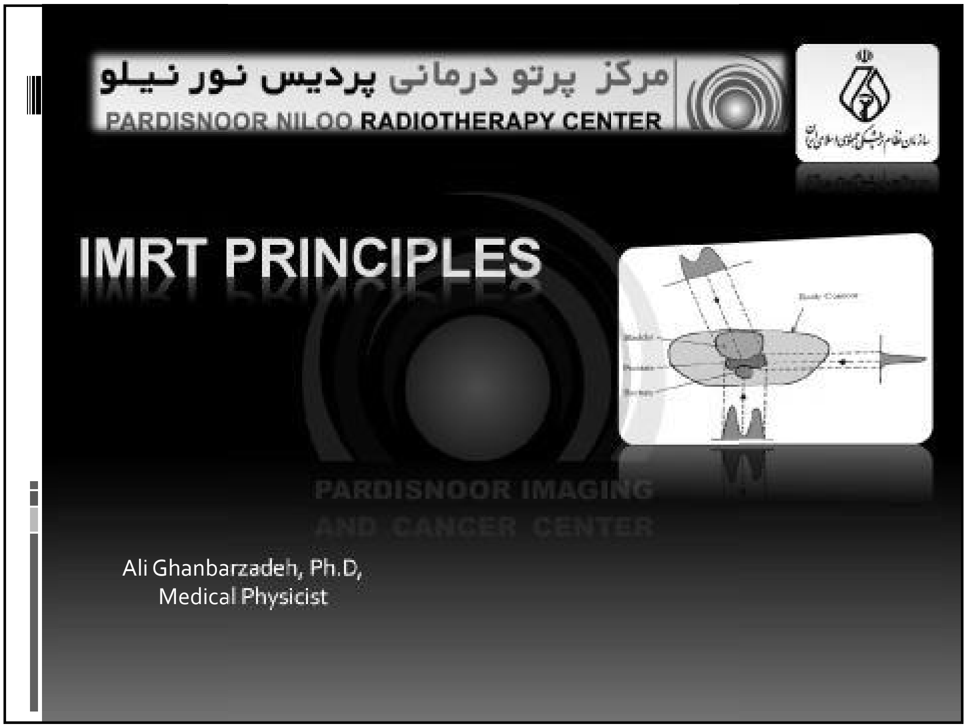
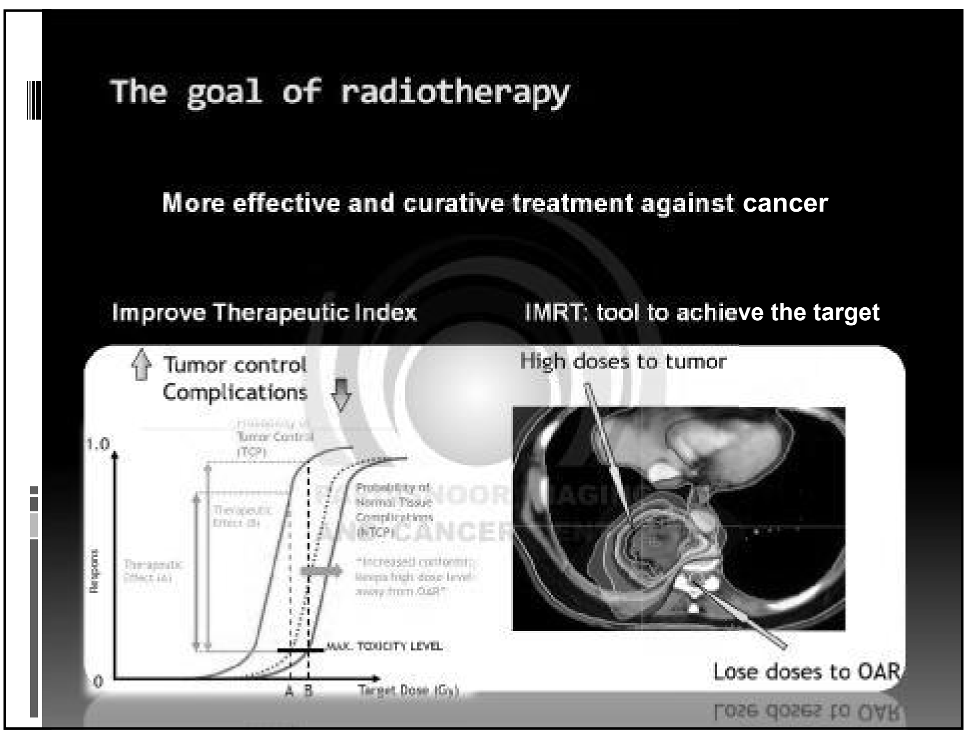
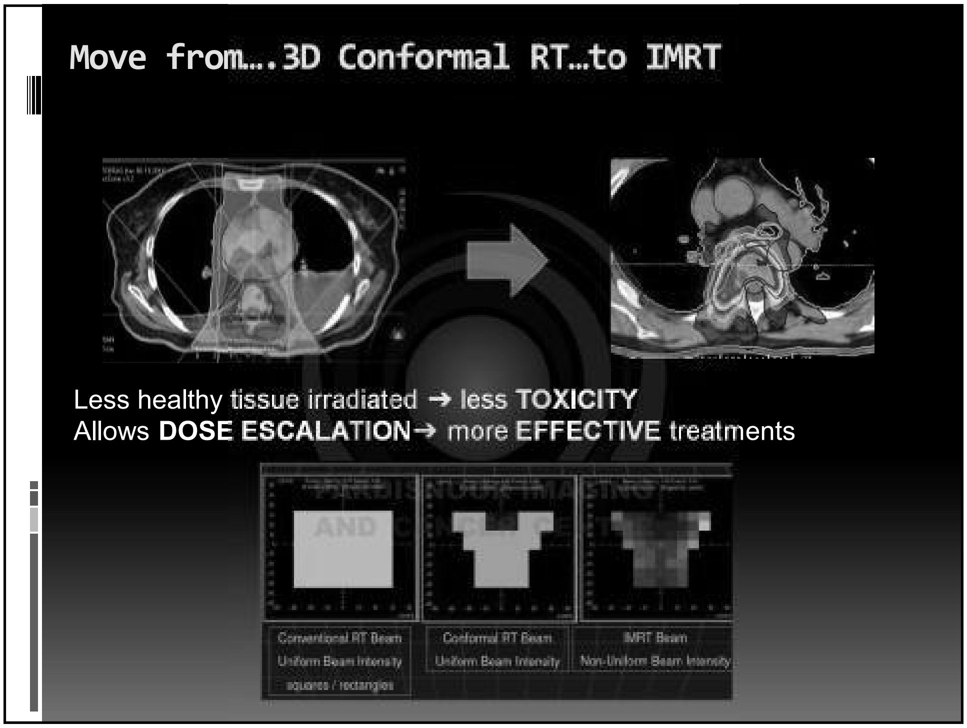
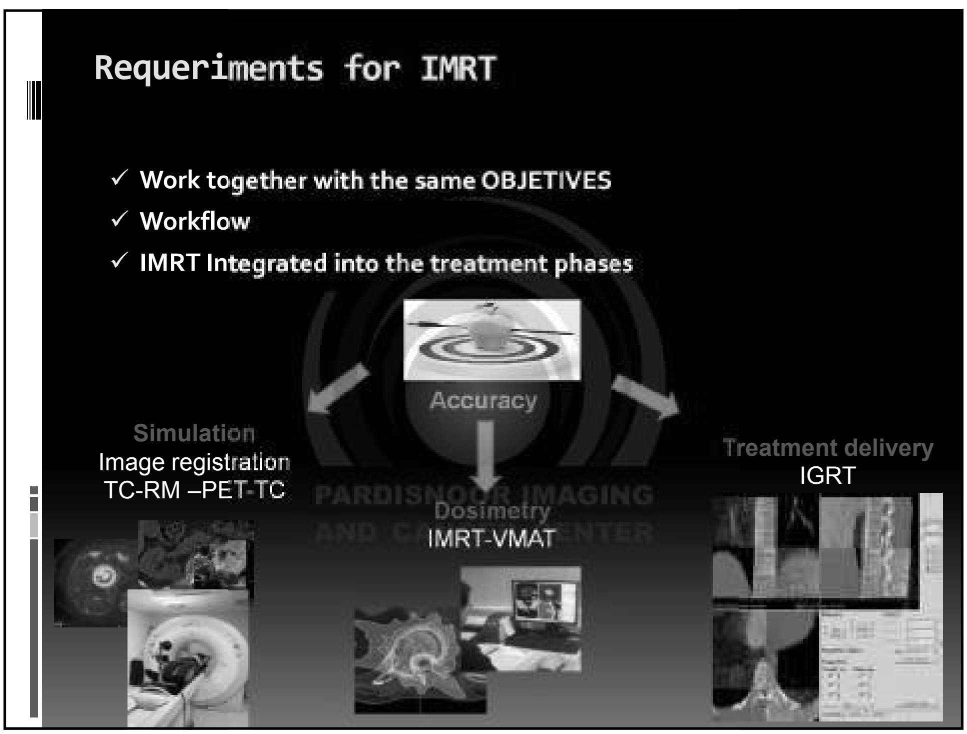
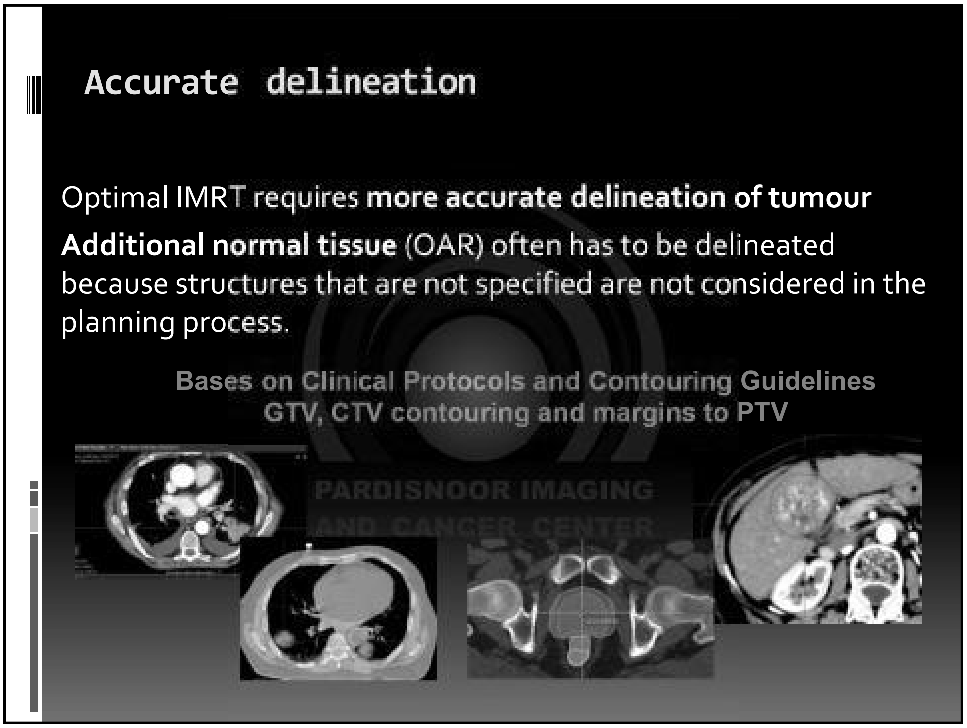
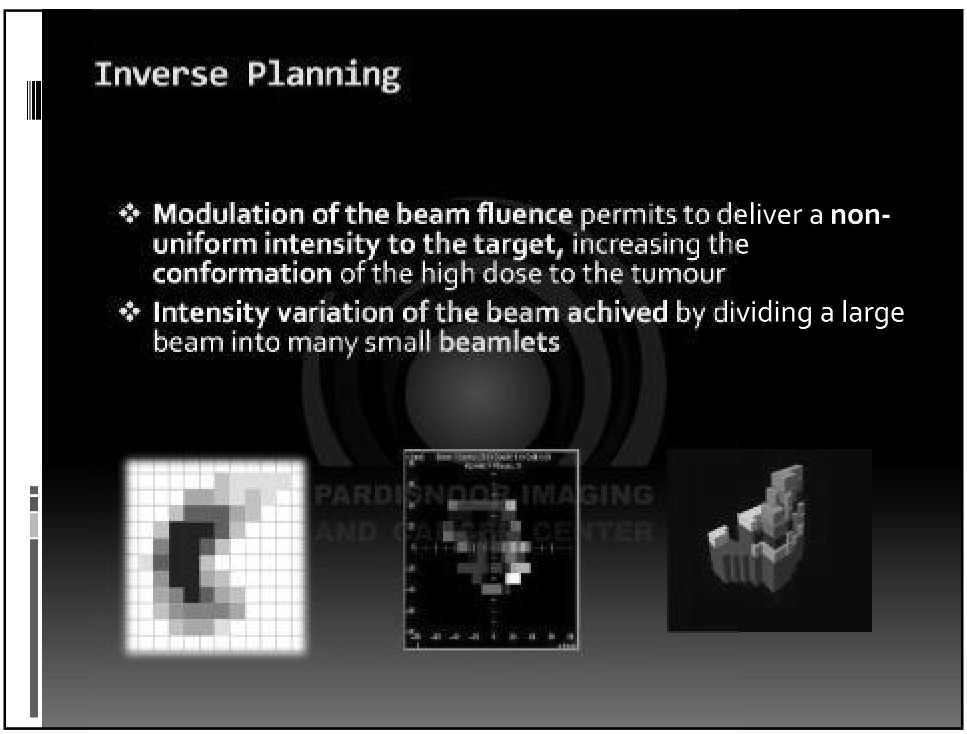

مرکز پرتو درمانی پردیس نور نیلو
PARDISNOOR NILOO RADIOTHERAPY CENTER
IMRT PRINCIPLES
PARDISNOOR IMAGING
AND CANCER CENTER
Ali Ghanbarzadeh, Ph.D,
Medical Physicist


The goal of radiotherapy
More effective and curative treatment against cancer
Improve Therapeutic Index
IMRT: tool to achieve the target
Tumor control
Complications
1.0
0
MAX. TOXICITY LEVEL
A B
Target Dose (Gy)
High doses to tumor
Lose doses to OAR


Move from….3D Conformal RT…to IMRT
Less healthy tissue irradiated → less TOXICITY
Allows DOSE ESCALATION→ more EFFECTIVE treatments
Conventional RT Beam
Uniform Beam Intensity
squares / rectangles
Conformal RT Beam
Uniform Beam Intensity
IMRT Beam
Non-Uniform Beam Intensity


Requeriments for IMRT
✓ Work together with the same OBJETIVES
✓ Workflow
✓ IMRT Integrated into the treatment phases
Accuracy
Simulation
Image registration
TC-RM –PET-TC
Dosimetry
IMRT-VMAT
Treatment delivery
IGRT


Accurate delineation
Optimal IMRT requires more accurate delineation of tumour
Additional normal tissue (OAR) often has to be delineated because structures that are not specified are not considered in the planning process.
Bases on Clinical Protocols and Contouring Guidelines
GTV, CTV contouring and margins to PTV
PARDISNOOR IMAGING
AND CANCER CENTER


Inverse Planning
Modulation of the beam fluence permits to deliver a non-uniform intensity to the target, increasing the conformation of the high dose to the tumour
Intensity variation of the beam achived by dividing a large beam into many small beamlets

Inverse Planning

- **BEAM MODULATION** based on **treatment OBJETIVES**
- **Clinical PROTOCOLS**
- **Prescription of dose and fractionation for each PTV and INTEGRATED in the same fractions**

Prescription % Volume For PTV64.5/30 70.00 % will receive 6450 cGy in 30 Fractions

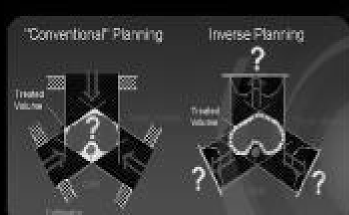
Target Objectives

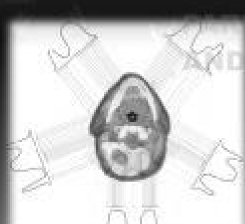
	Name	Overlap Priority	Use	Importance	Max Dose (cGy)	Max Dose Penalty	DVH Vol (%)	DVH Dose (cGy)	Min Dose (cGy)	Min Dose Penalty
	PTV64.5/30	1	✔	350	6450	100000	70.00	6450	6450	100000
	PTV 50 PHYSIC	2	✔	500	4900	100000	90.00	4900	4900	100000
	PTV 54 PHYSIC	3	✔	350	5400	10000	70.00	5400	5400	10000

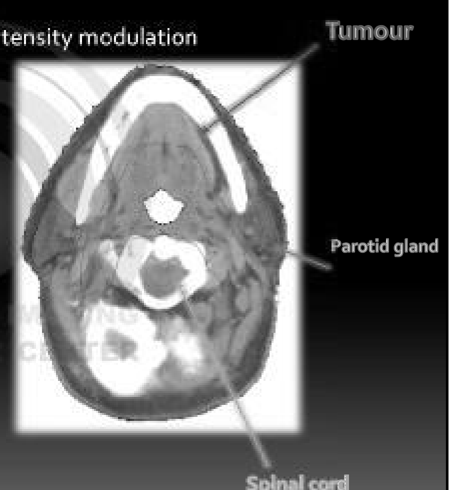
Inverse planning

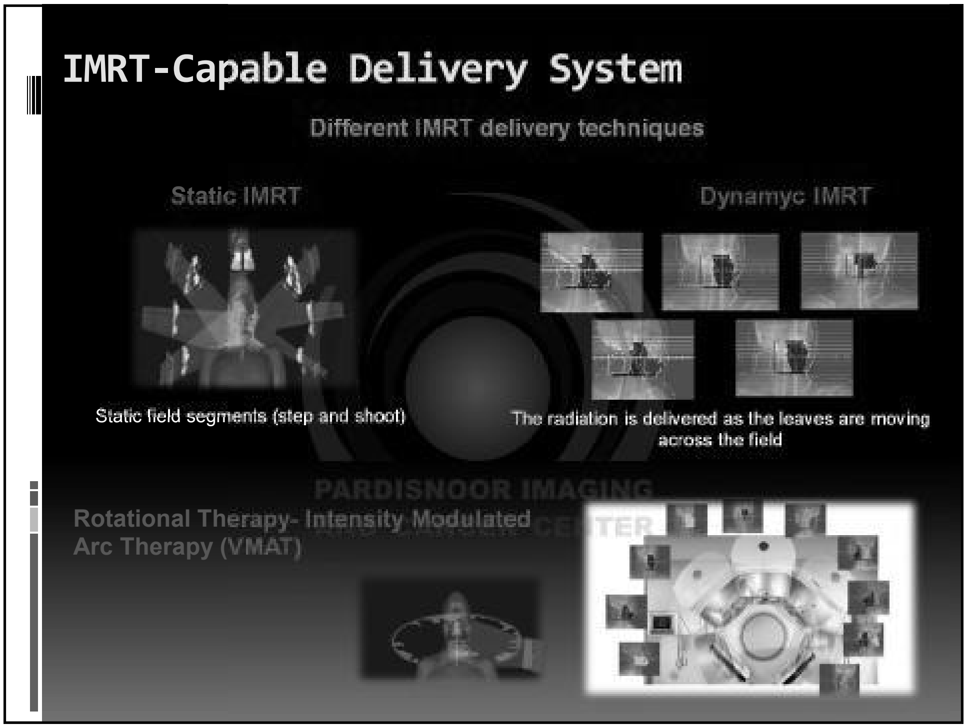
- IMRT treatment planning: careful delineation prescription of dose-volume constraints and objectives

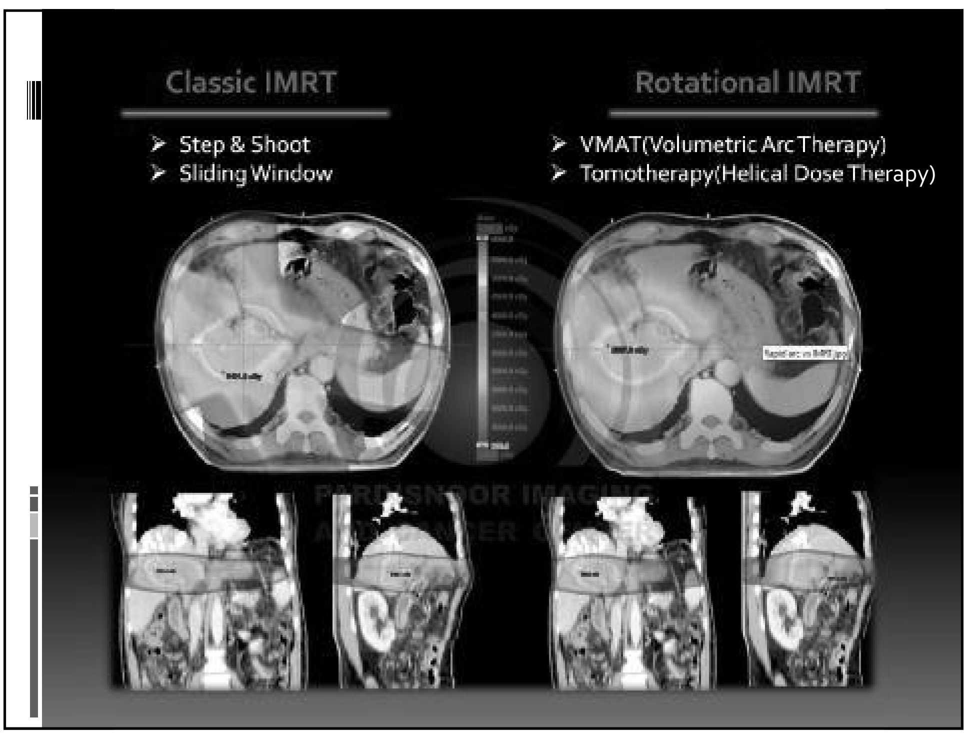
Then, the computer calculates thebeam intensity modulation





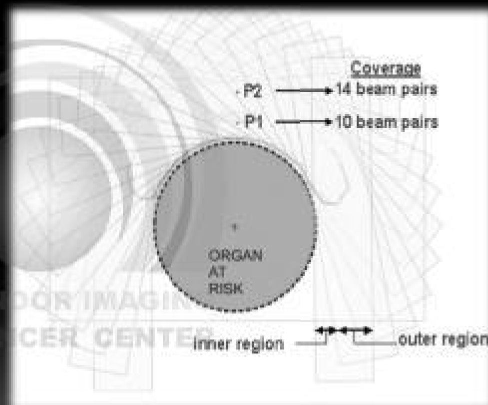



IMRT-Capable Delivery System
Different IMRT delivery techniques
Static IMRT
Dynamyc IMRT
Static field segments (step and shoot)
The radiation is delivered as the leaves are moving across the field
Rotational Therapy- Intensity Modulated Arc Therapy (VMAT)
PARDISNOOR IMAGING AND CANCER CENTER


Classic IMRT
Step & Shoot
Sliding Window
Rotational IMRT
VMAT(Volumetric Arc Therapy)
Tomotherapy(Helical Dose Therapy)

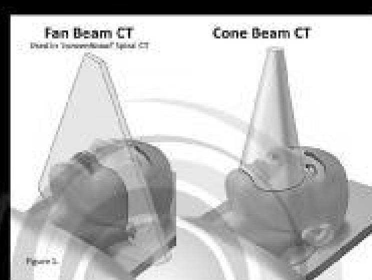
Why Arc techniques delivery ?

- Increasing field number means increasing degree of freedom
- Better conformal dose distribution (target is irradiated from many angles)
- Better OAR sparing in case of concave targets
- Faster delivery .....better efficiency
- Faster delivery.... intra-fraction movements reduction



Springer Ed. 2007

Arc IMRT techniques : Fan Beam vs. Cone Beam



Helical Tomotherapy

Dose is delivered in a continuously rotating fan-beam concomitant with couch translations

During this rotation the fluence is modulated by

- changing the field shapes (movement of MLC leaves)
- changing the beamlets weights (variation with fast binary MLC motion)

Volumetric modulated arc therapy (VMAT)

Dose is delivered in a single/multiple rotation(s) of the gantry

During this rotation the fluence is modulated by

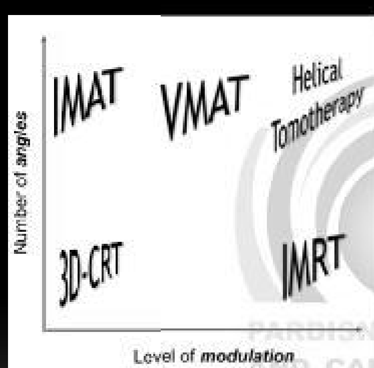
- changing the field shapes (movement of MLC leaves)
- changing the field weights (intensity variation)

Sara Broggi

Fan beam Arc IMRT: Helical Tomotherapy

- Synchronization movement between gantry rotation and longitudinal couch movement
- Continuous gantry rotation (360o) with 51 projection >> MLC shape and pattern is modified every 7o. Fastest rotation time 12 s.
- The modulation is obtained varying the fraction time in which every leaf is on/off.
- These binary MLC are designed for modulation.

VMAT vs. Helical Tomotherapy

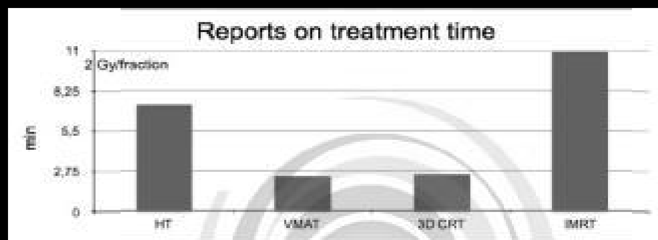


VMAT: plans quality could be improved (comparable with HT) in complex cases by increasing the arcs number and/or increasing the modulation degree (leaves/gantry speed) => **increase of treatment/delivery time**

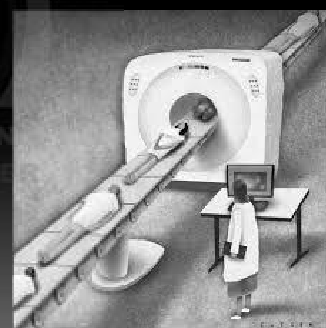
HT: treatment/delivery time could be reduced by decreasing the modulation factor => **decreasing of plan quality**

Sara Broggi

Treatment delivery times



Decreased risk of intra-faction motion with shorter treatment time



Palma et al

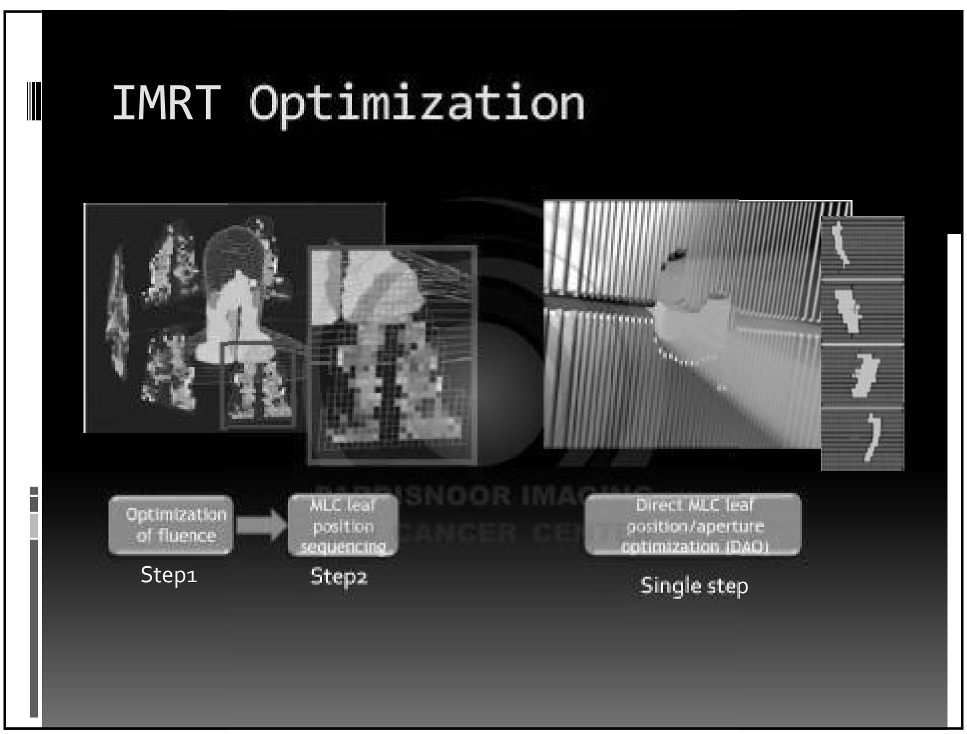
Introduction of invers planning

GOAL

- achieving a higher degree of uniform dosage for the planning target volume (PTV)
- decreasing the dose as much as possible to the organs at risk (OAR)

Optimization in IMRT
- Beam Angle Optimization
- Fluence Map Optimization
- Beam segmentation


Inverse Treatment Planning with computer optimization
FMO
BAO
BS

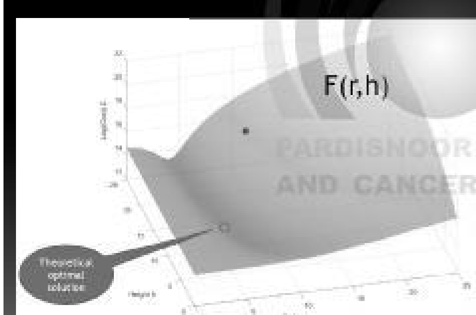

IMRT Optimization
Optimization of fluence
Step1
MLC leaf position sequencing
Step2
Direct MLC leaf position/aperture optimization (DAO)
Single step

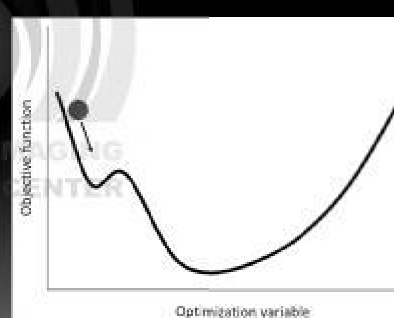
Mathematical Optimization

- An optimization problem consists of maximizing or **minimizing a real function**
- Which is performed **by systematically choosing input values** from within an allowed set and computing the value of the function

Optimization: Minimizing the Objective Function

- Virtually all algorithms use gradient information for the downhill search
- These algorithms are deterministic, so that given infinite time, they find a minimum, which is unique in the absence of delivery constraints
- The minimum sits in a flat-pan valley, the search direction is well defined, but vague in most dimensions



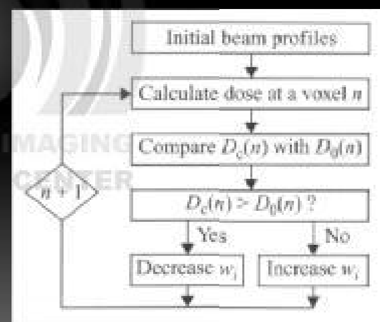


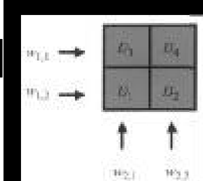
Fluence Map Optimization

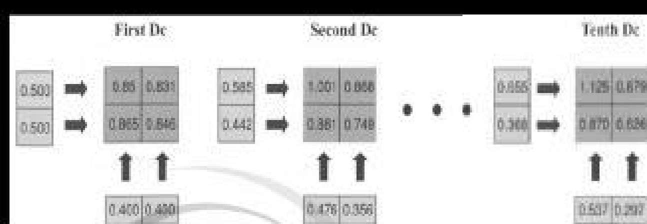
minimize F(d)
$w_{a,i}$

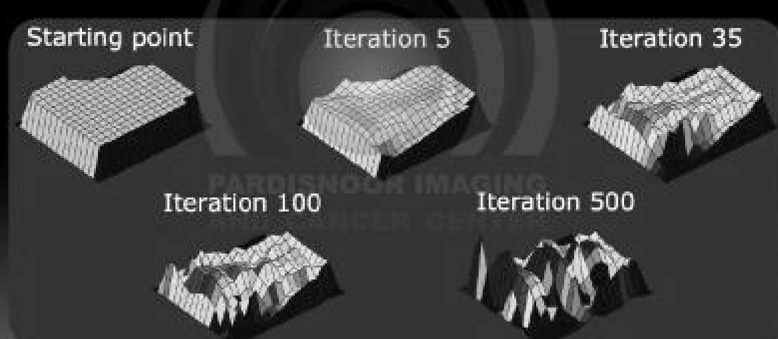
Subject to $d_p = \sum_{a \in \mathcal{A}} \sum_{i=1}^{m \times n} A_{(p,a,i)} \cdot w_{a,i}$ p=(x,y,z) $\in T \cup S \cup N$

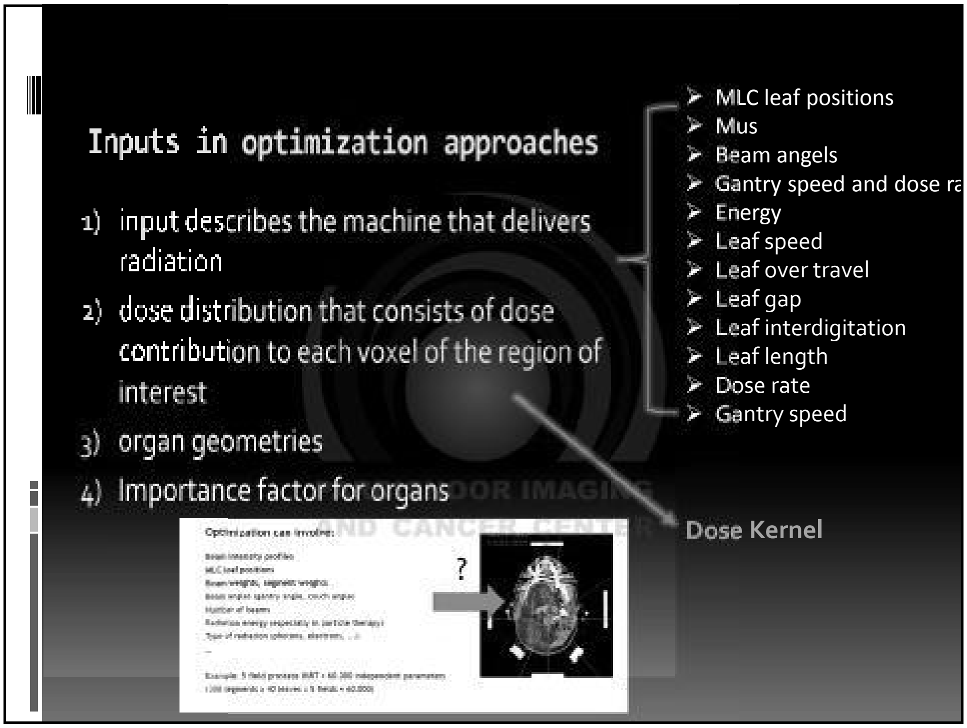
$w_{a,i} \geq 0 \quad \forall a \in \mathcal{A}$










Inputs in optimization approaches
1) input describes the machine that delivers radiation
2) dose distribution that consists of dose contribution to each voxel of the region of interest
3) organ geometries
4) Importance factor for organs
MLC leaf positions
Mus
Beam angels
Gantry speed and dose ra
Energy
Leaf speed
Leaf over travel
Leaf gap
Leaf interdigitation
Leaf length
Dose rate
Gantry speed
Dose Kernel
Optimization can involve:
?
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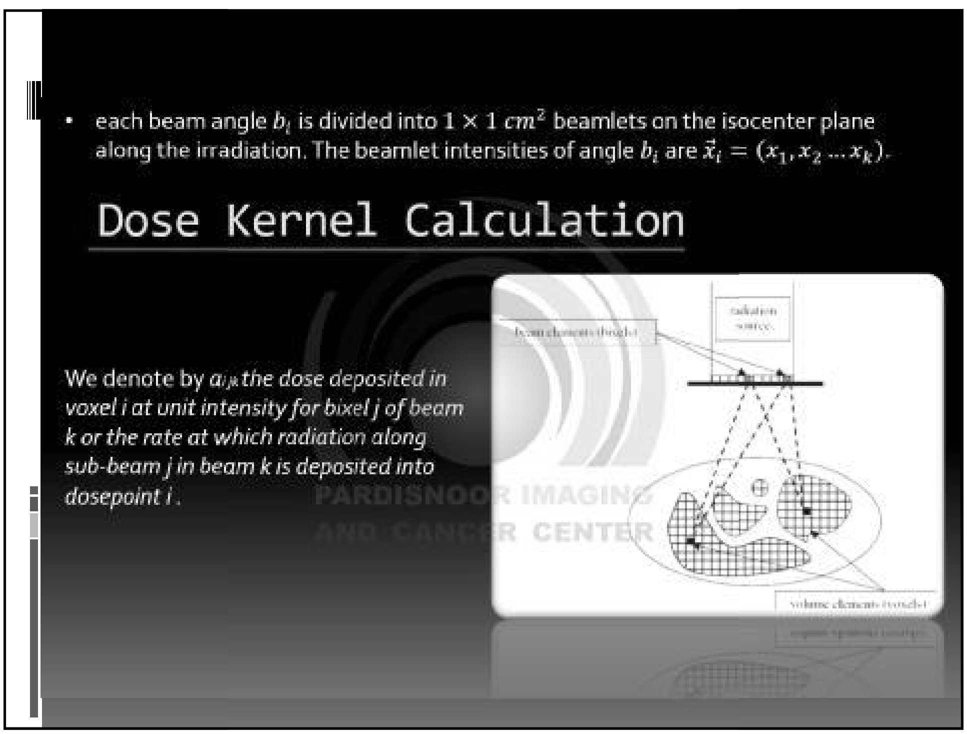
• each beam angle b_i is divided into $1 \times 1\ cm^2$ beamlets on the isocenter plane along the irradiation. The beamlet intensities of angle b_i are $\vec{x}_i = (x_1, x_2 \dots x_k)$.
Dose Kernel Calculation
We denote by a_{ijk} the dose deposited in voxel i at unit intensity for bixel j of beam k or the rate at which radiation along sub-beam j in beam k is deposited into dosepoint i.
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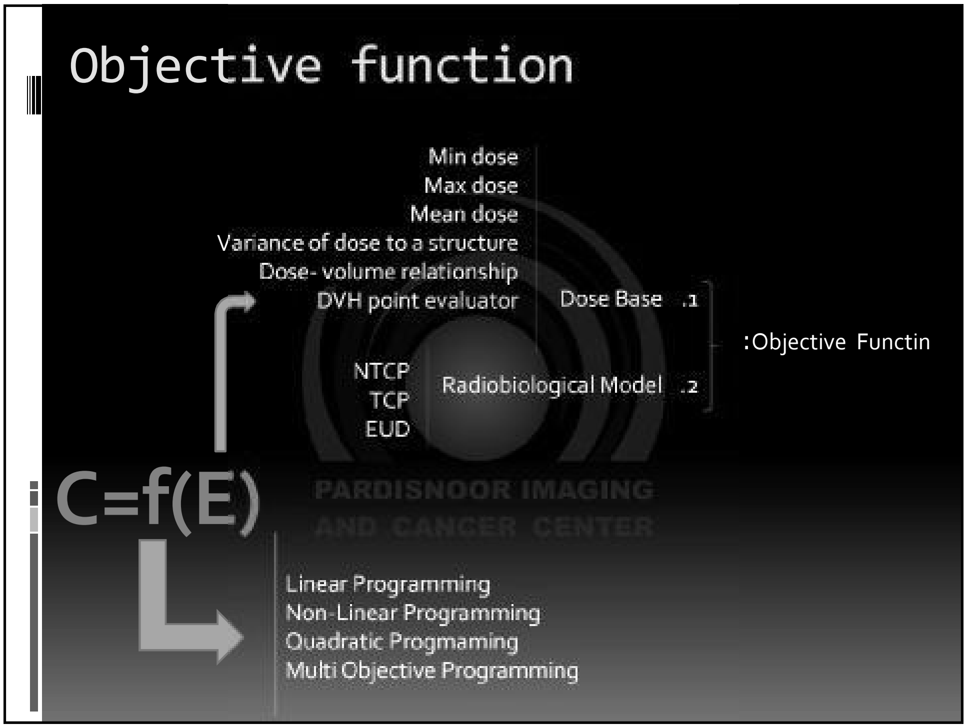
Objective function
Min dose
Max dose
Mean dose
Variance of dose to a structure
Dose- volume relationship
DVH point evaluator
Dose Base .1
:Objective Functin
NTCP
TCP
EUD
Radiobiological Model .2
C=f(E)
PARDISNOOR IMAGING
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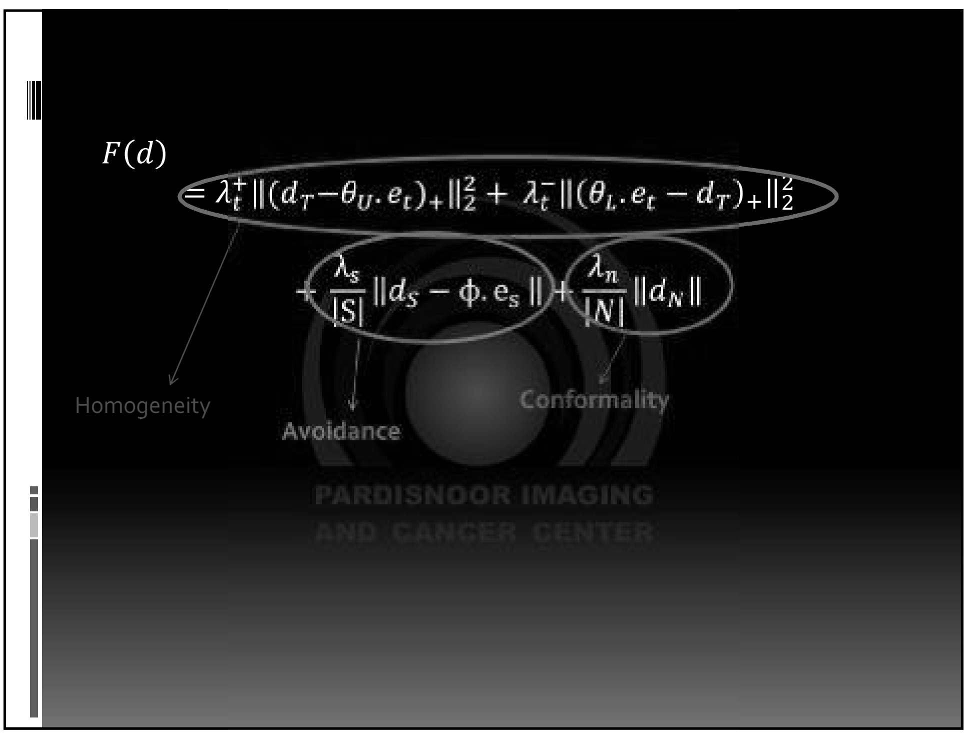
Linear Programming
Non-Linear Programming
Quadratic Progmaming
Multi Objective Programming


$F(d) = \lambda_t^{+} \|(d_T - \theta_U . e_t)_+\|_2^2 + \lambda_t^{-} \|(\theta_L . e_t - d_T)_+\|_2^2 + \frac{\lambda_s}{|S|} \|d_S - \phi . e_s\| + \frac{\lambda_n}{|N|} \|d_N\|$
Homogeneity
Avoidance
Conformality
PARDISNOOR IMAGING
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Objective Function

A quadratic objective function:

$$\min F(\vec{x}) = \sum_{i=1}^{NT_{PTV}} p_i\left(D_i(\vec{x}) - D_i^{pres}\right)^2 + \sum_{j=1}^{N_{OAR}} \sum_{i=1}^{NT_j} p_i\left[D_i(\vec{x}) - D_i^{max}\right]_+^2$$

$$\text{subject to} \quad D_i(\vec{x}) = \sum_{m=1}^{N_{ray}} K_{im} \cdot \vec{x}_m$$

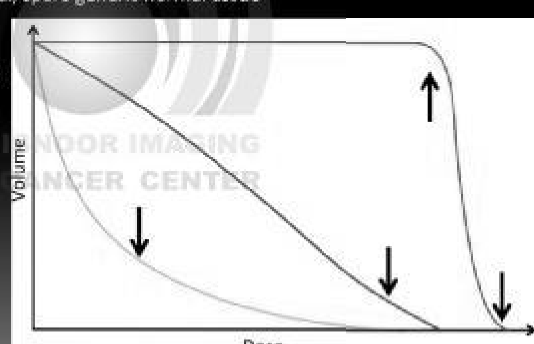
$$\vec{x}_m \geq 0$$

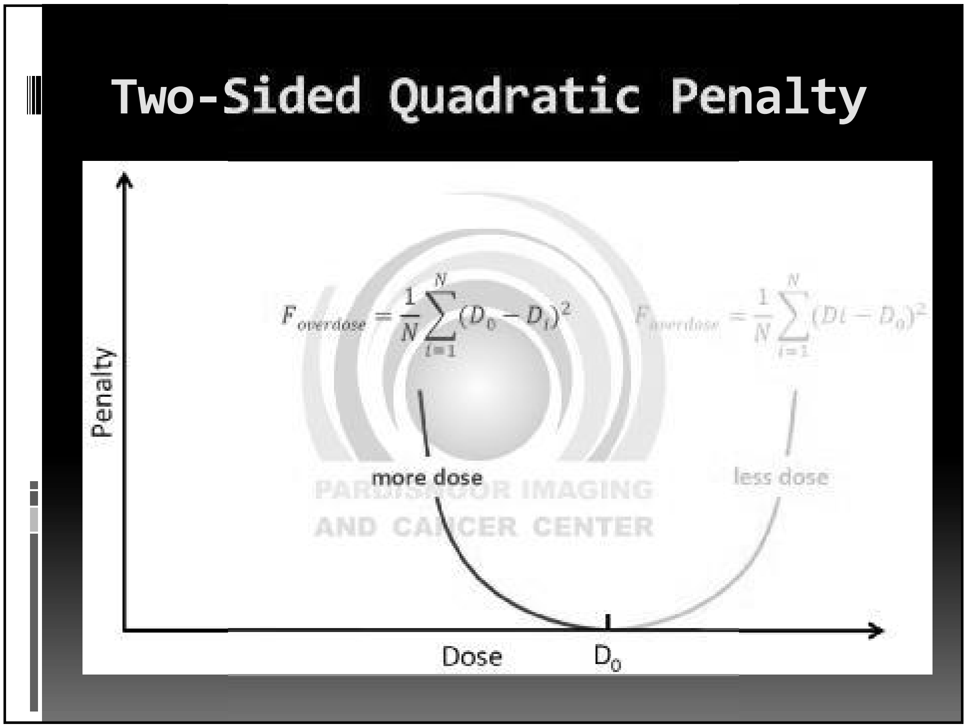
A conjugate gradient (CG) algorithm is used to solve the FMO problem in the proposed framework.

- Target Cost Function
  - Maximize minimum dose in target
- Normal tissue Cost Function
  - Minimize maximum or mean dose in OARs
- Conformality Cost Function
  - Minimize maximum dose to rings around target
- Homogeneity Cost Function
  - Minimize maximum dose in target

What Are Typical Treatment Goals?

- **Target goal**
  - Achieve a sufficient target dose
- **Normal tissue goals**
  - Do not exceed acceptable doses in OARs
- **Conformality goal**
  - Target dose should be conformal, spare generic normal tissue
- **Homogeneity goal**
  - No large or excessive hot spots in the target




Two-Sided Quadratic Penalty
$F_{overdose} = \frac{1}{N}\sum_{i=1}^{N}(D_0 - D_i)^2$
$\frac{1}{N}\sum_{i=1}^{N}(Di - D_0)^2$
Penalty
more dose
less dose
Dose
D_0
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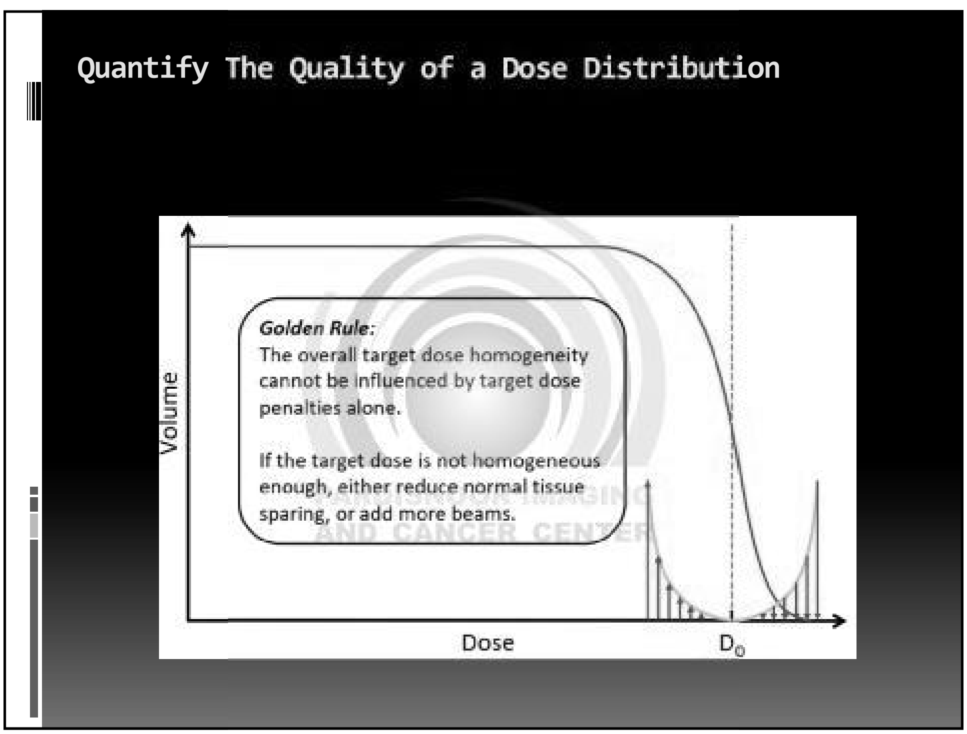
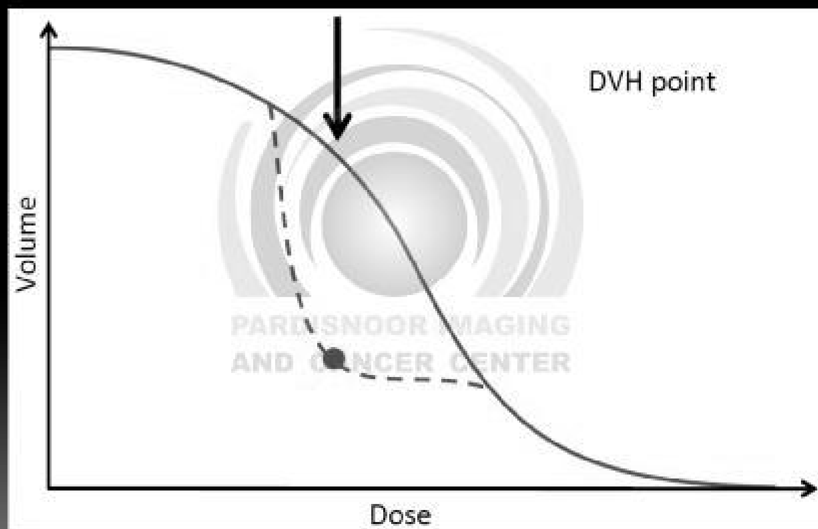
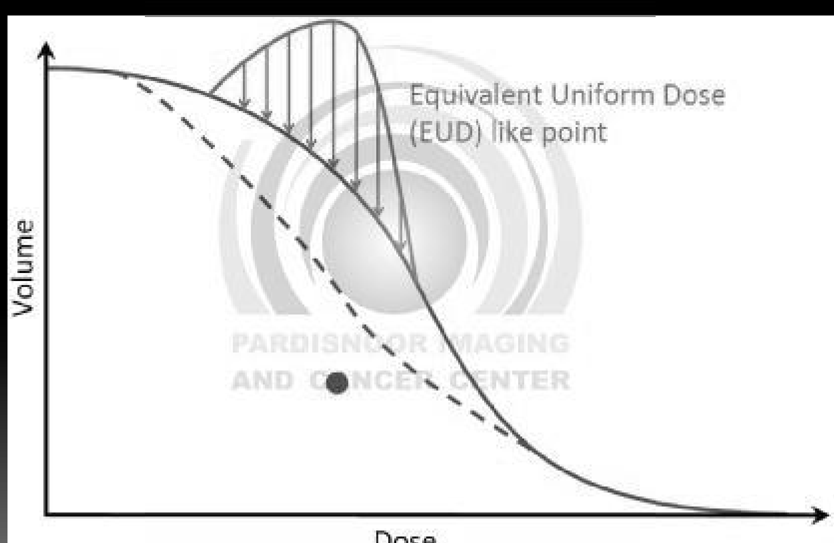

Quantify The Quality of a Dose Distribution
Golden Rule:
The overall target dose homogeneity cannot be influenced by target dose penalties alone.
If the target dose is not homogeneous enough, either reduce normal tissue sparing, or add more beams.
Volume
Dose
D_0

Dose-Volume Cost Functions: Local Effect

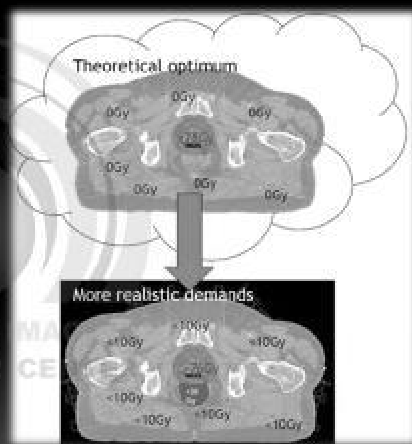


Dose-Volume Cost Functions: Local vs. Global Effect



IMRT optimization: “best” plan..?

How to communicate with a computer?



“computer has the computional power to lool through mullions of possible solutions … but which on to pick?”

“how do we define numerically what the best dose distribution/treatment plan is?”

Weighted Objective Function: Combining Cost Functions

Cost functions can be combined (or balanced) by weight factors

$$L = \sum_{i=1}^{N} \lambda_i CF_i$$

$$\sum_{i=1}^{N} \lambda_i = 1, \lambda_i \geq 0$$

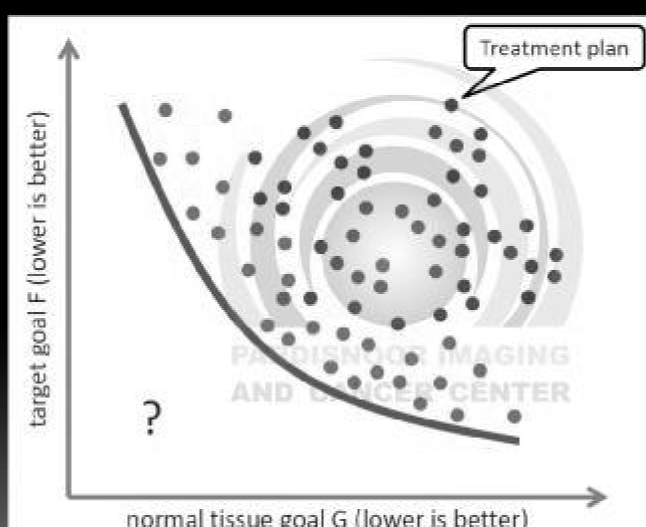
Weighted Objective Function: Combining Cost Functions

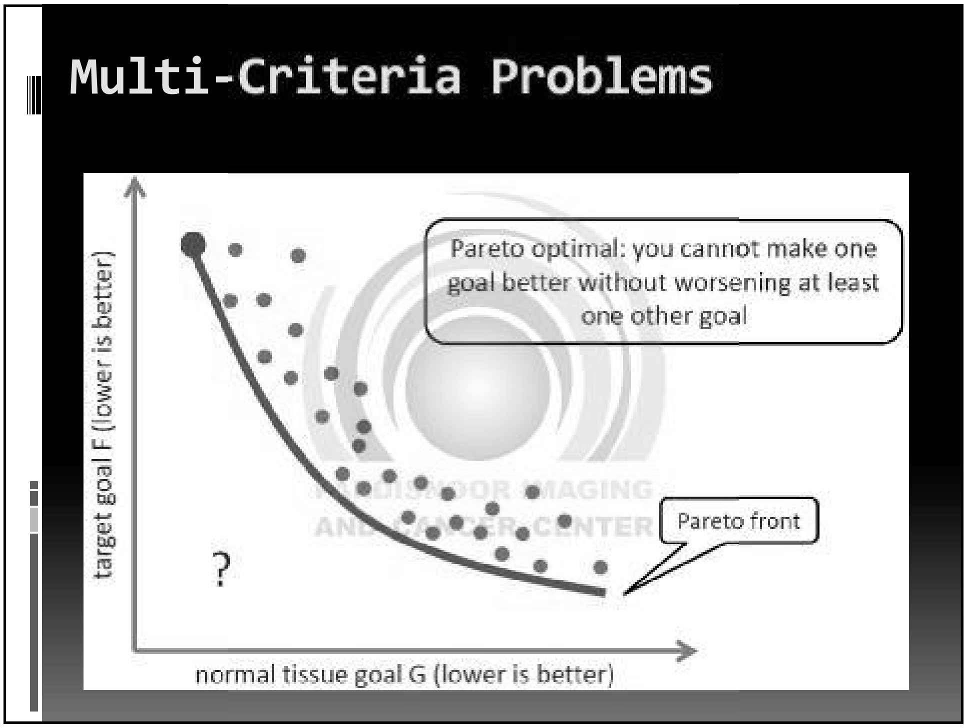
- Challenge is to find the right set of weight factors that produces a dose distribution which is ***"closest to the intended"*** treatment

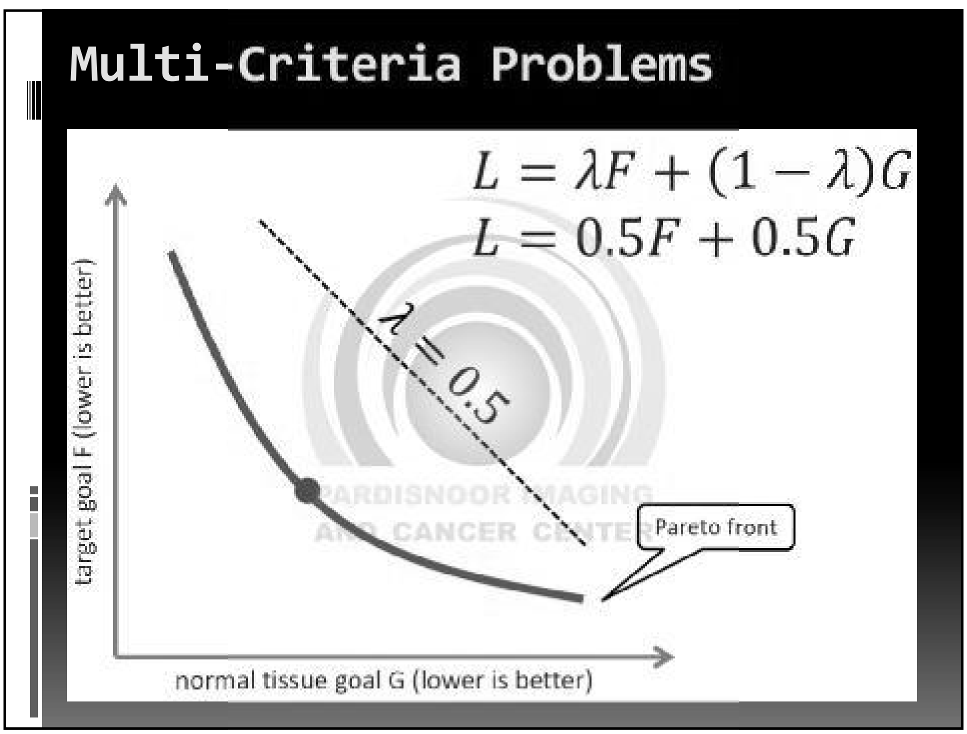
✓ **Treatment planning is finding the right objective function**

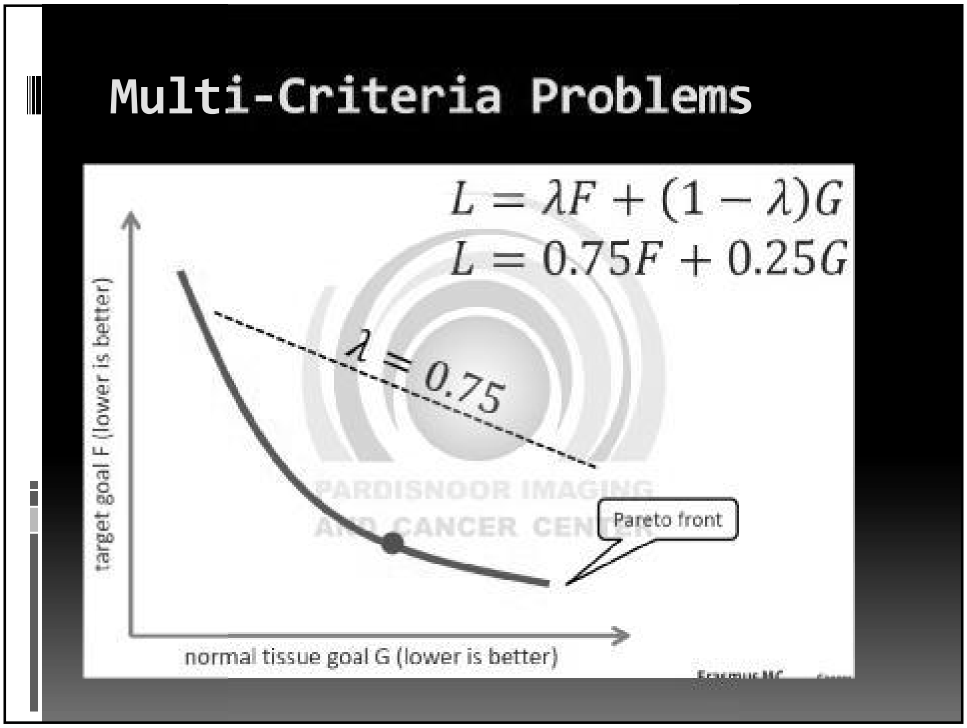
✓ **The right objective functionis patient specific**

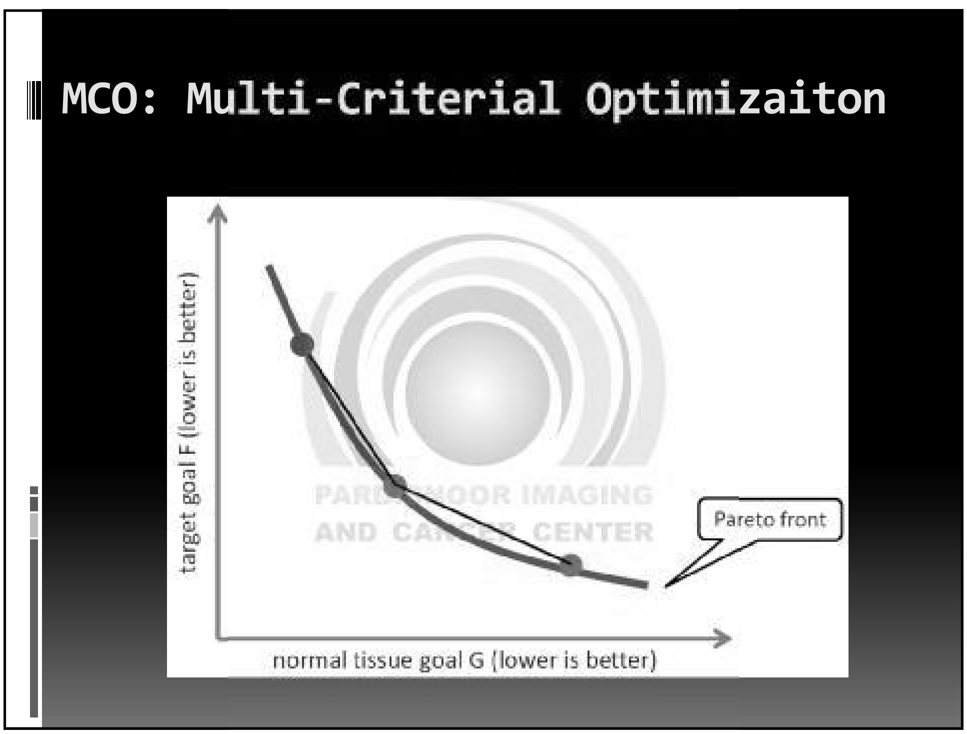
Multi-Criteria Problems

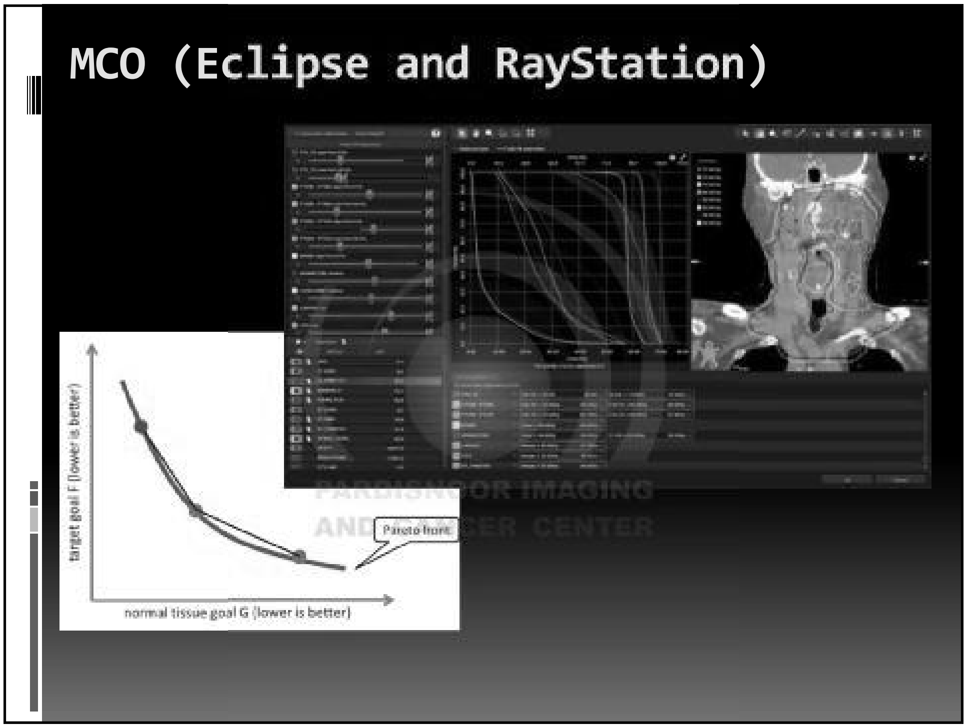


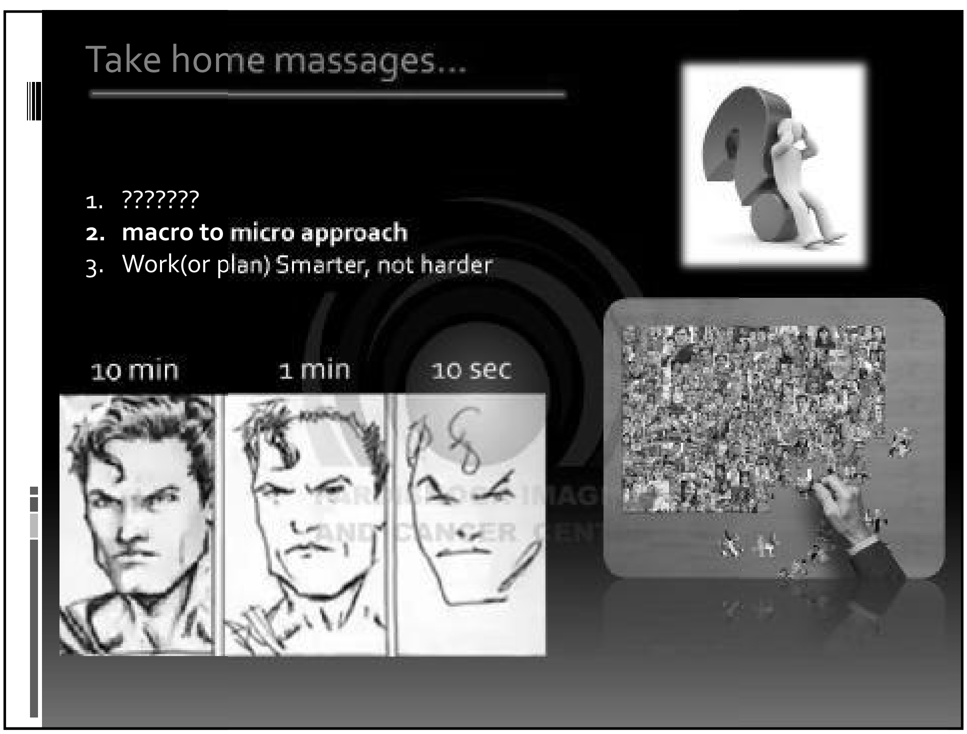

Multi-Criteria Problems
Pareto optimal: you cannot make one goal better without worsening at least one other goal
?
Pareto front
target goal F (lower is better)
normal tissue goal G (lower is better)

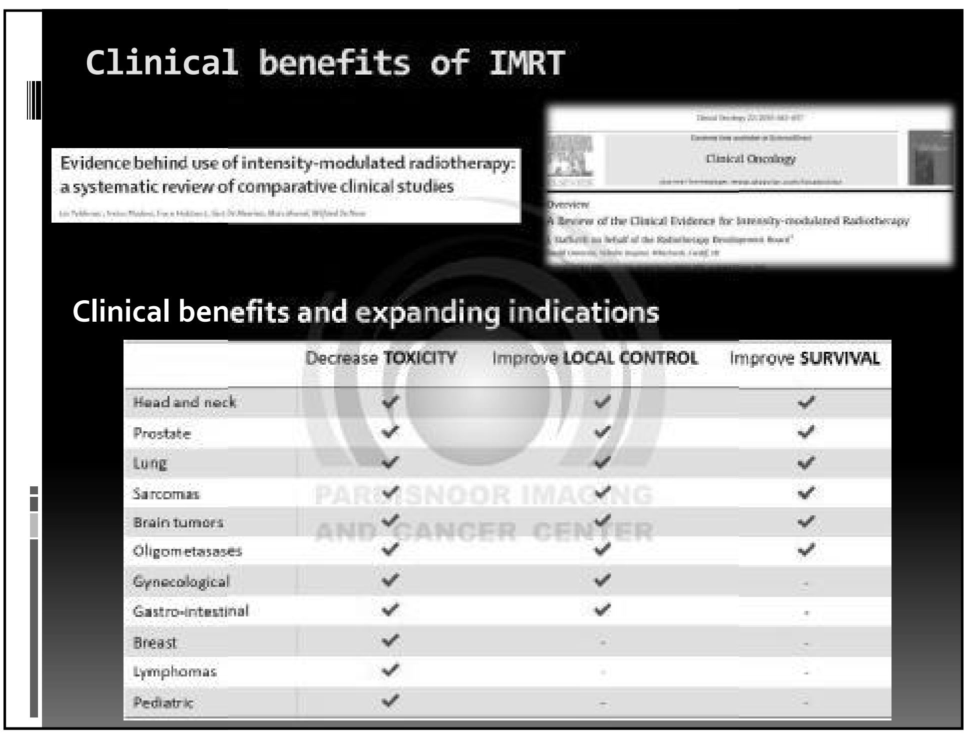

Multi-Criteria Problems
$L = \lambda F + (1 - \lambda)G$
$L = 0.5F + 0.5G$
$\lambda = 0.5$
Pareto front
target goal F (lower is better)
normal tissue goal G (lower is better)


Multi-Criteria Problems
$L = \lambda F + (1 - \lambda)G$
$L = 0.75F + 0.25G$
$\lambda = 0.75$
Pareto front
target goal F (lower is better)
normal tissue goal G (lower is better)
PARDISNOOR IMAGING AND CANCER CENTER


MCO: Multi-Criterial Optimizaiton
Pareto front
target goal F (lower is better)
normal tissue goal G (lower is better)
PARDISNOOR IMAGING AND CANCER CENTER


MCO (Eclipse and RayStation)
target goal F (lower is better)
normal tissue goal G (lower is better)
Pareto front
PARDISNOOR IMAGING
AND CANCER CENTER


Take home massages…
1. ???????
2. macro to micro approach
3. Work(or plan) Smarter, not harder
10 min
1 min
10 sec



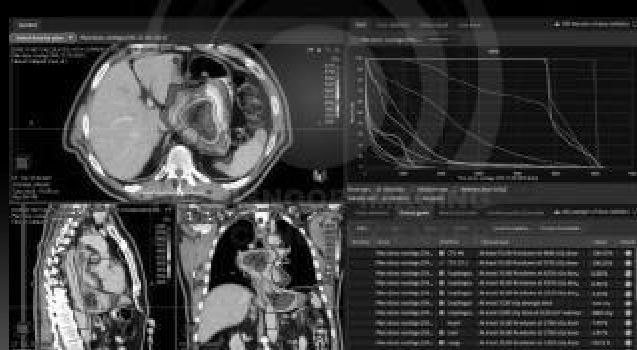
	Decrease **TOXICITY**	Improve **LOCAL CONTROL**	Improve **SURVIVAL**
Head and neck	✔	✔	✔
Prostate	✔	✔	✔
Lung	✔	✔	✔
Sarcomas	✔	✔	✔
Brain tumors	✔	✔	✔
Oligometasases	✔	✔	✔
Gynecological	✔	✔	-
Gastro-intestinal	✔	✔	-
Breast	✔	-	-
Lymphomas	✔	-	-
Pediatric	✔	-	-

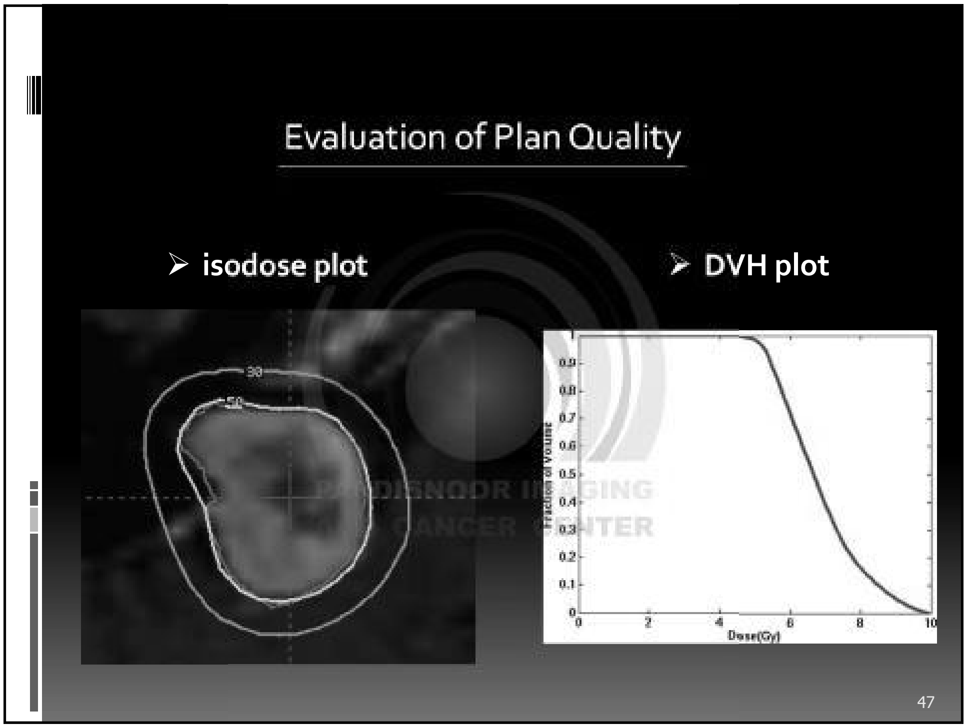
Clinical benefits of IMRT

Dose escalation, integrated boost, hypofractionation

Fracctionation	Type of Tumor	Number of fractions
Standard	Lung, GI, GU tumors, Brain... Lymphoma, Sarcomas Pediatric tumors	15-35
Boost Integrated	Head and Neck, Cervical cancer Rectum	25-30 23
Moderate +/- boost integrated	Prostate Breast Re-irradiations Brain	21 15 10-15 5-10
Extreme Hipofraccionation	Lung -Liver SBRT Prostate SBRT Pancreas SBRT	5
Extreme Hipofraccionation	Brain - SRS Spine SBRT	1

Evaluation of dose distribution and clinical goals




Evaluation of Plan Quality
➢ isodose plot
➢ DVH plot
90
50
Fraction of Volume
Dose(Gy)
PARDISNOOR IMAGING
AND CANCER CENTER
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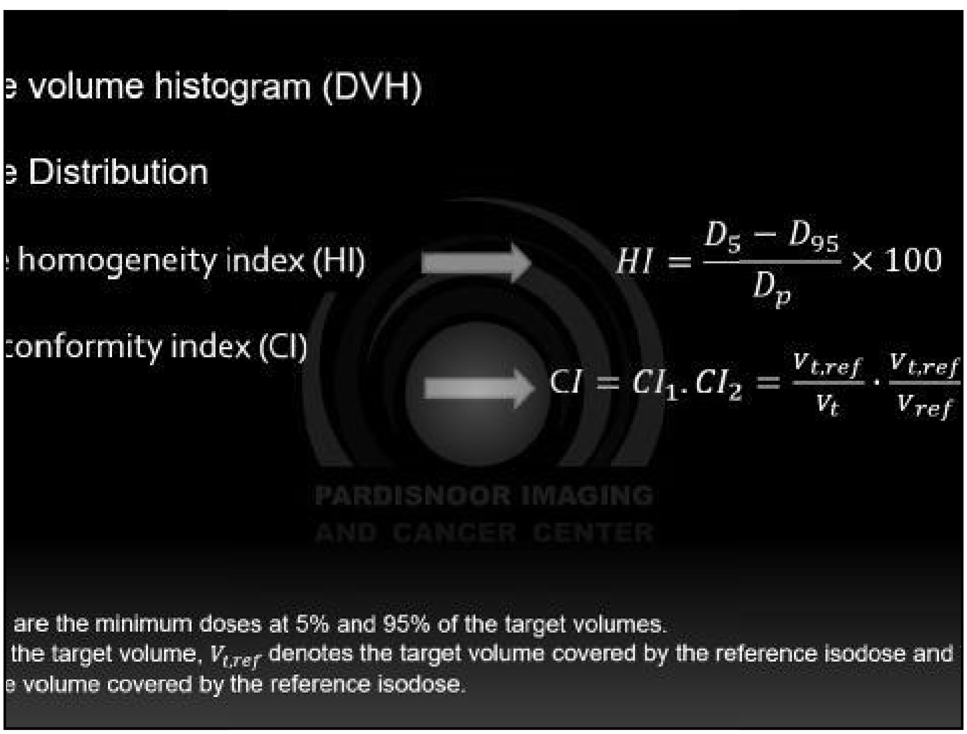
e volume histogram (DVH)
e Distribution
homogeneity index (HI)
conformity index (CI)
$HI = \frac{D_5 - D_{95}}{D_p} \times 100$
$CI = CI_1 . CI_2 = \frac{V_{t,ref}}{V_t} \cdot \frac{V_{t,ref}}{V_{ref}}$
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are the minimum doses at 5% and 95% of the target volumes.
the target volume, $V_{t,ref}$ denotes the target volume covered by the reference isodose and
e volume covered by the reference isodose.

Evaluation of Plan Quality

- **the conformity index**
- defined to score both dose conformity and target
- the conformity index as the volume of the prescription isodose surface divided by the target volume

Drawback → A plan with a complete geometric miss of the target could still give a perfect conformity index

- Lomax and Scheib have suggested a conformity index defined as "the ratio of the volume within the target irradiated to at least the prescription isodose over the total volume enclosed by the prescription isodose"
- As a planning goal, Lomax and Scheib suggest a conformity index of 0.6 or higher.

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Evaluation of Plan Quality

- **homogeneity index**
- equal to the maximum dose in the treatment volume divided by the prescription dose
- the RTOG considers a case to be per protocol if the isodose line equal to 90% of the prescribed dose completely encompasses the target

→ Lomax and Scheib suggest an alternative volumetric definition of coverage where target coverage is defined as the percentage of the target volume covered by the prescription

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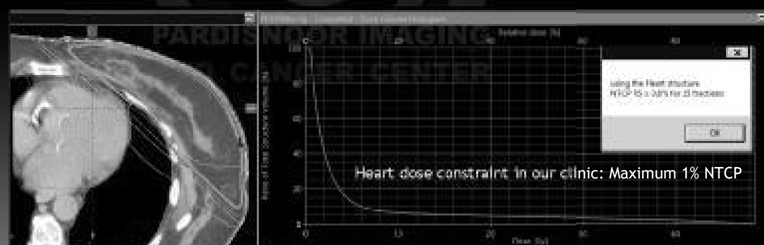
Why radiobiological model?

Currently: all tumoursof a certain type and stage prescribed the same dose

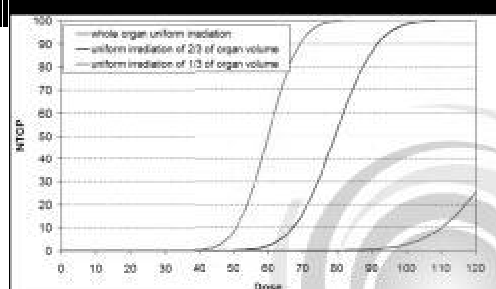
- based on perceived risk of toxicity in the population Wide variation in dose throughout the tissue
- Different anatomy = different dose distribution
- Prescription dose not a good measure of *normal-tissue complication probability* (NTCP) for an individual
- Good NTCP models could help us limit the risk for each individual

Example: Heart NTCP for breast cancer RT

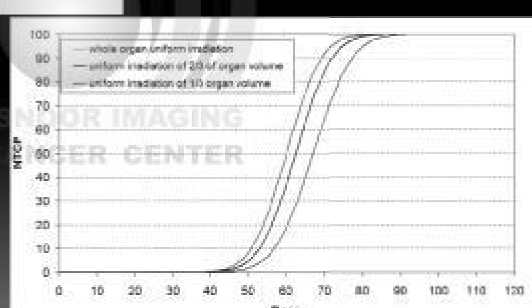


(Stockholm + Oslo): Gagliardi et al.1996

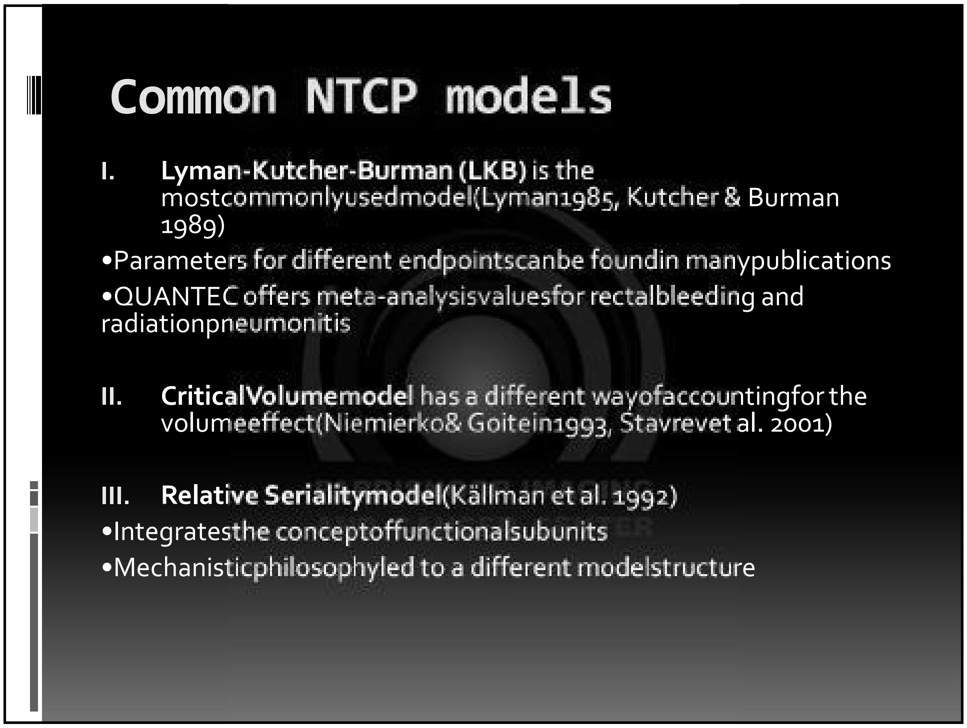
Large volume effect
Parallel organ (n = 0.7)



Small volume effect
Serial organ (n = 0.1)



Courtesy of Giovanna Gagliardi, 1991 -parameters for 28 complications Burman et al, IJROBP


Common NTCP models
I. Lyman-Kutcher-Burman (LKB) is the mostcommonlyusedmodel(Lyman1985, Kutcher & Burman 1989)
•Parameters for different endpointscanbe foundin manypublications
•QUANTEC offers meta-analysisvaluesfor rectalbleeding and radiationpneumonitis
II. CriticalVolumemodel has a different wayofaccountingfor the volumeeffect(Niemierko& Goitein1993, Stavrevet al. 2001)
III. Relative Serialitymodel(Källman et al. 1992)
•Integratesthe conceptoffunctionalsubunits
•Mechanisticphilosophyled to a different modelstructure