Strengthened Relaxations and Algorithms For Radiation Therapy Optimization Under Dose-Volume Restrictions

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Outline/Summary

- Radiation Therapy is a common treatment procedure for many types of cancer.
- Stages of Radiation Therapy Planning include:
  - Selection of beam angles.
  - Determination of beam/beamlet intensities through Fluence Map Optimization (FMO).
  - Segmentation.
- *Dose-Volume Restrictions* specify a tissue volume percentage and a dose limit to be applied to that percentage of the tissue volume.
  - Introduce a difficult combinatorial structure to FMO problems.
  - FMO problems under dose-volume restriction are NP-Hard.

Outline/Summary

- Mixed Integer Programming (MIP) Formulations of Fluence Map Optimization,
  - Allow precise modeling of dose-volume restrictions.
  - Are difficult to solve – partially due to weak linear programming relaxation (LPR).
- We show
  - How valid inequalities based on disjunctive programming can be derived to strengthen LPR.
  - How certain enumeration schemes can be utilized to effectively reduce optimality gaps.
- Computational Results

Radiation Therapy Planning

- External-Beam Radiation Therapy
  - Commonly used procedure in treating many types of cancer
  - Radiation is delivered by a linear accelerator, which can rotate around the patient to deliver radiation from different angles

- Main Goal of Radiation Therapy Planning
  - To make optimal delivery decisions such as,
    - which angles to deliver the radiation from
    - what intensity to assign to each beam angle
    - how to modulate the radiation intensity through out the beam surface (in Intensity Modulated Radiation Therapy)
  - So that infected tissues are sufficiently irradiated, while healthy organs at risk are protected from excess radiation.

Fluence Map Optimization

- Prior to Fluence Map Optimization:
  - CT/MRI/PET Scans
  - Identifying tissue boundaries on images.
  - Discretizing tissues into *volume elements (voxels)*
  - Discretizing beam surface into *beam elements (beamlets)* (IMRT only)
  - Construction of *dose matrix* $A=[a_{ij}]$, where a_{ij} is the dose delivered to voxel i from beam/beamlet j per unit intensity.
  - Determination of Beam Angles
- Fluence Map Optimization:
  - Determines optimal intensity assignment to each beam/beamlet of each selected angle in order to meet prescribed dose restrictions on different types of tissues.
  - Linear Dose Accumulation Assumption
    - $d=Ax$

      where A is the dose matrix, x is the vector of intensity variables for different beam angles and components, and d is the vector of dose amounts delivered to each voxel.

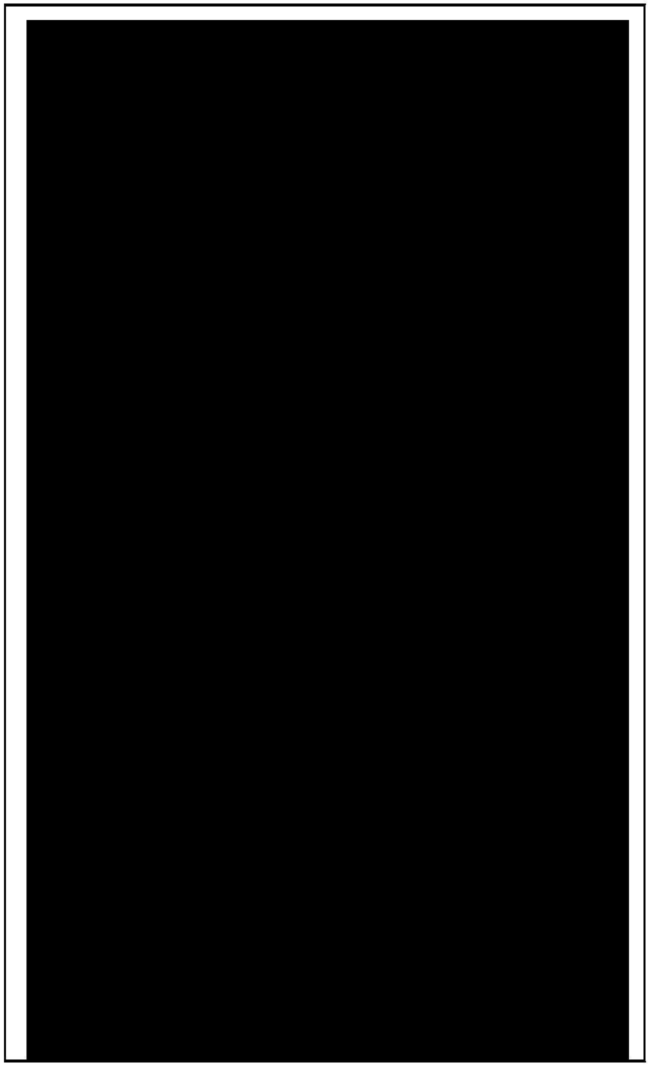
Dose-Volume Restrictions

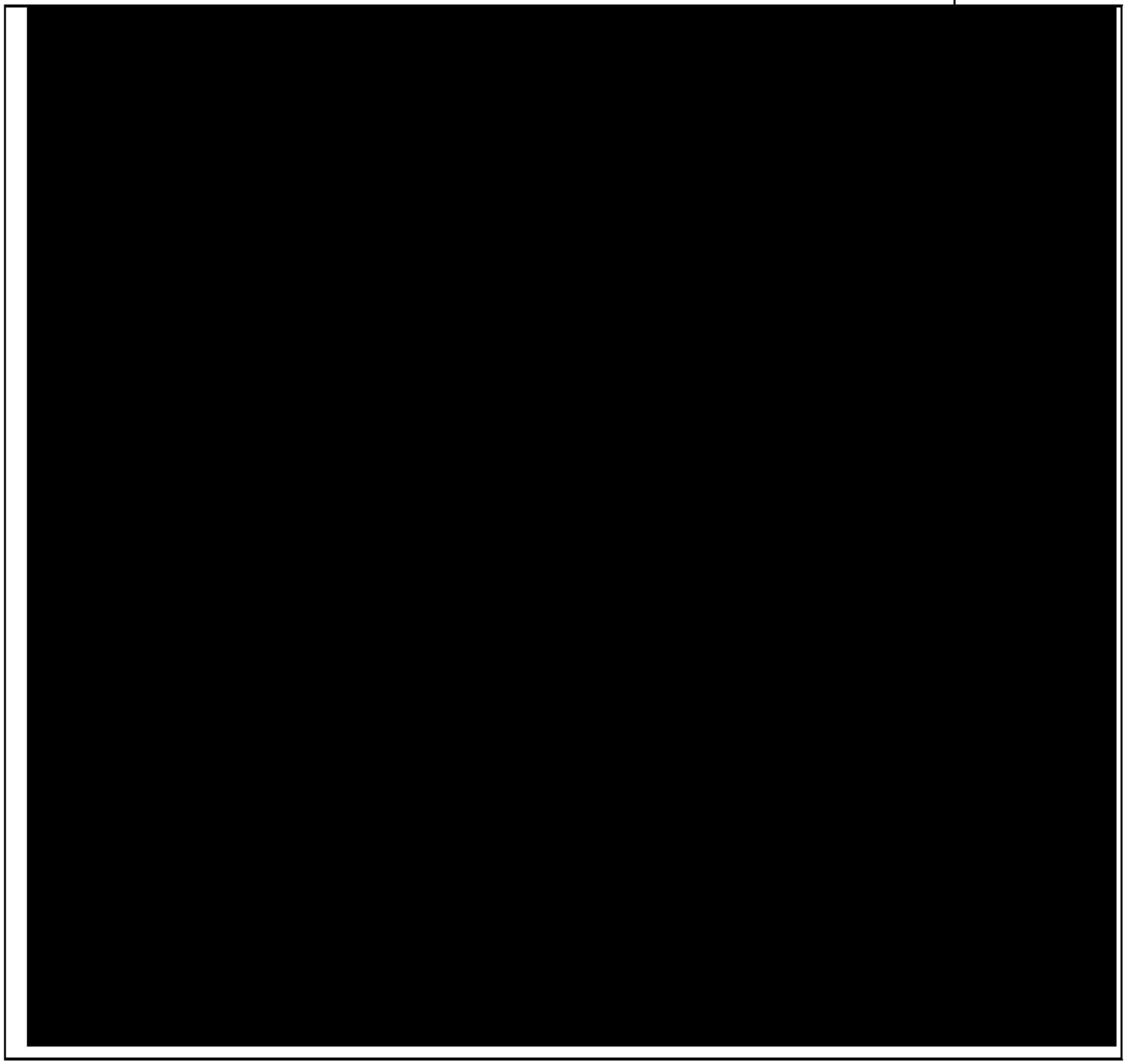
- A dose volume restriction on a particular tissue specifies a tissue volume percentage and a dose limit to be applied to that percentage of the tissue volume:
  - Ex: “At least 66% of the left lung volume should receive dose amounts no more than 20Gy”.
- Prescriptions and protocols are typically specified in terms of dose-volume restrictions.

FMO Models & Methods

- Unconstrained Nonlinear Models
  - Gradient Based Methods
  - Meta-heuristics
- Convex Approximation Models
  - Linear Programs
  - Quadratic Programs
- Goal Programming Models
- **MIP Models**
  - **Allow precise modeling of dose-volume restrictions**

A Mixed-Integer-Programming (MIP) Model for FMO





A Simplified Special Case - P

- Maximizes average primary target dose while considering dose restrictions of a single dose-volume tissue:
  - <u>Absolute Dose Restriction</u>: All *m* voxels should receive dose amounts no more than $\bar{b}$
  - <u>Dose-Volume Restriction</u>:
    - **<u>Cold Voxels</u>**: At least *L* of the *m* voxels should receive dose amounts no more than $\underline{b}$
    - **<u>Hot Voxels</u>**: At most $K = m - L$ of the *m* voxels can receive dose amounts more than $\underline{b}$

[redacted]

- Some Disadvantages of P:
  - <u>NP-Hard</u>: We can reduce partition (subset sum) problem to P.
  - <u>Weak Linear Programming Relaxation (LPR)</u>: LPR of P-MIP tends to get weaker as the difference between $\underline{b}$ and $\bar{b}$ increase.

OPCS: A Relaxation of P

- Optimization Problem with Constraint Selection (OPCS) is a relaxation of P <u>where absolute dose restrictions are dropped</u>.

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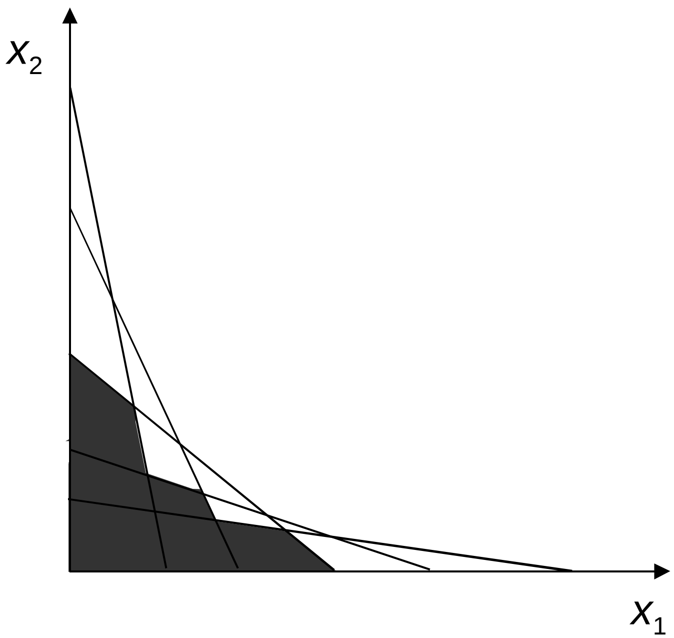
- OPCS is also NP-Hard.

Feasible Set of OPCS

m=5, *L*=3, *K*=2



$$A = \begin{matrix} 2 & 8 \\ 5 & 4 \\ 8 & 2 \\ 3 & 6 \\ 7 & 3 \end{matrix}$$

$\underline{b} = 20$

Valid Inequalities for OPCS – Disjunctive Programming

- Computationally effective valid inequalities for OPCS can be derived based on Disjunctive Programming principles.
- Disjunctive Programming:
  - Studies optimization problems whose feasible sets can be expressed as disjunction (union) of polyhedra
  - Provides a general principle to generate valid inequalities for disjunctive sets based on the following theorem:

[redacted]

Expressing OPCS as Union of Polyhedra

- Feasible set of OPCS can be expressed as union of polyhedra as follows:

[redacted]

Valid Inequalities for OPCS – Main Disjunctive Inequality

[redacted]

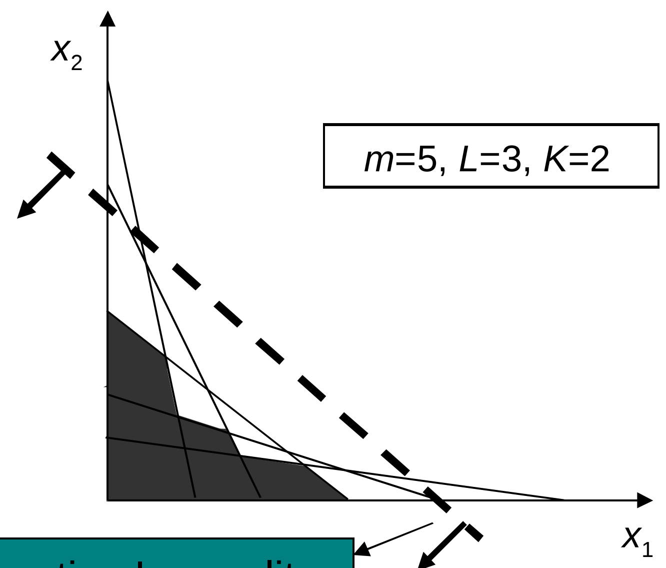
$\underline{b} = 20$

$$A = \begin{bmatrix} 2 & 8 \\ 5 & 4 \\ 8 & 2 \\ 3 & 6 \\ 7 & 3 \end{bmatrix} \qquad \breve{A} = \begin{bmatrix} 8 & 8 \\ 7 & 6 \\ \hdashline 5 & 4 \\ 3 & 3 \\ 2 & 2 \end{bmatrix}$$

Average of lowest 3 values

$$\frac{10}{3}x_1 + 3x_2 \quad 20$$

Main Disjunctive Inequality



Valid Inequalities for OPCS – A Family of Disjunctive Inequalities

[redacted]

[redacted]

- Each inequality of the family is the main disjunctive inequality of a relaxation OPCS($A(S,.)$,$\underline{b}$,K), where only the rows of A with indices in S are considered.
- The family has exponentially many inequalities (there is an inequality for each $S \subseteq I$ with $|S| > K$).

Valid Inequalities for OPCS – Disjunctive Support Inequalities

[redacted]

[redacted]

<u>b</u> = 20

$$A = \begin{matrix} \cancel{2} & \cancel{8} \\ 5 & 4 \\ 8 & 2 \\ \cancel{3} & \cancel{6} \\ 7 & 3 \end{matrix}$$

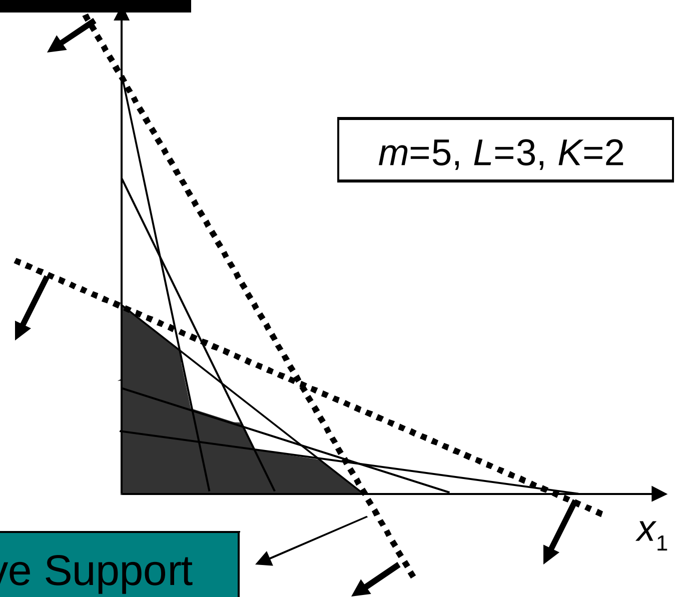
$$\breve{A} = \begin{matrix} 8 & 4 \\ 7 & 3 \\ \hline 5 & 2 \end{matrix}$$

Average of the lowest value

$$5x_1 + 2x_2 \quad 20 \longrightarrow$$

Disjunctive Support Inequality

m=5, *L*=3, *K*=2



Computational Results: Test Cases

[redacted]

[redacted]

Computational Results: Test Cases

[redacted]

[redacted]

The difference between $\underline{b}$ and $\overline{b}$ values influences the initial optimality gap.

Computational Results: Baseline Results

[redacted]

[redacted]

* All built-in CPLEX cuts are turned off due to extreme inefficiency of these cuts. All other CPLEX parameters are set to their default values.

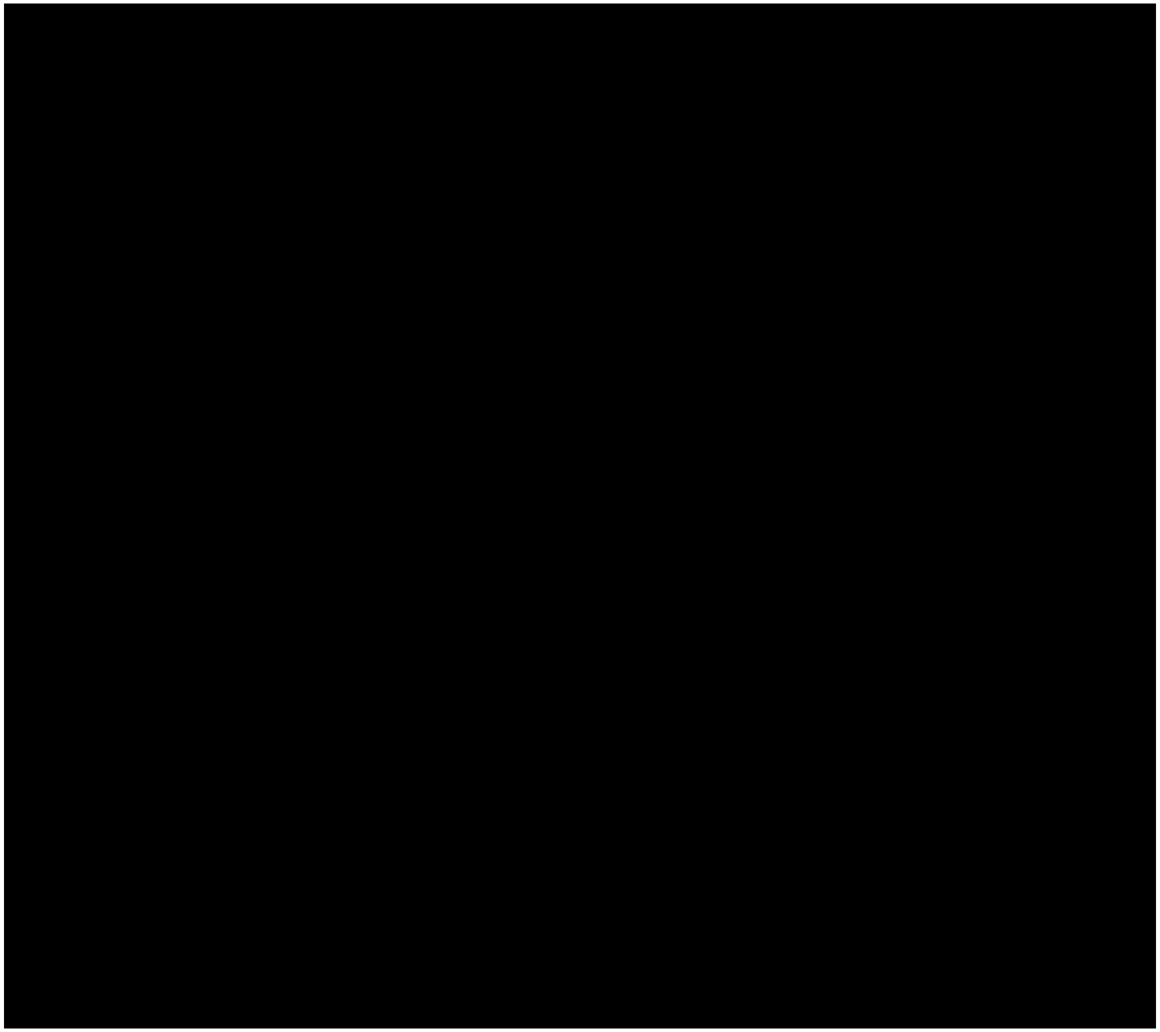
Computational Results: Disjunctive Inequalities

Single Cold Point Enumeration (SCPE) Procedure

The following steps are applied for each dose-volume tissue separately,

- **Initialization**: Obtain a feasible solution for FMOP-MIP using a heuristic and set *lb* to the best feasible solution value found. Relax integrality constraints to obtain the LPR of FMOP-MIP.
- **Single Cold Point Iterations**: For each voxel *i* in the dose-volume tissue,
  - Force voxel *i* to be cold, i.e. to receive a dose amount no more than $\underline{b}$.
  - Solve new problem and store its optimal solution in $\overline{x}^i$ and its optimal solution value in $\overline{z}_i$.
  - If $\overline{x}^i$ is feasible for FMOP-MIP and $\overline{z}_i > lb$, then set $\hat{x} = \overline{x}^i$ and $lb = \overline{z}_i$.
  - Remove the restriction on voxel *i*.
- **Sorting**: Sort $\overline{z}$ values in ascending order to obtain $\overline{z}_1, \ldots, \overline{z}_m$.
- **Finalization**: Return $\overline{z}_{K+1}$ as a valid upper bound. If $lb > -\infty$ return $\hat{x}$ as the best feasible solution found. Declare voxels where $\overline{z}_i < lb$ as hot voxels.

SCPE Procedure



SCPE Procedure – Computational Results

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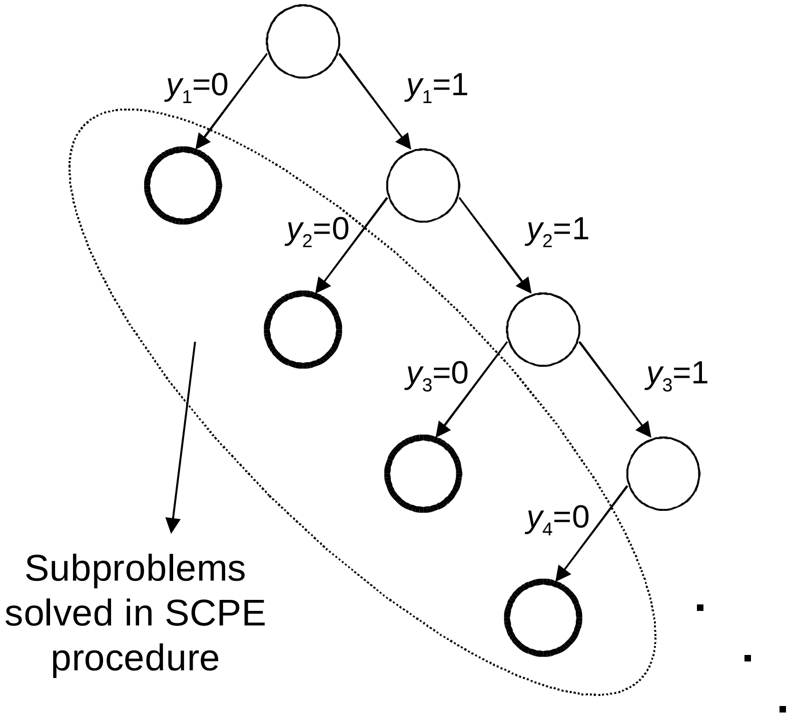
- Reduces upper bounds significantly (usually more than disjunctive cuts).
- Fixes the state of some dose-volume voxels.
- Computationally intensive.

Implementing SCPE Procedure Within Branch & Bound



- Built-in branching schemes of CPLEX are not effective in reducing the upper bounds in lung cases.
- Many commercial MIP solvers, including CPLEX, allow implementation of user-specified branching schemes.
- Considering the computational benefits of SCPE procedure, using this type of a branching scheme within a MIP branch-and-cut framework could be useful.

Combined Algorithm

- Integrates disjunctive cuts and SCPE procedure within the framework of rounding heuristic.
- Algorithm Outline
  - **Initialization:** Set up LPR model.
  - **Strengthen LP Relaxation:** Add main disjunctive cut and disjunctive support cuts for all dose-volume tissues.
  - **Rounding Heuristic:** Apply the rounding heuristic to obtain an upper bound and a feasible solution.
  - **SCPE:** Apply SCPE procedure to all dose-volume tissues. Update upper bound, lower bound values. Obtain the set of fixed dose-volume voxels.
  - **Update Cuts:** Adjust disjunctive cuts to take the fixed dose-volume voxels into account.
  - **Rounding Heuristic:** Apply the rounding heuristic again.

Combined Algorithm – Computational Results

[redacted]

[redacted]

- Reduced upper bounds and optimality gaps.
- Better feasible solutions.
- Less computation time on average compared to applying SCPE procedure alone.

Conclusions

- Linear Programming Relaxations of MIP formulations of FMO problems can be arbitrarily weak.
- Commercial MIP solver (CPLEX 10.1) is not effective in closing the initial large optimality gaps.
- Efficient valid inequalities based on disjunctive programming theory can be generated to:
  - Strengthen LPR and significantly reduce initial optimality gaps.
  - Help find better feasible solutions within the rounding heuristic framework.
  - Improve run times.

Conclusions

- SCPE procedure can be implemented as a stand-alone enumeration procedure or as a problem-specific branching scheme. The procedure,
  - Significantly reduces upper bound values.
  - Determines the optimal value of some of the binary variables.
  - In many cases, finds better feasible solutions.
- The combined algorithm utilizes disjunctive inequalities and SCPE procedure within the rounding heuristic framework. The algorithm produces lower optimality gaps and better feasible solution values than methods utilizing only disjunctive inequalities or only the SCPE procedure.