Clinical Implementation of IMRT

(TU-B2-01)

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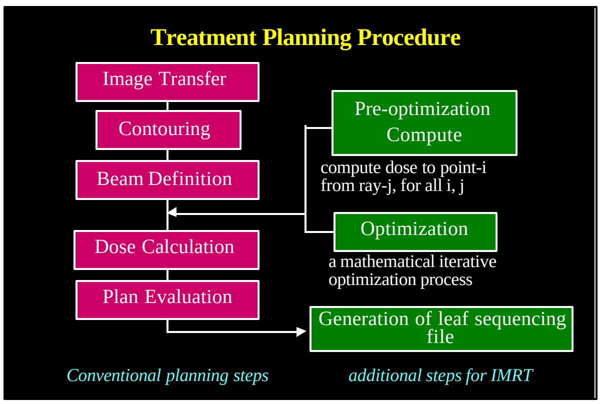
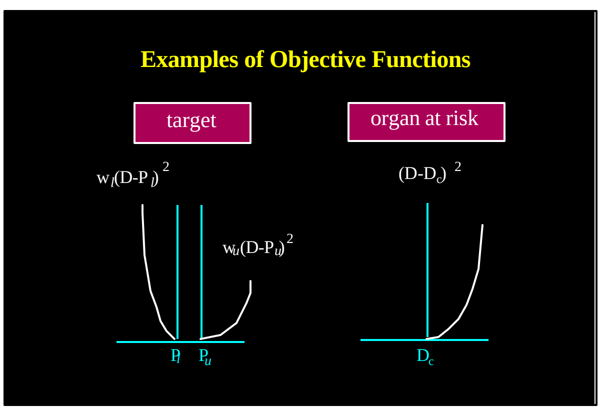
Optimization and Delivery of IMRT

- Optimization (Inverse Planning)
- Delivery
- Quality Assurance
- Radiation Safety



Objective Functions based on Dose, Dose/Volume

- Examples of commonly used objective functions:
  - target: $(D-P)^2$
  - critical organs: $(D-D_c)^2$, $(D-D_c)$ if $D>D_c$
  - dose volume conditions:
    no more than p% of the volume to exceed dose q.
- Reasonable and mathematically convenient.
- No fundamental physical basis.
- Could be any other forms such as $|(D-P)^m|$.



Objective Functions based on Biological Indices

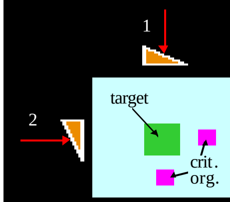
- Maximize TCP, minimize NTCPs.
- Used in place of or in conjunction with dose-, dose/volume-based objective functions.
- At present, clinical data are scarce and models not well-established yet.
- Not available on commercial system at present.

Examples of Optimization Methods

- **Deterministic:**
  - *Gradient, Conjugate gradient.*
  - *Maximum likelihood.*
- **Stochastic:**
  - *Simulated annealing.*
  - *Genetic algorithm.*

Global vs. Local Minimum

(example of local minima)



Objective Function

Uniform target dose (100% dose):
1 solution, beams 1&2 equally weighted.

Critical organs: no more than 1/2 to exceed 50% dose.
1 solution, beams 1&2 equally weighted.

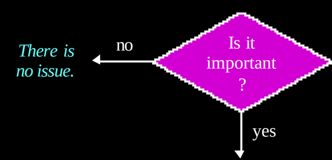
Critical organs: no more than 1/2 to exceed 10% dose.
2 solutions, beams 1&2 weighted either (a,b) or (b,a) Þ ***local minima !!***

Global Minimum

- **In Principle:**
  - *Stochastic methods can find global minimum.*
  - *Deterministic methods may get trapped in local minima.*
- **In Practice:**
  - *It is not easily known if current solution is at global or local minimum, regardless of which methods are used.*
  - *It may not be important if the solution is clinically satisfactory.*
  - *If solution not satisfactory:*
    - ý for stochastic methods: change random selection parameters (e.g.annealing schedule), increase number of iterations.
    - ý for deterministic methods: try different initial guess.
    - ý is the new solution better?

Dose Uniformity in the Target

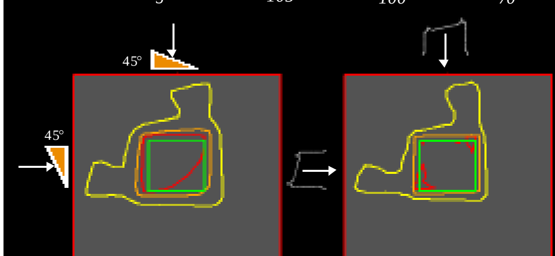
IMRT vs Conventional Conformal Plans



IMRT should do better (at least no worse), for there are more degrees of freedom.

Dose Distributions

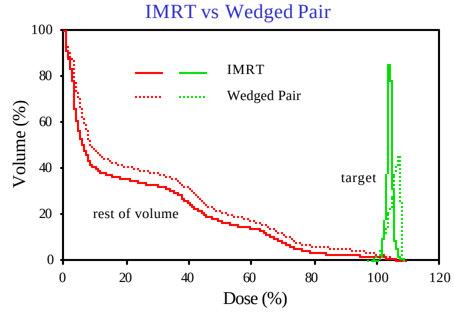
IMRT vs Conventional Conformal Plans



Wedged pair *IMRT pair*

Dose Volume Histograms

IMRT vs Wedged Pair



Nasopharynx IMRT and Conformal Plans

Beam arrangement

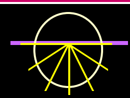
Prescription
- Gross disease: ≥70 Gy
- Micro. Disease ≥ 54 Gy
- Bid after 36 Gy

Normal tissues
- Cord, brainstem
- Mandible
- Parotids
- Temp. Lobes

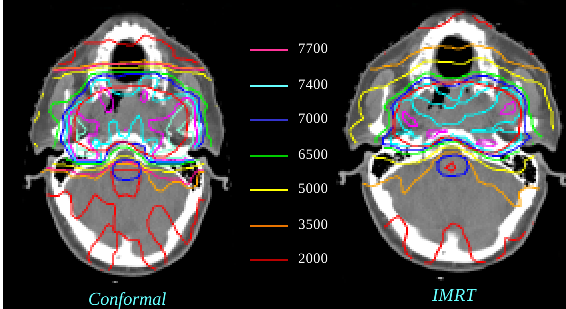
IMRT Constraints

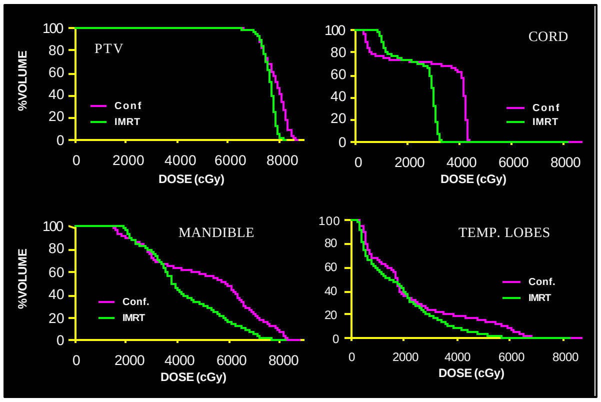
Target
Minimum: 100%
Uniformity: < 20%
Cord max: 40 Gy
Brainstem max: 45 Gy

Conformal Plan



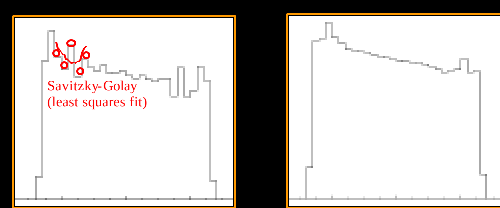
Nasopharynx Plan Comparison





1D Intensity Profiles

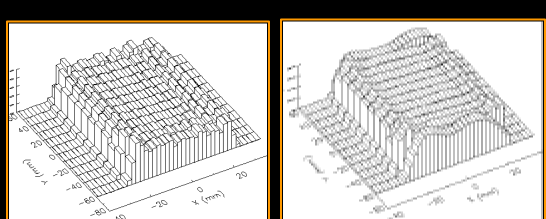
before & after smoothing



before smoothing *after smoothing*

2D Intensity Distribution

before & after smoothing



before smoothing *after smoothing*

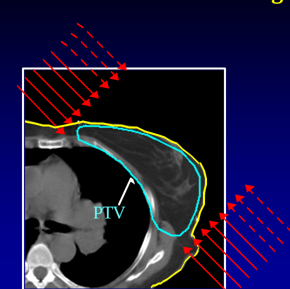
The 'Skin-Flash' Problem in Inverse Planning

Conventional:

Margin added to field edge to allow for uncertainties.

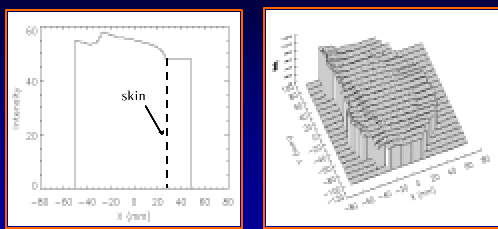
IMRT:

Intensity remains at 0 outside PTV. No skin-flash



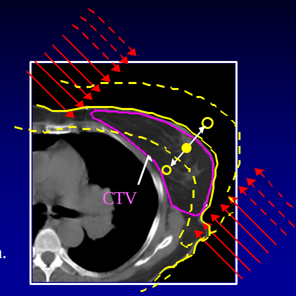
Skin-Flash for Intensity-Modulated Field

Simple, flat extension



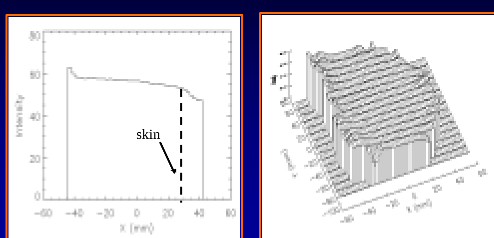
Incorporation of Uncertainties in Inverse Planning

- Each point in the region of interest *(e.g. CTV)* is split into multiple points *(typically 3)* to account for the range of uncertainties.
- Corresponding rays are brought into optimization.
- Performed in pre-optimization.



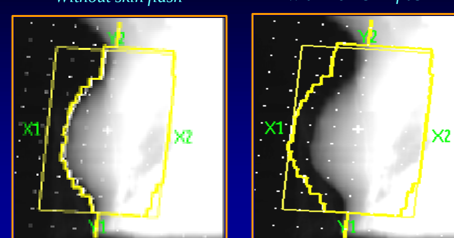
Skin-Flash for Intensity-Modulated Field

Incorporation of Uncertainties in Optimization



Beam's-Eye-View: Lateral Field

Without skin flash *With 2 cm skin flash*

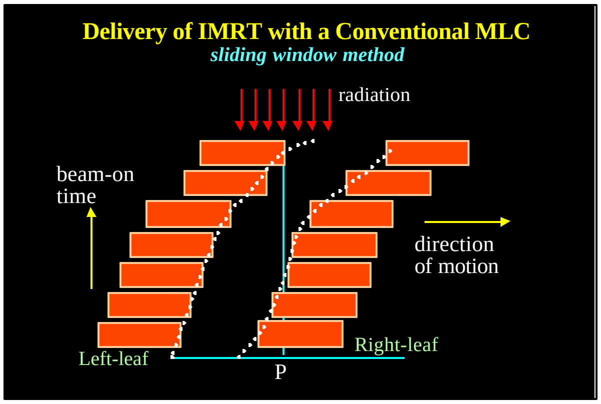


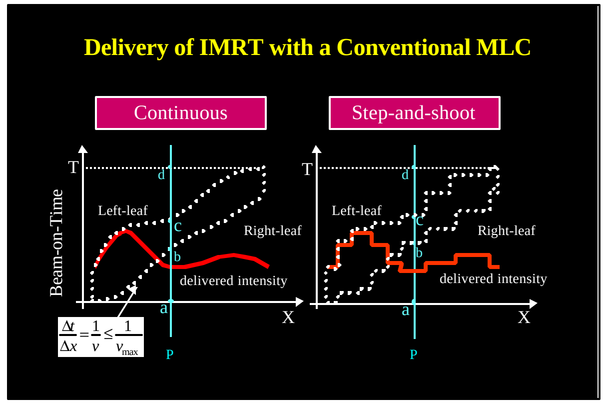
Summary - Optimization

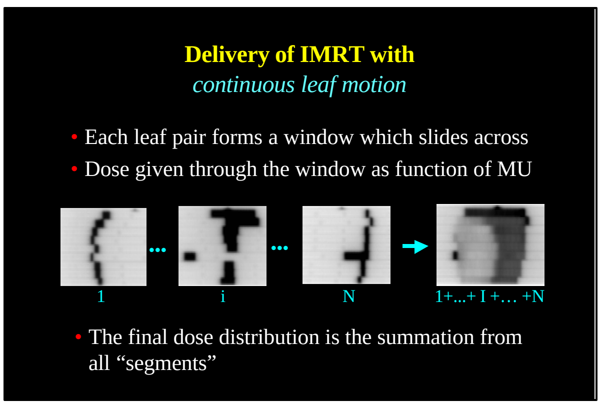
- Objective functions may be based on dose, dose/volume conditions, or biological indices.
- Optimization methods may be stochastic or deterministic.
- Local minima may exist, but there is no easy way to tell whether a solution is at a global or local minimum, *regardless of which optimization method is used*.
- Optimized intensity distribution should give better dose distribution than conventional conformal plans.
- Smoothing of intensity profiles may be useful for practical reasons.
- Other clinical considerations, such as "skin flash" problem.

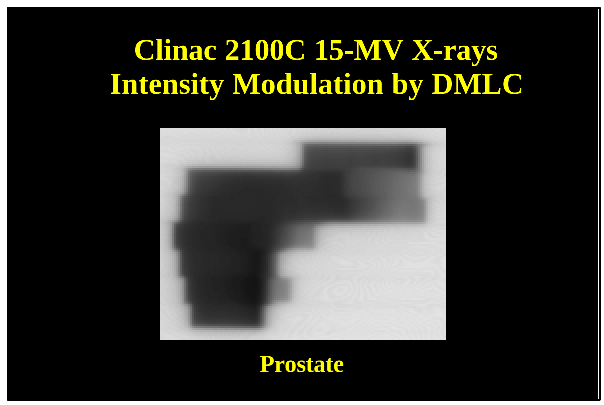
Delivery of IMRT

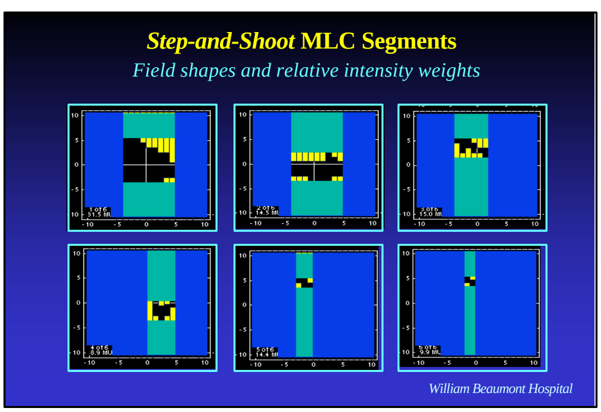
- Compensator: less efficient *(fabrication, re-entry into the room between fields).*
- Fixed field with conventional MLC:
  - *continuous leaf motion,*
  - *step-and-shoot.*
- Rotational field:
  - *conventional MLC,*
  - *NOMOS/MIMIC, Tomotherapy.*


Delivery of IMRT with a Conventional MLC
sliding window method
radiation
beam-on
time
direction
of motion
Left-leaf
Right-leaf
P


Delivery of IMRT with a Conventional MLC
Continuous
Step-and-shoot
Beam-on-Time
T
Left-leaf
Right-leaf
delivered intensity
a
b
c
d
X
P
$\frac{\Delta t}{\Delta x} = \frac{1}{v} \leq \frac{1}{v_{max}}$


Delivery of IMRT with
continuous leaf motion
• Each leaf pair forms a window which slides across
• Dose given through the window as function of MU
1
i
N
1+...+ I +… +N
• The final dose distribution is the summation from all "segments"


Clinac 2100C 15-MV X-rays
Intensity Modulation by DMLC
Prostate


Step-and-Shoot MLC Segments
Field shapes and relative intensity weights
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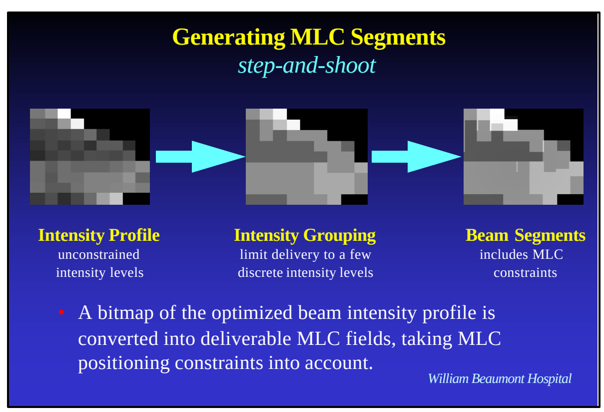
Generating MLC Segments
step-and-shoot
Intensity Profile
unconstrained intensity levels
Intensity Grouping
limit delivery to a few discrete intensity levels
Beam Segments
includes MLC constraints
• A bitmap of the optimized beam intensity profile is converted into deliverable MLC fields, taking MLC positioning constraints into account.
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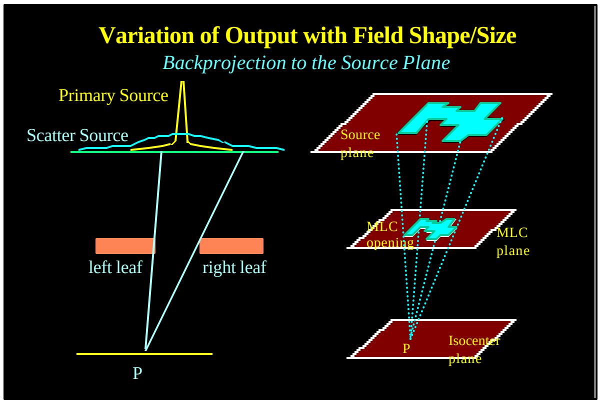
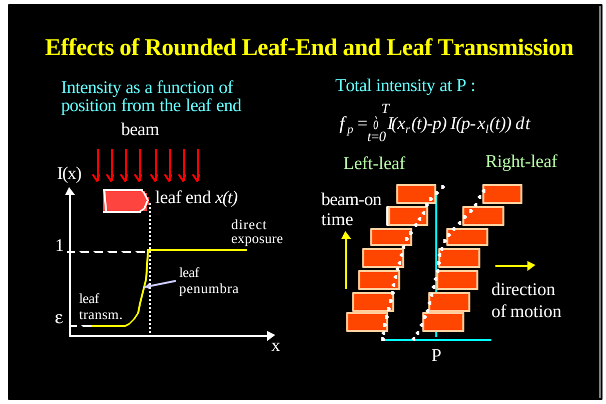
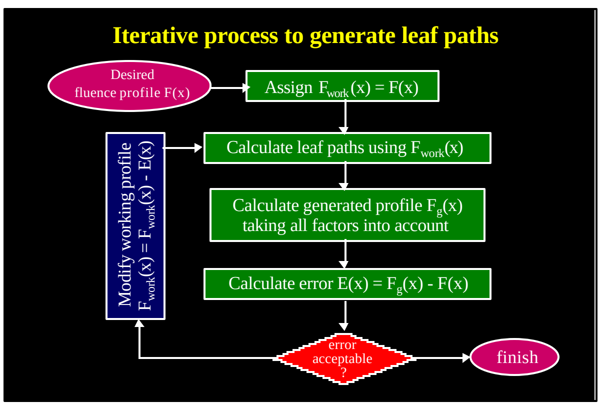
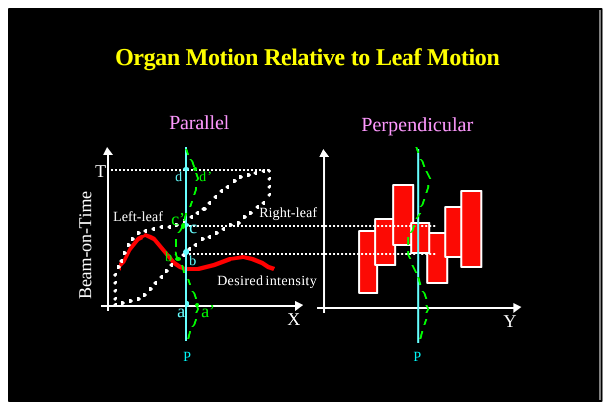
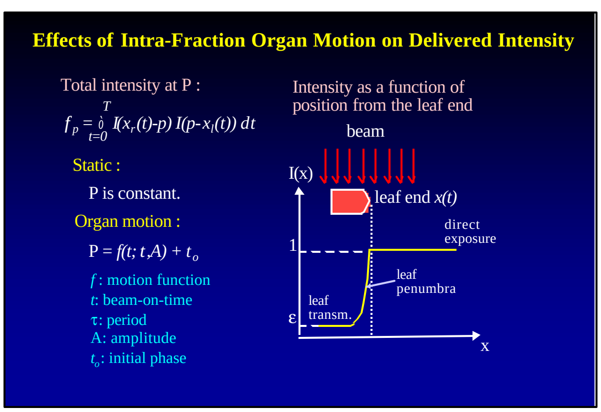
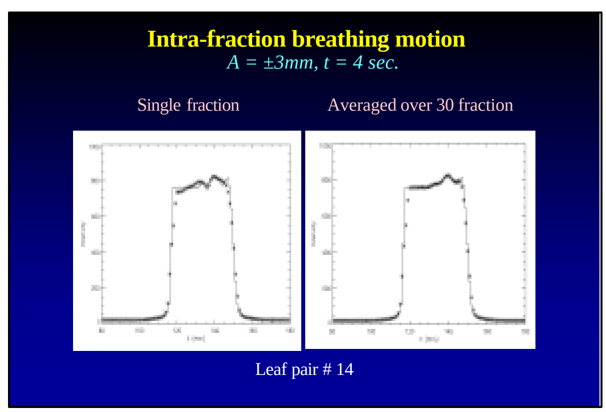

Variation of Output with Field Shape/Size
Backprojection to the Source Plane
Primary Source
Scatter Source
left leaf
right leaf
P
Source plane
MLC opening
MLC plane
P
Isocenter plane


Effects of Rounded Leaf-End and Leaf Transmission
Intensity as a function of position from the leaf end
beam
I(x)
leaf end x(t)
direct exposure
1
leaf penumbra
leaf transm.
ε
x
Total intensity at P :
$f_p = \int_{t=0}^{T} I(x_r(t)-p)\, I(p-x_l(t))\, dt$
Left-leaf
Right-leaf
beam-on time
direction of motion
P


Iterative process to generate leaf paths
Desired fluence profile F(x)
Assign $F_{work}(x) = F(x)$
Calculate leaf paths using $F_{work}(x)$
Calculate generated profile $F_g(x)$ taking all factors into account
Calculate error $E(x) = F_g(x) - F(x)$
Modify working profile $F_{work}(x) = F_{work}(x) - E(x)$
error acceptable ?
finish


Organ Motion Relative to Leaf Motion
Parallel
Perpendicular
Beam-on-Time
T
Left-leaf
Right-leaf
Desired intensity
X
Y
P
P


Effects of Intra-Fraction Organ Motion on Delivered Intensity
Total intensity at P :
$f_p = \int_{t=0}^{T} I(x_r(t)-p)\, I(p-x_l(t))\, dt$
Static :
P is constant.
Organ motion :
$P = f(t; \tau, A) + t_o$
f: motion function
t: beam-on-time
τ: period
A: amplitude
t_o: initial phase
Intensity as a function of position from the leaf end
beam
I(x)
leaf end x(t)
direct exposure
1
leaf penumbra
leaf transm.
ε
x

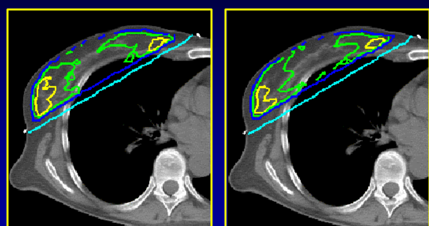

Intra-fraction breathing motion
A = ±3mm, t = 4 sec.
Single fraction
Averaged over 30 fraction
Leaf pair # 14

Intra-fraction breathing motion

A = ±3mm, t = 4 sec.

105 103 100 50

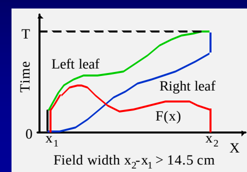
IMRT Planned IMRT Averaged over 30fx



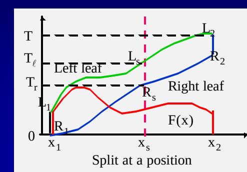
Transverse View

Splitting a Large IMRT Field

- Due to the design of MLC, the largest IMRT size that can be delivered without jaw repositioning may be limited *(e.g. 14.5 cm on the current Varian MLC).*
- The most straight forward solution is to split the field at an intermediate position X_s, but it is less efficient (T_ℓ-T_r) and prone to field matching uncertainties.



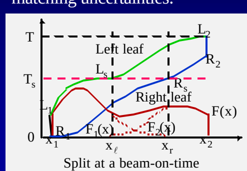
Field width x_2-x_1 > 14.5 cm



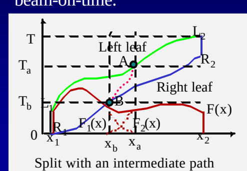
Split at a position

Splitting a Large IMRT Field (cont'd)

- The most efficient way is to split the field at an intermediate time T_s, if each segment meets the field size limitation. It is most efficient (same beam-on-time) and is insensitive to field matching uncertainties.
- Another way is to split the field at an intermediate path, with each segment satisfying the field size limitation. It provides a more general solution but is less efficient in beam-on-time.



Split at a beam-on-time



Split with an intermediate path

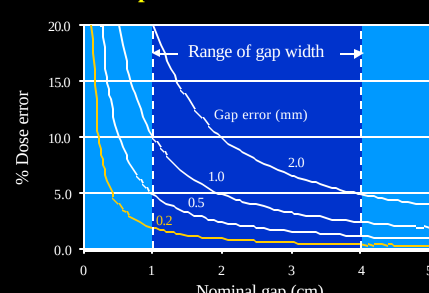
Summary - Delivery

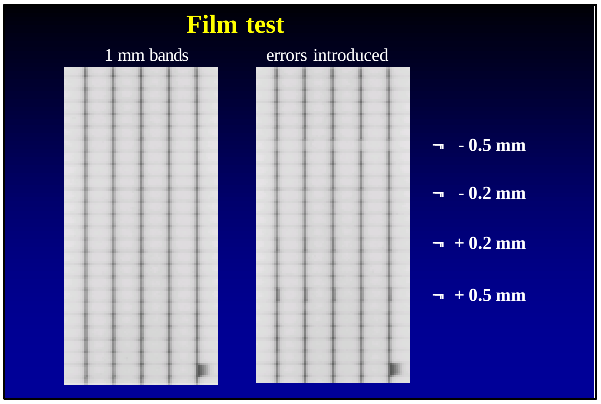
- Intensity-modulated field can be delivered with a conventional MLC, either in continuous or step-and-shoot mode.
- Need to account for leaf transmission, rounded leaf end, and head scatter.
- Increased beam-on-time comparing to conventional treatment:
  - *prostate, 2-3 times.*
  - *head & neck, 3-4 times.*
  - *breast, about the same.*
- Need to account for intra-fraction organ motion, if present: *single fraction & multiple fractions.*
- Split large field into 2 or more segments, if necessary.

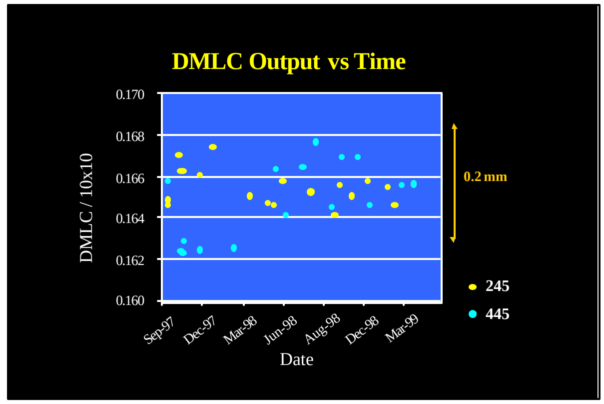
Quality Assurance

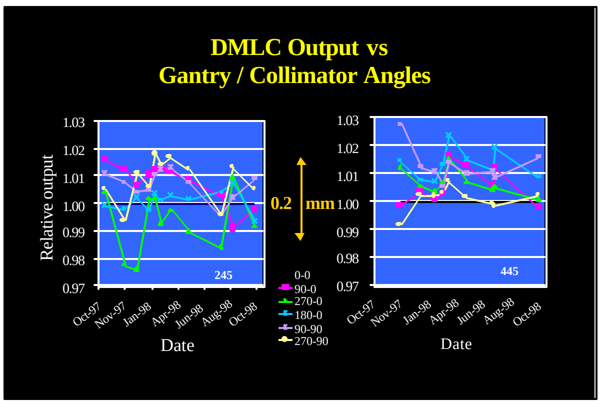
- Machine Performance:
  - Film test *(semi-weekly)*
  - Dosimetry test *(monthly)*
  - Drift test *(monthly)*
- Patient Dosimetry:
  - Record & verify, file check-sums *(each fraction)*
  - Independent MU check, portal image *(each patient)*
  - Log file analysis, chamber measurement, film dosimetry *(periodically or new technique, new site)*

Gap error ® Dose error



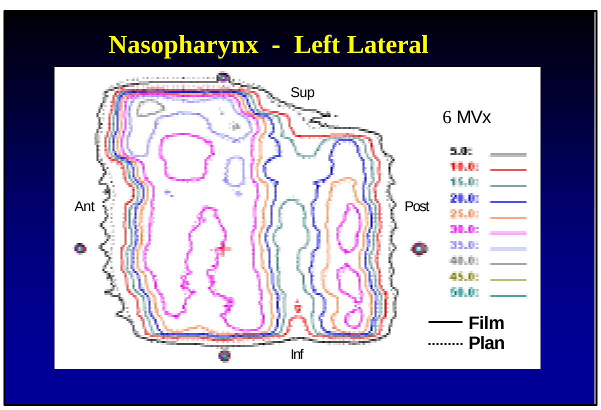


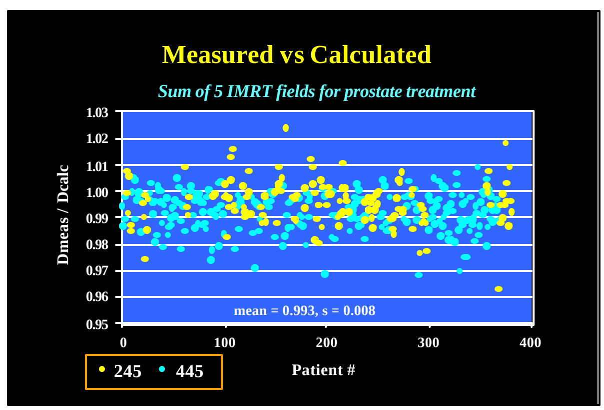




Independent Monitor-Unit (MU) Calculation

- Required by regulations, traditionally hand-calculation by the user, not part of the treatment planning system.
- For IMRT, such hand calculation is difficult. Independent program is needed to perform MU check.
- Uses the Beam-on-Time (MU) and leaf sequence file (DVA) as input, calculate dose distributions in a flat phantom.
- Takes into account rounded leaf-ends, extended source, and leaf transmission.
- Agreement between calculation & measurement, generally < 2% in dose or < 2mm
- Serves as independent check to treatment planning system.





Step-and-Shoot

Beam Stability: Dose Rate

- With *step-and-shoot* delivery, there is the potential for short irradiation times (MUs).
- Dose rate stability influences the treatment precision.
- Measure dose per MU versus total MU.
- Check short, and long term stability.
- For > 3MU, dose rate is within +/-2% (2s).

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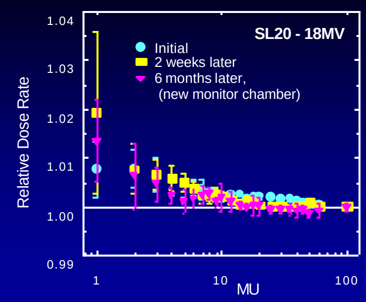
Beam Stability: Dose Rate



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Beam Stability: Flatness, Symmetry

- Stability of flatness and symmetry affects dose rate for small fields directed off the central axis.
- For an open 20x20cm^2 field, measure profiles for irradiation ranging from 1 to 100 MU.
  - Sun Nuclear Profiler (46 diodes, 10 profiles/sec).
- Flatness is less than +/-3% if more than 5MU delivered.
- Symmetry is less than +/-3% if more than 3MU delivered.

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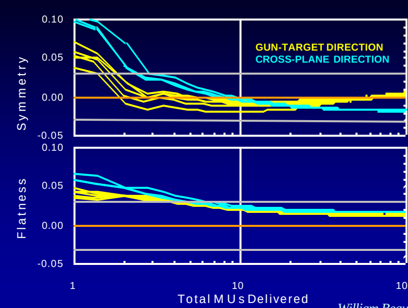
Beam Stability: Flatness, Symmetry



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Radiation Safety Considerations

• Whole Body Dose: *(for more details, see Followill et al. IJROBP.38: 667-672, 1997.)*

To estimate the total body dose delivered to patients by photons and neutrons outside the radiation fields when intensity modulated beams are used for treatment. These estimates are then used to compute the risk of induction of secondary cancers as a sequella of the radiation therapy.

• Room Shielding Requirement: *(for more details, see TU-D2-5)*

To calculate the shielding required as a result of increased beam-on-time due to delivery of intensity-modulated beams.

X-ray and Neutron whole-body dose equivalent (mSv) per unit calibration dose (cGy)

Radiation Type	*X-ray Beam Energy*		
	6 MV	**18 MV**	**25 MV**
x-ray	8.0×10^{-2}	6.5×10^{-3}	1.0×10^{-2}
neutron	0.0	4.6×10^{-2}	7.6×10^{-2}

MU/cGy to deliver conventional and modulated beam intensity radiotherapy

Beam Energy	Conventional		Beam Intensity Modulated	
	unwedged	wedged	Varian MLC	Nomos MLC
	(MU/cGy)	*(MU/cGy)*	*(MU/cGy)*	*(MU/cGy)*
6 MV	1.2	2.4	3.4	9.7
18 MV	1.0	1.5	2.8	8.1
25 MV	1.0	1.5	2.8	8.1

Total whole-body dose equivalent (mSv) for delivered dose of 7000 cGy at isocenter

	6 MV		18 MV		25 MV	
	no wedges	*wedges*	*no wedges*	*wedges*	*no wedges*	*wedges*
Conventional	67.	134.	326.	488.	602.	903.
MLC Modulated	190.	----	911.	----	1686.	----
Tomotherapy	543.	----	2637.	----	4876.	----

Estimated percent likelihood of a fatal secondary cancer due to a 7000 cGy course of IMRT

	6 MV		18 MV		25 MV	
	no wedges	*wedges*	*no wedges*	*wedges*	*no wedges*	*wedges*
Conventional	0.3%	0.5%	1.3%	2.0%	2.4%	3.6%
MLC Modulated	0.8%	---	3.6%`	---	6.7%	----
Tomotherapy	2.2%	---	10.5%	---	19.5%	----

Conclusion: Careful consideration should be made of the implications associated with secondary whole body radiation before implementation of beam intensity modulated conformal therapy using x-ray energies greater than 10 MV.

Shielding

- IMRT = relatively inefficient delivery
- New formalism required
- Evaluate
  - Primary
  - Scatter
  - Leakage
- Decouple the workload from MUs

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Primary Barrier

- Standard:
  - workload = TD = MU (50-100K/week) = dose equivalent
- DMLC
  - workload = TD (not MU) = dose equivalent
- Tomotherapy
  - workload = TD * N * F = dose equivalent
    - N = average number of indexes
    - F = fraction of arc subtended by primary beam

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Secondary Barrier

- Patient Scatter
  - Standard:
    - workload = TD = MU (50-100K/week) = dose equivalent
  - DMLC
    - workload = TD (not MU) = dose equivalent
  - Tomotherapy
    - workload = TD (not MU) * α = dose equivalent

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Secondary Barrier

- Leakage
  - Standard
    - workload = TD = MU (50-100K/week) = dose equivalent
  - DMLC
    - workload = TD * E = MU = dose equivalent
      - E = efficiency (approx 1.7)
  - Tomotherapy
    - workload = TD * N * E = MU = dose equivalent
      - N = average number of indexes
      - E = efficiency (approx 2.5)

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Neutron Shielding

- Standard
  - workload = TD = MU (50-100K/week)
- DMLC
  - workload = TD * E = MU
    - E = efficiency (approx 1.7)
- Tomotherapy
  - workload = TD * N * E = MU
    - N = average number of indexes
    - E = efficiency (approx 2.5)

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Conclusions

- Optimized IMRT plans can produce better dose distributions than conventional conformal plans, in terms of both target coverage and normal organ sparing.
- Delivery of IMRT with a conventional MLC is practical, either in continuous or in step-and-shoot mode. Delivery with MIMIC is also practical, but in general requires longer beam-on-time.
- Comprehensive QA is needed, for machine performance and patient-specific dosimetry.
- Radiation safety issues need to be considered.
- **PROCEED WITH CAUTION !**

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