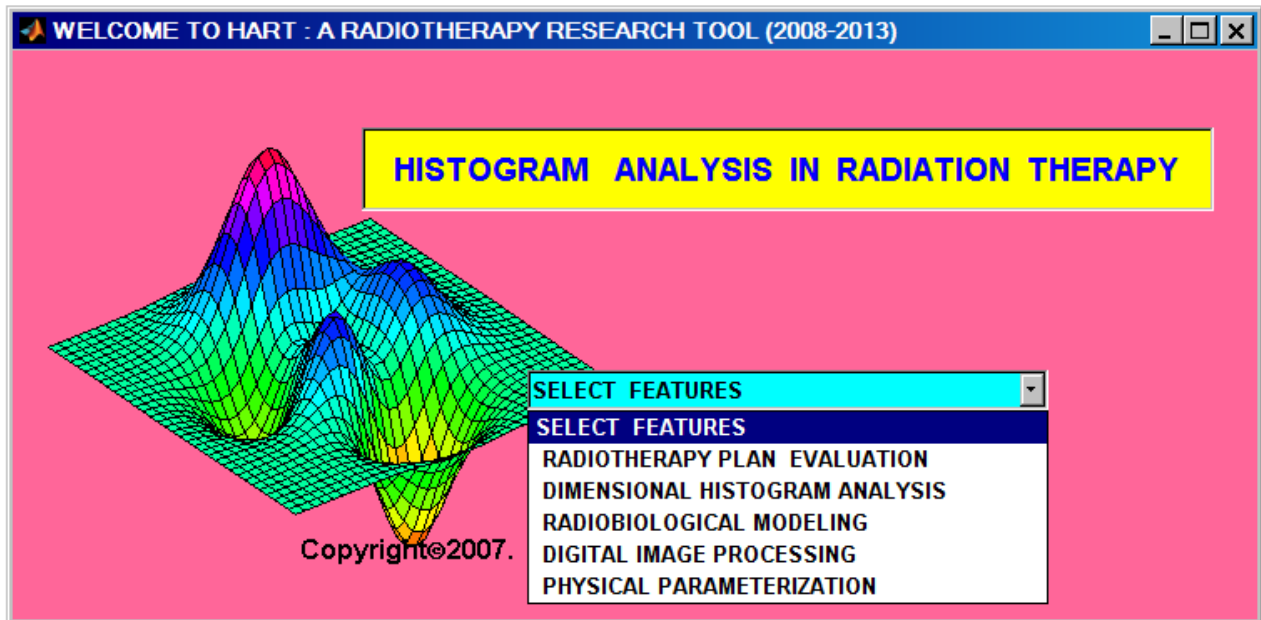


The Histogram Analysis in Radiation Therapy (HART*)

**An open source software system designed for clinical and research applications in radiation therapy*.*

2008-2014

[Software Manual and User-guide: Issue 2 (2014), Version: 01.08.2014]



Preface to the program

This work is dedicated to the cancer care community to improve the quality of radiation guided treatments in cancer. The program is primarily useful for the efficient and precise analysis of the multi-dimensional dose-volume histograms, evaluation of the advanced radiotherapy treatment plans, assessment of the radiobiological modeling outcomes, dose-response modeling and the physical parameterization of the normal organs using the radiotherapy treatment plans in the Radiation Therapy Oncology Group (RTOG) and the Digital Image Communication in Medicine for the Radiation Therapy (DICOM-RT) image formats respectively. The program was formally introduced in the 50th annual conference of the American Association of Physicists in Medicine at Houston, Texas, USA in 2008. Although the program has been successfully designed for research applications, it is also useful for direct clinical analysis of the advanced radiation therapy treatment plans following extensive validation of the dosimetric parameters.

Acknowledgement

The project is primarily supported by NIH-NIDCD grant and multi-institutional collaboration groups in Radiation Oncology throughout the United States.

Contact us

Anil Pyakuryal, PhD

Lead, HART Research Group (HRG)

National Cancer Institute / National Institutes of Health, Bethesda, MD 20850,

Northwestern University-Memorial Hospital, Chicago, IL 60610, and

University of Illinois at Chicago, Chicago, IL 60607.

E-mail: apyaku1@uic.edu

Website: <http://HART.Research.UIC.edu/>

Table of contents

I. Recommended settings for the system and file configuration	05
II. Download mechanism	05
III. HART program features	07
(a) Multi-dimensional histogram analyses	07
(i) Conventional dose-volume histogram (cDVH) analysis	07
(ii) Spatial dose-volume histogram (sDVH) analysis	12
(b) Radiobiological modeling and outcome analysis	16
(i) Therapeutic outcome analysis	17
(a) Tumor Control Probability (TCP: Poisson Statistics Model)	18
(b) Normal Tissue Complication Probability (JT Lyman; Kallman)	18
(c) Radiobiological Modeling Outcomes	29
(ii) Radiobiological model parameter optimization	33
(c) Universal Plan-Indices evaluation	36
(d) Image Registration and Processing	45
IV. File Transfer Protocol Service	49
V. Summary	50
Appendix A	51

HART Flow Chart

HART Program (2008-2013)	Multi-Dimensional Dose- Volume Histogram Analysis (Module 1)	Cumulative DVH Statistical Analysis (cDVH Analysis; RTOG or DICOM-RT Data Format)	Normalized cDVH Statistics	Extracts 5000 cDVH Statistics in 5-10 mins. Executes higher order polynomial simulations.
			Absolute cDVH Statistics	
			Effective cDVH Statistics(V95, V5 etc)	
		Spatial DVH (x-,y-, and z- DVHs) Statistical Analysis (RTOG or DICOM-RT Data Format)	xDVH (RTOG/DICOM-RT)	Extracts Hot, Cold and Critical spots profile.
			yDVH (RTOG/DICOM-RT)	
			zDVH (RTOG/DICOM-RT)	
	Universal Plan-Indices Evaluation (Module 2)	10 generic Plan - Indices overall Quality Factor (QF)	HI,MHI,COSI,CI,CN,PITV,DGI, TCI,RCI,TR,TVR,NCI, and QF	Ranks the plan
	Empirical Radiobiological Modeling Outcome Analysis (Module 3)	Tumor Control Probability (TCP) / Normal Tissue Complication Probability (NTCP) Parameters.	Poisson's TCP Index (Complicated & Uncomplicated Indices)	More practical outcomes assessments.
			JT Lyman / S. Kalman NTCP Index	
			Radiobiological Model Parameter Optimizations (JT Lyman)	
Image Registration (Module 4)		Rigid Registration	Registers Images	
Physical Parameterization of the Organs (Module 5)	Attenuation Coefficients, Centre of Mass of Organs.	Differential Attenuation Coefficients (μ)	Coefficients extraction	
		Centre of Mass (COM)		

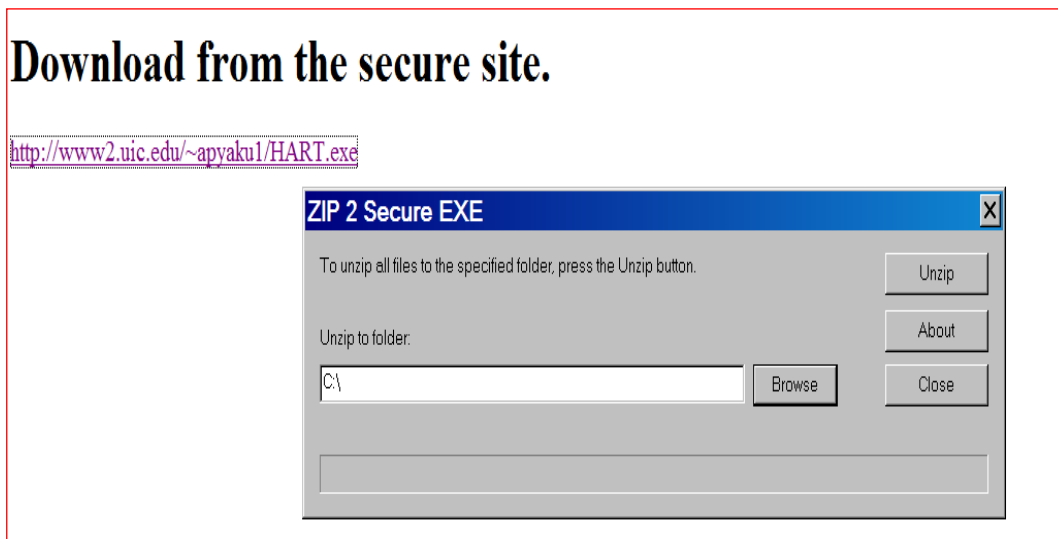
I. Recommended setting for system and file configuration:

- i. Platform: Windows-XP, 2000-2008, Vista, Linux, and MATLAB software.
- ii. IMRT/3DCRT/IGRT plans exported in RTOG and DICOM-RT formats.
- iii. Refer the publications and presentations on HART as indicated in our website.

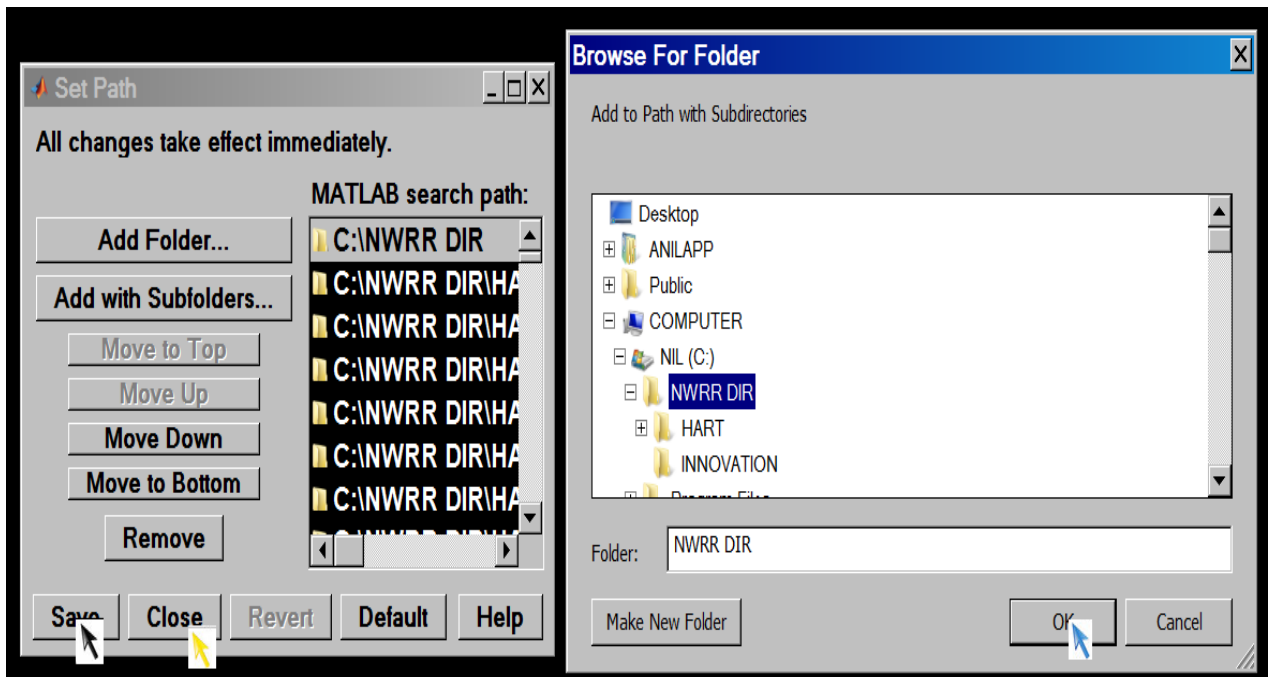
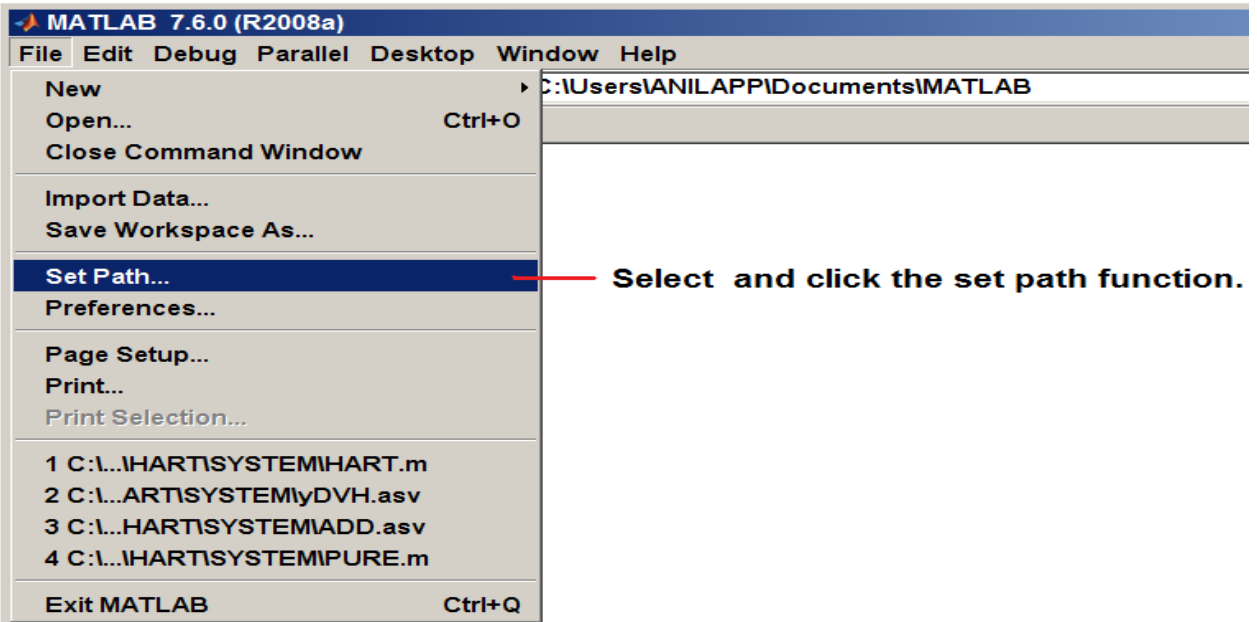
II. Download mechanism:

Save **HART.exe** application anywhere and unzip it using any unzip software, and extract it in C-drive as it would look like **C:\NWRR DIR** after the final extraction.

- (i) Unzip the **HART.exe** application into the C-drive of the personal computer using any types of unzip software as **C: \NWRR DIR** as shown below and in section II.



(ii) Launch MATLAB, Select the *Set Path* tab from the File Menu, and Select *Add with Subfolders* tab to direct all NWRR DIR and its sub-directories into the MATLAB original path immediately after the *Browse for Folder* windows pops up. Press and Click **Ok** → **Save** → **Close** as shown below step by steps.



III. HART Program features:

HART offers the following functionalities by processing RTOG and DICOM-RT data-file formats in the radiation therapy treatments*. It is highly recommended to the users to go through the full-papers/articles as mentioned in section I above for the detail information in the latest version of the program.

- (a) Multi-dimensional histogram (MDH) analyses :
 - i. Conventional dose volume histogram (cDVH)
 - ii. Spatial dose volume histogram (x,y, and z-DVHs)
- (b) Radiobiological-modeling for the outcome analysis (ROA),
- (c) Universal Plan-Indices (UPI) evaluation,
- (d) Digital Image Registration,
- (e) Dose response modeling (DRM) module,
- (f) Physical parameterization (PP) module,

a) Multi-dimensional histogram (MDH) analyses

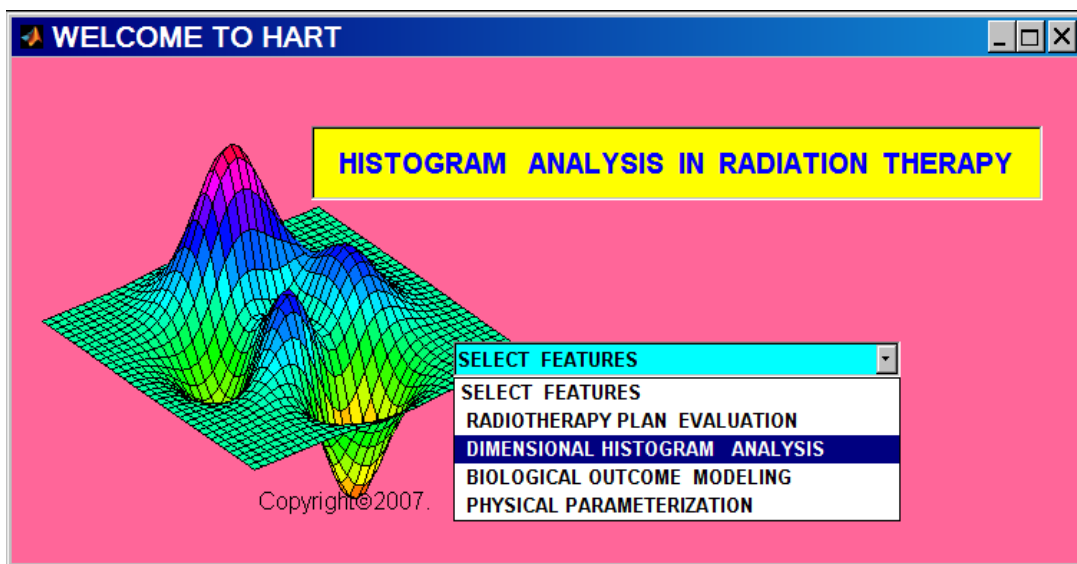
MDH analysis covers the space based DVH analysis and the conventional dose-volume histogram (cDVH) analysis options. The most common application of the multi-dimensional histogram analysis is the cDVH analysis of the radiation therapy treatment plans.

* Pyakuryal et. al, "An efficient computational toolresearch," Journal of Applied and Clinical Medical Physics, Vol 11 (1), p.3013 - 41, 2010.

(I) Conventional dose-volume histogram analysis

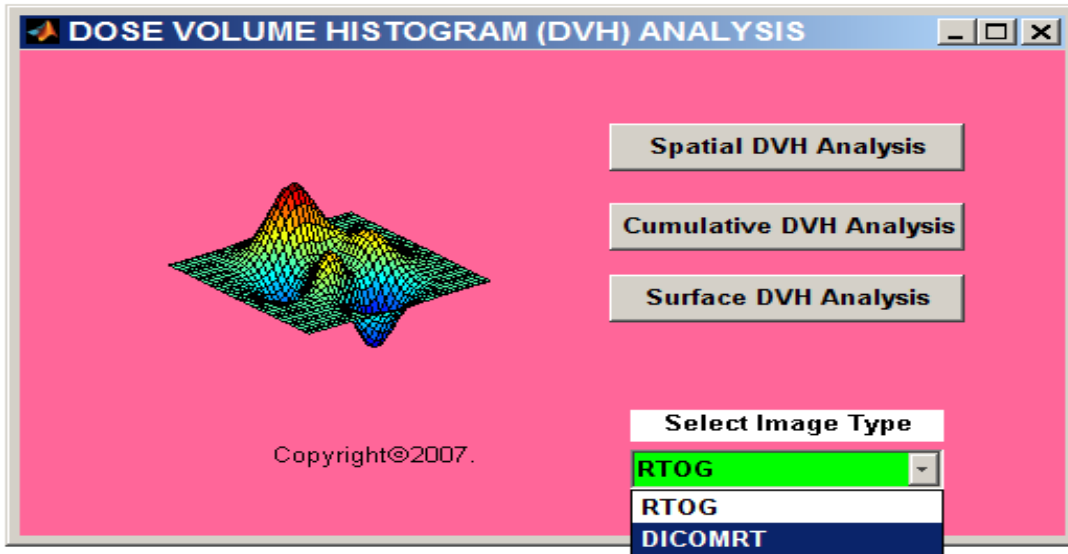
This section is especially prepared for the precise and efficient cDVH analysis, the most common application, using the fast statistical computational module. The user can simply follow the steps as shown below.

- (i) Type **HART** in the MATLAB command window. The Graphical User Interface (GUI) for the **HART** prompts quickly. Through **SELECT FEATURES** option select the **DIMENSIONAL HISTOGRAM ANALYSIS** option as shown below.



(Step (a))

→ Follow the **DOSE VOLUME HISTOGRAM (DVH) ANALYSIS** prompt panel.



(Step (b))

(ii) From the prompt panel of the *DOSE VOLUME HISTOGRAM (DVH) ANALYSIS* Window, please follow the steps as given below:

First select the Image type formats (**RTOG** or **DICOM-RT**) → (Select) *Cumulative DVH Analysis* button → the simulation runs in the specific path (RTOG or DICOM-RT) once the appropriate Treatment Planning System (TPS) is selected as shown below:

(a) RTOG path

(Select formats) either (a) Standard formats , or (b) Custom formats,[†] → Enter Name, Date, Plans (**PT1** for PTV1 plan, **PT2** for PTV2 plan, **PT3** for PTV3 plan, **COMPOSITE** for COMPOSITE plan only, **COMPLETE** for all RTOG plans), → Select Normal Mode (N) for RTOG plans, → Select the patient folder (eg. John_Smith folder that includes PTV1, PTV2, PTV3, COMP Plans in the corresponding **PTV1**, **PTV2**, **PTV3**, and **COMP**

folders respectively), —> Select output folder and assign a user-defined output excel file name (eg. Result.xls), —> Enter the prescription doses (PD1 for PTV1 plan, PD2 for PTV2 plan, and PD3 for PTV3 plan), —> Hold on 10-20 minutes, the computation and simulation automatically runs, —> End of application dialog box pops up, —> Push 'no' button if you are done, else push 'yes' button to restart the program for next cycle of computations, —> Search your output (eg. Result.xls) in the earlier user designated or the selected destination.

(↑Route (b): **Custom Format** allows arbitrary selections of fractional doses of interest for DVH analysis in the selected plans (PTV1, PTV2, PTV3, and COMPOSITE plans respectively. The successive steps of the DVH computation and simulation are shown below in a snap-shot for the **Custom Format** based DVH analysis.)

***** WELCOME to HART *****

CUSTOM FORMAT

STEP 1: Enter the Patient Name, Date of Analysis, Type of the Treatment Plan, and the Simulation Mode.

STEP 2: Select the Specific Patient Folder that contains the Treatment Plans, and hold on few seconds.

STEP 3: Select the Output Folder for the RESULTS.

STEP 4: Enter the reference doses to compute the corresponding volume statistics.

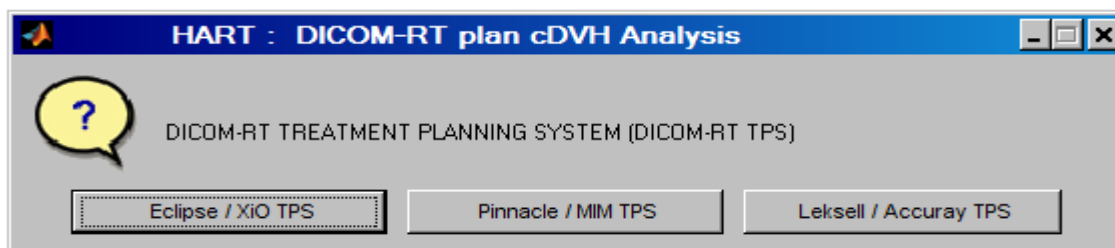
NOTE: Low(<) : Volume below reference dose; and High(>) : Volume above reference dose

STEP 5: Enter the Prescription Doses for the corresponding Plans.

Current Status : Simulation running for the COMPOSITE Plan.

(b) DICOM-RT path

Select the type of TPS for the DICOM-RT data files exported from the system.



Next select the specific patient plan or folder (eg. that PTV1 plan, PTV2 plans, PTV3 plan, or COMPOSITE Plan) → Select output folder and assign a user-defined output excel file name (eg. Result.xls) →[†]Enter the prescription dose (PD) and custom inputs for a specific plan → Hold on for 10-20 minutes until the computation and simulation execute → End of application dialog box pops up → Push 'no' button if you are done, else push 'yes' button to restart the program Search your output (eg. Result.xls) in the specific user designated location or folder.

[†] **Details on the Input prompts** [(< Volume) or (> Volume)]

"Enter Fraction (a) of PD (< Volume)" → Enter the ***fraction*** ('a' such as 0.10, 0.20, 0.30 etc) of the Prescription Dose (PD) as ***a reference point*** to calculate the relative volume coverage of the corresponding region of interest (ROI) below the specific dose (a*PD).

"Enter Fraction (c) of PD (>Volume)" → Enter the ***fraction*** ('c' such as 0.10, 0.20, 0.30 etc) of the Prescription Dose (PD) as ***a reference point*** to calculate the relative volume coverage of the corresponding region of interest (ROI) above the specific dose (c*PD).

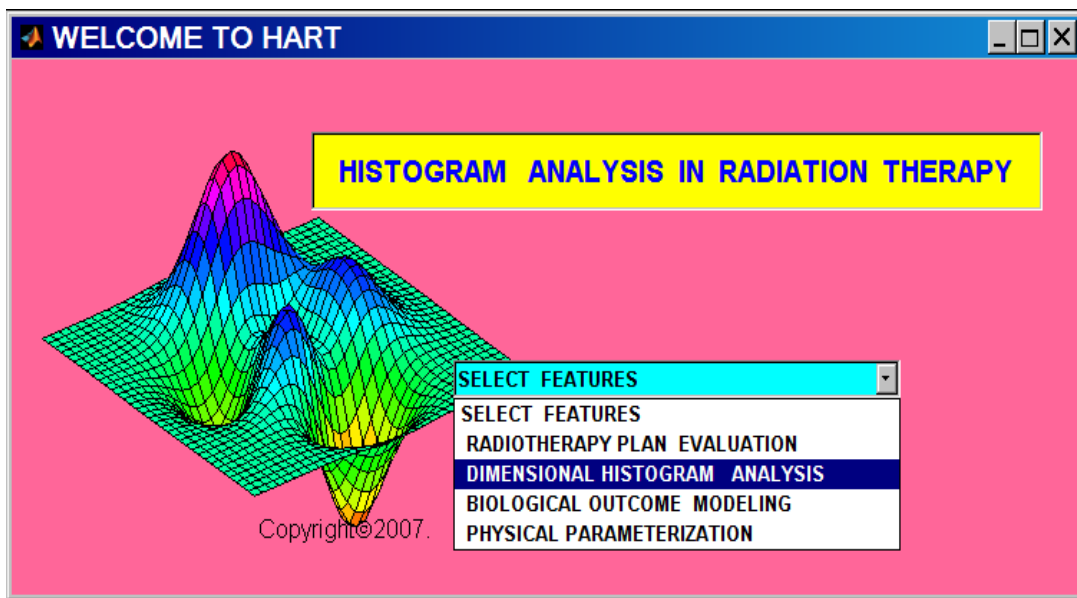
(Step (a))

(Step (b))

(II) Spatial dose-volume histogram (sDVH) analysis

This section is especially prepared for the sole users of the sDVH analysis, an extraordinary application in the program. The user can simply follow the steps by steps as shown below.

- (i) First type **HART** in MATLAB command window. **HART** GUI panel prompts quickly. From the prompt panel of the **HART** GUI: Select features → ***DIMENSIONAL HISTOGRAM ANALYSIS*** option as shown in Step (a).

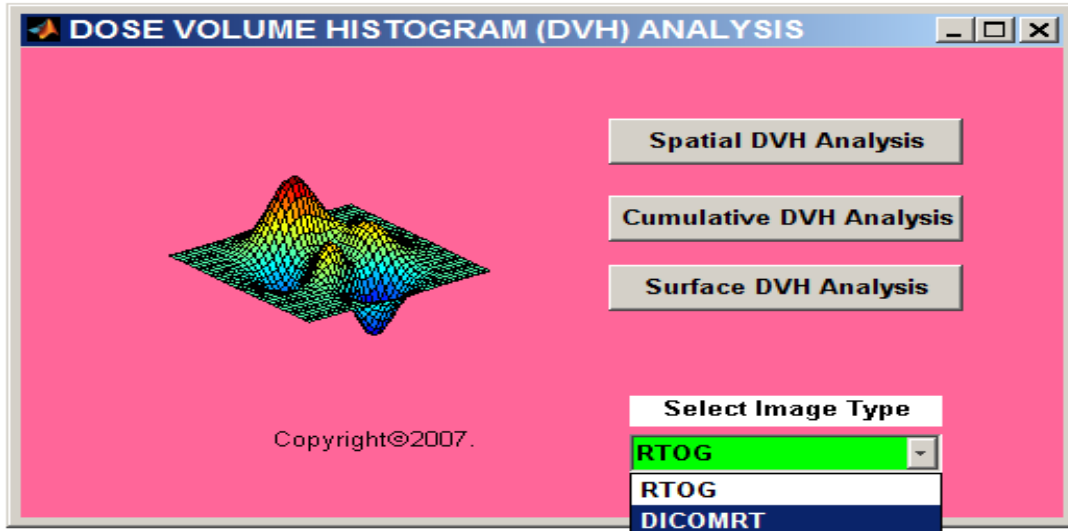


Step (a)

DOSE VOLUME HISTOGRAM (DVH) ANALYSIS panel prompts →

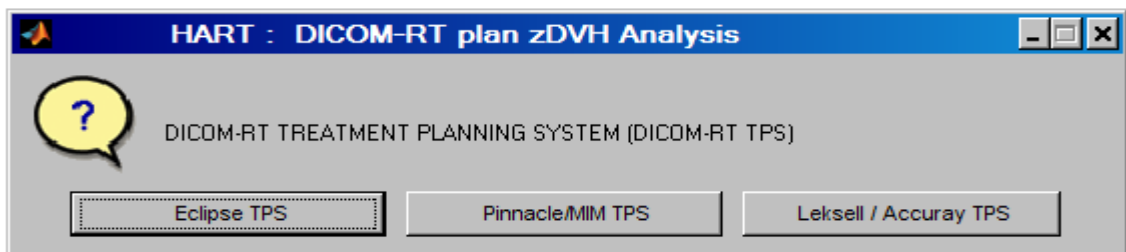
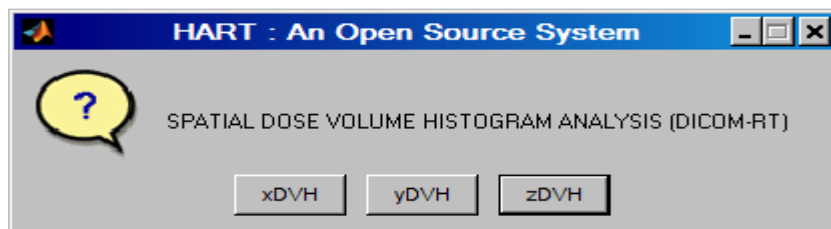
Select the type of the Image formats (**RTOG** or **DICOMRT**) → (Select)

Spatial DVH analysis button → **Step (b):**



(Step (b))

- (ii) From the prompt window of **HART** graphical user interface: **HART / sDVH** panel prompts users to select (a) appropriate type of sDVH analyses, and subsequently (b) the applicable type of Treatment Planning System (TPS) respectively:



The user can opt to select the type of the sDVH analyses using RTOG or DICOM-RT plans as follows:

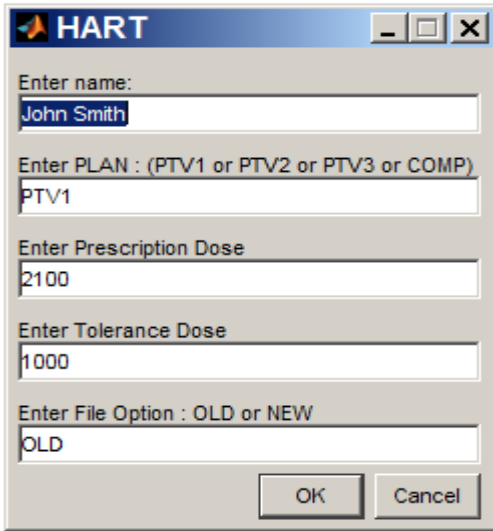
- (i) xDVH analysis of the region of interest along x-direction,
- (ii) yDVH analysis of the region of interest along y-direction, and
- (iii) zDVH analysis of the region of interest along z-direction,
based on the interest of their study using the RTOG data formats,

and

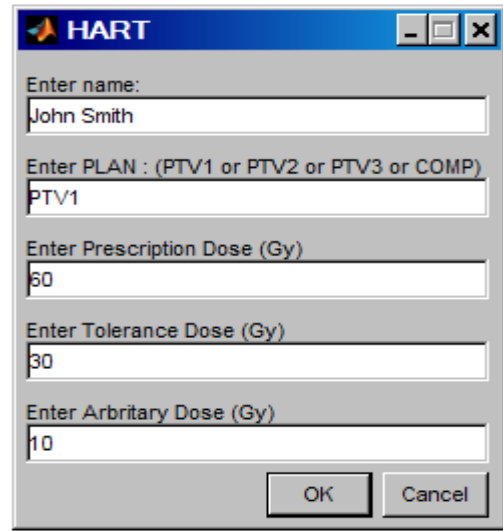
- (i) xDVH analysis of the region of interest along x-direction,
- (ii) yDVH analysis of the region of interest along y-direction, and
- (iii) zDVH analysis of the region of interest along z-direction, based
on the interest of their study for the DICOM-RT image data formats.

(iii) **HART / sDVH** panel prompts for the complete input information of the imported plan after selecting the x-,y- or z-DVHs in the step [II(ii)] as mentioned below:

- (a) Patient name under **Enter name** tab,
- (b) Plan of study under **Enter PLAN (PTV1 or PTV2 or PTV3 or COMP)** tab,
- (c) Prescription dose under **Enter Prescription Dose** tab,
- (d) Tolerance (& Arbitrary) dose under **Enter Tolerance (& Arbitrary) Dose** tabs respectively,
- (e) Users can repeat **Old run** or start a **New run** of the plan under **Enter File option: OLD or NEW** (Limited to **RTOG** file-path option).

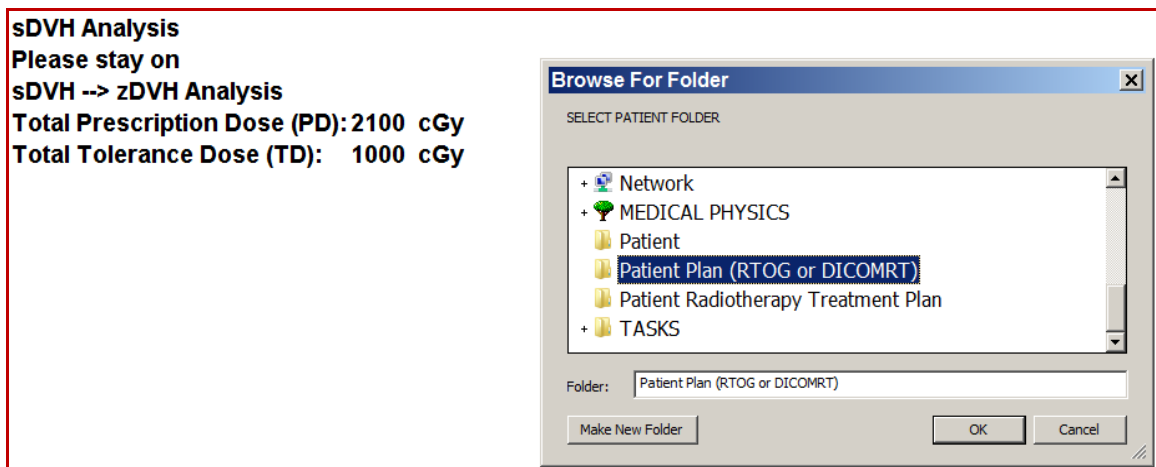


(RTOG path)

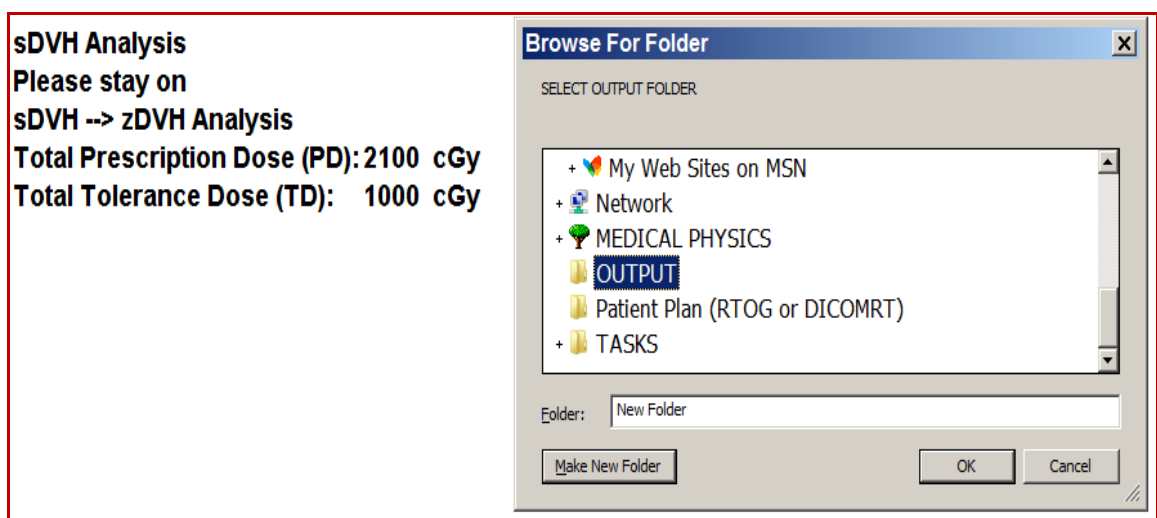


(DICOM-RT path)

- (iv) A panel prompts to search for the folder that contains the RTOG or DICOM-RT data files of your interest for a known radiation therapy treatment plan of a patient. Select the patient folder and click 'OK'. Please wait for few seconds until MATLAB finishes its copying task.



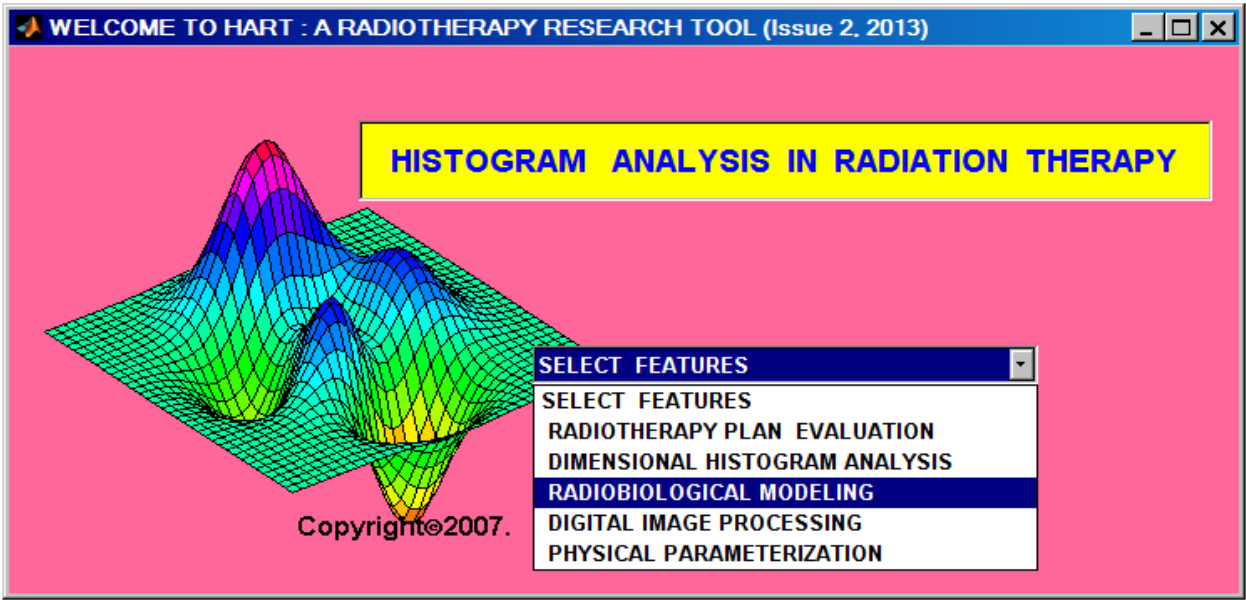
- (v) A panel prompts to search for the OUTPUT folder to dump the final output of the extracted sDVH statistics for all of the targets, regions of interest, and structures contoured in the radiation therapy treatment plan of a patient. Select the output folder of your interest and click 'OK'. Please hold on 5 to 15 minutes for the complete data extractions based on the strength of the processor.



b) Radiobiological modeling for outcome analysis

This section is especially prepared for the users of radiobiological modeling applications in the program. The user can simply follow the steps as shown below.

First type **HART** in the MATLAB command window. **HART** prompts quickly. The user can opt to select the types of **RADIOBIOLOGICAL OUTCOME MODELING** options as shown below.



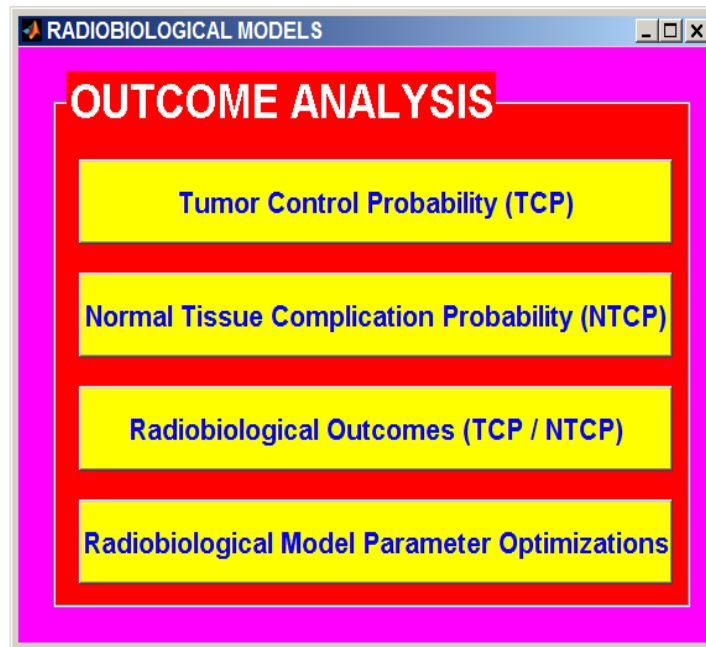
Biological modeling comprises of Poisson statistics based Tumor Control Probability (TCP) and JT Lyman based Normal Tissue Complication Probability (NTCP) models in the program. It also incorporates the radiobiological modeling parameter optimization feature for JT Lyman NTCP model.

i. Therapeutic outcome analysis (TCP/NTCP)

It is recommended to follow the directions as given below for several types of applications of the radiobiological modeling of the radiotherapy treatments.

Select (a) *Tumor Control Probability (TCP)* button to analyze Poisson Statistics tumor control probability, (b) *Normal Tissue Complication Probability (NTCP)* button to analyze JT Lyman normal tissue complication probability, and (c)

Radiobiological Outcomes (TCP/NTCP) button to analyze TCP index using the Poisson statistics, and NTCP index using JT Lyman model.

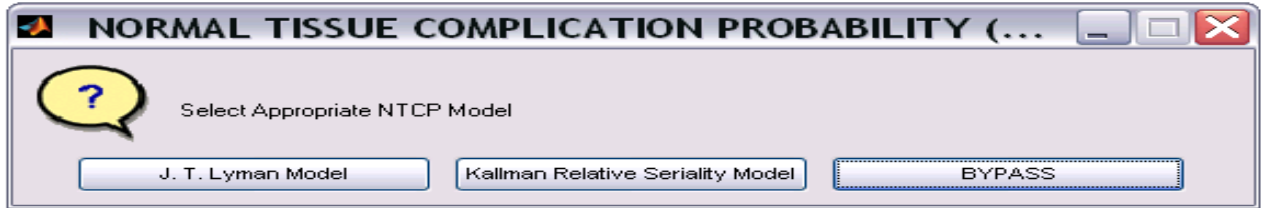


(a) Tumor Control Probability (TCP: Poisson-statistics model)

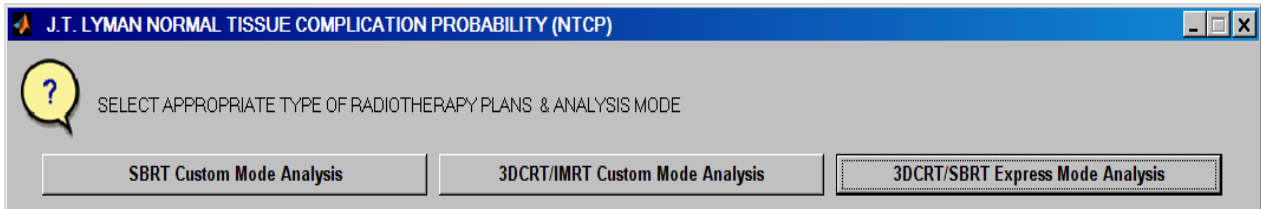
This command prompts the user to the *Radiobiological Outcomes (TCP/NTCP)* functionality that will redirect the analysis to the section (c) as discussed below.

(b-I) Normal Tissue Complication Probability (NTCP: JT Lyman model)

By clicking *Normal Tissue Complication Probability (NTCP)* button, NTCP dialog box prompts allowing users to select to JT Lyman or Kallman Relative Seriality Model based on their application as shown below:



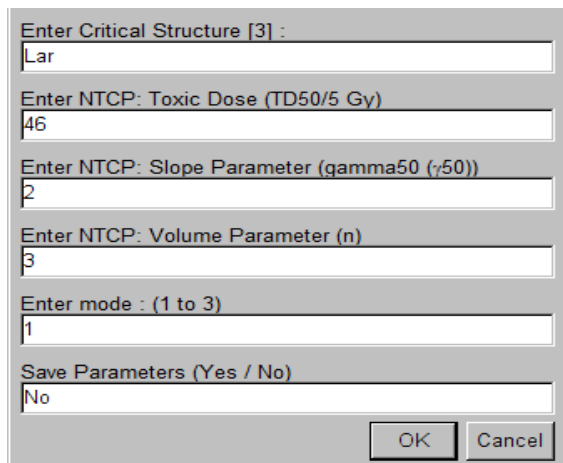
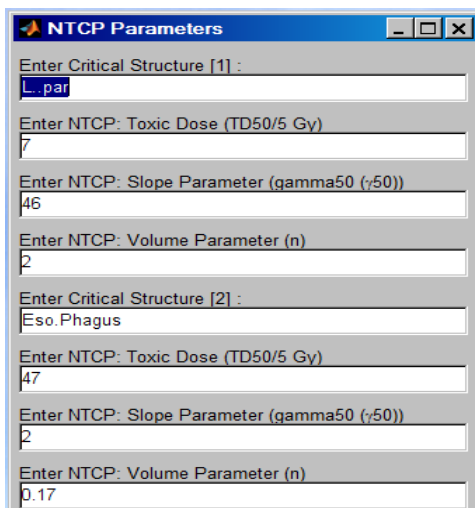
After clicking JT Lyman Model:



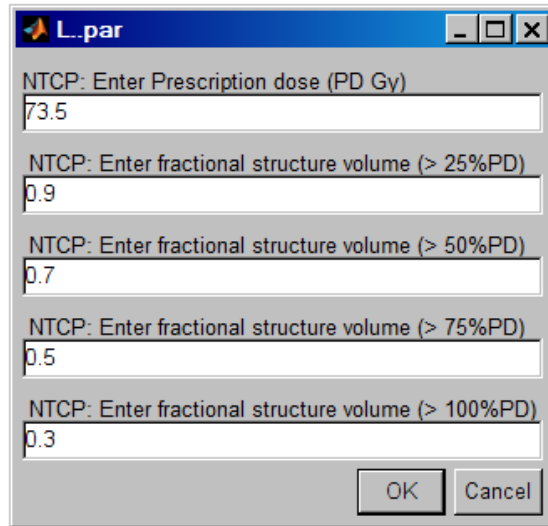
Part I: 3D Conformal Radiotherapy (3DCRT) / IMRT Custom Mode Analysis:

Selecting the *3D Conformal Radiotherapy (3DCRT) / IMRT Custom Mode Analysis*, the system requires user to follow the given steps below:

Step 1: Enter Toxic dose (TD50/5 Gy), Slope parameter (γ_{50}), and volume parameter (n) for each critical structure (1 to 3). Entered parameters can be stored for the next application by choosing ‘Yes’ or ‘yes’ options in Save Parameters box.



Step 2: Enter fractional volume DVH statistics for each critical structure below:

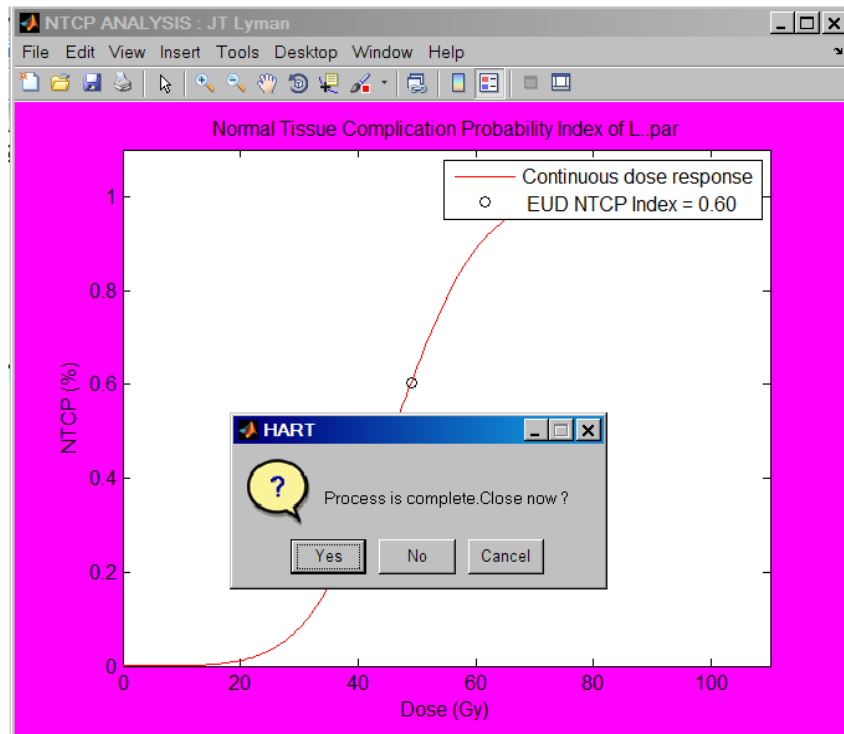


The screenshot shows a dialog box titled "L.par" with the following fields and values:

Field Label	Value
NTCP: Enter Prescription dose (PD Gy)	73.5
NTCP: Enter fractional structure volume (> 25%PD)	0.9
NTCP: Enter fractional structure volume (> 50%PD)	0.7
NTCP: Enter fractional structure volume (> 75%PD)	0.5
NTCP: Enter fractional structure volume (> 100%PD)	0.3

Buttons: OK, Cancel

Step 3: Simulation extracts the corresponding JT Lyman NTCP Indices as shown below in the legend of the graph.



Part II: Stereotactic Body Radiotherapy (SBRT) Custom Mode Analysis:

Step 1: If clicked the *Stereotactic Body Radiotherapy (SBRT) Custom Mode Analysis* button, then enter the **NTCP PARAMETERS** as the window prompts:

NTCP indices can be estimated for the 1– 4 structures contoured in the same plan using mode 1 - mode 4 options.

NTCP parameters as:

- (a) Enter the name of organ of interest,
- (b) Gamma50 (γ_{50}) for the organ of the interest,
- (c) Volume parameter (n) characteristic of seriality or parallel structure,
- (d) TD50,5 dose (Gy) for the specific type of organs,
- (e) Alpha (α) parameter of the organ,
- (f) Beta (β) parameter of the organ,
- (g) Dose per fraction size (Gy) of the organ,
- (h) Enter mode (1) for 1 organ, and mode (4) for 4 organs.

ENTER NTCP PARAMETERS

Enter major disease site :
Lung GTV

NTCP: Enter Critical Structure
Heart

Enter NTCP : gamma50 (γ_{50})
3.63

Enter NTCP : Volume Parameter (n)
0.5

Enter NTCP : Toxic Dose (TD50/5)
46

Enter Dose / Fraction Size (Gy)
7

Enter NTCP : alpha (α)
0.3

Enter NTCP : Beta (λ Beta)
0.1

Enter Mode : (1 or 4)
1

OK Cancel

Step 2: Enter the dose-volume statistics parameters as the DVH window prompts:

ENTER DVH PARAMETERS

NTCP: Enter Prescription dose (PD Gy)
35

NTCP: Enter structure volume > 25%PD
0.9

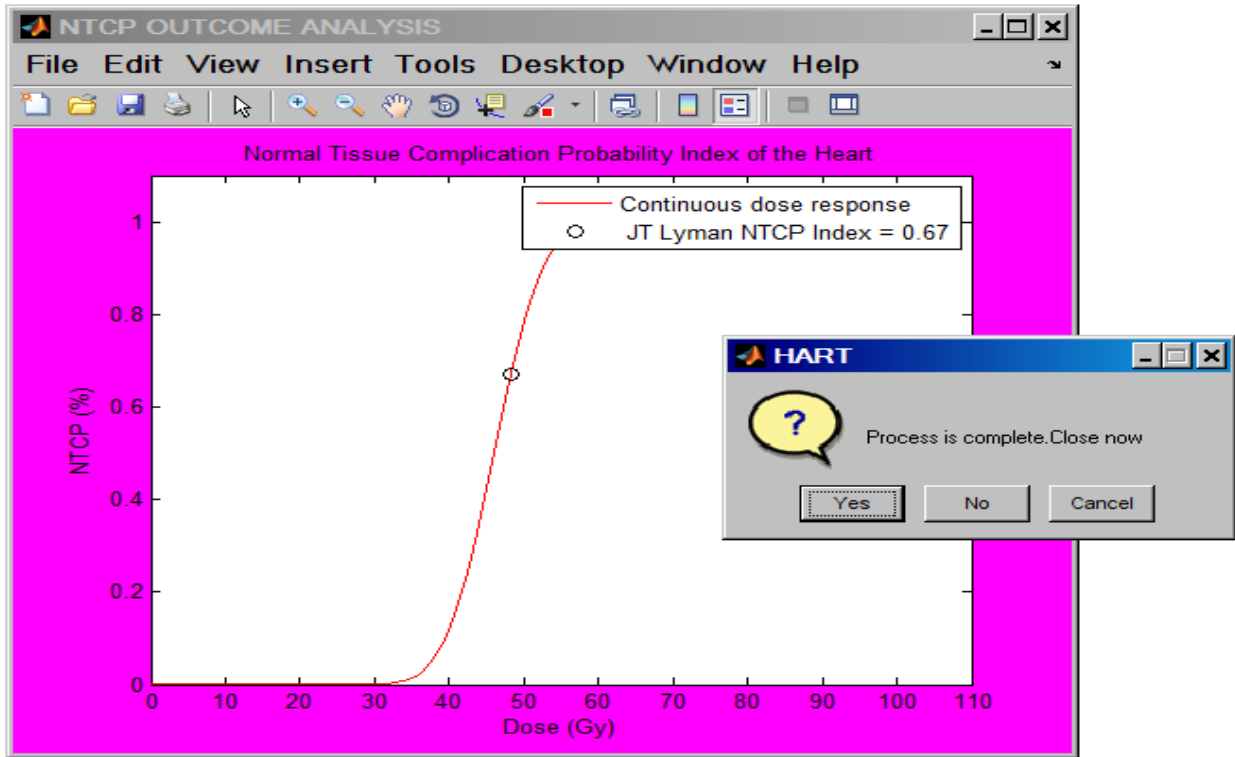
NTCP: Enter structure volume > 50%PD
0.7

NTCP: Enter structure volume > 75%PD
0.5

NTCP: Enter structure volume > 100%PD
0.3

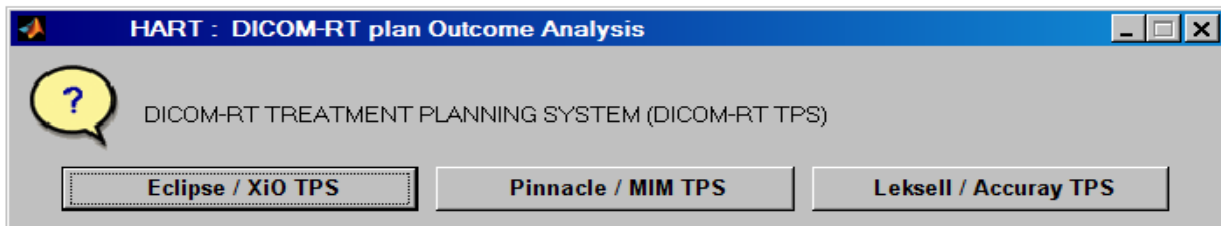
OK Cancel

Step 3: The final simulation executes: Exact NTCP index is displayed in the legend of the graph (JT Lyman NTCP index) as shown below:



Part III: 3DCRT/SBRT Express Mode Analysis:

Step 1: User can select an appropriate type of Treatment Planning System (TPS):

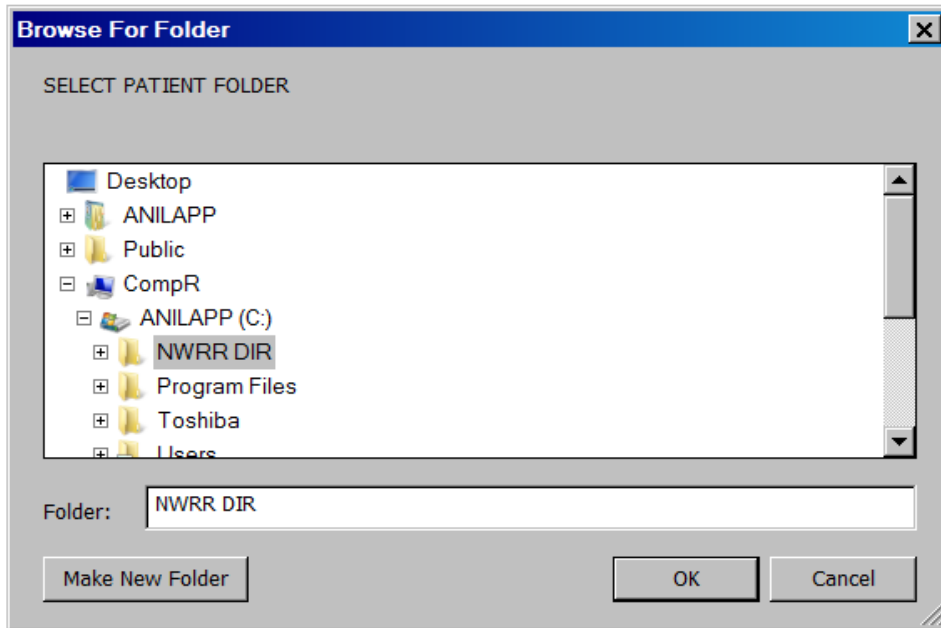


Note: (a) Eclipse / Xio TPS exports all CT-images, RT-plan, RT-structures, RT-dose files in a single patient folder, (b) Pinnacle/MIM TPS exports all CT-images, RT-

plan, RT-structures, RT-dose in 4 different folders in a single patient folder , and (c) Leksell/Accuray TPS exports all CT-images, RT-structures, RT-dose in 3 separate folders in a single patient folder respectively.

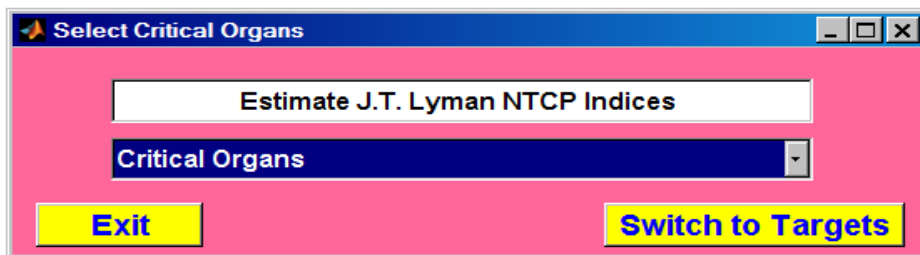
Step 2: User can select the appropriate *patient folder* for the corresponding data-set:

>> **System : Eclipse / XiO TPS.**

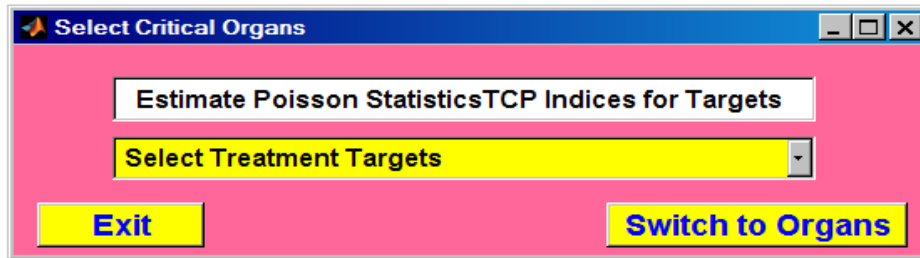


Step 3: User can select Organs for NTCP Analysis or Targets for TCP Analysis:

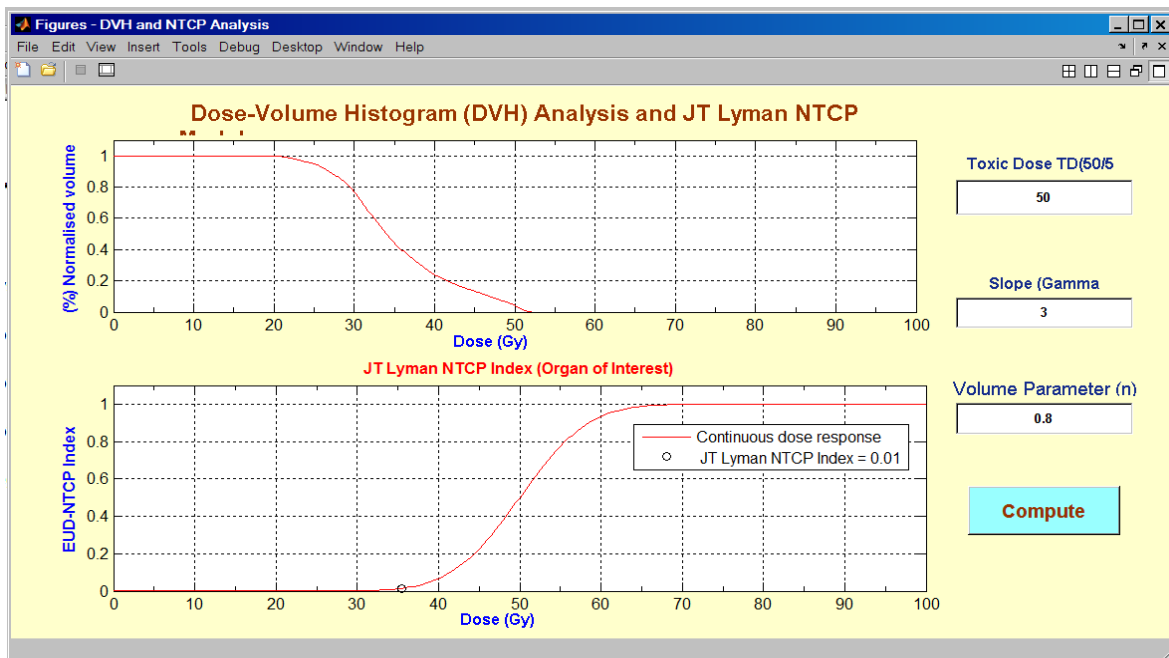
|>> **Now computing Normal Tissue Complication Probability (NTCP)**



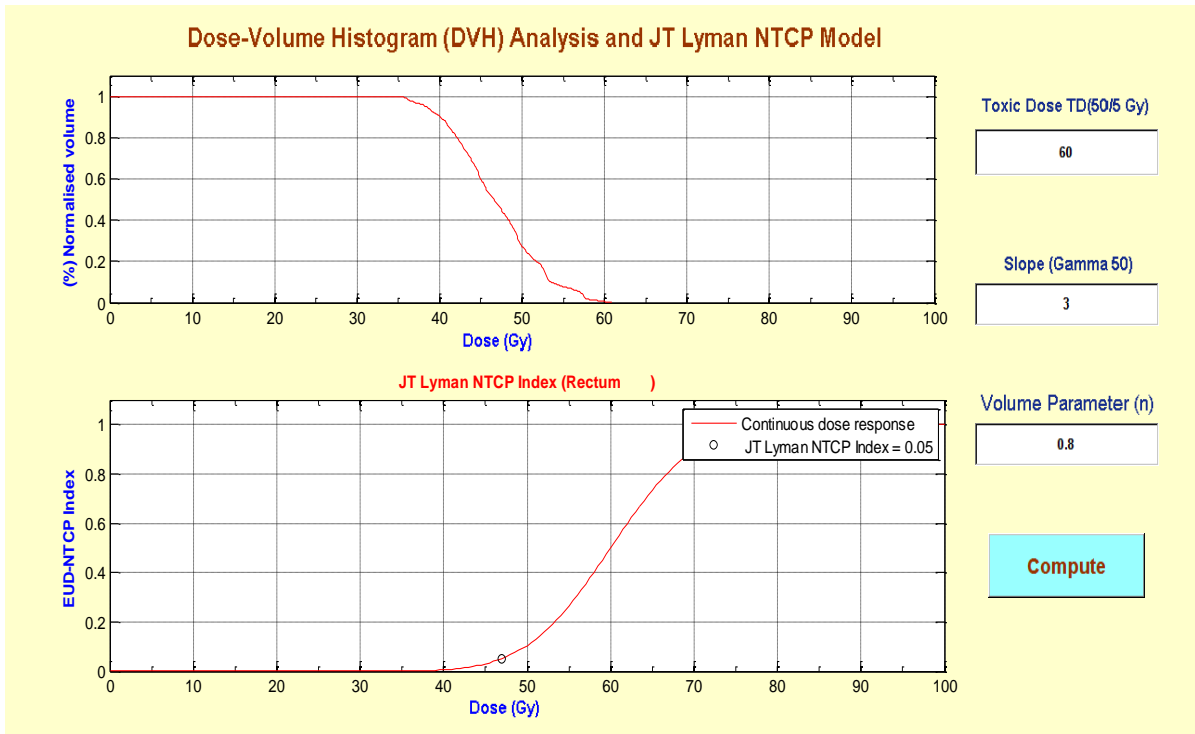
>> Now computing Tumor Control Probability (TCP)



Step 4: After selection of the organ or tumor target, user can execute the corresponding NTCP and TCP calculations and perform successive simulations and analyses in the corresponding panels using the switching systems as shown below by entering the appropriate radiobiological model parameters (JT Lyman parameters: TD50/5, Gamma50, and volume parameter (n) for NTCP analysis; Poisson statistics parameters: TCD50/5, Gamma50, and α/β Ratio for TCP analysis).



(Sample before simulation)



(Executed simulation)

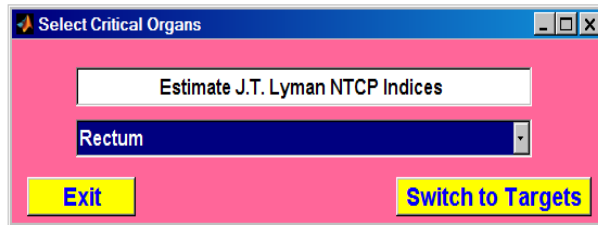
Step 5: Exit the simulation system: *Click Exit.*

```

Region of Interest : Rectum
Organ: Rectum TD50/5: 50; Gamma50: 3; Parameter (n): 0.8; JT Lyman NTCP Index = 0.32
Organ: Rectum TD50/5: 75; Gamma50: 3; Parameter (n): 0.8; JT Lyman NTCP Index = 0.00
Organ: Rectum TD50/5: 60; Gamma50: 3; Parameter (n): 0.8; JT Lyman NTCP Index = 0.05
  
```

```

>>
>>
>>
>>
>>
>>
>>
>>
>>
>>
  
```



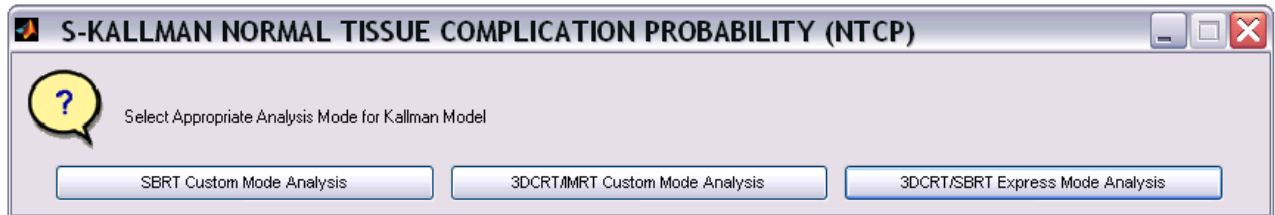
```

Region of Interest : spinal_cord
Organ: spinal_cord TD50/5: 50; Gamma50: 3; Parameter (n): 0.8; JT Lyman NTCP Index = 0.83
Elapsed time is 57.315627 seconds.
  
```

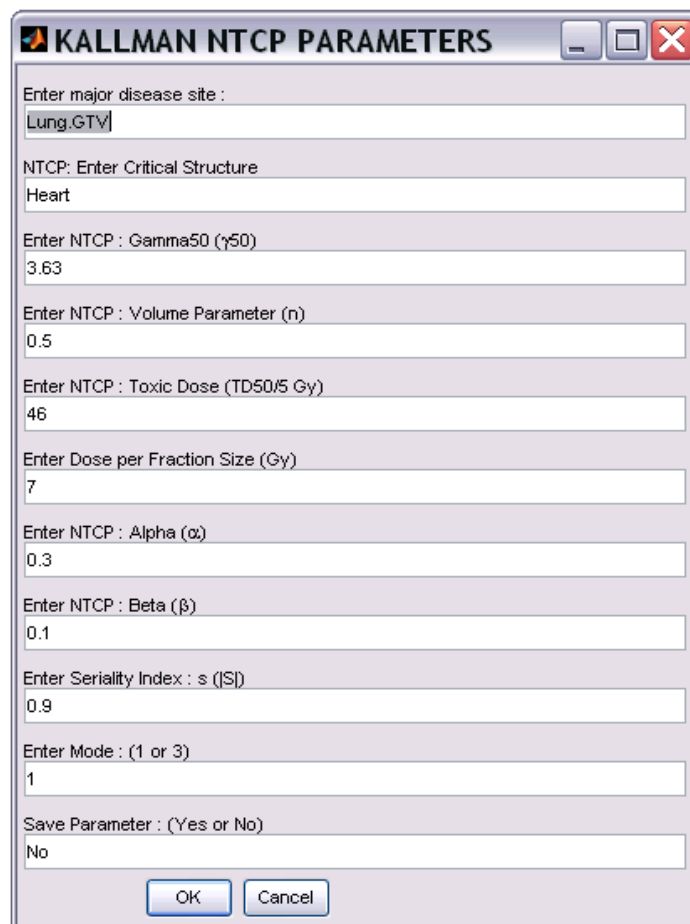
Thank you very much for choosing HART program : [Histogram Analysis in Radiation Therapy](#)

(b-II) Normal Tissue Complication Probability (NTCP: Kallman Serial model)

Step 1: Users can select custom mode analysis for SBRT and/or 3DCRT/IMRT modules based on their application or needs. However, 3DCRT express mode analysis is currently under construction.



Step 2: Enter organ specific model parameters for the Kallman Model at the prompt:



KALLMAN NTCP PARAMETERS

Enter major disease site :
Lung.GTV

NTCP: Enter Critical Structure
Heart

Enter NTCP : Gamma50 (γ_{50})
3.63

Enter NTCP : Volume Parameter (n)
0.5

Enter NTCP : Toxic Dose (TD50/5 Gy)
46

Enter Dose per Fraction Size (Gy)
7

Enter NTCP : Alpha (α)
0.3

Enter NTCP : Beta (β)
0.1

Enter Seriality Index : s (|S|)
0.9

Enter Mode : (1 or 3)
1

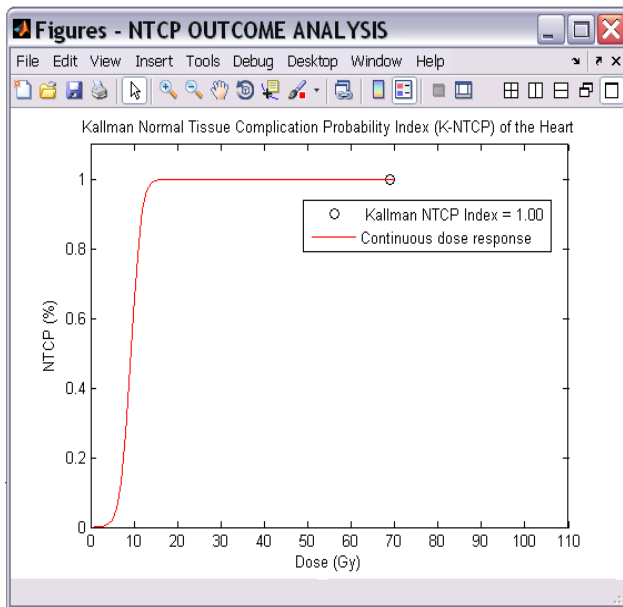
Save Parameter : (Yes or No)
No

OK Cancel

Step 3: Enter Prescription Dose (PD) of treatment, and a set of DVH statistics for the corresponding organ in the prompt as shown below:

Detailed description of the DVH:Heart dialog box: The window title is 'DVH:Heart'. It contains five text input fields, each with a label and a value. The labels are: 'NTCP: Enter Prescription dose (PD Gy)', 'NTCP: Enter Structure Volume > 25%PD', 'NTCP: Enter Structure Volume > 50%PD', 'NTCP: Enter Structure Volume > 75%PD', and 'NTCP: Enter Structure Volume > 100%PD'. The values entered are: 35, 0.9, 0.7, 0.5, and 0.3 respectively. At the bottom of the dialog are two buttons: 'OK' and 'Cancel'.

Step 4: Output indices and corresponding NTCP simulation would be displayed in the command windows platform as shown below:



Status: NTCP Analysis Mode.

Mode of Analysis: SBRT Custom Mode.

Kallman NTCP (K-NTCP) Index and Outcome Analysis:

Critical Structure:	Heart
01. Prescription Dose (PD):	35.000000 Gy
02. Dose Tolerance (TD50/5):	46.000000 Gy
03. Relative Seriality Index (s):	0.900000
04. Slope Parameter (Gamma50):	3.630000
05. Effective Dose (D-Eff):	69.000000 Gy
06. K-NTCP Index:	1.000000

(c) Radiobiological Modeling Outcomes (TCP/NTCP)

Step 1: Select *Radiobiological Outcomes (TCP/NTCP)* button, then **OUTCOME ANALYSIS¹** window pops up. One can easily enter:

TCP parameters as:

- (a) TCD50 dose for the specific type of treatments
(eg: Prostate: 38.9 Gy; Head and Neck: 63.5 Gy),
- (b) alpha (α ; 0.3 by default),
- (c) Beta (β ; 0.03 by default),
- (d) Gamma50 (γ_{50}) for Target,

NTCP indices can be estimated for the 1– 4 structures contoured in the same plan using mode 1 - mode 4 options.

NTCP parameters as:

- (a) Gamma50 (γ_{50}) for the organ of the interest,
- (b) Volume parameter (n),
- (c) TD50 dose (Gy) for the specific type of organs,
- (d) Enter mode (1) for 1 organ, and mode (4) for 4 organs.

OUTCOME ANALYSIS

Enter major disease site :
Prostate / Head & Neck GTV

Enter TCP: TCD50
38.9

Enter TCP: Lambda (Λ)
N/A

Enter TCP : Alpha (α)
0.3

Enter TCP : Beta (β)
0.03

Enter TCP : Gamma50 (γ 50)
0.74

NTCP: Enter Critical Structure
LAR

Enter NTCP : gamma50 (γ 50)
3.63

Enter NTCP : n
0.5

Enter NTCP : TD50
80

Enter mode : (1 or 4)
1

OK Cancel

(¹Fig: Outcome Analysis Prompt)

Step 2: Other **OUTCOME ANALYSIS**² prompt pops up: Enter the **TCP inputs** as:

(a) Prescription dose of the treatment (PD Gy)

(b) Normalized target volumes as

(**< 40% PD, < 60% PD, >80% PD, >100% PD, >110% PD, and >120% PD**)

and the **NTCP inputs** as:

(c) Normalized structure volumes (>25% PD, >50% PD, > 75% PD, >100% PD)

OUTCOME ANALYSIS

TCP/NTCP: Enter Prescription dose (PD Gy)
73.5

TCP: Enter target volume < 40% PD
0.02

TCP: Enter target volume < 60% PD
0.07

TCP: Enter target volume > 80% PD
0.6

TCP: Enter target volume > 100% PD
0.5

TCP: Enter target volume > 110% PD
0.4

Enter TCP target volume > 120% PD
0.3

NTCP: Enter structure volume > 25%PD
0.9

NTCP: Enter structure volume > 50%PD
0.7

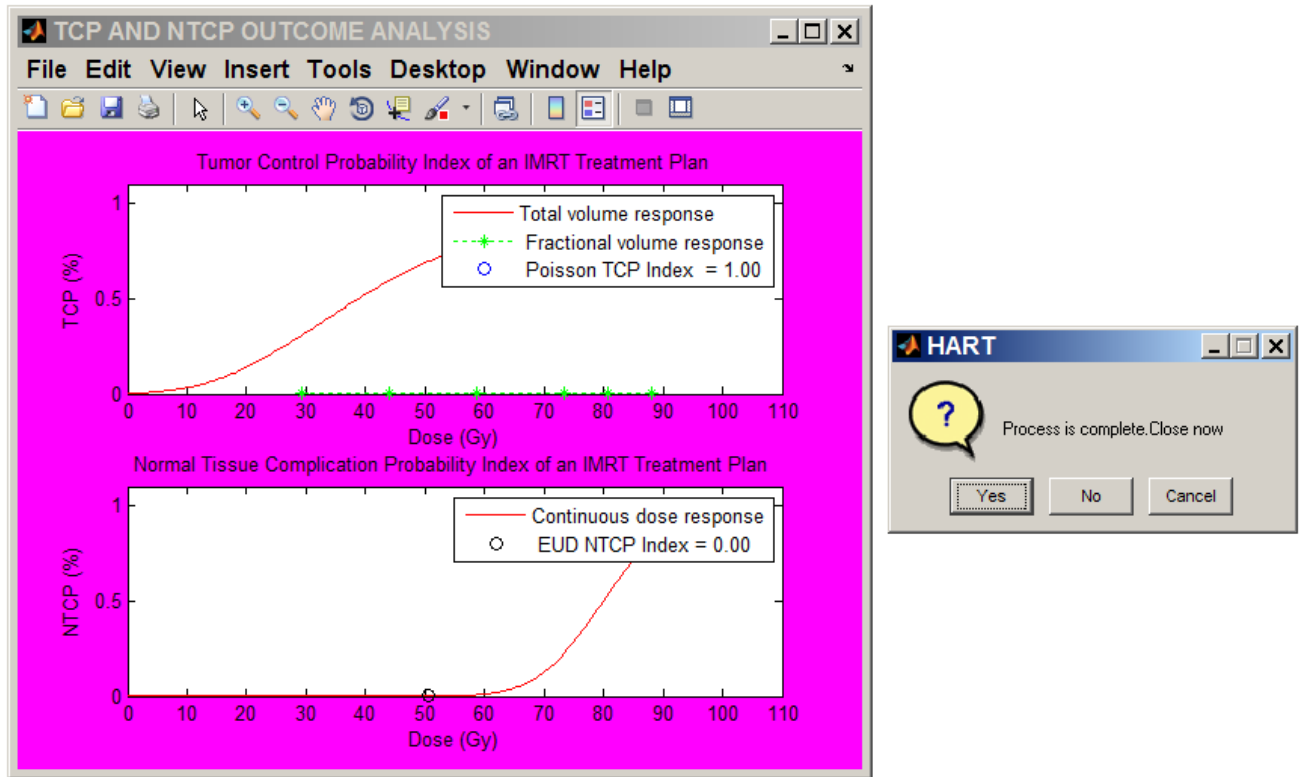
NTCP: Enter structure volume > 75%PD
0.5

NTCP: Enter structure volume > 100%PD
0.3

OK Cancel

(Fig²: Outcome Analysis Prompt)

Step 3: Final simulation pops up: Exact TCP and NTCP indices are displayed in the corresponding legends of the graph (TOP: TCP index; BOTTOM: NTCP index) as shown below:

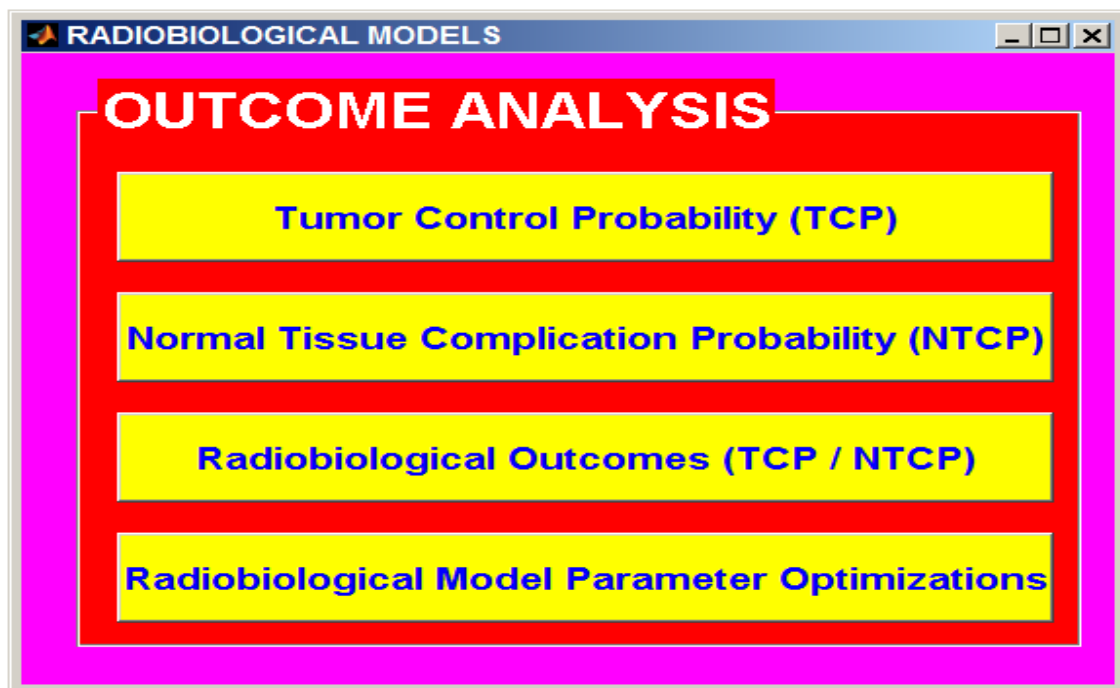


If clicked 'Yes', the plot closes in 15 seconds and if clicked 'No' the simulation stays there forever unless one cancels the GUI.

ii. Radiobiological model parameter optimization (JT Lyman model):

The proposed technique offers the analytical solution of the Probit function of the Lyman-Kutcher-Burman (LKB) model and the Logistic function of the Niemierko (NMK) model to determine the unknown slope parameter (m) of the JT Lyman NTCP model using the standard tolerance - dose (TD50,5) of the large volume fraction ($>2/3$) of the organ, the volume parameter (n), and the polynomial modeling extrapolation technique.

- (a) Select ***Radiobiological Model Parameter Optimization*** button to determine the slope parameter (m) in JT Lyman NTCP model using prescription dose (PD), Toxic dose (TD50,5), volume parameter (n), and the corresponding DVH statistics of the critical organs or Region of Interests (ROIs).



- (b) Enter structure identification, prescription dose (PD), Toxic dose ($TD_{50,5}$), and volume parameter (n), and mode (1 or 4 structures) respectively.

LYMAN PARA... - □ ×

NTCP: Enter Critical Structure
LAR

Enter NTCP: Prescription Dose (PD Gy)
70

Enter NTCP: TD50/5 (Gy)
46

Enter NTCP: Volume Parameter (n)
0.5

Enter mode: (1 or 4)
1

OK Cancel

- (c) Enter fractional doses relative to prescription dose (x1% PD, x2% PD, x3% PD, x4% PD) and the normalized structure volumes (>25% PD, >50% PD, >75% PD and >100% PD) of the irradiated critical structure or organ.

DVH Statistics - □ ×

NTCP: Enter Prescription dose (PD Gy)
70

NTCP: Enter Fractional Dose 1 (x1%PD)
0.25

NTCP: Enter Fractional Dose 2 (x2%PD)
0.50

NTCP: Enter Fractional Dose 3 (x3%PD)
0.75

NTCP: Enter Fractional Dose 4 (x4%PD)
1

NTCP: Enter Relative Volume > (x1%PD)
1

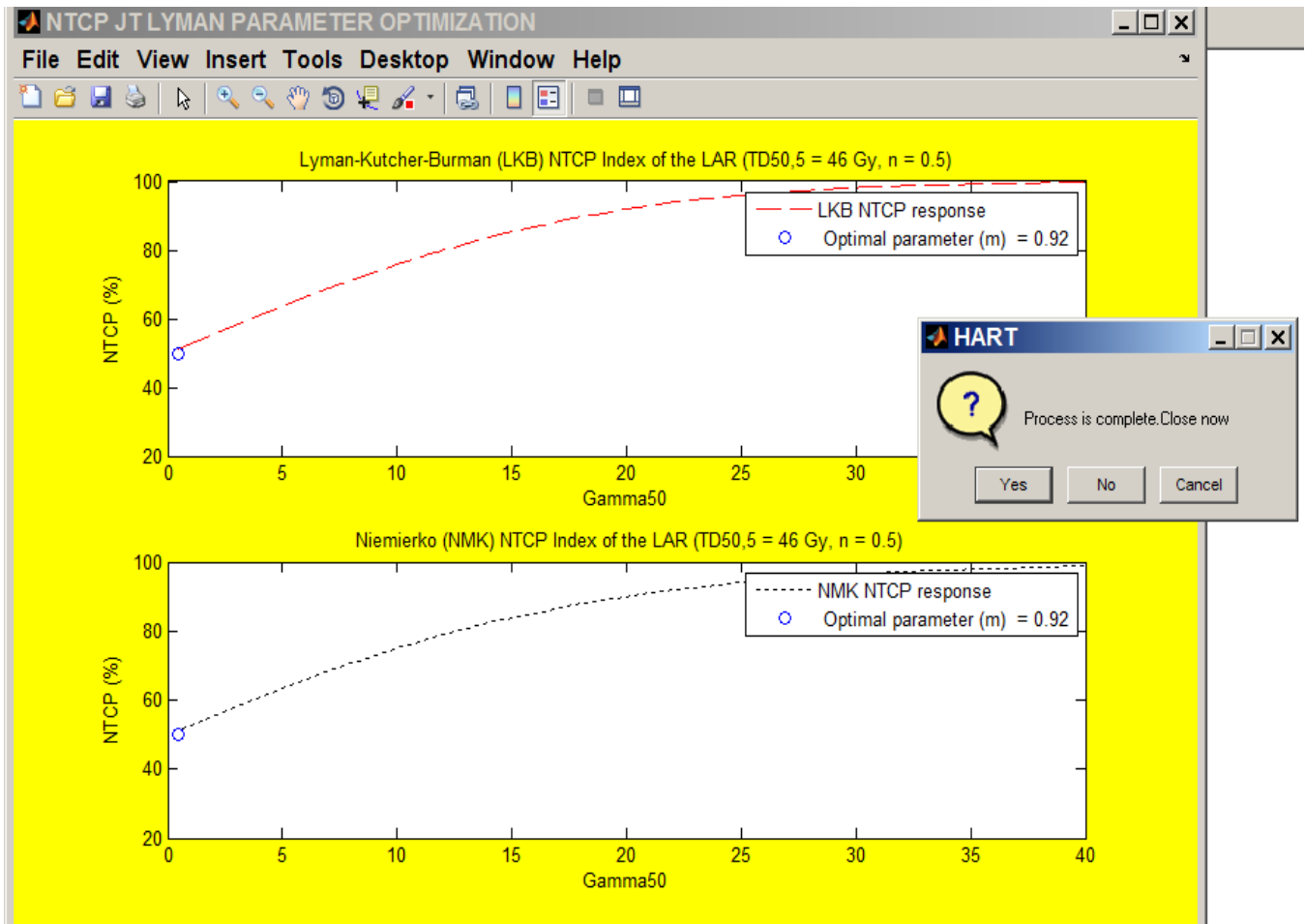
NTCP: Enter Relative Volume > (x2%PD)
0.8

NTCP: Enter Relative Volume > (x3%PD)
0.5

NTCP: Enter Relative volume > (x4%PD)
0.2

OK Cancel

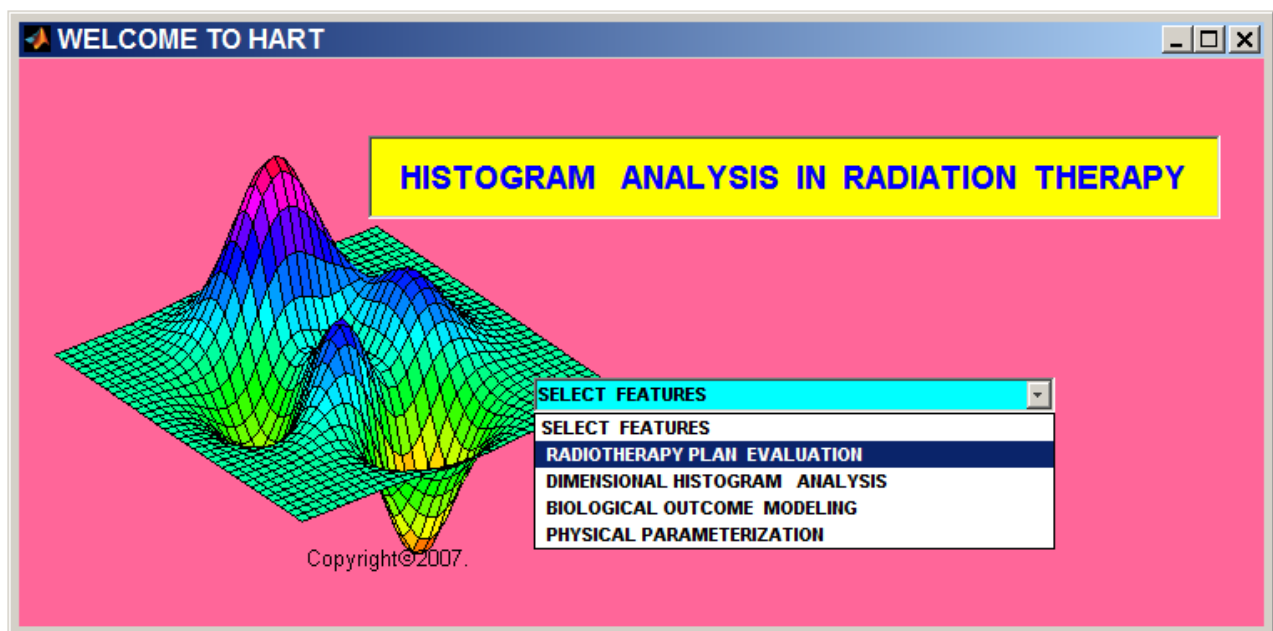
(d) Simulation executes. The optimal value of ‘m’ would be displayed in the legend of the figure as shown below. Furthermore if clicked ‘Yes’ on the dialog box that prompts immediately, the plot closes in 5 seconds and if clicked ‘No’ the simulation stays there forever unless the GUI is cancelled.



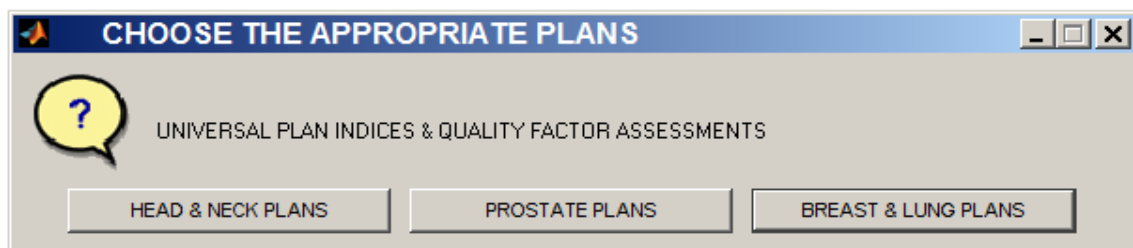
c) Universal Plan-Indices evaluation

This section is especially prepared for the users of universal plan indices (UPI) applications in program. Users can simply follow the steps as given below.

- (i) Type **HART** in the MATLAB command window. **HART** prompts quickly. Select the *Radiotherapy Plan Evaluation* option as shown below.

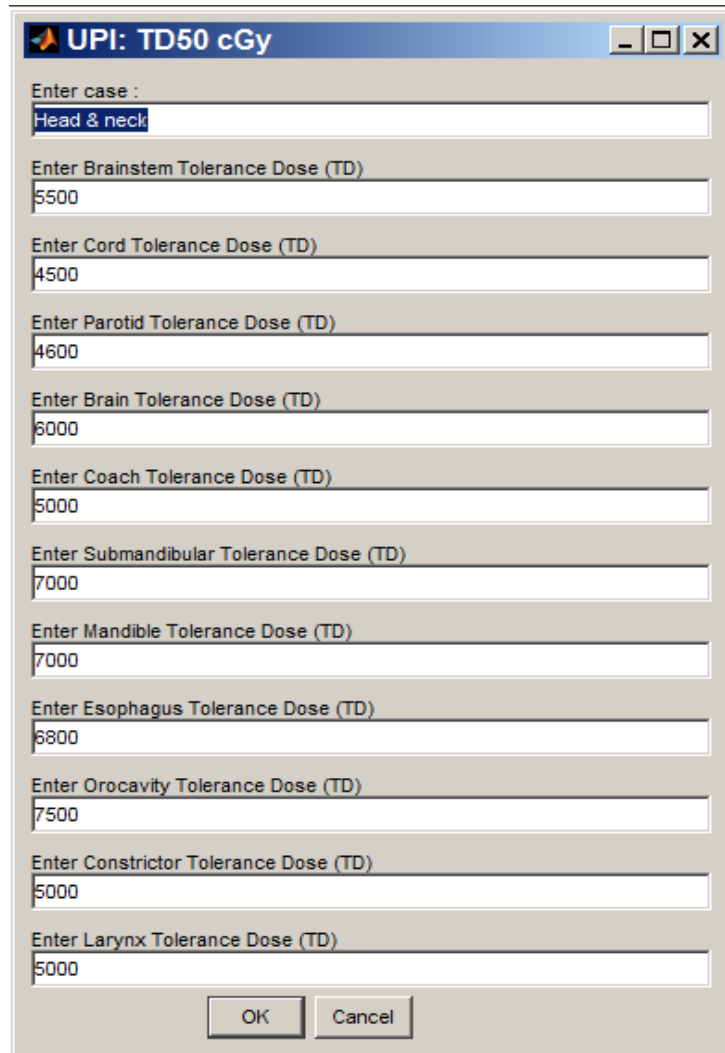


- (ii) Select the appropriate plans such as **HEAD & NECK** Plans, **PROSTATE** Plans, and **BREAST & LUNG** Plans. The **Head& Neck** cases cover a large no. of organs.



(iii) Currently UPI evaluation forms are available for two different cases :

(a) **Head and Neck Plans:** *Enter Tolerance doses (cGy) for all neighboring organs of the tumor target as shown below in the **Step (i)**.*



The image shows a software dialog box titled "UPI: TD50 cGy". It contains several input fields for entering tolerance doses (TD) in cGy for different organs. The "Enter case :" field is filled with "Head & neck". The other fields and their values are: "Enter Brainstem Tolerance Dose (TD)" is 5500; "Enter Cord Tolerance Dose (TD)" is 4500; "Enter Parotid Tolerance Dose (TD)" is 4600; "Enter Brain Tolerance Dose (TD)" is 6000; "Enter Cochlea Tolerance Dose (TD)" is 5000; "Enter Submandibular Tolerance Dose (TD)" is 7000; "Enter Mandible Tolerance Dose (TD)" is 7000; "Enter Esophagus Tolerance Dose (TD)" is 6800; "Enter Oropharynx Tolerance Dose (TD)" is 7500; "Enter Constrictor Tolerance Dose (TD)" is 5000; and "Enter Larynx Tolerance Dose (TD)" is 5000. At the bottom, there are "OK" and "Cancel" buttons.

Organ	Tolerance Dose (TD) (cGy)
Brainstem	5500
Cord	4500
Parotid	4600
Brain	6000
Cochlea	5000
Submandibular	7000
Mandible	7000
Esophagus	6800
Oropharynx	7500
Constrictor	5000
Larynx	5000

Step (i)

Enter the normalized volume above **TD50 (cGy)** dose for the corresponding organ as shown below in the **Step (ii)**.

OAR: Normalised volume (%) >TD50

Enter Brainstem Volume above TD
0.0

Enter Cord Volume above TD
0.0

Enter L. Parotid Volume above TD
0.0

Enter R. Parotid Volume above TD
0.0

Enter Brain Volume above TD
0.0

Enter R. Cochlea volume above TD
0.0

Enter L. Cochlea volume above TD
0.0

Enter L. Submandible Volume above TD
0.0

Enter R. Submandible Volume above TD
0.0

Enter Mandible Volume above TD
0.0

Enter Esophagus Volume above TD
0.0

Enter Orocavity Volume above TD
0.0

Enter Constrictor Volume above TD
0.0

Enter Larynx Volume above TD
0.0

OK Cancel

Step (ii)

Enter the absolute volume above the PD (cGy) for the corresponding organs at risk (OARs) as shown below in the **Step (iii)**.

OAR: Absolute Volume (cc) > PD

Enter Brainstem Volume above PD
0.0055

Enter Cord Volume above PD
0.0055

Enter L. Parotid Volume above PD
0.0055

Enter R. Parotid Volume above PD
0.0055

Enter Brain Volume above PD
0.0055

Enter R. Cochlea volume above PD
0.0055

Enter L. Cochlea volume above PD
0.0055

Enter L Submandible Volume above PD
0.0055

Enter R Submandible Volume above PD
0.0055

Enter Mandible Volume above PD
0.0055

Enter Esophagus Volume above PD
0.0055

Enter Orocavity Volume above PD
0.0055

Enter Constrictor Volume above PD
0.0055

Enter Larynx Volume above PD
0.0055

OK Cancel

Step (iii)

Enter (a) **Prescription dose (PD; cGy)** of the treatment;

(b) **Maximum dose (D_{Max} ; cGy)** at the planning target volume (PTV);

(c) Corresponding **absolute volumes** of the PTV above the specified fractions (**100%, 95%, and 50%** respectively) of the PD;

(d) Corresponding **Doses (D_{95} and D_5 cGy** respectively) at the specified fractions (**95% and 5%** respectively) of the PTV respectively; and

(e) **Total volume of PTV** target as shown below in the **Step (iv)**.

UPI: Target dose (cGy) and Volume (cc)

Enter Prescription Dose
1000

Enter maximum PTV dose
1500

Enter PTV volume (cc) above PD
1.0

Enter PTV volume (cc) above 95% PD
1.0

Enter PTV volume (cc) above 50% PD
1.0

Enter Dose at 95% of PTV Volume
950

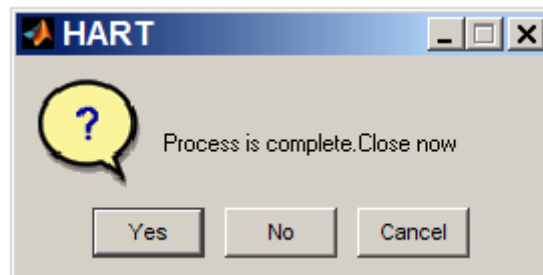
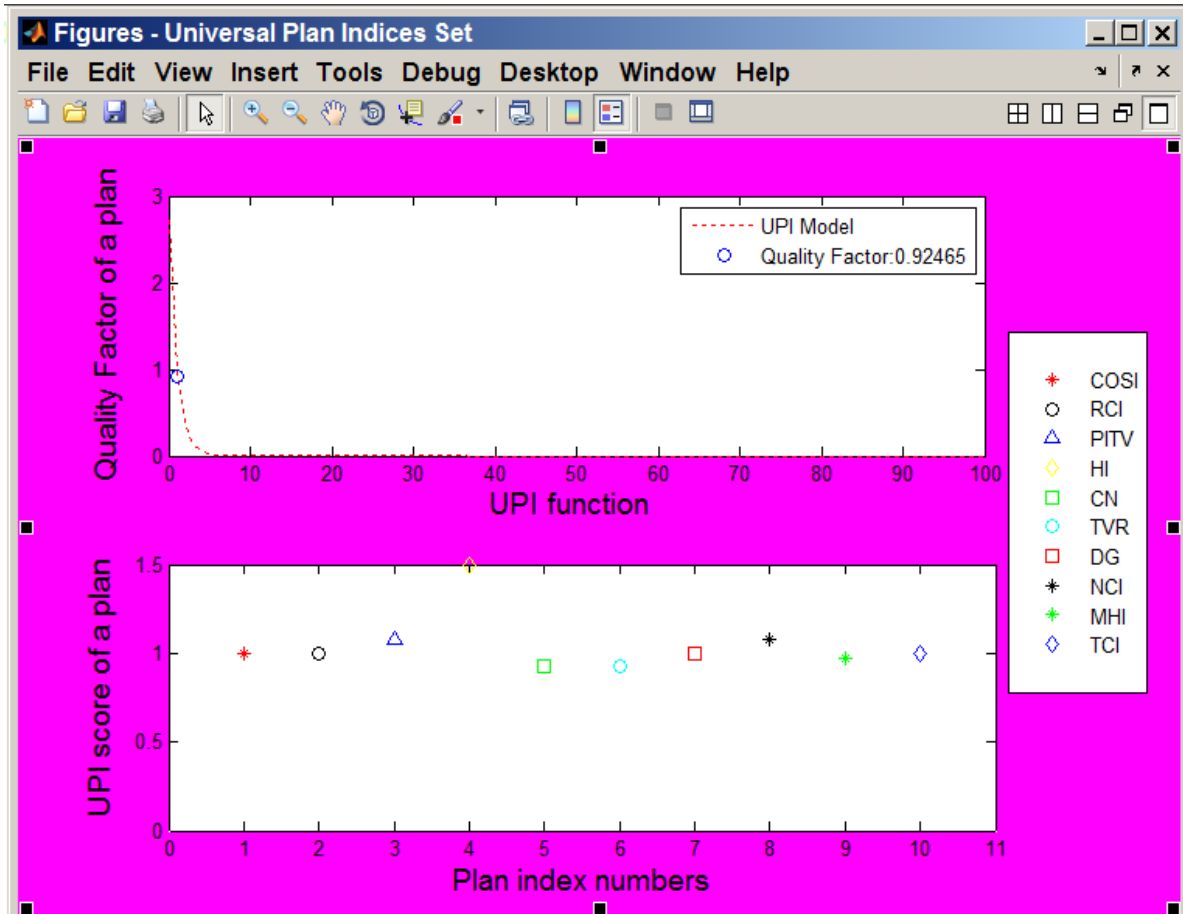
Enter Dose at 5% of PTV Volume
975

Enter PTV Volume (cc)
1

OK Cancel

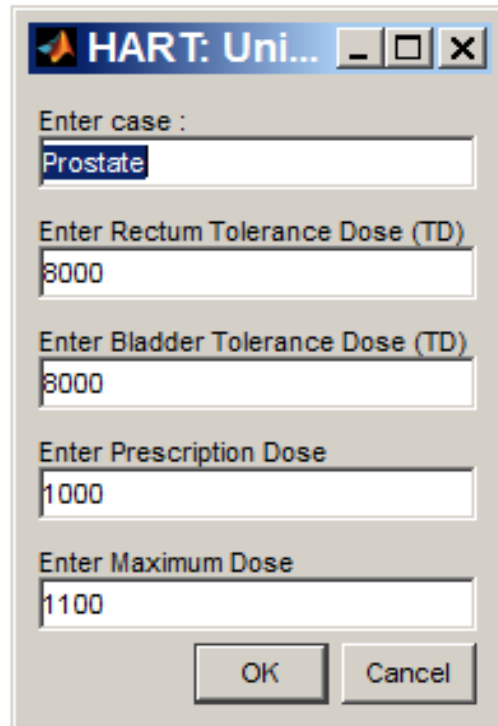
Step (iv)

Final simulation displays the values of all **UPI scores** and the quality factor (**QF**) of the treatment plan as shown below in **Step (v)**.



Step (v)

(b) **Prostate and/or Pelvin plans**: *Enter Tolerance doses (cGy) for all neighboring organs of the target, prescription dose (PD) of the treatment, and the maximum dose (cGy) in the target as shown below in the **Step (i)**.*



The image shows a dialog box titled "HART: Uni...". It contains five input fields and two buttons. The fields are labeled as follows: "Enter case :", "Enter Rectum Tolerance Dose (TD)", "Enter Bladder Tolerance Dose (TD)", "Enter Prescription Dose", and "Enter Maximum Dose". The values entered in the fields are "Prostate", "8000", "8000", "1000", and "1100" respectively. At the bottom of the dialog box are "OK" and "Cancel" buttons.

Step (i)

*Enter the normalized volume above the **TD50 (cGy)** dose and the normalized volume above the **95% Prescription dose (PD)** for the corresponding organs as shown below in chart in **Step (ii)**. Also enter normalized volume of the*

planning target above **95%**, **90.25%**, **47.5%** of the **PD**, and the absolute dose (cGy) above **95%** and **5%** volume of the planning target volume.

HART: Universal Plan Indices

Enter case :
Prostate

Enter Rectum Volume above TD
0.05

Enter Bladder Volume above TD
0.05

Enter Rectum Volume above 95% PD
0.10

Enter Bladder Volume above 95% PD
0.10

Enter PTV volume above 95% PD
0.95

Enter PTV volume above 90.25% PD
0.95

Enter PTV volume above 47.5% PD
1.0

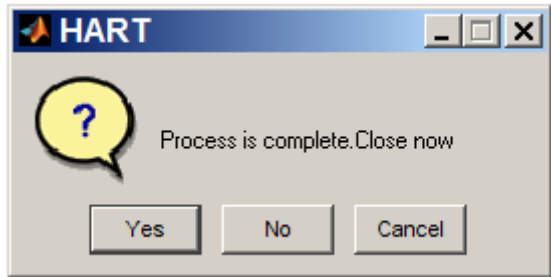
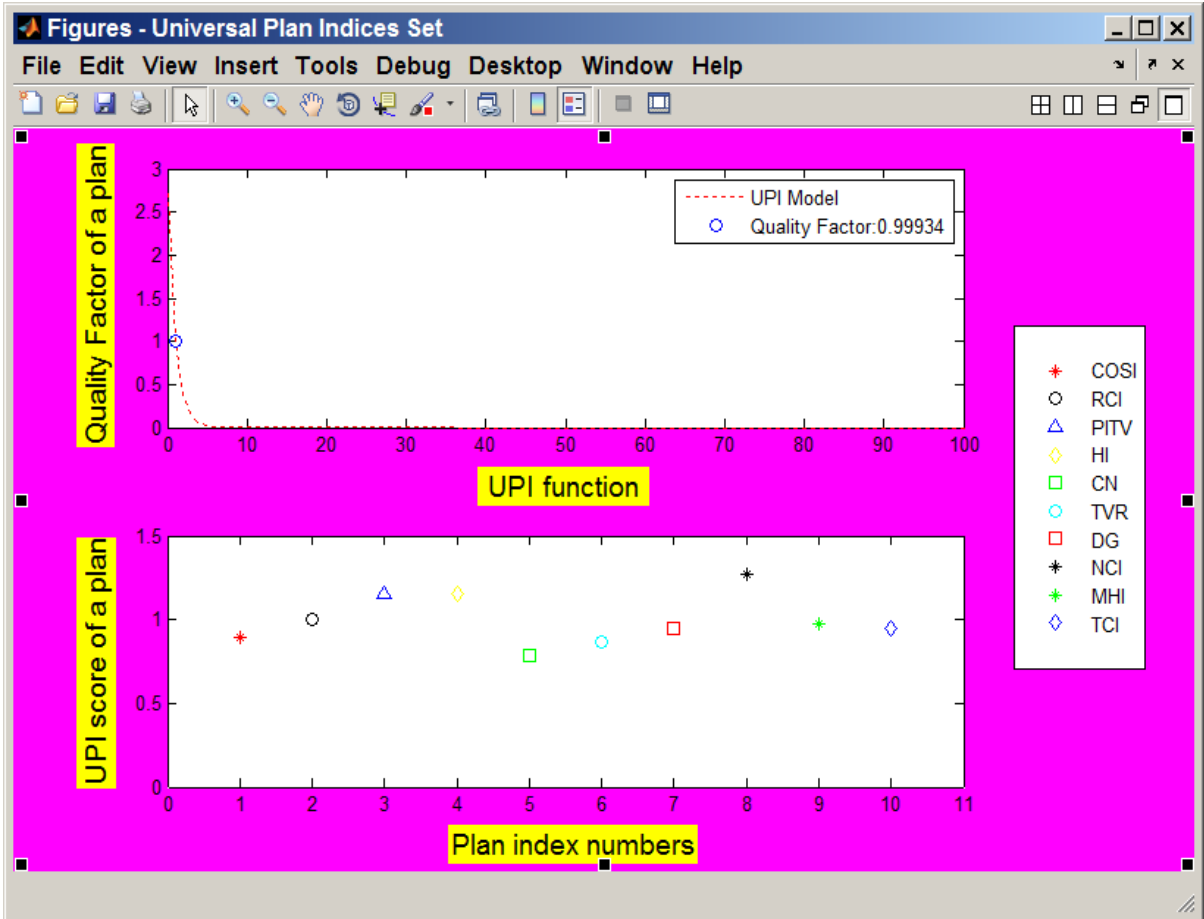
Enter Dose at 95% of Volume
950

Enter Dose at 5% of Volume
975

OK Cancel

Step (ii)

Final simulation displays the values of all **UPI scores** and the quality factor (**QF**) of the treatment plan as shown below in **Step (iii)**.

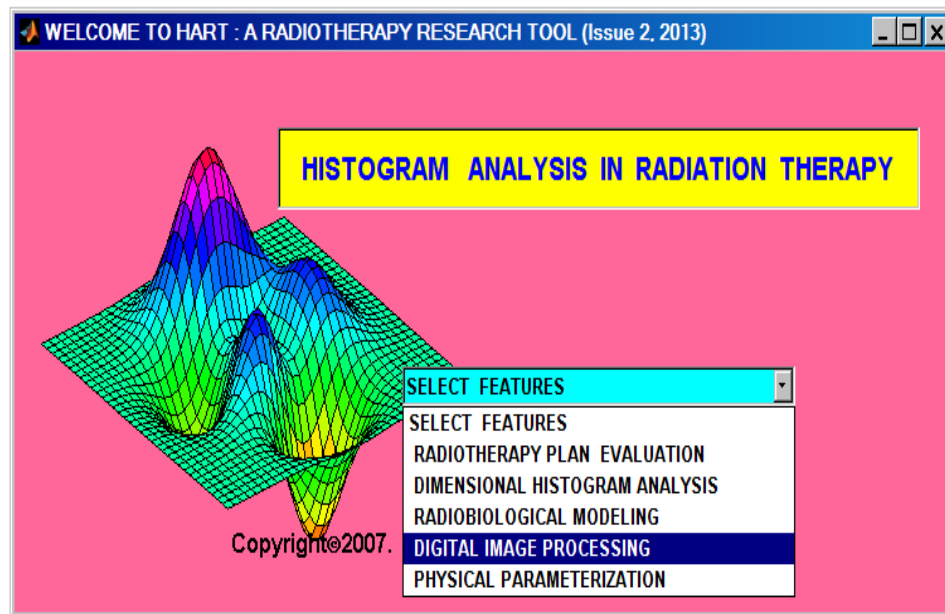


Step (iii)

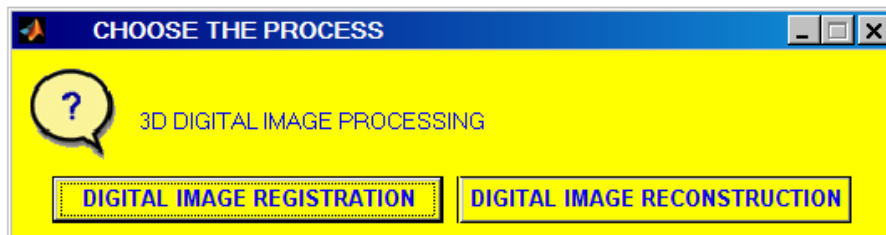
d) Image Registration and Processing:

Rigid Registration of the digital images of the types (.dcm, .fig) can be performed systematically through the steps as shown below:

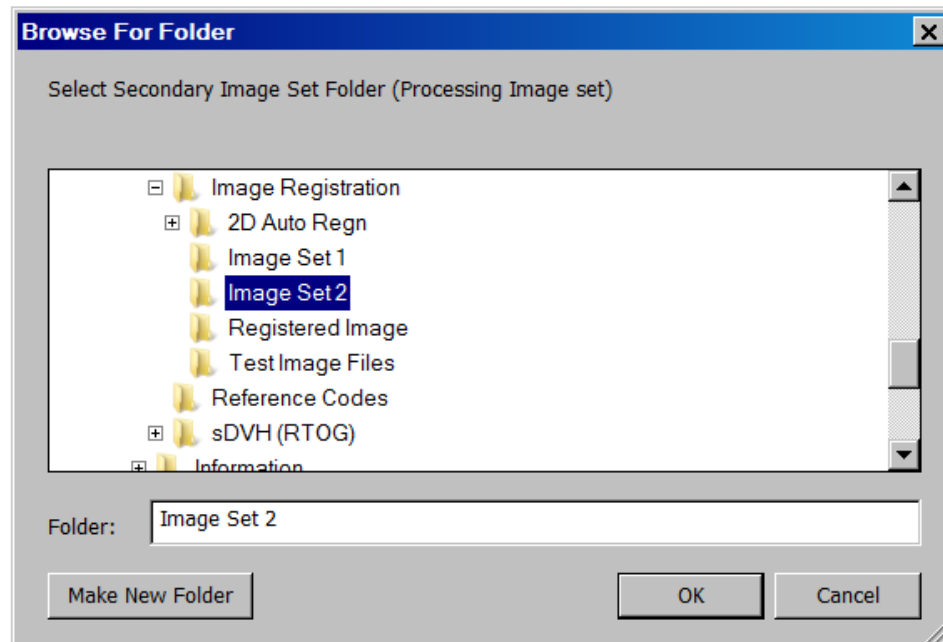
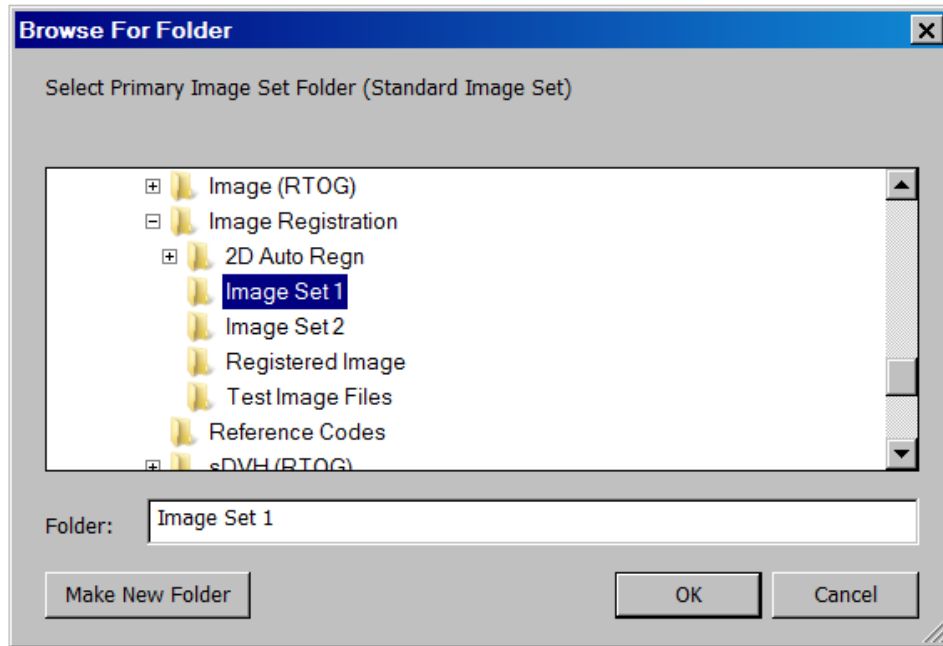
Step 1: Select *Digital Image Processing* option:



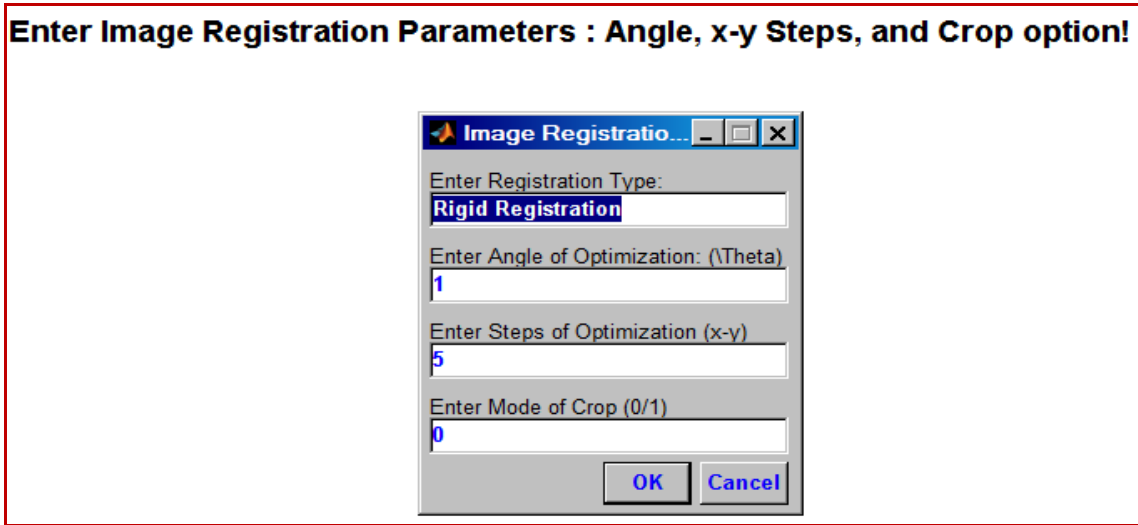
Step 2: Select *Digital Image Registration* option as an appropriate process in the prompt shown below:



Step 3: Select *Primary Image Set 1 (Base or Reference Images)* folder and successively *Secondary Image Set 2 (Processing Images)* folder as shown below:



Step 4: Enter Image Registration Type (*Rigid Registration by Default*), Angle of Optimization (*1°-rotation by Default*), Steps of Optimization (*5 pixels along x- and y-axes by Default*), and Mode of Crop (**0 or 1; 0 for no-crop by Default**) as:

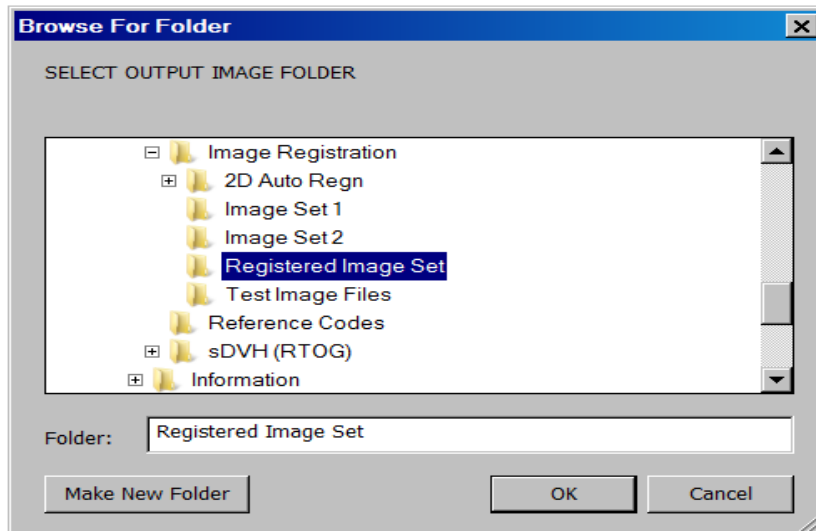


Step 5: Designate the *Output Image Folder* to collect the complete *Set of Registered Images* after completion of the registration process as shown below:

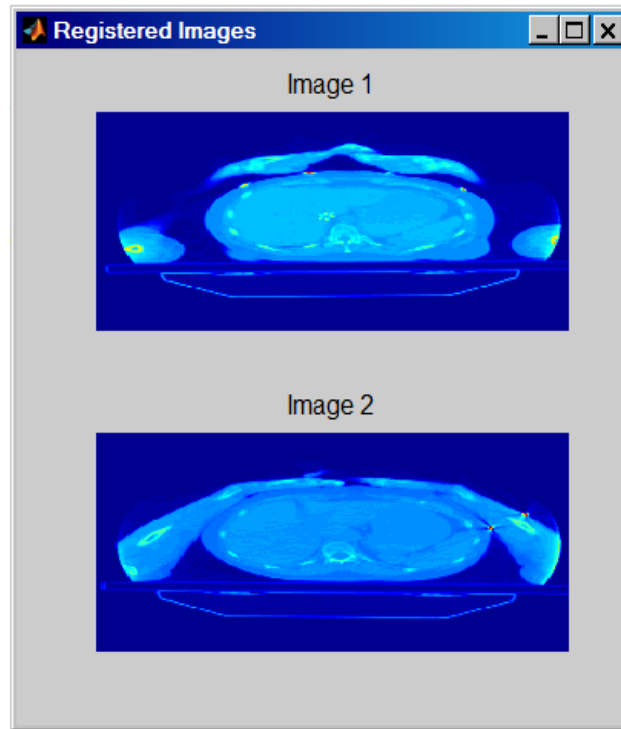
Enter Image Registration Parameters : Angle, x-y Steps, and Crop option!

Image Registration --> Rigid Registration

Note: Select Correct Output Image Folder.



Step 6: *Registered Image Set* would also be displayed in the front panel GUI as shown below (Eg. A Set of 2 Registered Images):



IV. File Transfer Protocol (FTP) Service

The users have the privilege and accessibility to upload and download their test files at our remote server directed by the **HART** research group. Users and clients are strongly recommended to utilize the service, however they have their sole responsibility to anonymize the treatment plans and data-files of the patients while exporting their files in- and out- of their local servers.

V. Summary

HART is an open-source software system designed to support research and clinical applications in radiation oncology and therapeutic treatments of cancer. The complete program package is issued 3 times a year with supplements for AAPM and ASTRO conference. The program is distributed as a free package online taking account of feedbacks and suggestions from the users around the globe. The free technical support is also available through emails, Skype, and the social networking site Facebook (<http://www.facebook.com/hartprogram>). Any feedbacks and suggestions to improve the outcome and efficiency of the program would be highly appreciated. Users are always encouraged to contact through email correspondences at *hartprogram@uic.edu* or *apyaku1@uic.edu*.

Appendix A