**Using Optimization to Cure Cancer**

**Abstract**

The advancements in current software technologies and faster computing machines has enabled us to use OR concepts and techniques in various industries. Here, we use linear programming to solve a healthcare problem with the objective to send maximum radiations through tumour cells and minimum radiations through critical cells in the patient’s body.

We define the various sets and parameters for the formulation as follows-

Let,

*B* – set of matrices for beamlet intensity

*R* – set of rows

*C* *-* set of columns

*U* - upper limit of radiation on critical cells

L – lower limit of radiation on tumor cells

*bijk* – parameter indicating beam intensity from beamlet i on row j and column k

a*jk –* parameter indicating presence or absence of critical cell on row j and column k

e*jk* – parameter indicating presence or absence of tumor cell on row j and column k

*Xi* - decision variable indicating intensity to be set for beam i for treating

**Task 1**

1. We formulate a basic LP model for the problem proposed here by the Oncologist which will satisfy the upper limit on the critical cells and lower limit on tumor cells while maximizing radiation on tumor cells and minimizing the same on critical cells. We decide to set the function to minimize the radiation on critical cells and adding a penalty function for radiations on the tumor cells.

Objective function:

Minimize (∑i∈B ∑j∈R ∑k∈C  ajk \* bijk \* Xi) - (∑i∈B ∑j∈R ∑k∈C  ejk \* bijk \* Xi)

Subject to:

∑i∈B  ajk \* bijk \* Xi <= U for j∈R, k∈C

∑i∈B  bijk \* Xi >= L \* ejk  for j∈R, k∈C

This model when formulated in AMPL did not gave 0 as the solution for both small and actual example. Hence, we reformulated the objective function so as to only minimize the radiations on the critical area. Even with this formulation, we were able to find a feasible solution for the small example, but no feasible solution was found for the actual example.

**Model 1 - Image for visualizing the radiations in small example:**



1. As we did not get feasible solution in the first formulation, we now try to relax our constraints to get a feasible solution for the actual example and we can also see the corresponding changes in the small example. We will introduce slack variables to the constraints from the previous formulation and change our objective to minimize the sum of these slack variables.

This formulation will give us the values for slack variables and this would help the oncologist in adjusting the limits on the critical and tumor areas to obtail a fesible solution using the first model.

Minimize ∑i∈B ∑j∈R ∑k∈C  ajk \* bijk \* Xi

Minimize ∑j∈R ∑k∈C (pjk + qjk)

Subject to:

∑i∈B  ajk \* bijk \* Xi <= U + qjk for j∈R, k∈C

∑i∈B  bijk \* Xi >= (L – pjk) \* ejk  for j∈R, k∈C

Where pjk and qjk are slack variable to minimize.

**Model 2 - Image for visualizing the radiations in small example:**



**Model 2 - Image for visualizing the radiations in actual example:**

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1. For penalizing the radiations that are incident at the bordering regions of the non-critical region, we use rolling indexes m and n to which range from -1 to 1 to locate the bordering regions of the critical region and we then penalize our objective function using multipliers on these bordering binary indexes.

Minimize ∑i∈B ∑j∈R ∑k∈C  ajk \* bijk \* Xi

Minimize

∑j∈R ∑k∈C ((pjk + qjk) + ∑i∈B ∑-1<=n<=1 ∑-1<=m<=1 (1-ajk) \* aj+n,k+m\* bijk \* Xi )

Subject to:

∑i∈B  ajk \* bijk \* Xi <= U + qjk for j∈R, k∈C

∑i∈B  bijk \* Xi >= (L – pjk) \* ejk  for j∈R, k∈C

**Model 3 - Image for visualizing the radiations in small example:**

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**Model 3 - Image for visualizing the radiations in actual example:**

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1. **Suggested Enhancements**
2. **Weighted Slacks** - From model 2, we see that the value of the slack variables can be used by the oncologist as a reference for the range of adjustments to the upper and lower limit on critical and tumor regions respectively. By intuition, we can compromise on changing the limits on the tumor region, but we would not want to change the limits on tumor region. So, we propose adding weights to the critical and tumor slacks in the objective function such that the sum of slacks corresponding to critical region are minimised and we can make minimum adjustments in the limits of the critical region.

For implementing this, we would not need additional data. The only additional task is to figure out the weights that will give us the most effective solution.

1. **Minimizing total Radiation** –As we know, no radiation is beneficial to the human body whether it is on the tumor area, critical area or the non-critical area. The goal is to enhance the quality of the life of the patient and by minimizing the total radiation sent over all the cells would be a decent objective with the same limits on tumor and critical regions.

To implement this, we use the same formulation as in model 2. Here, we update our objective function by including penalties on radiations passing through both critical and tumor regions. Also, the model will automatically try to send zero or no radiations in the non-critical regions.

Again, there is no additional data needed for implementing this model. Only additional task is to put a weight on the part of objective with sum of slacks so that there is enough room for the penalties. In the objective function.

1. **Including cell recovery data –** It is obvious that no tumor cell can be treated with one sesion of radiation therapy. We can obtain past data and analyse the recovery time for certain critical cells in the body. Doing this we might be able to up the minimum limit on critical area. We can run the model before every session of therapy with updated limits on critical and tumor regions.

We can also think of a future advancement where passing a negative beam intensity will heal the cell and not damage. Implementing this would not be difficult as we would set out X variable free so that it can also take negative values. Hence, with the set of positive intensity beams which damage the tumor cells, we will have beams with negative intensities which will heal the critical cells.

1. Now, we try to propose models for the first two suggested enhancements proposed above:
   1. **Weighted Slacks**

**Model 4**

Minimize ∑j∈R ∑k∈C ((wt \* pjk) + (wc \* qjk))

Subject to:

∑i∈B  ajk \* bijk \* Xi <= U + qjk for j∈R, k∈C

∑i∈B  bijk \* Xi >= (L – pjk) \* ejk  for j∈R, k∈C

Where pjk and qjk are slack variable to minimize and wt and wc are weights for corresponding slack variables for tumor and critical regions respectively.

For calculation of slacks, we tried different combinations of wt and wc including complete elimination of critical slacks. We observed that the model was maximizing slacks for the tumor region while adjusting radiations in the allowed range of the critical areas. So we came up with a logic to get the weights. We used the ratio of total critical cells to that of total tumor cells and used this ratio as the weights.

This ratio worked because we have less area of critical region as compared to tumor region in the current instance. There might be instances where the critical area is equal or even larger. For this, one might have to use different combinations to come u with the best solution.

**Model 4 - Image for visualizing the radiations in small example:**

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For the small example, we get the same solution as obtained from model 1

**Model 4 - Image for visualizing the radiations in actual example:**



We can see a significant reduction in the amount of radiations in the critical area as compared to previous models.

* 1. **Minimizing total Radiation –**

**Model 5**

Minimize

∑j∈R ∑k∈C (w\*(pjk + qjk)) + ∑i∈B ∑-1<=n<=1 ∑-1<=m<=1 (ejk+ajk) \* aj+n,k+m\* bijk \* Xi )

Subject to:

∑i∈B  ajk \* bijk \* Xi <= U + qjk for j∈R, k∈C

∑i∈B  bijk \* Xi >= (L – pjk) \* ejk  for j∈R, k∈C

Where w is the weight attached to the part of the objective which sums the sacks

**Model 5 - Image for visualizing the radiations in small example:**

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**Model 5 - Image for visualizing the radiations in small example:**

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**CONCLUSION**:

After building all these models, we were curious to know which model performed the best. For this, we calculated total radiations on critical and tumor regions separately.

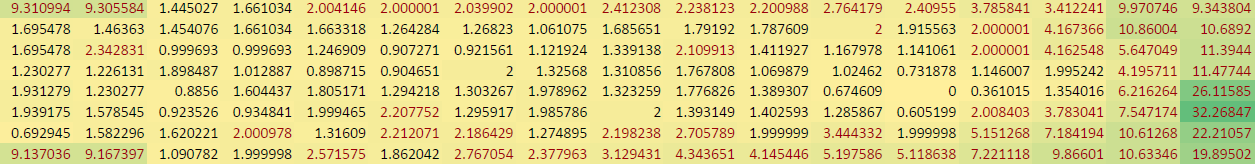
The following table summarises the total radiations obtained from all models on actual example (excluding model 1)

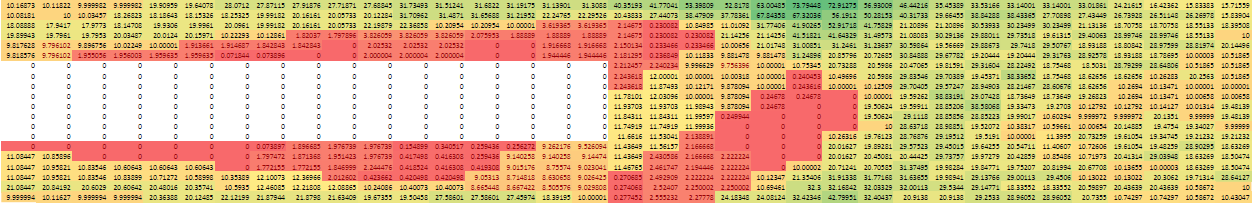
|  |  |  |
| --- | --- | --- |
| Total Radiations | On Tumor area | On Critical area |
| Model 2 | 11314 | 627 |
| Model 3 | 8980 | 118 |
| Model 4 | 10405 | 978 |
| Model 5 | 11314 | 479 |

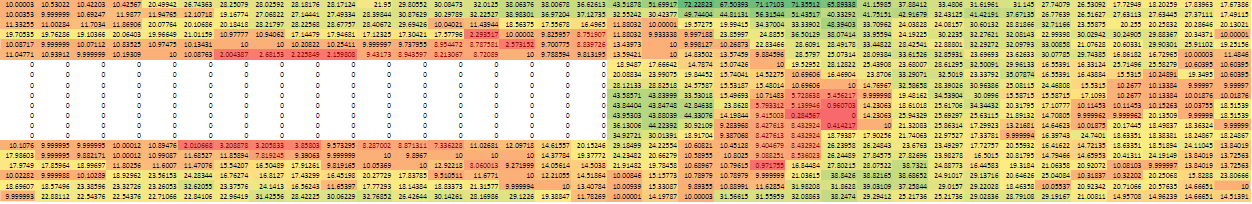
We can observe that model 3 gives us minimum radiation on the critical area whereas model 5 gives maximum on the tumor area. Additionally, model 5 was also derived from model 5 with a few adjustments in the objective function.

Hence, we dived in deep to visualize the radiations on specific areas. Of course, the visuals obtained from Maple were helpful but we took help of the colorscaling option in excel to visualize the data from the radiations.

**Model 3 – Critical region**

**Model 5 – Critical region**

**Model 3 – Tumor Region**

**Model 5 – Tumor Region**

From above color scale visuals, we can see that while model 3 has minimum total radiations on the critical region, it violates upper limits only on a few critical cells (highlighted in green). Doing this, many tumor cells (highlighted in red) in red have been left out without any radiation incident on them.

On the other hand, model 5 has more upper limits violated for critical cells (highlighted in green) than model 3 but it is able incident the required amount of radiation on the tumor cells (highlighted in red)

One thing that catches our attention here is that while model 5 violates the upper limits on the critical cells, it violates those with large intensities incident on them. This means, that a few of the critical cells have high chances of damaging completely which may not be desirable. Model 3, on the other hand violates only a few critical cell upper limits and that too with smaller impact. Yes model 3 leaves out quite a good number of tumor cells untreated but we cant afford to loose critical cells for the cost of damaging a few extra tumor cells

We conclude and suggest model 3 to be used by the Oncologist and treat the patient in 2 stages. We can have a new and reduced tumor region after the first stage and a similar model can be run for treatment in the second stage. The total radiations on the critical region are such small that we can afford to have two radiation sessions in the same setup which will double the radiations in the critical region which would still be much lesser total radiations from other models.

**Appendix**

1. **Model 1 – AMPL code**

**param** num\_beams; #number of avaiable beamlets

**param** num\_rows >= 1;

**param** num\_cols >= 1;

**set** ROWS:= 1..num\_rows;

**set** COLS:= 1..num\_cols;

**set** BEAM:= 1..num\_beams;

**param** beam\_value {BEAM, ROWS, COLS} >= 0;

**param** tumor\_value {ROWS, COLS} >= 0;

**param** critical\_value {ROWS, COLS} >= 0;

**param** critical\_max;

**param** tumor\_min;

**param** a {j **in** ROWS, k **in** COLS} = **if** critical\_value[j,k] > 0 **then** 1 **else** 0;

**param** e {j **in** ROWS, k **in** COLS} = **if** tumor\_value[j,k] > 0 **then** 1 **else** 0;

**var** X {i **in** BEAM} >= 0;

**minimize** critical\_dosage: (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

**subject** **to** tumor\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} X[i] \* beam\_value[i,j,k] >= tumor\_min \* e[j,k];

**subject** **to** critical\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} a[j,k] \* X[i] \* beam\_value[i,j,k] <= critical\_max;

1. **Model 2 – AMPL code**

**param** num\_beams; #number of avaiable beamlets

**param** num\_rows >= 1;

**param** num\_cols >= 1;

**set** ROWS:= 1..num\_rows;

**set** COLS:= 1..num\_cols;

**set** BEAM:= 1..num\_beams;

**param** beam\_value {BEAM, ROWS, COLS} >= 0;

**param** tumor\_value {ROWS, COLS} >= 0;

**param** critical\_value {ROWS, COLS} >= 0;

**param** critical\_max;

**param** tumor\_min;

**param** a {j **in** ROWS, k **in** COLS} = **if** critical\_value[j,k] > 0 **then** 1 **else** 0;

**param** e {j **in** ROWS, k **in** COLS} = **if** tumor\_value[j,k] > 0 **then** 1 **else** 0;

**var** X {i **in** BEAM} >= 0;

# slack variables

**var** P {j **in** ROWS, k **in** COLS} >= 0;

**var** Q {j **in** ROWS, k **in** COLS} >= 0;

# minimize total slacks

**minimize** total\_slacks: **sum** {j **in** ROWS, k **in** COLS} (P[j,k] + Q[j,k]);

#minimize dosage

**minimize** treatment\_dosage: (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

**subject** **to** tumor\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} X[i] \* beam\_value[i,j,k] \* e[j,k] >= (tumor\_min - Q[j,k]) \* e[j,k] ;

**subject** **to** critical\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} a[j,k] \* X[i] \* beam\_value[i,j,k] <= critical\_max + P[j,k];

1. **Model 3 – AMPL code**

**param** num\_beams; #number of avaiable beamlets

**param** num\_rows >= 1;

**param** num\_cols >= 1;

**set** ROWS:= 1..num\_rows;

**set** COLS:= 1..num\_cols;

**set** BEAM:= 1..num\_beams;

**param** beam\_value {BEAM, ROWS, COLS} >= 0;

**param** tumor\_value {ROWS, COLS} >= 0;

**param** critical\_value {ROWS, COLS} >= 0;

**param** critical\_max;

**param** tumor\_min;

**param** a {j **in** ROWS, k **in** COLS} = **if** critical\_value[j,k] > 0 **then** 1 **else** 0;

**param** e {j **in** ROWS, k **in** COLS} = **if** tumor\_value[j,k] > 0 **then** 1 **else** 0;

**var** X {i **in** BEAM} >= 0;

# slack variables

**var** P {j **in** ROWS, k **in** COLS} >= 0;

**var** Q {j **in** ROWS, k **in** COLS} >= 0;

# minimize total slacks

**minimize** total\_slack: **sum** {j **in** ROWS, k **in** COLS} ( (P[j,k] + Q[j,k]) + **sum** {i **in** BEAM} **sum** {m **in** -1 .. 1} **sum** {n **in** -1 .. 1} (1 - a[j,k]) \* (a[min(max(j+m,1), num\_rows),min(max(k+n,1),num\_cols)]) \* X[i] \* beam\_value[i,j,k]);

**minimize** treatment\_dosage: (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

**subject** **to** tumor\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} X[i] \* beam\_value[i,j,k] \* e[j,k] >= (tumor\_min - Q[j,k]) \* e[j,k] ;

**subject** **to** critical\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} a[j,k] \* X[i] \* beam\_value[i,j,k] <= critical\_max + P[j,k];

1. **Model 4 – AMPL code**

**param** num\_beams; #number of avaiable beamlets

**param** num\_rows >= 1;

**param** num\_cols >= 1;

**set** ROWS:= 1..num\_rows;

**set** COLS:= 1..num\_cols;

**set** BEAM:= 1..num\_beams;

**param** beam\_value {BEAM, ROWS, COLS} >= 0;

**param** tumor\_value {ROWS, COLS} >= 0;

**param** critical\_value {ROWS, COLS} >= 0;

**param** critical\_max;

**param** tumor\_min;

**param** a {j **in** ROWS, k **in** COLS} = **if** critical\_value[j,k] > 0 **then** 1 **else** 0;

**param** e {j **in** ROWS, k **in** COLS} = **if** tumor\_value[j,k] > 0 **then** 1 **else** 0;

**var** X {i **in** BEAM} >= 0;

# slack variables

**var** P {j **in** ROWS, k **in** COLS} >= 0;

**var** Q {j **in** ROWS, k **in** COLS} >= 0;

**param** W\_C > 0; #weight for slack variable reated to critical region

**param** W\_T > 0; #weight for slack variable reated to tumor region

# minimize total slacks

**minimize** total\_slacks: **sum** {j **in** ROWS, k **in** COLS} ((W\_C\*P[j,k]) + (W\_T\*Q[j,k]));

#minimize dosage

**minimize** dosage: (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

**subject** **to** tumor\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} X[i] \* beam\_value[i,j,k] \* e[j,k] >= (tumor\_min - Q[j,k]) \* e[j,k] ;

**subject** **to** critical\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} a[j,k] \* X[i] \* beam\_value[i,j,k] <= critical\_max + P[j,k];

1. **Model 5 – AMPL code**

**param** num\_beams; #number of avaiable beamlets

**param** num\_rows >= 1;

**param** num\_cols >= 1;

**set** ROWS:= 1..num\_rows;

**set** COLS:= 1..num\_cols;

**set** BEAM:= 1..num\_beams;

**param** beam\_value {BEAM, ROWS, COLS} >= 0;

**param** tumor\_value {ROWS, COLS} >= 0;

**param** critical\_value {ROWS, COLS} >= 0;

**param** critical\_max;

**param** tumor\_min;

**param** a {j **in** ROWS, k **in** COLS} = **if** critical\_value[j,k] > 0 **then** 1 **else** 0;

**param** e {j **in** ROWS, k **in** COLS} = **if** tumor\_value[j,k] > 0 **then** 1 **else** 0;

**param** s {j **in** ROWS, k **in** COLS} = 1;

# slack variables

**var** P {j **in** ROWS, k **in** COLS} >= 0;

**var** Q {j **in** ROWS, k **in** COLS} >= 0;

**var** X {i **in** BEAM} >= 0;

#minimize dosage: (sum{i in BEAM} sum {j in ROWS, k in COLS} s[j,k] \* X[i] \* beam\_value[i,j,k]) - (sum{i in BEAM} sum {j in ROWS, k in COLS} e[j,k] \* X[i] \* beam\_value[i,j,k]) + (sum{i in BEAM} sum {j in ROWS, k in COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

# minimize total slacks

**minimize** total\_slacks: **sum** {j **in** ROWS, k **in** COLS} (10\*(P[j,k] + Q[j,k])) + (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} e[j,k] \* X[i] \* beam\_value[i,j,k]) + (**sum**{i **in** BEAM} **sum** {j **in** ROWS, k **in** COLS} a[j,k] \* X[i] \* beam\_value[i,j,k]);

**subject** **to** tumor\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} X[i] \* beam\_value[i,j,k] \* e[j,k] >= (tumor\_min - Q[j,k]) \* e[j,k] ;

**subject** **to** critical\_limit {j **in** ROWS, k **in** COLS} : **sum** {i **in** BEAM} a[j,k] \* X[i] \* beam\_value[i,j,k] <= critical\_max + P[j,k];

1. We used Excel to multiply and add the solution matrix X obtained from running the LP models.