Coverage-based treatment planning to accommodate organ deformable motions and contouring uncertainties for prostate treatment

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Content

For prostate IMRT treatment planning,

• What are the major contributing factors to target and normal tissue coverage probability?

• What are the similarities and differences of coverage-based planning techniques?

• What are the benefits and limitations of coverage-based planning techniques?
Geometric uncertainties (GUs) in multi-fractional prostate IMRT

- **A. Setup uncertainties**
- **B. Contouring uncertainties**
- **C. Interfraction and intrafraction organ variations**

Planned geometry ≠ Treatment geometry
Conventional method to consider GUs

• Apply safety margins and use surrogate volumes
  – Expand CTV to PTV (and sometimes OAR to PRV) for treatment planning

  – Then, the planned dose to PTV / PRV is assumed to be the dose received by CTV / OAR with GUs
Conventional method to consider GUs

- Margins are usually determined empirically by the planner

Empirical margin formula, e.g., CTV-to-PTV margin = 2.5\(\Sigma\) + 0.7\(\sigma\) (van Herk 2000)
- \(\Sigma\) = quadratic sum of SD of all systematic errors
- \(\sigma\) = quadratic sum of SD of all random errors

Therefore, CTV-to-PTV margin is ~1cm for \(\Sigma = \sigma = 3\) mm

- A high target coverage + acceptable normal tissue sparing is expected
coverage probability $q$

- $q$ is the probability that $D_v \geq \text{dose } d$ for an ROI (Gordon and Siebers)
- To compute $q$, usually a large number of sampled treatment scenarios are simulated.

*Simulated “moving” CTVs:* positional and shape changes based on the mathematical model of GUs.

*Isodose surface of dose $d$:*
For prostate IMRT plans, invariant dose distribution is sufficiently accurate. (Sharma et al)

Coverage $q$ distribution of 28 prostate patients

- For all the IMRT plans
  - Same margin: 1cm PTV van Herk margin (for $\Sigma = \sigma = 3$mm)
  - Same simulated setup uncertainties:
    - $\sigma$ is always 3mm with $\Sigma = 1, 3, 5$mm, respectively

$\Sigma$ (mm)  
\begin{tabular}{c|cccc}
 & 1 & 3 & 5 & 7 \\
\hline
$q$ (%) & 100 & 80 & 40 & 20 \\
\end{tabular}

Often, the coverage probabilities ≠ the value implied by margin formula

Major contributing factor to coverage

• Geometric uncertainties vs. “Dosimetric margin (DM)”
  – where DM = CTV-to-TV margin, and “Treated volume (TV)” is the volume enclosed by a critical isodose surface (ICRU 62).

• Dependent on patient-specific anatomy and plan design such as beam arrangement.
To achieve desirable coverage for each patient,

A potential solution is ...

Using coverage probability for plan optimization
Coverage-based planning (CP)

• An approach of probabilistic treatment planning that uses **probabilistic DVH (pDVH)** criteria
  – The corresponding DVH criteria are replaced.
  – Coverage probability is repeatedly computed and optimized to generate a dose distribution that is immune to the geometric uncertainties.
pDVH

• Metrics in the format of $D_{v,q}$
  – with $D_v$ being the dose delivered to the fractional volume $v$ of a structure
  – with $q$ being probability that $D_v \geq$ the objective value

• Examples of pDVH criteria
  – CTV: $D_{98,95} \geq$ TargetDose
    • 95% probability that $D_{98} \geq$ TargetDose
  – bladder/rectum: $D_{25,5} \leq$ OarDose
    • 5% probability that $D_{25} \geq$ OarDose
    • 95% probability that $D_{25} \leq$ OarDose
DVH samples to get pDVH for current plan

• Simulate a large number of (e.g., 1000) virtual treatment courses that are sufficiently representative to all the possible GUs
• Compute dose for each fraction and accumulate dose for each treatment course
• Get e.g., 1000 DVHs for each ROI
pDVH criteria for optimization

CTV: $D_{98,95} \geq \text{TargetDose}$

- Get CTV pDVH of $q=95\%$ by connecting the Dv values below 95% CTV DVHs.
- Find $D_{98}$ on this pDVH and compare it with $\text{TargetDose}$
- If $D_{98,95} < \text{TargetDose}$, increase dose to CTV until the criterion is met
pDVH criteria for optimization

**bladder/rectum: $D_{25,5} \leq OarDose$**

- Get OAR pDVH of $q=5\%$ by connecting the $D_v$ values below $5\%$ OAR DVHs
- Find $D_{25}$ on this pDVH and compare it with $OarDose$
- Optimize the dose until $D_{25}$ is lower than $OarDose$ for at least $95\%$ cases
Two CP techniques

- Optimized margin (OM) planning
- Coverage-optimized planning (COP)
Optimized margin (OM) planning

- Adjust PTV until target pDVH criteria are met

For example:
\[ D_{98,95} \geq 78\text{Gy} \text{ (CTV}_{\text{prostate}}) \]
and
\[ D_{98,95} \geq 66\text{Gy} \text{ (CTV}_{\text{SV}}) \]

Coverage-optimized planning (COP)

- No need of PTV or PRV
- TPS optimizes “dosimetric margins” directly based on pDVH criteria

COP pDVH criteria

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTV prostate</td>
<td>$D_{98.95} \geq 78 {100}, D_{2.5} \leq 81 {50}$</td>
</tr>
<tr>
<td>CTV SV</td>
<td>$D_{98.95} \geq 66 {100}$</td>
</tr>
<tr>
<td>Bladder</td>
<td>$D_{70.5} \leq 18, D_{50.5} \leq 36, D_{30.5} \leq 57, D_{20.5} \leq 66,$</td>
</tr>
<tr>
<td></td>
<td>$D_{14.5} \leq 69, D_{9.5} \leq 75, D_{2.5} \leq 81 {10}$</td>
</tr>
<tr>
<td>Rectum</td>
<td>$D_{50.5} \leq 36, D_{30.5} \leq 51, D_{20.5} \leq 66, D_{5.5} \leq 69, D_{2.5} \leq 75 {10}$</td>
</tr>
</tbody>
</table>

COP pDVH objective functions

\[
f = \begin{cases} 
\sum_{v_n \in \text{ROI\_neighborhood}, DAPC \leq d_n \leq T_{Rx}} \omega^2 (d_n - T_{Rx})^2 & \text{(min pDVH)} \\
\sum_{v_n \in \text{ROI\_neighborhood}, O_{Rx} \leq d_n \leq DAPC} \omega^2 (d_n - O_{Rx})^2 & \text{(max pDVH)}
\end{cases}
\]

- **ROI\_neighborhood** includes all voxels with potential contribution to the coverage probability of ROI.
COP pDVH objective functions

\[ f = \begin{cases} 
\sum_{v_n \in \text{ROI\_neighborhood}, DAPC \leq d_n \leq T_{Rx}} \omega^2 (d_n - T_{Rx})^2 & \text{ (min pDVH)} \\
\sum_{v_n \in \text{ROI\_neighborhood}, O_{Rx} \leq d_n \leq DAPC} \omega^2 (d_n - O_{Rx})^2 & \text{ (max pDVH)} 
\end{cases} \]

- Voxel-specific \( \omega \)
- Optimize dose to the voxels with more significant coverage contribution in priority
COP pDVH objective functions

\[ f^* = \begin{cases} 
\sum_{v_n \in \text{ROI}_\text{neighborhood}} & (DAPC \leq d_n \leq TRx) \\
\sum_{v_n \in \text{ROI}_\text{neighborhood}} & (ORx \leq d_n \leq DAPC)
\end{cases} \omega^2 (d_n - TRx)^2 \quad \text{(min pDVH)}
\omega^2 (d_n - ORx)^2 \quad \text{(max pDVH)}
\]

Optimize ROI_neighborhood voxels with dose between \textbf{DAPC} and \textbf{TRx} (or \textbf{ORx})

\textbf{DAPC}: current dose at prescribed coverage on pDVH,
\textbf{TRx}: target dose, or \textbf{ORx}: OAR tolerance dose
Studies of COP and OM

- 19 high-risk prostate cancer patients treated by multi-fractional IMRT
  - Interfraction organ deformable motions for treatment with prostate centroid aligned
  - contouring uncertainties
Interfraction deformable motions

- Complex deformable motions are of higher dimensionality than rigid motions
- For prostate, can vary significantly during the treatment course due to differential bladder and rectal filling
- The suggested PTVs in many studies are population-based and should be used with caution for individual patient.

• The planning image

• One fractional image
Interfraction deformable motions

- In our study, DVF is used to represent ROI positional and shape changes for treatment with CTV_{prostate} centroid aligned.

- DVF is calculated based on grayscale and contour information on the patient CT images (Christensen et al).

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Principal analysis component (PCA) model

19 patients treated with prostate centroid aligned, each with 8–13 prostate CT images

Patient-specific PCA model

Input: 7-12 DVFs for one patient

In reality, a reduced number of input images or population-based data might suffice.

Output: patient-specific synthetic DVFs
Synthetic anatomy generated by PCA

Planning anatomy + Synthetic DVF = Synthetic deformed anatomy in a virtual treatment fraction simulation
CP vs. conventional planning

- **CP: COP**
  - “Dosimetric margins” generated by TPS for each patient
  - No PTV

- **CP: OM**
  - Optimized PTV margins for each patient
  - 0-10mm for prostate, 0-18mm for seminal vesicles

- **FM** (conventional technique)
  - Fixed PTV margins for all the patients:
  - 5mm for prostate and 8mm for seminal vesicles

(Mutanga et al)

Which plan is the best?

- **Primary comparison criteria**
  - $D_{98,95}$ values for $CTV_{prostate}$ and $CTV_{SV}$
Which plan is the best?

When primary metric is comparable...

- **Secondary criteria**
  - $P^+$, the probability of uncomplicated tumor control, a function of TCP and NTCP distribution for e.g., 1000 treatment courses

\[
P^+ = E[TCP_{CTV_{prostate}}] \times (1 - E[NTCP_{bladder}]) \times (1 - E[NTCP_{rectum}])
\]
Benefit of CP for organ deformable motions

- **CP techniques can produce better plans than FM**
  - Either (12/19) OM plans or (7/19) COP plans were preferred

- **The relative advantages between the three plans are patient-specific**
  - *Relative to FM plans:*
    - COP and OM plans improve up to 5% CTV $D_{98,95}$ and obtain 1-23% P+ gain
  - *COP vs. OM:*
    - In general, COP plans have higher P+ gain and OM plans improve more CTV coverage

Contouring uncertainties

- E.g., Inter-observer difference

- Are challenging regarding
  - the microscopic spread of disease
  - the inability to reproducibly distinguish tumor – normal tissue boundaries in anatomical images

- May be the dominant geometric uncertainties, when positioning and shape error components are reduced by e.g., image guidance
Contouring uncertainties

• Quantified by the deviation between the physician contoured volume and alternative possible volumes in our study.
• Use vectors $D$ for the deviations caused by inter-observer contour variability and CT image quality limitations.
Vector $D = F_{CT} \times F_{SD}$

- $F_{SD}$ (SD factor), SD of inter-observer contouring difference
  - Direction: expansion or contraction for conservative or liberal contouring
  - Magnitude follows an inverse standard normal cumulative density function,
    - mean = 0, as the average of the delineated ROI surface is assumed the best available estimate of the true ROI surfaces,
    - standard deviation in RL (x), PA (y) and SI (z) direction are listed below.

<table>
<thead>
<tr>
<th>ROI</th>
<th>SDx</th>
<th>SDy</th>
<th>SDz</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>$CTV_{prostate}$</td>
<td>1.7</td>
<td>2</td>
<td>2.5</td>
<td>van Herk, Rasch et al</td>
</tr>
<tr>
<td>$CTV_{SV}$</td>
<td>1.7</td>
<td>2</td>
<td>3</td>
<td>Fiorino et al, Deurloo et al</td>
</tr>
<tr>
<td>bladder</td>
<td>0.7</td>
<td>0.7</td>
<td>3</td>
<td>Weiss et al</td>
</tr>
<tr>
<td>rectum</td>
<td>1.3</td>
<td>1.3</td>
<td>3</td>
<td>Weiss et al</td>
</tr>
</tbody>
</table>
Vector $\mathbf{D} = \mathbf{F}_{\text{CT}} \times \mathbf{F}_{\text{SD}}$

- $\mathbf{F}_{\text{CT}}$: CT factor, a function of CT image contrast around ROI boundary

2D D vector field with vector magnitude $= \mathbf{F}_{\text{CT}}$
CP vs. conventional planning

• **CP: COP**
  – “Dosimetric margins” generated by TPS for each patient
  – No PTV

• **CP: OM**
  – Optimized PTV margins for each patient
  – 2-5mm for prostate, 0-4mm for seminal vesicles

• **FM (conventional technique)**
  – Fixed PTV margins for all the patients:
    – $PTV_{\text{Prostate}} = 4,5,6\text{mm}$, $PTV_{\text{SV}} = 4,5,7\text{mm}$ for RL, PA, SI directions (based on van Herk margin formula)
Benefit of CP for contouring uncertainties

- **CP techniques can produce better plans than FM**
  - Either (7/19) OM plans or (11/19) COP plans were preferred

- **The relative advantages between the three plans were patient-specific**
  - *Relative to FM plans:*  
    - COP and OM plans improve up to 3.5% CTV $D_{98.95}$ and obtain 1-22% P+ gain
  - *COP vs. OM:*  
    - In general, COP plans have higher P+ gain and OM plans has better CTV coverage
Benefit of CP

- Right table, monitor units per fraction of COP, OM, FM plans for 19 patients
- CP plan delivery complexity does not get increased significantly.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Interfraction deformable motions</th>
<th>Contouring uncertainties</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID</td>
<td>COP</td>
<td>OM</td>
</tr>
<tr>
<td>1</td>
<td>483</td>
<td>-3%</td>
</tr>
<tr>
<td>2</td>
<td>448</td>
<td>6%</td>
</tr>
<tr>
<td>3</td>
<td>636</td>
<td>-1%</td>
</tr>
<tr>
<td>4</td>
<td>531</td>
<td>-2%</td>
</tr>
<tr>
<td>5</td>
<td>489</td>
<td>0%</td>
</tr>
<tr>
<td>6</td>
<td>401</td>
<td>-1%</td>
</tr>
<tr>
<td>7</td>
<td>406</td>
<td>-1%</td>
</tr>
<tr>
<td>8</td>
<td>361</td>
<td>3%</td>
</tr>
<tr>
<td>9</td>
<td>440</td>
<td>16%</td>
</tr>
<tr>
<td>10</td>
<td>537</td>
<td>1%</td>
</tr>
<tr>
<td>11</td>
<td>478</td>
<td>7%</td>
</tr>
<tr>
<td>12</td>
<td>565</td>
<td>-1%</td>
</tr>
<tr>
<td>13</td>
<td>555</td>
<td>-2%</td>
</tr>
<tr>
<td>14</td>
<td>541</td>
<td>-2%</td>
</tr>
<tr>
<td>15</td>
<td>434</td>
<td>-2%</td>
</tr>
<tr>
<td>16</td>
<td>441</td>
<td>-1%</td>
</tr>
<tr>
<td>17</td>
<td>552</td>
<td>-1%</td>
</tr>
<tr>
<td>18</td>
<td>476</td>
<td>1%</td>
</tr>
<tr>
<td>19</td>
<td>405</td>
<td>0%</td>
</tr>
</tbody>
</table>

Avg.±SD(MU) 483±71 486±20 490±12 518±80 464±57 497±61
One limitation of current CP

- Sometimes, the tradeoff between CTV and OAR may not be balanced optimally.
  - For example, COP plans may fail \( \text{CTV}_{\text{prostate}} \) or \( \text{CTV}_{SV} \) coverage objective:
    - 4/19 plans, by >5% for interfraction deformable motions
    - 3/19 plans, by up to 3.5% for contouring uncertainties
Future work of CP techniques

- Optimization of the objective function weights (CTV vs. OAR) on a patient-specific basis may be desirable...

<table>
<thead>
<tr>
<th>Optimization criteria for $CP_{COP}$ plans</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTV$_{prostate}$</strong></td>
</tr>
<tr>
<td><strong>CTV$_{SV}$</strong></td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
</tr>
</tbody>
</table>
Other limitations of CP

- Optimization time is longer
  - Approximately, COP 4hr vs. OM 1hr vs. FM 10min
- May potentially introduce uncertainties
  - Representativeness of the mathematical model of geometric uncertainties
  - Deformable image registration
  - Sampling of treatment scenarios
  - Any involved approximation ...
- Therefore, more researches are needed.
Summary

• Coverage probability is a function of geometric uncertainties and dosimetric margin between ROI and treated volume. Coverage probability depends on the patient individual anatomy and plan design.

• CP, a PTP approach, is characteristic with pDVH criteria.
  – OM optimizes PTV based on CTV pDVH criteria
  – COP does away PTV/PRV and uses pDVH criteria for both CTVs and OARs.
Summary

Based on the studies for interfraction deformable motions and contouring uncertainties for prostate patients

• With similar plan complexity, both CP techniques (COP and OM) generate better plans than conventional planning using fixed PTV.
• The benefit of CP is patient-specific, some in target coverage, others in OAR sparing.
• The limitations of CP (e.g., tradeoff, time and potential uncertainties) call for more researches.
Thank you for your attention!