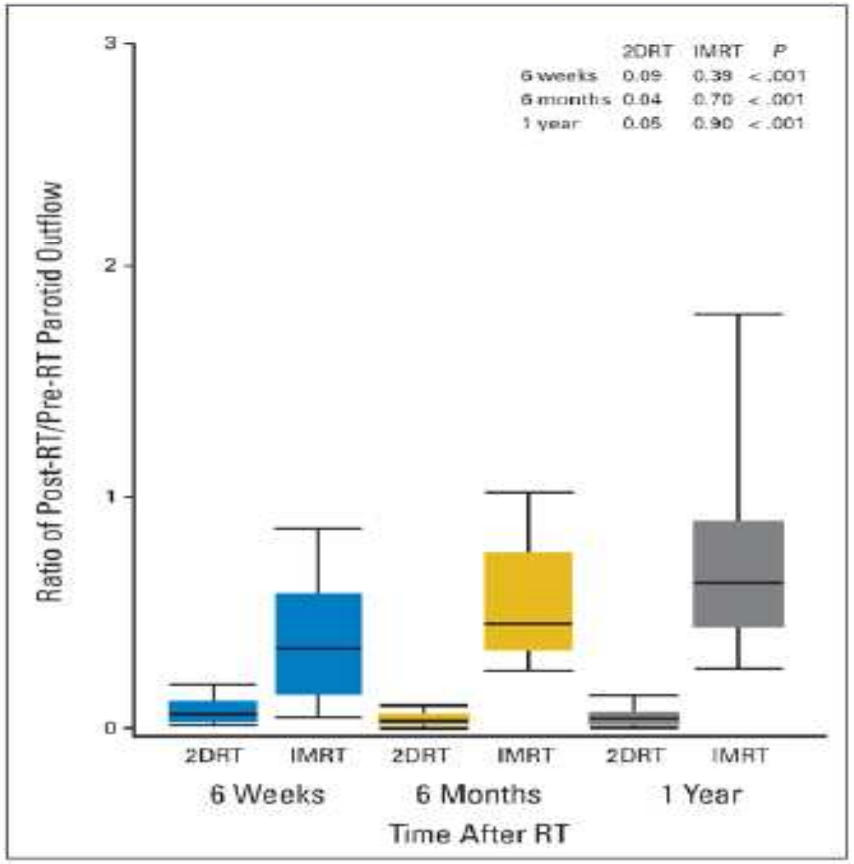
CVRT (3 yrs)	76%
IMRT (3 yrs)	82%

XEROSTOMIA

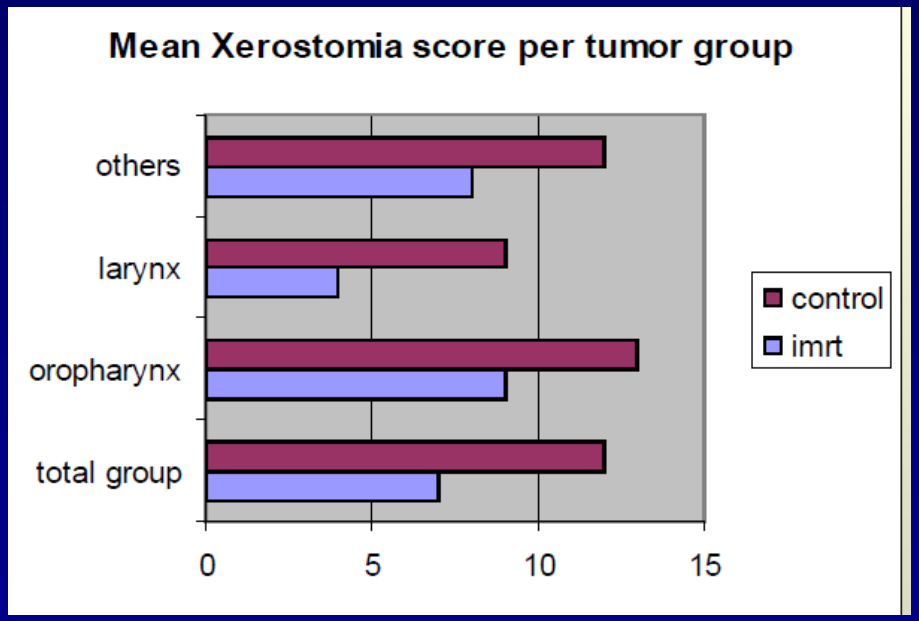
Phase III trial

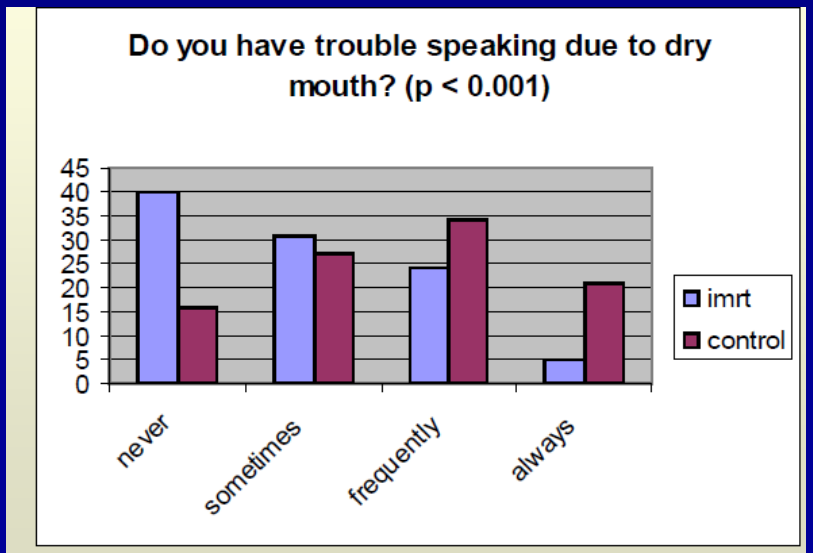
Kam et al,JCO-2007



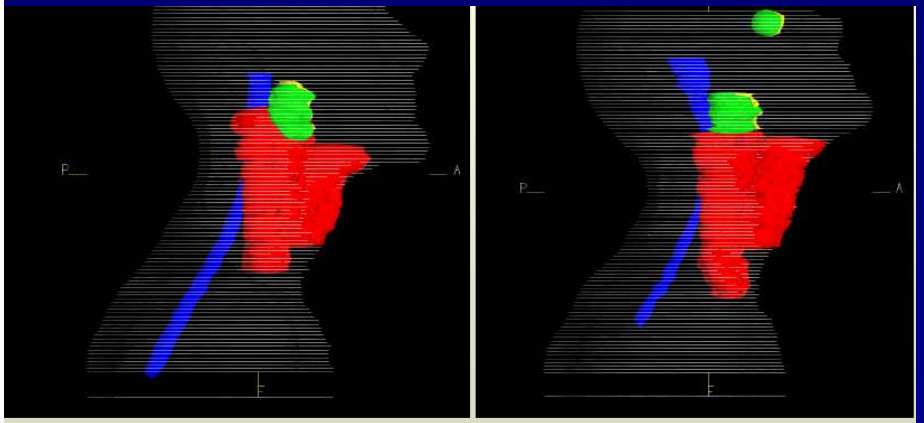


HN CANCER

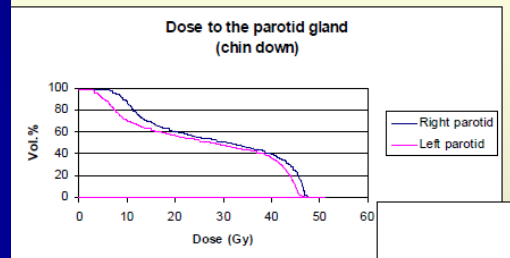


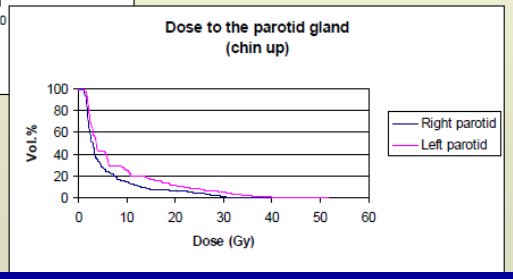


Van Rij et al (Radiation Oncology 2008)



atient position and parotid dose





Tomo vs IMRT (sequential)

[Fiorino et al, Rdiother.Oncol. 2006]

- 5 H&N pts
– IMRT SS (5 fields, 10 levels) vs Tomo-a (same constraints used for IMRT) vs Tomo-b (stressed parotids and mandible sparing)

- ***Better PTV coverage and homogeneity with Tomo***:
V95% : 90% (IMRT) – 96-97% (Tomo);
Dmax: 60.3Gy (IMRT) – 57.4 Gy (Tomo-a) – 58.7 Gy (Tomo-b)

- ***Spinal cord Dmax reduction***: Dmax : 31.6 Gy (IMRT) – 26.5 Gy (Tomo-a) – 24.6 Gy (Tomo-b) (non stressed in the optimisation)

- ***Reduction of Parotid mean dose***: 26.1 Gy (IMRT) – 25.1 Gy (Tomo-a) – 20.8 (Tomo-b)

- ***Mandible dose reduction***: 34.9 Gy (IMRT) – 34 Gy (Tomo-a) – 30.7 Gy (Tomo-b)

IMRT:- WHAT HAS BEEN LEARNT

- IMRT IS FEASIBLE
- IMRT HAS GOOD LOCOREGIONAL CONTROL but NO SURVIVAL ADV
- IMRT ALLOWS PRESERVATION OF SALIVA,ESPECIALLY WITH MEAN DOSE </= 25 Gy

CARCINOMA PROSTATE

Disease characteristics

		Stage	Gleason score	PSA (ng/ml)
Risk group	Low risk	T1-2a	2-6,and	<10
	Intermediate risk	T2b-2c, or	7,or	10-20
	High risk	T3a, or	8-10	>20
	Locally advanced	T3b-T4	any	Any
	metastatic	N1 and/or M1	any	any

Pathological diagnosis of adenocarcinoma of prostate

Risk group classification

Clinical stage

PSA

Gleason

★ **May be defined as ≥ 50% positive biopsy cores ,>50% core length involvement,annual PSA velocity >2 ng/ml/year**

Low risk
Stage T1-2a
GS 2-6
PSA <10 ng/ml

Treatment option
Active surviellance
Brachytherapy
High dose EBRT
Radical prostatectomy

Volume of EBRT
Prostate only

Role of androgen supression therapy
no

Intermediate risk (Favourable)
Stage 2b-2c,N0,M0
PSA 10-20
GS 7

Treatment option
High dose EBRT
Radical prostatectomy

Volume of EBRT
Prostate and seminal vesicle

Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concuttent(2m)

Intermediate risk (Unfavourable) ★
Stage 2b-2c,N0,M0
PSA 10-20
GS 7

Treatment option
1) High dose EBRT
2) EBRT with brachy boost
3) Radical prostatectomy

Volume of EBRT
Prostate and seminal vesicle
Consider whole pelvic radiotherapy

Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concuttent(2m)
± adjuvant HT 2 yrs

High risk (Favourable)
Stage 3a,N0,M0
GS 8-10, or
PSA 10-20

Treatment option
1) High dose EBRT
2) EBRT with brachy boost

Volume of EBRT
Whole pelvic RT
followed by prostate boost

Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concuttent(2m)
adjuvant HT 2 yrs

Treatment volume

Prostate alone

T1c-T2a,Gleason score <6,PSA <10 ng/ml

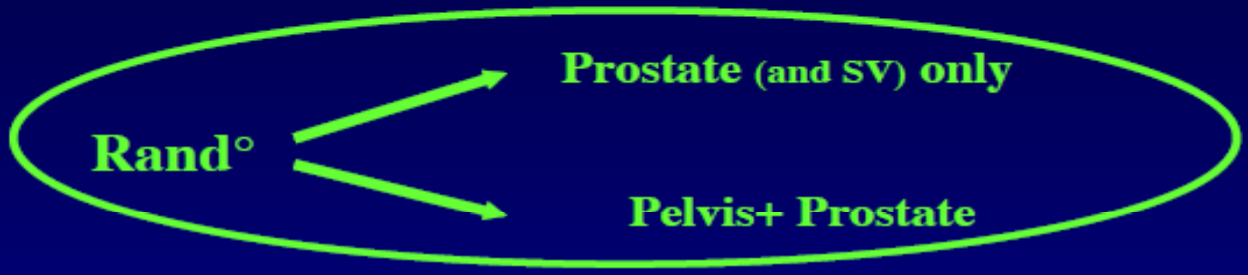
Prostate + SV

If seminal vesicle involvement >15%
= PSA + (GS - 6) ×10

Whole pelvis

Pelvis LN risk >15% (pertins table / Roach's formula
Patient with suspisious pelvic LN

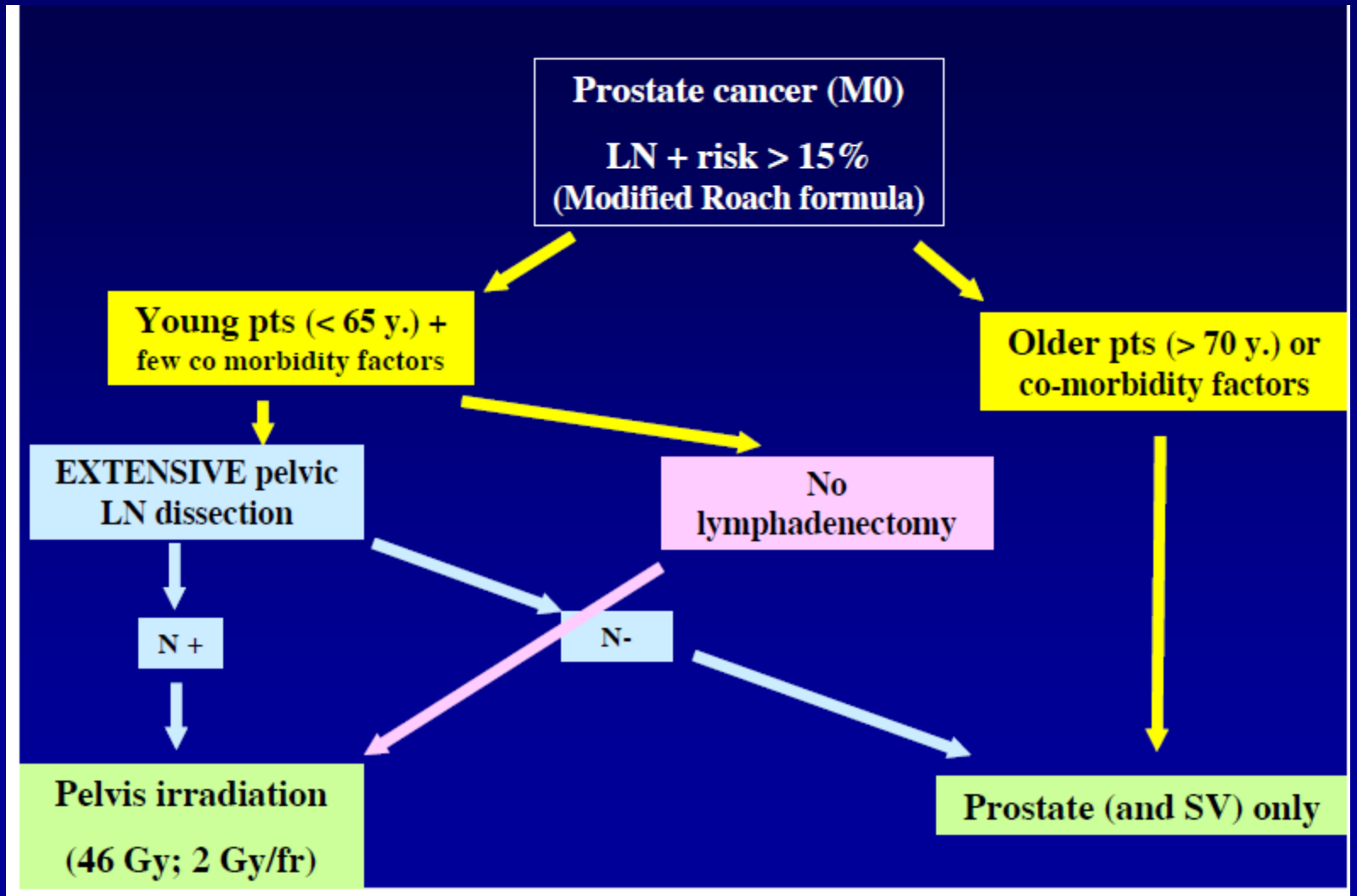
Benefit of pelvis irradiation ? (randomized studies)



	Follow-up	Biochemical control	Toxicity
RTOG 94-13 *(IJROBP 2007)*	6 years	No difference	Grade 3: < 3%
GETUG 01 *(JCO 2007)*	3.3 years	No difference	Grade 2-4 rectal and bladder toxicities not different

…RT of the pelvic lymph nodes = still debated

CA PROSTATE


Prostate cancer (M0)
LN + risk > 15%
(Modified Roach formula)
Young pts (< 65 y.) +
few co morbidity factors
Older pts (> 70 y.) or
co-morbidity factors
EXTENSIVE pelvic
LN dissection
No
lymphadenectomy
N +
N-
Pelvis irradiation
(46 Gy; 2 Gy/fr)
Prostate (and SV) only

WHY DOSE ESCALATION

- With dose 70Gy of conv. EBRT alone T2c-T4, 30-50% of patient develop local recurrence within 10yrs & majority will develop distant mets.
- Standard dose of RT doesn’t have the capacity to completely eradicate the prostate disease in majority.
- Thus dose escalation is needed.

CA PROSTATE

Randomized studies showing the benefit of dose escalation

R° → Standard dose (67-70 Gy)

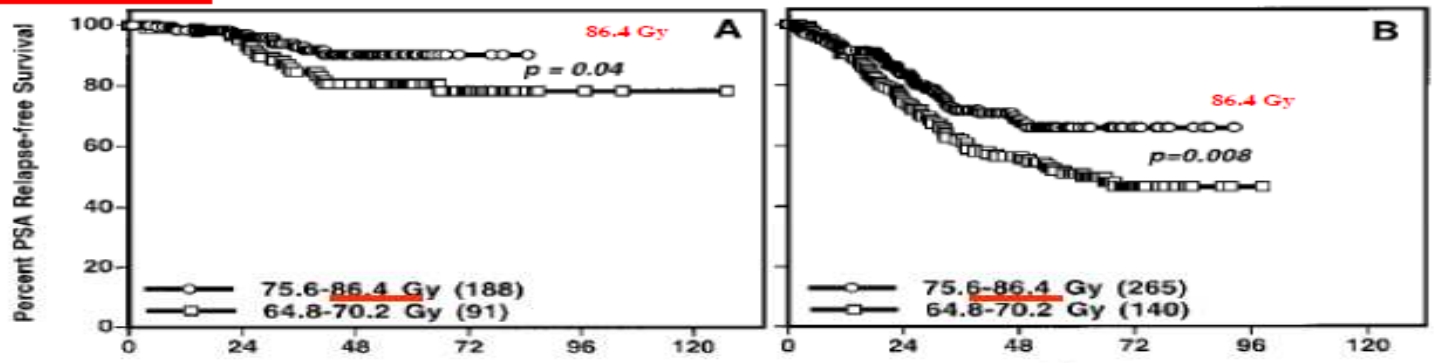
R° → High dose (76-80 Gy)

	Local control (negative biospy)	Freedom from biochemical failure	Freedom from clinical failure	Specific survival
Shipley 1995	GI 8: 19% vs 64%	No PSA available	NS Median folow-up = 10 years	NS
Pollack, Kuban 2000, 2002, 2008	72% vs 65% NS	PSA≤10 NS PSA>10 p=0.012	7% vs 15% (p= 0.01)	P<0.05
Zietman 2005	48% vs 67% (p<0.001)	61% vs 80% (p<0.001) including low risk group	NS	NS
Dutch 2008	NS	45% vs 56% (p<0.001), mainly intermediate risk group	NS	NS
GETUG 06 2010	NS	PSA>15 p=0.03	NS	NS

CA PROSTATE

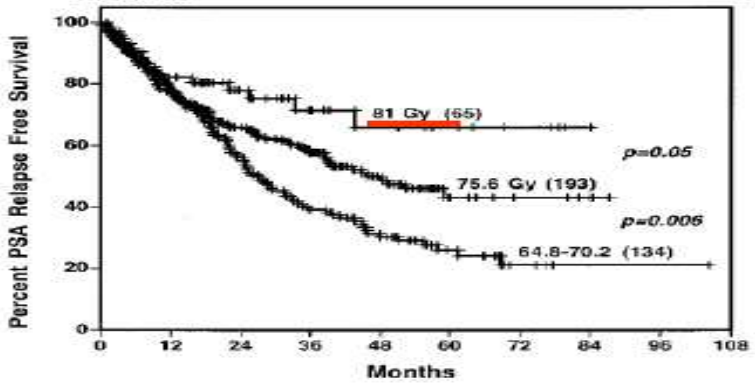
HIGH DOSE RADIATION DELIVERED BY INTENSITY MODULATED CONFORMAL RADIOTHERAPY IMPROVES THE OUTCOME OF LOCALIZED PROSTATE CANCER

Up to 86.4 Gy !!!



Low risk

Intermediate risk



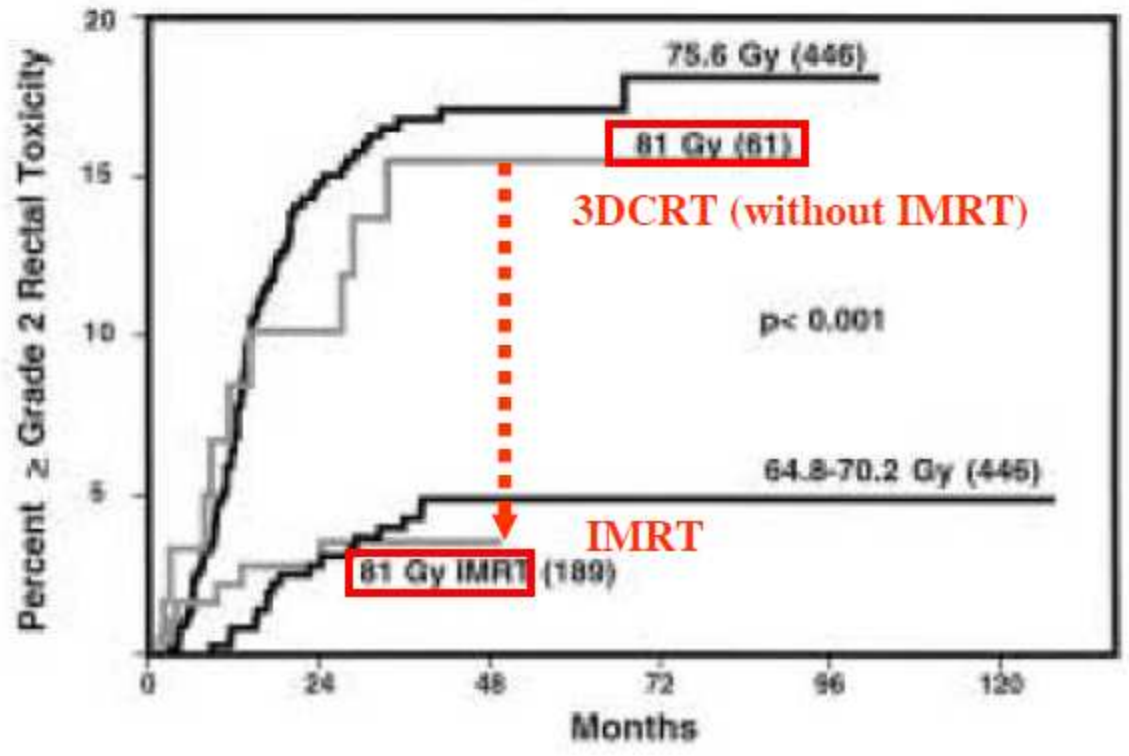
High risk

Zelefsky, J Urol 2001

CA PROSTATE

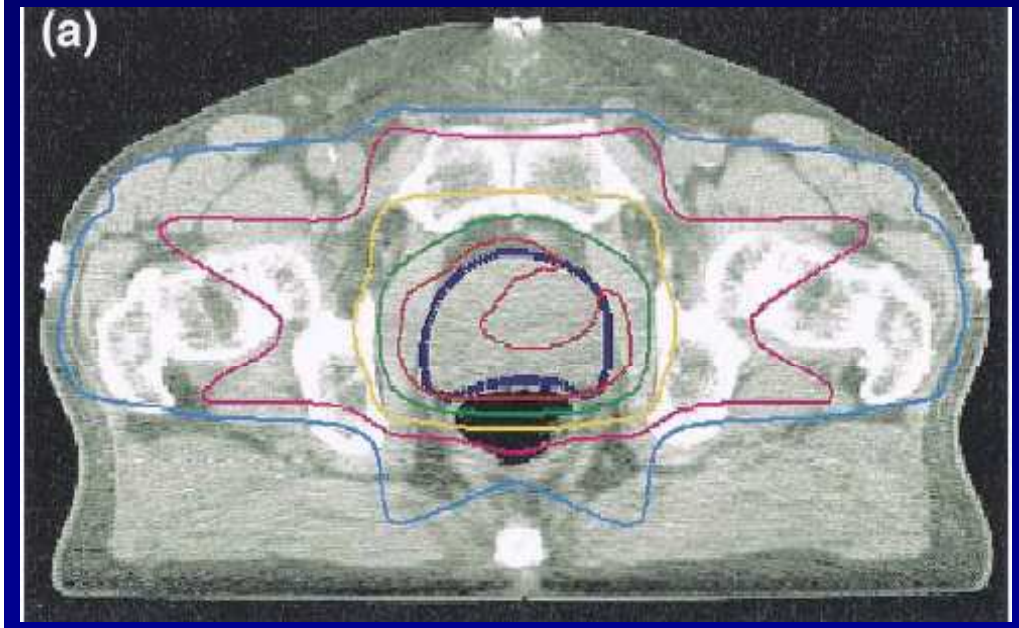
IMRT decreases GI toxicity compared to 3DCRT

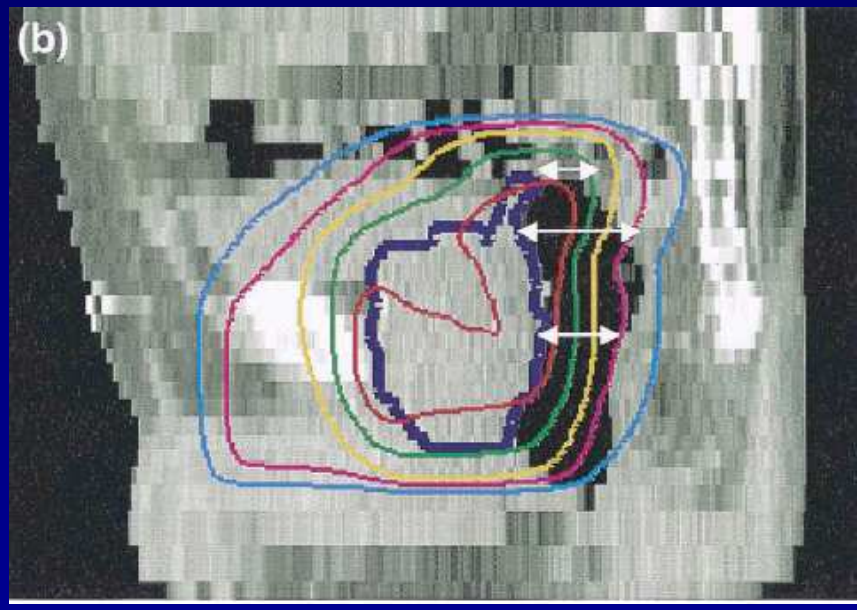
(non randomized study)



Zelefsky, J Urol 2001

RECTAL DISTENSION &PSA CONTROL



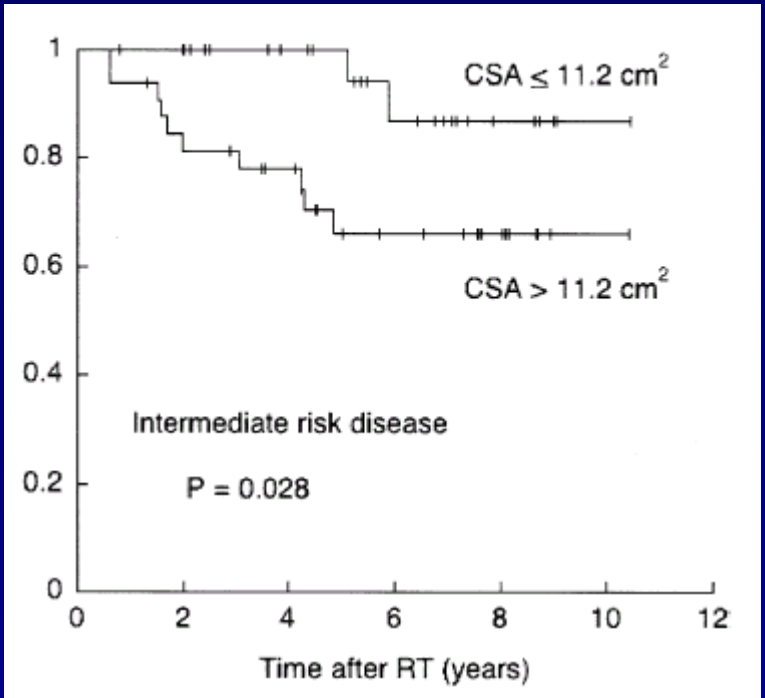


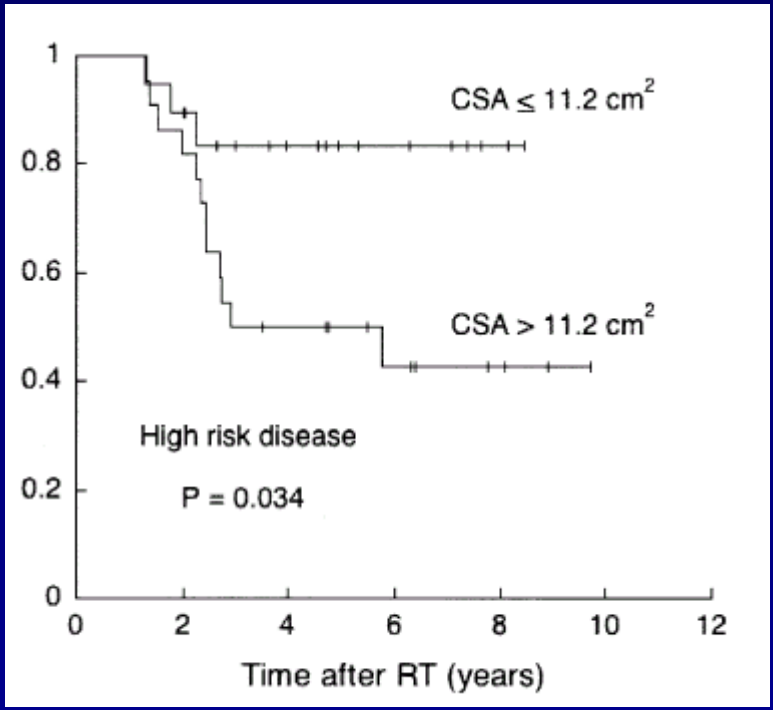
- **127 patients -3 D CRT - total dose of 78 Gy**

- **Rectal distension = average cross- sectional rectal area (CSA; defined as the rectal volume divided by length) and measuring three rectal diameters on the planning CT.**

de Crevoisier et al. Int J Radiat Oncol Biol Phys. 2005; 62: 9

RECTAL DISTENSION & PSA CONTROL





- **Rectal distension decreased the probability of biochemical control, local control, and rectal toxicity in patients without daily IGRT**
- **Therefore, an empty rectum is warranted at the time of simulation.**
- **Emphasize the need of empty rectum for IGRT to improve LC**

de Crevoisier et al. Int J Radiat Oncol Biol Phys. 2005; 62: 965-73

Benefit of IMRT in high dose prostate cancer radiotherapy (Rennes, France)

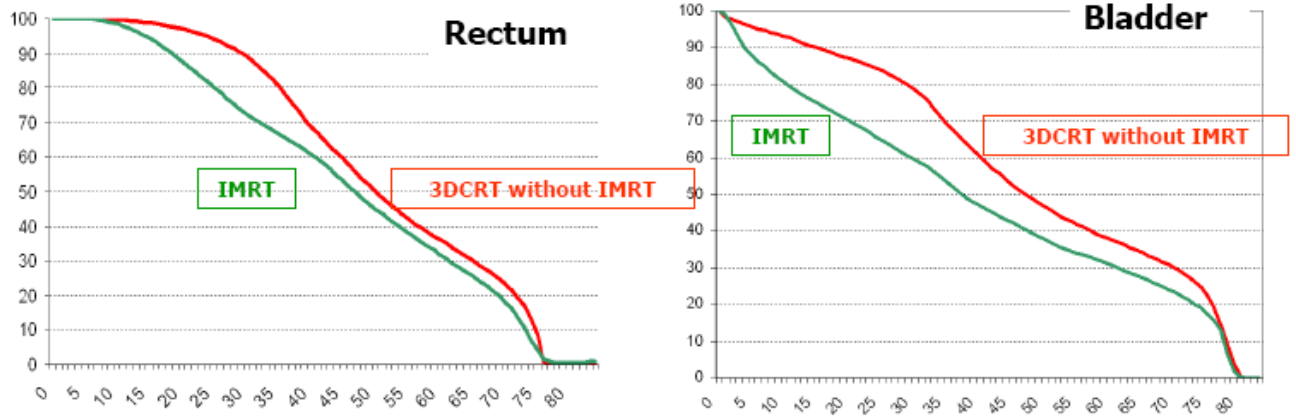
Dosimetric benefit of IMRT

80 Gy in the prostate

(no pelvis)

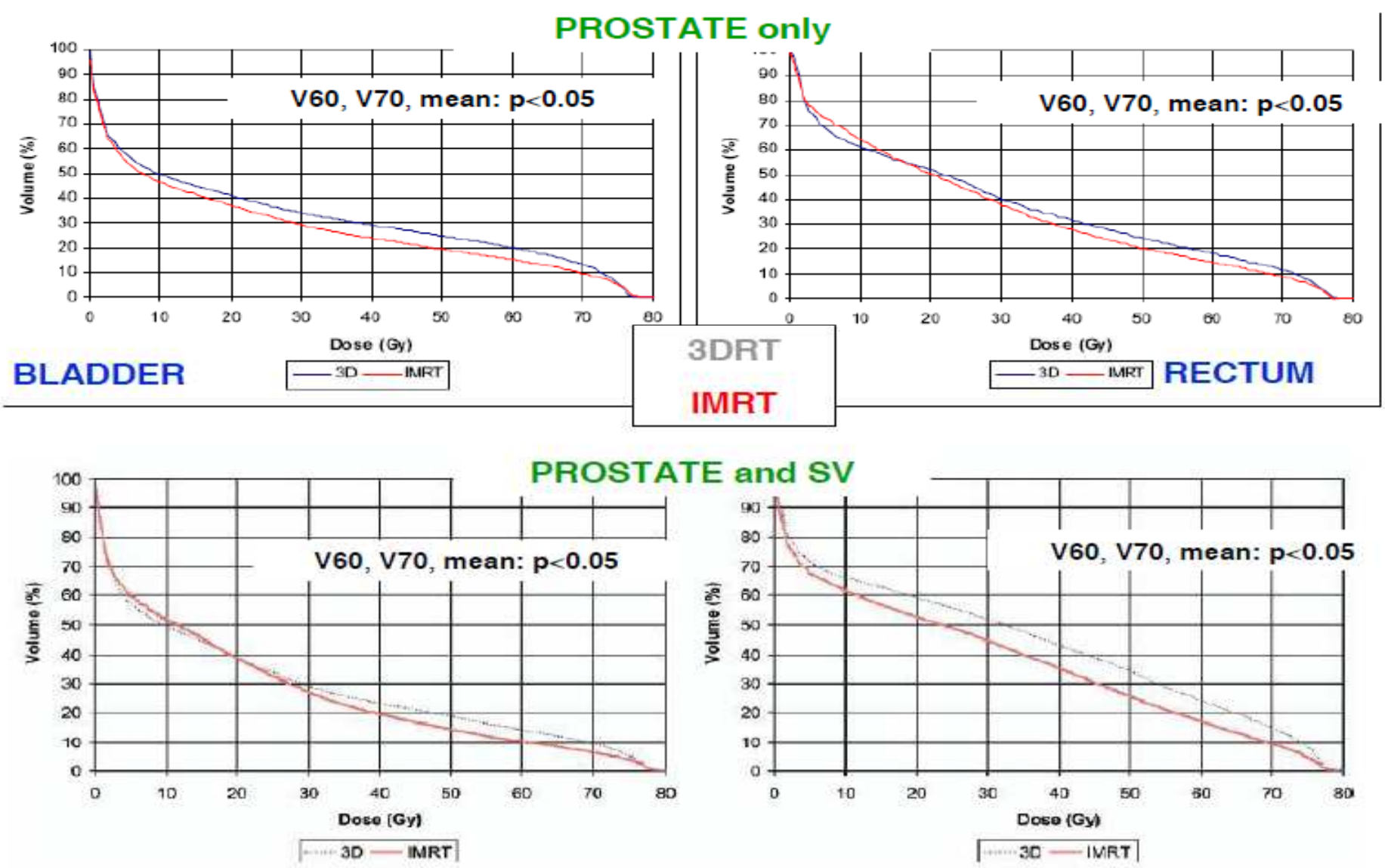
- 3DCRT — 77 pts
- IMRT — 80 pts

IMRT decreased significantly the dose in:
- the rectal wall (V10 to V79) and NTCP/2
- the bladder wall (V4 to V79)



De Crevoisier ASTRO 2010

CA PROSTATE

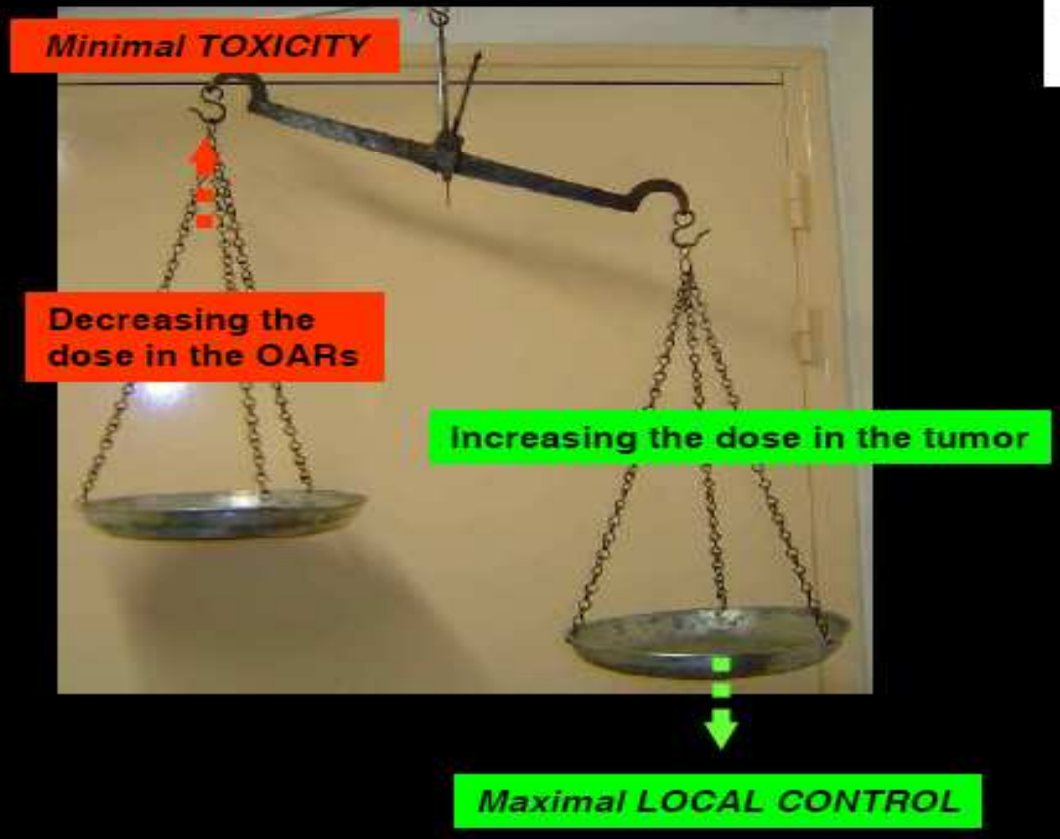

PROSTATE only
V60, V70, mean: p<0.05
Volume (%)
Dose (Gy)
3D
IMRT
BLADDER
3DRT
IMRT
V60, V70, mean: p<0.05
Volume (%)
Dose (Gy)
3D
IMRT
RECTUM
PROSTATE and SV
V60, V70, mean: p<0.05
Volume (%)
Dose (Gy)
3D
IMRT
V60, V70, mean: p<0.05
Volume (%)
Dose (Gy)
3D
IMRT

TOXICITIES

- Conventional EBRT:- Grade 2/ higher rectal/ bladder morbidity; needs medication in 60%.
- The risk of complication increases when RT dose exceeds 70Gy.
- Rectal complication depends on % of rectum treated to 70Gy/ higher dose.
- Rectal complication increases with increased dose of radiation.
- IMRT reduces the incidence of acute & late rectal effect compared to 3DCRT but not acute & late urinary complication.
- At present time IMRT doesn’t appear to significantly reduce the urinary symptoms compared to 3DCRT.
- With EBRT + Brachytherapy, the complication rates are high.

CA CERVIX

IMRT in gynaecological tumor



DOSIMETRIC benefit of IMRT ?

IMRT reduces the dose to the:

-**small bowel**

-rectum

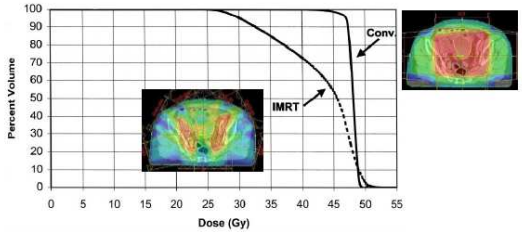
-bladder

-bone marrow

-kidney

DOSIMETRIC STUDY: standard 3DCRT versus IMRT

IMRT spares the bladder



Bladder comparison of conventional and IMRT plans

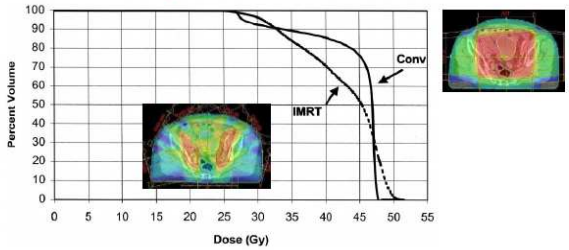
Dose (Gy)	Percent volume—conventional	Percent volume—IMRT	*p* value
10	100 ± 0	100 ± 0	1.0
20	100 ± 0	99.9 ± 0.3	0.34
30	100 ± 0	96.5 ± 2.3	0.05
40	99.8 ± 0.4	86.1 ± 7.2	0.0001
45	99.3 ± 1.3	76.6 ± 11.7	0.0005
50	5.3 ± 9.0	2.5 ± 2.6	0.37

average volume of bladder irradiated at the prescription dose reduced by 23% (p<0.001)

Roeske, IJROBP 2002

DOSIMETRIC STUDY: standard 3DCRT versus IMRT

IMRT spares the rectum



Rectum comparison of conventional and IMRT plans

Dose (Gy)	Percent volume—conventional	Percent volume—IMRT	*p* value
10	100 ± 0	100 ± 0	1.0
20	100 ± 0	99.9 ± 0.2	0.34
30	97.9 ± 2.8	94.5 ± 4.2	0.001
40	91.9 ± 4.9	73.9 ± 9.7	0.0002
45	80.3 ± 5.3	57.7 ± 13.8	0.0002
50	0 ± 0	1.9 ± 2.0	0.01

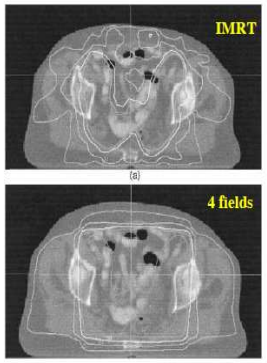
average volume of rectum irradiated at the prescription dose reduced by 23% (p<0.001)

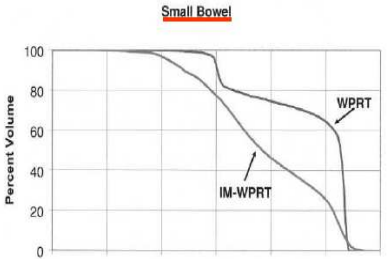
Roeske, IJROBP 2002

DOSIMETRIC STUDY: standard 3DCRT versus IMRT

IMRT spares the small bowel

36 gynecological tumor pts





IMRT spares the bone marrow

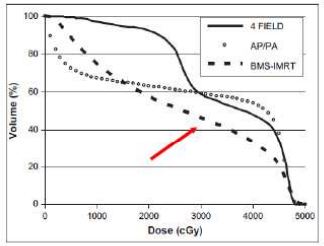
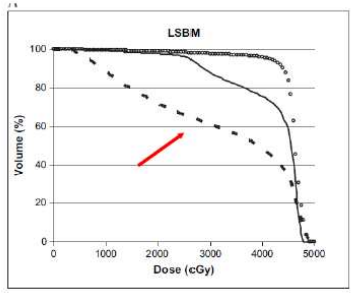


Fig. 3. Dose–volume histograms for pelvic bone marrow compar-



Lower pelvic bone marrow

Table 1. Pelvic bone marrow dose–volume comparison

Dose (Gy)	BMS-IMRT	Four-field box	AP–PA	*p* (IMRT vs. four-field box)	*p* (IMRT vs. AP–PA)
5	90.4	99.6	72.4	<0.05	<0.05
10	76.5	97.3	66.9	<0.05	<0.05
20	57.5	92.7	62.9	<0.05	<0.05
30	46.1	59.9	59.1	<0.05	<0.05
40	33.7	48.9	54.1	<0.05	<0.05

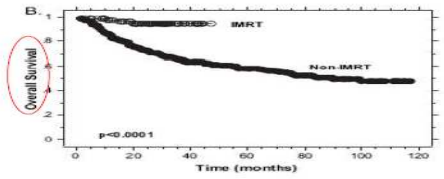
Mell, IJROBP 2005

IMRT for gynecological tumor is safe: provides high local control and survival

Locally advanced cervical cancer

Non randomized study : 135 pts IMRT vs 317 pts 3D technique

Recurrence	IMRT	Non-IMRT	Total	*p* Value
Overall	39 (28.9%)	139 (43.8%)	178	0.036



Kidd, IJROBP 2010

CA PANCREAS

Clinical benefit of IMRT in pancreas

46 pts with pancreatic cancer:
IMRT (50.4 Gy) + concurrent chemo (5-FU ± capecitabine)

➔ **acute GI toxicity** compared with those from RTOG 97-04 (3DCRT witout IMRT)

Toxicity	3-D conformal *n* (%)		IMRT *n* (%)	*p*
Nausea/vomiting				
Grade 0–2	402 (89)		46 (100)	0.016
Grade 3–4	49 (11)		0 (0)	
Diarrhea				
Grade 0–2	373 (83)	>	44 (96)	0.02
Grade 3–4	78 (17)		2 (4)	
Anorexia				
Grade 0–2	442 (98)		44 (96)	> 0.05
Grade 3–4	9 (2)		2 (4)	

Yovino, IJROBP 2011

A randomized controlled trial of 300 patients comparing IMRT with standard wedged tangential fields at the Institute of Cancer Research and Royal Marsden Hospital.

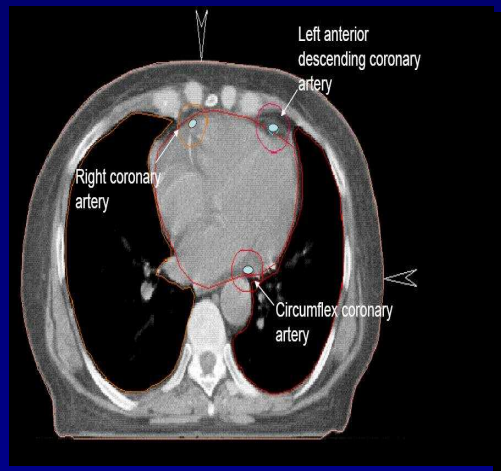
Ref: Yarnold JR, Donovan EM, Reise S, et al. Randomized trial of standard 2D radiotherapy versus 3D intensity modulated radiotherapy in patients prescribed breast radiotherapy. Radiother Oncol 2002;65:(S15)64.

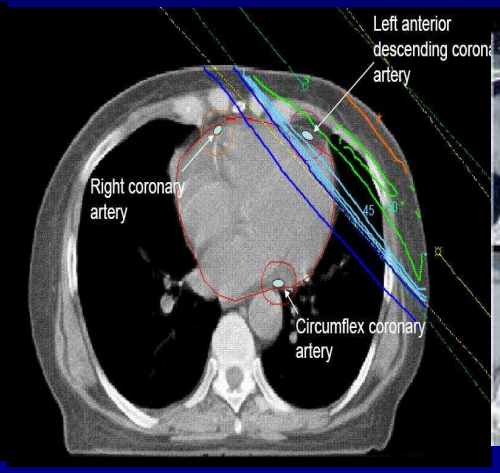
WITH IMRT:

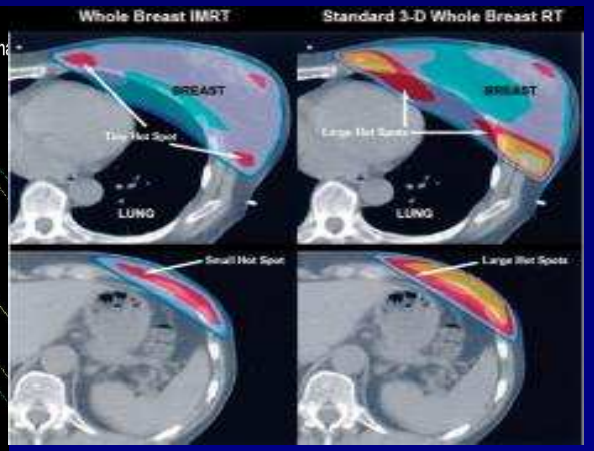
Dose inhomogeniety only in 4% of patients treated with IMRT Vs 70% of patients treated with standard techniques

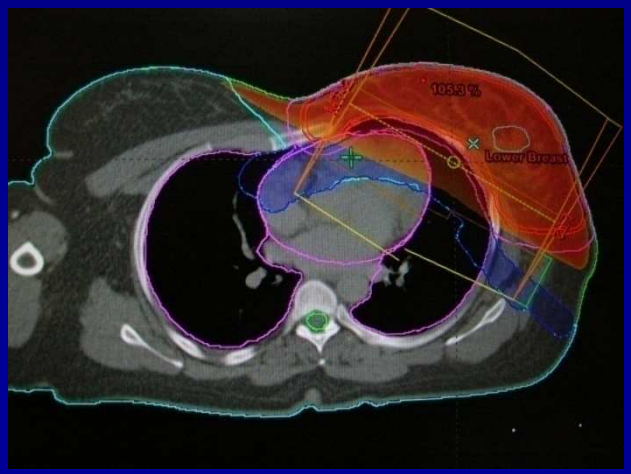
- 25% reduction in the dose to the heart
- 42% reduction in the mean dose to the contralateral breast
- 30% reduction in the ipsilateral lung volume

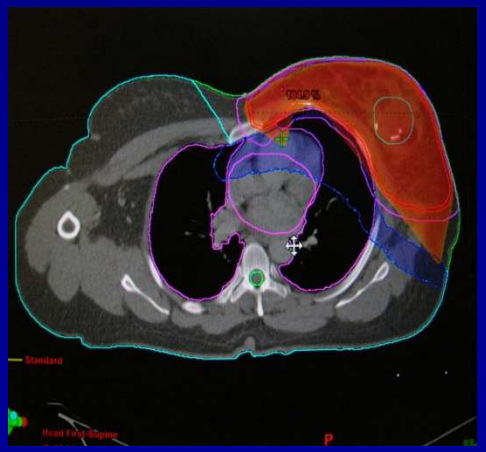
LATE COMPLICATION











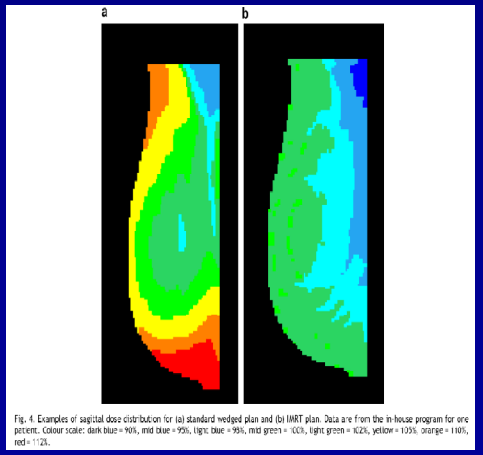


Fig. 4. Examples of sagittal dose distribution for (a) standard wedged plan and (b) IMRT plan. Data are from the in-house program for one patient. Colour scale: dark blue = 90%, mid blue = 95%, light blue = 98%, mid green = 100%, light green = 102%, yellow = 105%, orange = 110%, red = 112%.

Scope of IMRT in Whole Breast RT

- Reducing dose inhomogeneity across the treatment volume
- Increasing Conformity of the dose
- Internal mammary node irradiation
- Simultaneous Integrated Boost to tumor cavity
- Possibly reduce morbidity

IMRT/IGRT in pelvis/abdomen : conclusions

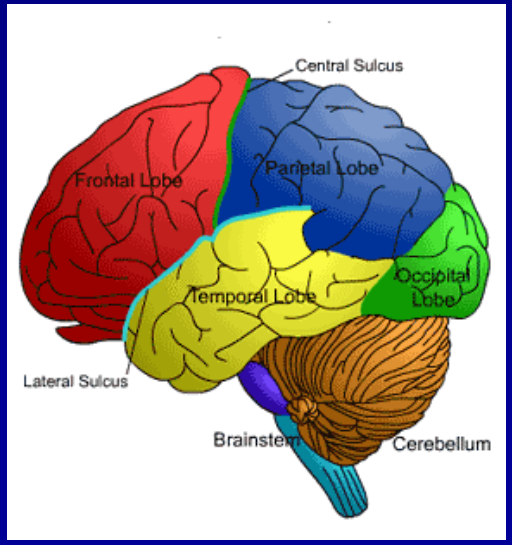
		IMRT			IGRT	
		Experience	Dosimetric benefit	Clinical benefit	Rational	Experience
Prostate	« in place »	+++++++	-rectum -bladder -bowel	-GU/GI toxicity (acute/late) - local control	+++++	+++
	+ pelvic LN	+++++			++	++
	post-op	+++			++	+
Gynecol	cervix	++	- rectum - bladder - bowel - kidney - bone - ParaoLN	-GU/GI toxicity (acute/late) -hemato toxicity -local control ?	+++	+
	endometrium	++			++	
Digestive	anal canal	++	- rectum - bladder - bowel - kidney - bone - perineum	- GI toxicity - dermato toxicity	+	
	rectum	++		GI toxicity (acute)	+++	+
	pancreas	+	- rectum - bladder - bowel - kidney	GI toxicity (acute)	+	

CYBERKNIFE-INDICATIONS

- Intracranial lesions: single fraction, or fractionated
- Head and neck:
  - Nasopharynx & base of skull, primary or recurrent
  - Other sites, as boost following conventional RT, or recurrent
- Spine: where surgery indicated but not feasible, and conventional RT less effective or not possible
- Lung: where surgery indicated but not feasible
- Liver: where surgery indicated but not feasible
- Pancreas: unresectable but localized tumors
- Kidney: where surgery indicated but not feasible
- Previously irradiated tumors: retreatment w/ conventional RT not possible, for severe symptoms, Karnofsky $\geq$ 40

Clinical Applications

- Benign conditions
  - Acoustic neuroma/Vestibular schwannoma, AVM
  - Meningioma
  - Pituitary adenoma, Craniopharyngioma
  - Glomus jugulare tumors
  - Trigeminal neuralgia



INDICATIONS OF TOMOTHERAPY

Magnafield radiotherapy – Large Field IMRT

-Total Marrow Irradiation (TMI) & Total Lymphoid Irradiation (TLI)

- Whole Abdominopelvic Radiotherapy (WAR)

- Craniospinal Irradiation (CSI)

- Mantle, Mini-Mantle, Extended Mantle field

- Inverted-Y, Spade field

Simultaneous targeting of multiple lesions

- Synchronous double primaries

- Multiple metastases closely or far apart

- Primary plus metastatic lesions

Conformal avoidance

- Whole Brain sparing scalp radiotherapy

- Scalp sparing Whole brain radiation therapy (WBRT)

- Hippocampal & neural stem cell sparing WBRT

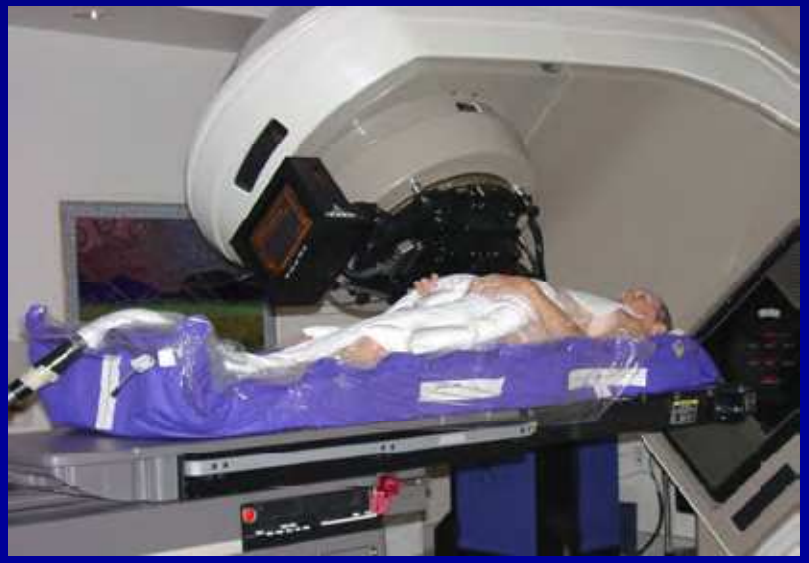
- Cardiac sparing mediastinal radiotherapy

Indications of SBRT

- **Lung**
  - Stage I (T1–2 N0 M0) NSCLC
  - Lung mets
- **Liver**
  - Hepatocellular carcinoma
  - Liver mets
- **Spine**
  - Spinal mets (primary trt, postop, re-irradiation
  - Benign spinal tumors
- **Promising early results**
  - Prostate cancer
  - Renal cell carcinoma
  - Pancreatic cancer

Immobilization—Blue Bag

Medical Intelligence BodyFIX



SBRT Dose

Most Commonly Reported SBRT Prescriptions for Spine Tumors (n=170)

Fractions (%)	Common Dose/ Fraction, Gy (%)	Median Dose/ Fraction, Gy (range)	Median IDL, % (range)
1 (57%)	18 (40%), 16 (34%)	18 (7-24)	85 (70-100)
3 (22%)	8 (51%), 7 (14%)	8 (6-12)	80 (75-95)
5 (18%)	6 (60%), 7 (10%)	6 (4-12)	100 (90-100)

Most Commonly Reported SBRT Prescriptions for Lung (n=262)

Fractions (%)	Common Dose/ Fraction, Gy (%)	Median Dose/ Fraction, Gy (range)	Median IDL % (range)
3 (47%)	20 (46%), 18 (45%)	18 (10-20)	80 (70-100)
4 (21%)	12 (78%), 12.5 (11%)	12 (10-16)	85 (80-100)
5 (30%)	10 (51%), 12 (34%)	10 (3-20)	90 (75-100)

Most Commonly Reported SBRT Prescriptions for Liver (n=142)

Fractions (%)	Common Dose/ Fraction, Gy (%)	Median Dose/ Fraction, Gy (range)	Median IDL % (range)
3 (48%)	15 (40%), 20 (25%)	15 (8-20)	80 (70-100)
4 (9%)	12 (77%), 10 (8%)	12 (8-12)	80 (80-95)
5 (38%)	10 (38%), 12 (19%)	10 (5-12)	90 (70-100)

Pan H et al, A Survey of Stereotactic Body Radiotherapy Use in the United States. Cancer 2011 Oct 1;117(19):4566-72

SBRT in early stage NSCLC

Study	Trial type	Disease stage	Number of patients	Radiation dose	Follow-up period (months)	Outcomes
McGarry *et al.* (2005)[27]	Prospective (phase I)	Medically inoperable stage I	47	24–72 Gy in 3 fractions at 80%	27.4 for T1 19.1 for T2	LC: 78.7%
Fakiris *et al.* (2009)[28]	Prospective (phase II)	Medically inoperable stage I	70	T1 tumors: 60 Gy in 3 fractions at 80% T2 tumors: 66 Gy in 3 fractions at 80%	50.2	LC: 88.1% at 3 years OS: 42.7% at 3 years CSS: 81.7% at 3 years
Nagata *et al.* (2005)[30]	Prospective (phase I–II)	IA and IB	45	48 Gy in 4 fractions at isocenter	30 for T1 tumors 22 for T2 tumors	LC: 98% (crude) OS: 92% and 83% at 1 and 3 years, respectively DFS: 80% and 72% at 1 and 3 years, respectively
Baumann *et al.* (2009)[31]	Prospective (phase II)	Medically inoperable stage I	57	45 Gy in 3 fractions at 67%	35	LC: 92% at 3 years OS: 86%, 65% and 60% at 1, 2 and 3 years, respectively CSS: 93%, 88% and 88% at 1, 2 and 3 years, respectively PFS: 52% at 3 years

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SBRT for Lung Metastases

Study	Trial type	Number of patients	Number of targets	Radiation dose	Median follow-up (months)	Outcomes
Uematsu *et al.* (1998)[3]	Retrospective	22	43	30–75 Gy in 5–15 fractions prescribed to 80%	9	LC: 98% (crude) No or minimal adverse effects
Hara *et al.* (2002)[49]	Retrospective	14	18	20–30 Gy in one fraction prescribed to periphery of PTV	12	LC: 78% at 13 months. No grade 3 or higher toxic effects
Lee *et al.* (2003)[50]	Retrospective	19	25	30–40 Gy in 3–4 fractions (10 Gy per dose) prescribed to periphery of PTV	18	LC: 88% at 2 years OS: 88% at 2 years No symptomatic or late serious complications
Hof *et al.* (2007)[51]	Retrospective	61	71	12–30 Gy in one fraction prescribed to isocenter	14	LPF: 88.6%, 73.7% and 63.1% at 1, 2 and 3 years, respectively OS: 78.1%, 65.1% and 47.8% at 1, 2 and 3 years, respectively No clinically significant toxic effects
Okunieff *et al.* (2006)[52]	Retrospective	42	125	50 Gy in 10 fractions (5 Gy per dose) prescribed to 80%	18.7	LC: 94% (crude), 91% at 3 years PFS: 25% and 16% at 1 and 2 years, respectively Grade 3 toxic effects: 4%

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SBRT for Liver Metastases

Study	Type	Number of patients	Number of targets	Radiation dose	Median follow-up (months)	Outcomes
Katz *et al.* (2007)[58]	Retrospective	69	174	30–55 Gy in fractions of 2–6 Gy prescribed to 80%	14.5	LC: 76% and 57% at 10 and 20 months, respectively OS: 46% and 24% at 6 and 12 months, respectively Grade 3 or higher toxic effects: 0%
Wulf *et al.* (2001)[47]	Retrospective	23	23	30 Gy in 3 fractions of 10 Gy prescribed to 65%	9.0	LC: 76% and 61% at 1 and 2 years, respectively* OS: 71% and 43% after 1 and 2 years, respectively* Grade 3–5 toxic effects (acute): 0%
Gunvén *et al.* (2008)[60]	Retrospective	7	9	20–40 Gy in 2–4 fractions, 30–45 Gy in 2–3 fractions, or 40 Gy in 2 fractions prescribed to 65%	117.0	LC: 100% (crude) OS: 100% (crude)
Herfarth *et al.* (2001)[61]	Prospective (phase I–II)	33	56	14–26 Gy in 1 fraction prescribed to 80%	5.7.0	LC: 78% (crude); 75%, 71% and 67% at 6, 12 and 18 months, respectively† OS: 72% at 1 year† RILD: 0%

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Biologically Guided Radiotherapy: Theragnostics

- "Theragnostic": use of molecular imaging to prescribe the distribution of radiation doses in 4 dimensions

  - Tumor burden / clonogenic density
  - Hypoxia
  - Proliferation
  - Receptor expression (EGFR) etc

  } targeted

TAKE HOME MESSAGE

- GEOMETRIC FIELD SHAPING:-3DCRT
- GEOMETRIC FIELD SHAPING+MODULATION OF THE FLUENCE:- IMRT
- GEOMETRIC FIELD SHAPING+MODULATION OF THE FLUENCE+IMAGE GUIDANCE:-IGRT

HEAD AND NECK :

- HIGH RISK CTV → ≥ 70 Gy.
  INT. RISK CTV → 63 Gy.
  LOW RISK → 50- 55 Gy.

- POSITION AS COMFORTABLE AS POSSIBLE.

- TARGET VOLUME :

  GTV + subclinical disease = CTV.

  CTV + IM + SM = PTV.

  OAR = serial , parallel, serial in parallel, combination of serial and parallel.
- BEAMS EYE VIEW → looking from the source.
- CONVENTIONAL AND 3D CRT → forward planning .
- IMRT → inverse planning.
- DIFFERENTIAL DVH → exact volume of tissue received that particular dose.

- CUMULATIVE DVH → entire volume received specified dose.
- Inhomogenity should be within + 7% to – 5%.
- Motion may be Interfractional/ Intrafractional.
- IGRT → planning -> EPID, Cyberknife.
  volumetric -> CT on rail, Tomo, MVCT, CVCT.
- 3D CT + Respiratory gating → 4 D.
- PAROTID dose less in chinup position.
- IMRT IN H& N→ less xerostomia, better speaking.

- PROSTATE → Biochemical control no difference in prostate Vs pelvis + prostate Radiation.
  4 year PFS improved but more toxicity.
  Dose escalation → Better freedom from biochemical failure and better PSA relapse free survival.
- Ca Cervix → Less toxicity , better overall survival.
- Ca Pancreas → Less toxicity.
- SBRT indicated in :
  T1, T2 NSCLC
  Lungs metastasis
  Hepatocellular carcinoma.
  Spinal RT.


THANK YOU