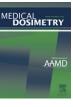


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Comp Plan: A computer program to generate dose and radiobiological metrics from dose-volume histogram files

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ABSTRACT

Treatment planning studies often require the calculation of a large number of dose and radiobiological metrics. To streamline these calculations, a computer program called Comp Plan was developed using MATLAB. Comp Plan calculates common metrics, including equivalent uniform dose, tumor control probability, and normal tissue complication probability from dose-volume histogram data. The dose and radiobiological metrics can be calculated for the original data or for an adjusted fraction size using the linear quadratic model. A homogeneous boost dose can be added to a given structure if desired. The final output is written to an Excel file in a format convenient for further statistical analysis. Comp Plan was verified by independent calculations. A lung treatment planning study comparing 45 plans for 7 structures using up to 6 metrics for each structure was successfully analyzed within approximately 5 minutes with Comp Plan. The code is freely available from the authors on request.

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Introduction

Radiotherapy treatment planning studies have been undertaken for many different treatment techniques and many different clinical sites.^{1–3} Treatment planning studies allow several treatment options to be compared for a single patient dataset. Within these studies, a large number of dose and radiobiological metrics may be used as a surrogate for patient outcome.

Dose metrics are indicators providing a single value to represent the physical dose distribution, *e.g.*, the use of V20 and mean lung dose for assessing likely lung toxicity.⁴ Radiobiological metrics incorporate parameters representing the tissue concerned as well as physical dose. Radiobiological metrics include equivalent dose models, such as that proposed by Niemerko and colleague,^{5,6} and outcome probability models. Outcome probability models attempt to predict the likelihood of a given dose distribution resulting in the eradication of all tumor cells for tumor control probability (TCP)^{7–10} or a given clinical end point for normal tissue complication probability (NTCP).^{11,12}

Calculation of dose and radiobiological metrics can be timeconsuming. For a given treatment planning study, there may be a large number of metrics per structure, structures per treatment plan, and

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treatment plans per patient. It is often necessary to modify planning parameters and repeat these calculations several times.

There are a number of programs that have been published to calculate dose and radiobiological metrics,^{5,13–16} with the selection of metrics and input data format specific to each program. Bioplan¹⁴ and Calc_NTCP¹⁶ require dose-volume histogram (DVH) data, whereas CERR¹⁷ and DREES¹³ use radiotherapy dicom datasets. The program described here provides another option for calculating and comparing dose and radiobiological metrics. The unique features of this computer program, called Comp Plan, are its ability to use DVH data to adjust the fraction size according to the linear quadratic model, to use a simple program structure so that additional models could be added, and to export results in a manner easily used for statistical analysis.

Materials and Methods

The metrics considered in this program together with parameters required for calculations, references for the models, and references containing parameter values where available are detailed in Tables 1–4. Each of these metrics can be calculated with or without conversion to standard effective dose (SED).¹⁸ SED is also known as biological effective dose (BED)¹⁹ and fraction size– equivalent dose (FED),²⁰ and when the conversion is to 2–Gy fractions it is equivalent to EQD2²¹ and normalized tolerance dose (NTD).²² Within the parameters for the SED calculation, a saturation SED limit can also be set, such that if the SED is determined to be above this value, then it is replaced by the saturation SED value. This accounts for the possibility of an isoeffect threshold beyond which any further damage has no further clinical significance.²³ For each of the structures considered a homogeneous boost dose, of a specified total dose and fraction number, can also be added. In most circumstances, it is expected that the SED conversion will be used with the boost option to account for changes in fractionation.

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Table 1

SED, EUD, and logitEUD models used in the Comp Plan program

Model name and description	Equation(s)	Parameters required	References	
SED		α/β = tissue parameter, as described by the	For the model: 18	
This model uses the linear quadratic model to	$SED = \frac{D(1 + (D/n)/(\alpha/\beta))}{(1 + X/(\alpha/\beta))}$	linear quadratic model	For parameter values: 26	
determine the equivalent dose values in a	$3ED = \frac{1 + X/(\alpha/\beta)}{(1 + X/(\alpha/\beta))}$	D = the dose matrix for the given structure		
given fraction size.		X = the standard dose per fraction		
All models within Comp Plan can be		n = the number of fractions		
calculated for SED instead of physical dose				
if chosen by the user				
EUD	$\sum_{n=1}^{\infty} \left(\sum_{i=1}^{n} \left(\sum_{j=1}^{n} \left(\sum_{i=1}^{n} \left(\sum_{j=1}^{n} \left($	v_i = the normalized volume for the voxel or	For the model: 5,6	
This model generates an equivalent dose from	$EUD = \left(\sum_{i} \left(v_i D_i^a\right)\right)^{Va}$	dose bin being considered	For the parameters: 5	
DVH data representing a uniform dose that		$D_i =$ the dose to the voxel or dose bin being		
leads to the same probability of injury as		considered		
the given inhomogeneous distribution		a = a parameter related to the considered		
		structure determining the behavior of the EUD-based model		
LogitEUD		$D_{50} = dose for 50\%$ control or complication	For the model: 5	
A logit dose-response model, using EUD	1	γ_{50} = slope of the dose response curve	For the parameters: 5, 27	
values. This can be used for both TCP and	$Probability = \frac{1}{(D_{11})^{4\gamma_{50}}}$	γ_{50} – slope of the dose response curve	For the parameters, 5, 27	
	$Probability = \frac{1}{1 + \left(\frac{D_{50}}{D_{50}}\right)^{4\gamma_{50}}}$			
NTCP	$1 + \left(\frac{EUD}{EUD}\right)$			

Comp Plan structure

Comp Plan was written using MATLAB R2007a (The MathWorks, Natick, MA) and designed so that the user can choose multiple dose and radiobiological metrics for each treatment plan and structure. Separate functions for each metric were written so that additional metrics can be added easily.

The structure of Comp Plan is detailed in Fig. 1. Comp Plan reads the plan, structure, and metric details, which are specified by the user in a text file, opens the appropriate DVH file formatted in Excel as a column of dose and volume data, calculates DVH variations, and then calculates each of the required metrics. For each structure, if the structure string starts with "boostDXny_", a homogeneous boost dose with a prescription dose of X Gy delivered in y fractions is added to the DVH. In a similar fashion for each metric, if the metric string starts with "SED_", the dose is first converted to a chosen standard fractionation before calculation of the metric. Once the metrics for each structure are determined, the metric results are exported to an Excel spreadsheet.

Comp Plan requires details of a "base directory" containing the text files described above (see Fig. 1) and the DVH files are placed into a directory structure according to plan and structure names. The user specifies the format of DVH data, *e.g.*, *c*Gy or Gy and cumulative or differential volume data. To allow calculation of the different metrics, all dose data are converted to Gy and differential and cumulative as well as absolute and normalized volume matrixes are calculated.

For each of the radiobiological models, a related function was written to read in parameter values. This function scans the text file to find the appropriate structure name and returns the parameter values for that structure. These parameter files are stored in the base directory as seen in Fig. 1. Once these files are established, they could be used for many treatment planning studies. Individual functions were written for each of the metrics and can also be used independently of the overarching program. The resulting spreadsheet contains a new sheet for each structure. Within each sheet, the name of the plan is given in the left column, and the names of the metrics are given in the top row (Fig. 2).

Verification of data input into the program can be achieved with a number of options in the main script. First, the parameter verification option can be selected. In this situation, the parameters used for the calculation of each metric for each plan and structure are printed in a corresponding worksheet in the resulting spreadsheet. Second, each of the DVHs generated, including the absolute and normalized as well as cumulative and differential for each structure, can be plotted in the main structure

I dDIC 2

Dose	metrics	used	in	the	Comp	Plan	program

Model name	Model description
Max	Maximum dose delivered to the structure considered
Min	Minimum dose delivered to the structure in question
Mean	Mean dose delivered to the structure in question
Median	Median dose delivered to the structure in question
Vol	Volume of the normal structure in question
Vy	Volume of the organ receiving at least the dose yGy
isoX	The volume receiving dose above %X of the
	prescription dose (<i>i.e.</i> , the volume encompassed by
	the X% isodose line)

spreadsheet together with dose vs. SED when this conversion has been used. As the verification options slow down calculation time, they can be selected to be on or off.

Program Verification

To ensure Comp Plan was calculating metrics correctly, an example dataset was tested. For each of the metrics, the Comp Plan calculated data were compared with independent calculations. These calculations were undertaken using Excel or by manual observation for simple metrics, as detailed in Table 5. First, dose data were converted to Gy. Second, normalized and absolute, as well as differential and cumulative volume data were generated. These datasets were then used to calculate each of the values. Simpson's rule was used to approximate the integral in the TCP Poisson linear quadratic (LQ) values with α distribution; other values were calculated without approximations.

A lung treatment planning study undertaken in our department²⁴ comparing 45 plans and 7 structures and requiring calculation of up to 6 metrics per structure was used to investigate the performance of this program in a realistic environment. Factors affecting the time required for the initial data to be set up for calculation and for recalculation of metrics were noted for this dataset.

Results

Comp Plan ran successfully on MATLAB version 2007a and 2010b. It is anticipated that it would also run effectively on other versions of MATLAB; however, this has not been confirmed. All plan files, structure and metric files, and DVH files were read successfully. Figure 2 shows a screen capture of the exported excel file.

Program verification

The conversion to SED of the dose matrix was verified when the metric label specified SED. Each of the SED values for the sample dataset was compared with the values from Comp Plan, showing agreement with at least 4 significant figures. The addition of the boost dose was also verified, comparing a sample dataset with values from Comp Plan showing agreement to at least 4 significant figures. The verification results for each of the metrics together with the method of verification are given in Table 5. Only the TCP Poisson, LQ values with α distribution showed a minor discrepancy as a result of using Simp-

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