Clinical Implementation of IMRT
(TU-B2-01)

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Optimization and Delivery of IMRT

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

Treatment Planning Procedure

Image Transfer
Contouring
Beam Definition
Dose Calculation
Plan Evaluation

Pre-optimization Compute
Optimization
Generation of leaf sequencing file

Conventional planning steps
additional steps for IMRT

Objective Functions

Based on Dose, Dose/Volume

- Examples of commonly used objective functions:
  - target: $(D-P)^2$
  - critical organs: $(D-D_c)^2, (D-D_D)^2$ if $D > D_D$
  - dose volume condition:
    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 $|D-P|^p$.

Examples of Objective Functions

$$w(D-P_j)^2$$

$$w(D-D_j)^2$$

$$D_j$$

$$P_j$$

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.
Critical organs: no more than 1/2 to exceed 10% dose.
2 solutions, beams 1 & 2 weighted either (a,b) or (b,a) ⇒ 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:
    - for stochastic methods: change random selection parameters (e.g., annealing schedule).
    - increase number of iterations.
    - for deterministic methods: try different initial guess.
    - is the new solution better?

Dose Uniformity in the Target
IMRT vs Conventional Conformal Plans

There is no issue.

Is it important?

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

Dose Distributions
IMRT vs Conventional Conformal Plans

IMRT vs Wedged 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**
- LATS TO 36 Gy
- Plan for 34 Gy

**Nasopharynx Plan Comparison**

**1D Intensity Profiles**
before & after smoothing

**2D Intensity Distribution**
before & 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

- Continuous sliding window method
- Beam-on time
- Direction of motion
- Left-leaf
- Right-leaf
- Delivered intensity

Delivery of IMRT with a Conventional MLC

- Continuous
- Step-and-shoot
- Beam-on time
- Left-leaf
- Right-leaf
- Delivered intensity

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
- 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

Generating MLC Segments
step-and-shoot

- Intensity Profile
- Intensity Grouping
- Beam Segments

- A bitmap of the optimized beam intensity profile is converted into deliverable MLC fields, taking MLC positioning constraints into account.
Variation of Output with Field Shape/Size

Backprojection to the Source Plane

Primary Source
Scatter Source
left leaf
right leaf
P

Primary Source
Scatter Source
left leaf
right leaf
P

Effects of Rounded Leaf-End and Leaf Transmission

Total intensity at P:
\[ \Phi = \int_{t_0}^{T} I(x_r(t)) I(p-x_l(t)) \, dt \]

Effects of Intra-Fraction Organ Motion on Delivered Intensity

Total intensity at P:
\[ \Phi = \int_{t_0}^{T} I(x_r(t)) I(p-x_l(t)) \, dt \]

Static:
P is constant.
Organ motion:
P = f(t; A) + t_o
f: motion function
r: beam-on-time
A: amplitude
t_o: initial phase

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 \( E(x) = F_g(x) - F(x) \)

error acceptable?
Modify working profile
\( F_{work}(x) = F_{work}(x) - E(x) \)

Iterative process to generate leaf paths

Effects of Intra-Fraction Organ Motion on Delivered Intensity

Static:
P is constant.
Organ motion:
P = f(t; A) + t_o
f: motion function
r: beam-on-time
A: amplitude
t_o: initial phase

Desired intensity
Parallel
Perpendicular

Intra-fraction breathing motion
\[ A = \pm 3 \text{mm}, \ t = 4 \text{ sec.} \]

Single fraction
Averaged over 30 fraction

Leaf pair # 14
Intra-fraction breathing motion

\[ A = \pm 3\text{mm}, t = 4\text{ sec.} \]

IMRT Planned \hspace{1cm} IMRT Averaged over 30fx

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 straightforward solution is to split the field at an intermediate position \( X_s \), but it is less efficient (\( T_r - T_l \)) and prone to field matching uncertainties.

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.

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)
Film test

1 mm bands
errors introduced

- 0.5 mm
- 0.2 mm
+ 0.2 mm
+ 0.5 mm

DMLC Output vs Time

Date

DMLC / 10x10
245
445

DMLC Output vs Gantry / Collimator Angles

Date

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.

Nasopharynx - Left Lateral

Sup  Post

Film  Plan

6 MVx

Data / Tests

mean = 0.993, s = 0.008

Measured vs Calculated

Sum of 5 IMRT fields for prostate treatment

Patient #
**Beam Stability: Dose Rate**

- With step-and-shoot delivery, there is the potential for short irradiation times (MU's).
- 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).

**Beam Stability: Flatness, Symmetry**

- Stability of flatness and symmetry affects dose rate for small fields directed off the central axis.
- For an open 20x20 cm² field, measure profiles for irradiation ranging from 1 to 100 MU.
- gan 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.

**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 sequela 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)**

<table>
<thead>
<tr>
<th>Radiation Type</th>
<th>X-ray Beam Energy</th>
<th>6 MV</th>
<th>18 MV</th>
<th>25 MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray</td>
<td></td>
<td>8.0 x 10⁻²</td>
<td>6.5 x 10⁻³</td>
<td>1.0 x 10⁻²</td>
</tr>
<tr>
<td>Neutron</td>
<td></td>
<td>0.0</td>
<td>4.6 x 10⁻²</td>
<td>7.6 x 10⁻²</td>
</tr>
</tbody>
</table>
Conventional Beam Intensity Modulated Beam Energy (MU/cGy) wedged Varian MLC Nomos MLC
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

<table>
<thead>
<tr>
<th>Beam Energy</th>
<th>Conventional no wedges</th>
<th>wedged</th>
<th>Tomotherapy no wedges</th>
<th>wedges</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 MV</td>
<td>67.134</td>
<td>326.488</td>
<td>190.911</td>
<td>911.1686</td>
</tr>
<tr>
<td>18 MV</td>
<td>190.543</td>
<td>2637.602.903</td>
<td>1686.19.5</td>
<td></td>
</tr>
<tr>
<td>25 MV</td>
<td>543.2637.602.903</td>
<td>2637.602.903</td>
<td>4876.19.5</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Beam Energy</th>
<th>Conventional no wedges</th>
<th>wedged</th>
<th>MLC Modulated no wedges</th>
<th>wedged</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 MV</td>
<td>0.3% 0.5%</td>
<td>1.3% 2.0%</td>
<td>2.4% 3.6%</td>
<td></td>
</tr>
<tr>
<td>18 MV</td>
<td>0.8%</td>
<td>3.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 MV</td>
<td>2.2% 10.5%</td>
<td>19.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 MU's

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
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

• 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)

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)

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!**