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Radiotherapy 3D Isodosezones Graphical Optimization for Hyperfractionated Treatment Planning Dosimetry in Lung and Head-Neck Tumors with Biological Effective Dose Model

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ARTICLE INFO	ABSTRACT
Published Online:	In recent lung and prostate cancer-radiotherapy contributions, [101-5], 3D imaging-processing
24 June 2024	Isodosezones [Casesnoves, 2022], delimited by 3D Isodoselines were explained in lung cancer and other tumor types, such as prostate or lung. The radiotherapy model applied was
	the classical BED one algorithm. Modern biological-model-based Treatment Planning Optimization can get objective improvements by using Isodosezones/lines when selecting the optimal dose delivery/schedule for any personalized treatment. Improved programming, from [Casesnoves, May 7 th , 2024], and engineered software is perfectioned-developed for numerical hyperfractionated 3D TPO lung and head-neck cancer imaging-processing with upgraded previous database. Mathematical algorithms are explained-detailed. Developed
	programming patters and arrays are briefed. A series of imaging-processing graphics results obtained with the 3D Isodosezones Pareto-Multiobjective Optimization programming database
Corresponding Author:	are shown and explained in detailed. Applications in radiotherapy-oncology medical physics
Dr F Casesnoves PhD	are subsequently briefed.

KEYWORDS: Pareto-Multiobjective Optimization (PMO), Mathematical Methods (MM), Biological Models (BM), Radiation Therapy (RT), Initial Tumor Clonogenes Number Population (N₀), Effective Tumor Population Clonogenes Number (N_{Effective}), Linear Quadratic Model (LQM), Integral Equation (IE), Tumor Control Probability (TCP), Normal Tissue Complications Probability (NTCP), Biological Effective model (BED), Tumor Control Cumulative Probability (TCCP), Radiation Photon-Dose (RPD), Nonlinear Optimization, Radiotherapy Treatment Planning Optimization (TPO), Source-Surface Distance (SSD), Software Engineering Methods, Radiation Photon-Dose, Attenuation Exponential Factor (AEF), Nonlinear Optimization, Radiotherapy Wedge Filter (WF), Anisotropic Analytic Model (AAA), Fluence Factor (FF), Omega Factor (OF), Treatment Planning Optimization (TPO), Breast Tumor (BT), Artificial Intelligence (AI), Pareto-Multiobjective Optimization (PMO), Genetic Algorithms (GA).

I. INTRODUCTION AND RESEARCH OBJECTIVES

Previously, [101,102-5], Nonlinear Graphical and Interior Optimization engineering software was improved with matrix algebra constraints and designed in programs/patterns for BED model. Namely, for hyperfractionated RT in lung and head-neck tumors Isodosezones and Isodoselines, [Casesnoves, May 7th, 2024]. Thorough hyperfractionated radiotherapy TPO findings are presented both in 2D graphics and inset dataset. The matrix-algebra constraints and the extensive comparison among several parameters selection constitutes the innovation of the study. At 3D graphics, Isodosezones and Isodoselines ar sharply indicated.

3D Isodosezones and Isodoselines (Casesnoves imaging-processing-programming and optimization creation, 2022) are obtained from a series of previous papers about 3D Isodoselines and 3D Isodosezones that set their definition-invention [101,102-5]. This new computational radiotherapy application was mainly developed for lung and head-neck tumors treatment planning optimization (TPO). The study continues further with programming details and 3D graphical-numerical results inset in images as an enhancement stage. A series of 3D imaging-processing charts have been proven [101,102-5]. Isodoselines and Isodosezones are proven be practical and complementary

useful in individual TPO. The 3D images are acquired with functional combinations of BED model parameters [84]. The BED function is a several variables one, and a brief mathematical analysis reminder is included, related to programming precision, smooth and running time [1-21, 28, 84, 86,88,89,99,101,102-5].

Therefore, the objectives of the study are to get and demonstrate 3D graphical optimization for BED model isodosezones and isodoselines. Programming is based in Pareto-Multiobjective software dataset from previous contributions [101, 102-5]. Secondly, to demonstrate the efficacy of the improved program writing that was developed [101, 102-5] by showing the charts with their numerical precise data. It is not an objective of this paper to discuss the deliberation between hyper and hypo fractionated dose delivery. In other words, hyper/hypo fractionated TPO depends on multiple clinical conditions and patient personalized treatment, whose discussion is beyond the computational optimal TPO task.

The radiotherapy Treatment Planning Optimization utility and applications for these Isodosezones-Isodoselines comprises the optimization of BED main parameter magnitudes, namely, number of fractions, total dose, treatment total time, TPotential and others for BED model. In this research, it is proven the 3D different selection of BED parameters, [Algorithm 1, 101, 102-5].

Results show 3D Isodosezones and Isodoselines imaging-processing visuals for lung cancer with a total dose in the interval: DTotal $\approx [\ 30\ ,\ 115\]$ Gy. However, Isodosezones within graphs are related to standard lung cancer dose magnitudes, namely DTotal $\approx [\ 70\ ,\ 80\]$ Gy, [$90,\ 96\]$. Numerical values are detailed inset at all imaging-processing figures. Tables 1-2 show BED in vivo parameters selection. For head-neck3D Isodosezones and Isodoselines, the dataset from previous studies is applied.

Grosso modo, improved software for imaging-processing of isodosezones/lines in lung cancer was obtained. Head-neck computational refinements are included. Results comprise new series of 3D graphics, mathematical method, algorithms, and radiotherapy TPO medical physics applications. A constrained extension of previous Nonlinear Pareto-Multiobjective GA optimization database was performed for radiotherapy BED models in lung and head-neck tumors [87,88, 101, 102-5]. Applications for radiotherapy TPO and future improvements in RT are explained in short.

II. MATHEMATICAL ALGORITHMS AND COMPUTATIONAL METHODS

This section comprises the radiotherapy experimental in vivo standard dataset that was implemented for programming-software improvements from [101-5]. The mathematical algorithms and software methods are also

developed from [86,88,89,99,101-5]. The basic dataset reminder of *in vivo* is included in Tables 1-2 from [98].

From [101, 102-5], for necessary understanding, the following essential concepts are highlighted:

Definition 1.- In RT-3D Treatment Planning, a 3D Isodoseline is demarcated by a line whose dose-distribution parameters can vary for optimal planner choice while keeping constant the magnitude of total radiation dose delivered [Casesnoves, 2022] .

Definition 2.- In RT-3D Treatment Planning, a 3D Isodosezone is demarcated by a polygon whose dose-distribution parameters can vary for optimal planner choice while keeping constant the total dose delivery magnitude [Casesnoves, 2022].

The mathematical method constitutes an evolution from the previous lung and prostate cancer publications [101, 102-5]. The main algorithm formulation for imagingprocessing and developments of improved isodosezones/lines charts is based on Tikhonov regularization algorithms presented in a number of previous studies [Algorithms 1-5 from 86, 88, 89, 98, 99, 101, 102-5] and literature records [20-25,68,74,75,80,81,85-94,99,101-5]. Tables 1-2 presents the numerical-figures parameter dataset implemented in software in Matlab ® . Just to remark that BED model is a nonlinear several variables function, with implications in numerical results analysis.

The biological effective dose, a nonlinear quadratic several variables equation, has an important Tpot parameter that was set for in vivo experimental data. Then, the simplest Pareto multiobjective optimization and Graphical Optimization BED-numbers for lung and head-neck cancer, [24,88,89,98, 101,102-5] (Algorithm 1) reads,

$$\begin{split} &\text{Chebyshev} \quad \text{L}, \, \text{Optimization}, \\ &\text{for} \quad i=1,2... \, \text{min imize pareto}, \\ &|\text{DOSE}_i| - |\text{BED}_{\text{Effective}}|_{\text{L}_i} \, \, \text{with}, \\ &|\text{BED}_{\text{Effective}}| = \text{k} \times \text{d} \times \left[1 + \frac{\text{d} \times \beta}{\alpha}\right] - ... \\ &|\text{...} - \frac{\text{Ln}(2)}{\alpha} \times \left[\frac{T_{\text{Treatment}} - T_{\text{Delay}}}{T_{\text{Delaystate}}}\right]; \end{split}$$

(Algorithm 1) where,

BED: The basic algorithm for Biological Effective Dose initially developed by Fowler et Al. [22-25, 89-94,98].

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- k : Optimal Number of fractions for hyperfractionated TPO. Optimization parameter. [22-25,89-94,98].
- d : Optimal Dose magnitude for every fraction. Optimization Parameter [Gy]. [22-25, 89-94].
- α : The basic algorithm constant for Biological Effective Dose models. Radiobiological experimental parameter in vivo. [Gy-1]. [22-25, 89-94].
- β : The basic algorithm constant for Biological Effective Dose models in vivo. Radiobiological experimental parameter . [Gy-2]. Note that it is very usual to set in biological models [α / β in Gy].

TTreatment: The overall Treatment Planning Optimization radiation-sessions summatory time. This parameter varies according to authors' and institutions/hospitals criteria. [22-25, 89-94,98]. The overall TPO time delay for clonogens re-activation. This parameter varies according to authors' experimental research.

TDelay: This BED parameter changes related to different authors' and institutions/hospitals criteria. [22-25, 89-94,98, 101-7].

TDelay: The TPO time delay for cell clonogens reactivation after radiation damage.

The overall TPO time delay for clonogens re-activation. This parameter varies according to authors' experimental research.

TPotential: The potential time delay for tumor cell duplication. This parameter varies according to authors' experimental-theoretical research.

DOSE : The dose magnitudes for lung cancer simulation algorithm for Biological Effective Dose [22-25, 89-94,98]. The programming patterns and arrays were set for intervals of DOSE ϵ [70 , 80] Gy.

A number of necessary, rather mandatory, conditions in software design to obtain a convenient imaging-processing graphics are:

- -Setting an ordered code for fast running time of images.
- -Avoid excessive arrays and subroutines.
- -Select the optimal subroutine imaging-processing commands in the program, and well ordered [1-20,24,68,74,88,89,98,99, 101,102-5].

Table 1. The implemented programming lung tumor dataset obtained from literature source references [38,43-45,98, 101, 102, 103].

GRAPHICAL OPTIMIZATION PARAMETER INTERVALS FOR LUNG TUMORS [1-20,24,68,74,88,89,98,99, 101,102, 103]						
Dose fractions number	[34, 42]	Usual protocol in literature [1 21,74-86, 101-103].				
Dose fraction magnitude	[0.8, 2.2] Gy	Usual protocol in literature [1 21,74-86]. Set with intervals according to different criteria				
Trestnert	[30,40] Days	Usual protocol in literature [1 21,74-86]. Set with intervals according to different criteria The RT treatment varies according to weekends break secondary effects, patient circumstances, etc.				
TDolay	[20,25] Days	Usual protocol in literature [1 21,74-86]. Set with intervals according to different criteria				
TPolential	[22, 32] Days	Usual protocol in literature [1 21,74-86]. Set with intervals according to different criteria				
Dose interval in Objective Function	[70, 80] Gy	Usual protocol in literature [1 21,74-86, 101, 102]. Set with two total dose Pareto Functio according to different criteria Note: at graphic for imaging processing reasons the interv is wider.				
α, α/β	0.38 Gy ⁻¹ , 8.2 Gy	From [89,103]. Remark, for average between early and medium tumor, it is acceptab to set alpha as 0.3 Gy-1				
β	0.042 Gy ⁻²	From [89,103]				

In the next sections, results and applications are presented. The imaging quality of the demonstrating Figures 1-2 was intended be good. In Table 1, software implemented dataset in vivo for programming with source references [38,43-45,98,100, 101, 102, 103-5].

Table 2. Matlab Constrained GA optimization dataset. Note the values of constraints matrix in Algorithm 1. In this system and other similar ones, the constraints can be set as a matrix equation, or as an array of vectors. As in Tables 2-3 of [87,88], the simulations were done with approximate numerical-experimental data from several authors. T_{Potential} in Head and Neck cancer is about 4 days as average. Simulation dataset from [20-25,74,75,80,81,85-88].

,/4,/5,80,81,85-88].								
	CONSTRAINED GENETIC ALGORITHM							
OPTIMIZATION								
	IETER INTERVAL FOR							
HEAD AND NECK TUMOR								
	ALGORITHM 2							
	rences at Tables 2-3]							
Parameter	Magnitude Interval							
Constraints								
Interval	[77.0 , -56.0]							
Algorithm 2								
	[Note that there are two linear							
	inequality constraints in matrix]							
Dose Fraction	[25 , 35]							
Number								
Dose Fraction	[1,2] Gy							
Magnitude								
T _{Treatment}	[30 , 40] Days							
T _{Delay}	21 Days							
T _{Potential}	[3.5 , 4.5]							
α [Gy-1]	[0.19 , 0.61] Gy ⁻¹							
β [Gy-2]	[,,							
Parameters	[0.0581] Gy ⁻² fixed							
	[
Dose Interval in	45 Gy for Pareto F 1 function							
Objective	55 Gy for Pareto F 2 function							
Function								
	+							

III. OPTIMIZATION GRAPHICAL RESULTS

3D Graphical results for 3D Graphical results for lung first constrained graphical optimization are shown in Figures 1-2. The simple constrained graphical optimization head-neck tumors results are presented in Figures 3-5. In general, constrained optimization with algorithm 1 shows be acceptable with high-precision.

In this improved-advanced study, 3D Interior-Graphical Optimization techniques are implemented in parallel refined-programs to verify results from [98, 101, 102] with the *in vivo* dataset from [23,24,97,98,10-5]. Those 3D processed imaging-graphs, Figures 1-2, prove definitely the results got with 3D IO in [101,102-5]. The pictures of 3D Isodosezones-Isodoselines are detailed with cursor-marked inset within every 3D graph. The cursor-marks give the numerical data for every point at surface. Therefore, the radiotherapy planner obtains the optimal combination of fractions number (k), and fraction dose (d), and other BED parameters for a fixed total BED dose delivery. That is considered a proven-consistent, easy, fast-running, and simple advance in modern TPO and RT research.

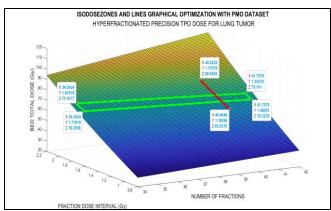


Figure 1.-3D Isodosezone for two variables. Namely, the choice is number of fractions dose and total treatment dose in lung TPO. Namely, marked inset, [70,75] Gy isodosezone (green boundaries). Marked inset, [70,75] Gy isodosezone delimited by isodoselines. In literature, T_{Potential} is usually set as 28-30 days for early stage lung cancer. Precision can be checked setting in Algorithm (1) at every extreme values of any long Isodosezone. Inset (red), and Isodoseline constrained to 40 fractions and for an interval of [65,85] Gy . The 3D Isodosezone fundamentals for IO calculations, [101,102-5], are implemented into this 3D surfactal isodosezone. Imaging-pattern numerical-intervals for plotting were obtained from PMO but with with *in vivo* lung tumor BED model parameters.

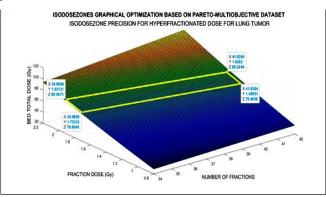
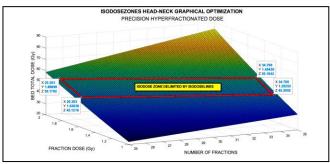


Figure 2. 3D Isodosezone for two variables, at XY plane, number of fractions and dose per fraction, the choice. Namely, Number of fractions and dose per fraction in lung TPO. Marked inset, [70,80] Gy isodosezone delimited by isodoselines. The precision can be checked calculating the product between fraction dose and number of fractions at each extreme of the long isodoselines. For instance, at lower isodoseline (yellow), 34 x 1.7 is approximately equal to 41 x 1.4 (taking one digit is exactly equal). The Isodosezone fundamentals from IO calculations, [101-5], are implemented into this 3D surface. The software-programming pattern intervals for plotting were taken from previous pareto multiobjective optimization developments but with in vivo lung tumor BED parameters. Each and every BED total dose is set along 3D Isodoszone, while (k) and (d), and other BED model parameters change along the isodoselines-isodosezones surfactal length when cursor is moved over the surface. Enhanced in Appendix.

HEAD AND NECK ISODOSEZONES-ISODOSELINES RESULTS

The following section includes the 3DImage-Processing graphical optimization charts, Figures 3-5. Precision is high.



One Isodoseline is demonstrated in Figure 5.

Figure 3. Head-Neck tumor TPO with Isodosezones-Isodoselines for approximate interval (d ϵ [45 , 55] Gy). Precision is high.

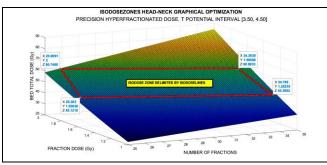


Figure 4. Head-Neck tumor TPO with Isodosezones-Isodoselines for approximate interval (d ϵ [45, 60] Gy). Precision is high. Note that the model has a negative factor that changes the product (d fraction dose) x (k number of fractions).

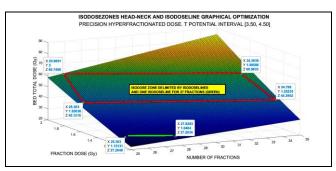


Figure 5. Head-Neck tumor TPO with Isodosezones-Isodoselines for approximate interval (d ϵ [45, 60] Gy). Precision is high. Note that the model has a negative factor that changes the product (d fraction dose) x (k number of fractions). One Isodoseline is proven inset.

IV. NUMERICAL RESULTS

Constrained optimization numerical data can be obtained from 3D graphics, Figures 1-5, and Appendix Figures 1-2. From there, Isodosezones and Isodoselines emerging data for TPO can be guessed. Precision is high, specially for lung 3D Graphical Optimization.

V. RADIOTHERAPY TREATMENT PLANNING OPTIMIZATION APPLICATIONS

Tables 3-4 show a resume of radiotherapy applications in head and neck tumors. Medical physics principal applications for radiotherapy TPO are explained briefly. Table 4, improved and completed from [101, 102-5], presents some radiotherapy applications for RT-TPO based on this study, and in general for biological models. Radiotherapy medical physics principal applications for personalized TPO are detailed briefly. Note that the applications are multifunctional.

Table 3 . Developed from previous publications, [23,24,97,98,101, 102-5], brief of radiotherapy and radioprotection applications derived from imaging results.

BRIEF RADIOTHERAPY COMPUTATIONAL MEDICAL PHYSICS APLICATIONS					
FUNCTIONAL TYPE	USAGE	ADDITIONAL			
Isodoseline	Selection of a lined-range of BED parameters	Personalized TPO application			
Isodosezone	Selection of a surface-range of BED parameters	Personalized TPO application			
BED parameters selection	Automatic TPO optimization	Extent variety of applications, depending on patient requirements, circumstances, etc			
RT research	Improvements of RT-TPO software and BED modelling.	Upcoming future investigation			

Table 4. Some radiotherapy and radioprotection for RT lung and head-neck cancer TPO Medical Physics study applications derived from results.

MODEL RESULTS APPLICATIONS FOR RADIOPROTECTION IN HEAD AND NECK TUMOR RT							
TYPE	CLINICAL	RESEARCH	MIXED	COMMENTS			
BM Treatment planning optimization	TPO precise for head and neck tumors with BMs	TPO Modelling BMs developments according to Neffective	Clinical improvements with BMs after research according to Nethective	Inverse planning system set up on BMs according to Neffective			
LINAC OPTIMIZATION	Optimization of photon- dose for BMs	LINACS BMs Usage for IMRT, IMPT according to Neffective	Exploration of new possibilities for Nemective models	Manufacturing adaptation of LINACs fro BMs according to Netective			
Theoretical improvements for new models	Dosimetry improvements in accuracy according to radiobiology experimental Neffective	From tumor survival clinical statistics advances in BMs according to Nemedive	According to Nemective new BMs research sources, both theory and clinical experimental trials	BMs got experimental evidences to be set on TPO according to Nerrective			

VI. DISCUSSION AND COMPUTATIONAL-MEDICAL PHYSICS CONCLUSIONS

First remark is the precision-achieved improvements in software-engineering from first publications-series till the recent ones, [101-5]. The purpose-objectives of the study were to develop precise 3D imaging-processing charts for isodosezones/lines. Complementary, the mathematical part comprised algorithm and programming specific characteristics and conditions. In addition, to put forward a brief of radiotherapy medical physics applications. In other words, explicitly the objective of the study was to apply further constrained GA Optimization for Head and Neck hyperfractionated RT treatment with BED model. Secondly to compare/review to simple constrained results [87,88].

Radiotherapy Treatment planning Optimization, and oncology-medical physics applications are diverse. Isodosezones processed-graphics, Figures 1-5, can give perfected and sharpened graphical-evidence and demonstrate the results from [98,101,102,103-5] in lung and head-neck cancer, specifically for tumors hyperfractionated RT treatment with BED-Polynomial model.

The programming method has the inconvenient that the 3D surfaces are specific for each and every model and cancer type. However, to change formulas and/or parameters in software is not complicated. Running time for 3D surfactal Isodoselines is acceptable.

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Software and programming was based on previous contributions [87,88]. The Matlab function handle have to be carefully programmed to get acceptable results. In plain language, handle functions got to get built with same precision than the classical FORTRAN subroutines. As a rule for the strict FORTRAN language, the programming design with FORTRAN requires more time and accuracy.

Imaging-numerical results can be considered accurateacceptable and subject to future further refinements. The 3D image quality is clear and sharp. The programming software, therefore, is proven be functional and fast-running. The average time for graphs display is about 4-5 seconds, and the setting of Isodoselines-zones inset is usually about 10-20 minutes, depending on the image difficulties. Thanks to the explained conditions, and order to design the codes. improvement related to previous [98,101,102,103-5] is the development of a parameters selection variety within the BED model implemented data and 3D visual graphics. The mathematical analysis for the model variables was justified.

In summary, a further research for 3D imaging-procesing isodosezones/lines in lung and prostate tumors were presented. Mathematical algorithms and software were detailed. Radiation-oncology medical physics usages are briefly included.

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SCIENTIFIC ETHIC STANDARDS

Important remarks: images and table-data reminders from previous contributions are intended for explicit improved understanding [101-5]. This study contains improved programming, [Casesnoves, May 7th, 2024], and engineered software that was developed for numerical hyperfractionated 3D TPO lung cancer imaging-processing database. Formulas applied/included are from previous prostate article with in vitro data. Model is a modification from several authors, based also on [20,24,25,83,86,88,89,99,101-5] techniques. Mathematical Algorithms 1-4 formulas are modificated from previous

publications [20,24,25,83,88,89]. RT applications methods for these publications were created by Dr Casesnoves in 2021-2. Methods from were created by Dr Francisco Casesnoves in 3rd November 2016, and Interior Optimization Methods in 2019. BED model setting in Algorithms and programming were developed by Dr Casesnoves from previously published BED models. This article has previous papers information, from [1-21], whose inclusion is essential to make the contribution understandable. This study was carried out, and their contents are done according to the International Scientific Community and European Union Technology and Science Ethics [39,44-46]. References [39,44-46]: 'European Textbook on Ethics in Research'. European Commission, Directorate-General for Research. Unit L3. Governance and Ethics. European Research Area. Science and Society. EUR 24452 EN. And based on 'The European Code of Conduct for Research Integrity'. Revised Edition. ALLEA. 2017. This research was completely done by the author, the computational-software, calculations, images, mathematical propositions and statements, reference citations, and text is original for the author. When a mathematical statement, proposition or theorem is algorithm, presented, demonstration is always included. When a formula is presented, all parameters are detailed or referred. If any results inconsistency is found after publication, it is clarified in subsequent contributions [Note 1: in at least one article of theses series, it was written by mistake that radiation is previous to tumor-surgery. That is a mistake, for cancer treatment, surgery, when possible, is previous to radiation, Note 2: in previous publications, [101-5], a matrix operation error was found and corrected here]. When a citation such as [Casesnoves, 'year'] is set, it is exclusively to clarify intellectual property at current times, without intention to brag. The article is exclusively scientific, without any commercial, institutional, academic, any religious, religious-similar, non-scientific theories, personal opinions, political ideas, or economical influences. When anything is taken from a source, it is adequately recognized, or put anu mber in a remark. Ideas and some text expressions/sentences from previous publications were emphasized due to a clarification aim [39, 44-46]. Number of references is large to provide literature in open access for public health care institutions.

"Radiotherapy 3D Isodosezones Graphical Optimization for Hyperfractionated Treatment Planning Dosimetry in Lung and Head-Neck Tumors with Biological Effective Dose Model"

AUTHOR'S BIOGRAPHY



Dr Francisco Casesnoves earned the Engineering and Natural Sciences PhD by Talllinn University of Technology (started thesis in 2016, thesis Defence/PhD earned in December 2018, official graduate Diploma 2019). He works as independent research scientist in computationalengineering/physics. Dr Casesnoves earned MSc-BSc, Physics/Applied-Mathematics (Public Eastern-Finland-University, MSc Thesis in Radiotherapy Treatment Planning Optimization, which was developed after graduation in a series of Radiation Therapy Optimization-Modelling publications [2007-present]). Dr Casesnoves earned Graduate-with-MPhil, in Medicine and Surgery [1983] (Madrid University Medicine School, MPhil Radioprotection Low Energies Dosimetry [1985]). Casesnoves resigned definitely to his original nationality in 2020 for ideological reasons, anti-monarchy-corruption, democratic-republican ideology, and ethical-professional reasons, and does not belong to Spain Kingdom anymore. Besides, for his anti-corruption ethical ideas, has no any collaboration-links in research for that country. His constant service to the International Scientific Community and Estonia Republic technological progress involves about 80 articles, more than 100 total publications, and about 4 books. Recent advances published are in Superconductors Mathematical Modelling and Radiotherapy Brain Neurobiological Models, 3D-AI Isodosezones and Isodoselines. Among Dr Casesnoves inventions and scientific creations are:

Numerical Reuleaux Method

Radiotherapy Omega Factor correction for AAA model wedge filters dose delivery

Integral-Differential materials erosion model

Graphical Optimization

Interior Optimization

Superconductors Molecular Effect Model

Superconductors Multifunctional Transmission Line

BED radiotherapy model GA optimization

RT Isodoselines and Isodosezones

Artificial-Intelligence applications with GA for Treatment Planning Optimization in applied Nuclear Physics.

APPENDIX

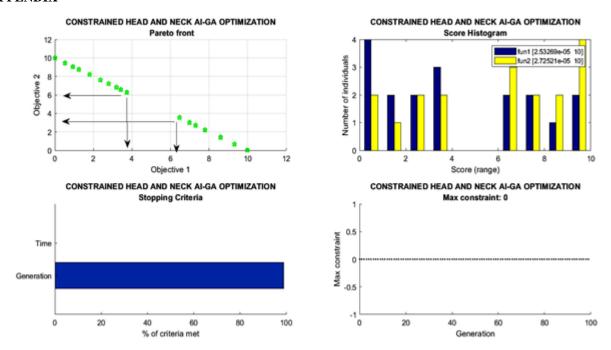


Figure 1 (Reminder of previous publications, 104-5).-Head-neck tumors, a review of PMO Optimization concepts-results from constrained optimization Multifunctional GA 2D graph (100 generations). This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f 1 and f 2 show low residuals. Therefore, results are acceptable in first optimization for function 1 and function 2.

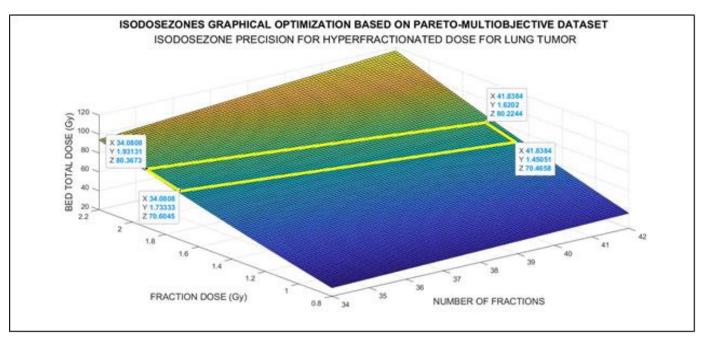


Figure 2, (enhanced).- 3D Isodosezones for two variables, at XY plane, number of fractions and dose per fraction, the choice. Namely, Number of fractions and dose per fraction in lung TPO. Marked inset, [70,80] Gy isodosezone delimited by isodoselines. The precision can be checked calculating the product between fraction dose and number of fractions at each extreme of the long isodoselines. For instance, at lower isodoseline (yellow), 34 x 1.7 is approximately equal to 41 x 1.4 (taking one digit is exactly equal). The Isodosezone fundamentals from IO calculations, [101,102], are implemented into this 3D surface. Pattern intervals for plotting were taken from PMO but with in vivo lung tumor parameters. Each BED total dose is fixed along 3D Isodozone, while (k) and (d) parameters vary when cursor is moved over this Isodosezone. This software numerical method was also developed in F # and Fortran.