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Radiotherapy Treatment Planning Optimization Improved 3D-Surfactal Isodoselines Series for Prostate Cancer with Bed Pareto-Multiobjective Model 3D-Dataset

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ABSTRACT

3D Isodoselines innovation with Interior Optimization (IO) for prostate tumor BED model hyperfractionated Treatment Planning Optimization (TPO) application is further demonstrated. The implemented data was got with additional-dual constrained evolutionary algorithm for BED-LQ model (Biological Effective Dose) in this cancer type. Results for TPO with 3D IO-Graphical Optimization show a number of surfactal IO 3D Isodoselines with proven accuracy-feasibility of the novelty of the technique. Programming software for surfactal-isodoselines methods solutions show a series of 3D IO graphs for TPO. Applications for prostate tumors radiotherapy and stereotactic radiosurgery treatments are briefed.

KEYWORDS: Pareto-Multiobjective Optimization (PMO), Mathematical Methods (MM), Biological Models (BM), Radiation Therapy (RT), Initial Tumor Clonogenes Number Population (N_0), Effective Tumor Population Clonogenes Number ($N_{Effective}$), Linear Quadratic Model (LQ), 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), Nonlinear Optimization, Treatment Planning Optimization (TPO), Artificial Intelligence (AI), Pareto-Multiobjective Optimization (PMO), Genetic Algorithms (GA) .

I. INTRODUCTION AND OBJECTIVES

In a previous 3D Isodoselines published definition-invention [100], for prostate treatment planning optimization (TPO), a primary group of demonstrating graphs were shown. This study deals with an extension/improvement of 3D Graphical-Interior Optimization obtained with perfected software.

Therefore, a series of imaging processing 3D charts are presented for Isodoselines in prostate cancer BED model for TPO. The BED parameters used are based on ***in vivo*** tumor radiobiological parameters (α , β), Treatment-Time variable, $T_{K\ (delay)}$, and $T_{Potential}$ ones. The previous publications ***in vitro*** dataset is shown for comparison in Table 2, [98].

The results comprise illustrative examples for BED model TPO refined with 3D Isodoselines series for several magnitudes of total doses.

In brief, a number of 3D imaging processing graphics for prostate tumors TPO by using BED model are proven and explained. Confirmation of findings of [100] is got. Applications for radiotherapy TPO are explained in brief.

II. MATHEMATICAL AND PROGRAMMING METHOD

This section comprises the dataset that was used for programming improvements from [100]. The mathematical algorithms and software methods are also developed from [100]. A reminder of ***in vitro*** dataset is included in Table 2 from [98].

Matlab Constrained GA optimization dataset is detailed, Table 1. Constraints matrix algebra are implemented through [Algorithms 1-5 from 100]. In Matlab and other similar systems, the constraints can be set as a matrix equation. Simulation dataset from comes from [20-25,68,74,75,80,81,85-94,100] . The GA simulations results that were done [98,100] with numerical-experimental interval-data for GA implemented arrays were used for imaging process. $T_{Potential}$ in prostate for *in vitro* experimental data is about [2 , 19] days. Table 1 shows all dataset implemented with references for *in vivo* parameters at BED-LQ model at low doses [100]. Table 2 shows all dataset implemented with references for *in vitro* parameters at BED-LQ model at low doses [98]. The reason to use *in vitro* dataset, [98], in this first prostate study is that currently the *in vivo* radiobiological differences differ in the literature, note that at Tables 1,2.

Table 1.- Software implemented dataset for GA programming with source references [38,43-45,98].

***IN VIVO* LQ MODEL PARAMETERS IMPLEMENTED**	
LQ MODEL PARAMETERS [Chapman, Nahum, 2015, Joiner, Kogel, 2019]	
BED-PARAMETER	**MAGNITUDE/INTERVAL**
T_{Pot}	[26.00 , 30.00] (Days)
T_K	21 (Days)
$T_{Treatment}$	[30 , 40] (Days)
α [Gy^{-1}]	[0.09 , 0.43] [Gy^{-1}]
β [Gy^{-2}]	0.0313 [Gy^{-2}]
Number of Fractions	[37 , 45] (Fractions)
Fraction Dose	[1.00 , 2.00] (Gy)
Pareto Total Prostate Dose Objective Function [89]	Pareto 1 : 70 Gy Pareto 2 : 78 Gy

Table 2.- From [98], software implemented *in vitro* dataset for GA programming with source references [38,43-45].

***IN VITRO* LQ MODEL PARAMETERS IMPLEMENTED [Chapman, Nahum, 2015]**		
Asynchronous populations of human tumor cell lines [Chapman, Nahum, 2015]	**α [Gy^{-1}]**	**β [Gy^{-2}]**
TSU	0.06	0.048
PC-3	0.24	0.068
DU-145	0.31	0.048
LnCap	0.49	0.015
INTERVAL/AVERAGE FOR SOFWARE	**[0.06 , 0.049]**	**0.0421**
LQ MODEL PARAMETERS IMPLEMENTED [From author's refs 23,24]		
BED-PARAMETER	**MAGNITUDE/INTERVAL**	
T_{Pot}	[2.00 , 19.00] (Days)	
T_K	21 (Days)	
$T_{Treatment}$	[30 , 40] (Days)	
Number of Fractions	[37 , 45] (Fractions)	
Pareto Total Prostate Dose Objective Function [89]	Pareto 1 : 70 Gy Pareto 2 : 78 Gy	

III. 3D ISODOSELINES-INVENTION SURFACTAL-SERIES RESULTS

In this extended study, 3D Interior and Graphical Optimization methods are used in parallel-refinement to confirm results from [98,100], with the ***in vivo*** dataset from [23,24,97,98, 100] . The 3D imaging process, Figures 1-5, programming demonstrate the results got with 3D IO in [100]. Isodoselines are cursor-marked inset within every 3D graph. The radiotherapy planner obtains the desired combination of fractions (**k**), and fraction dose (**d**), for a fixed total BED dose delivery. That is considered an easy, fast, and simple advance in modern TPO and RT research.

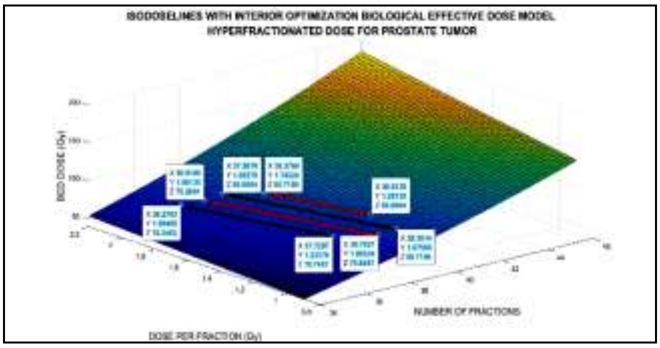

Figure 1.- Isodoselines for a series of BED doses. Namely, marked inset, 70,75,80,85 Gy. The Isodoselines fundamentals for IO calculations are implemented into a 3D surface with two examples. Pattern intervals for plotting were taken from PMO but with ***in vivo*** parameters. Each BED total dose is fixed along Isodoseline, while (**k**) and (**d**) parameters vary when cursor is moved along this Isodoseline.

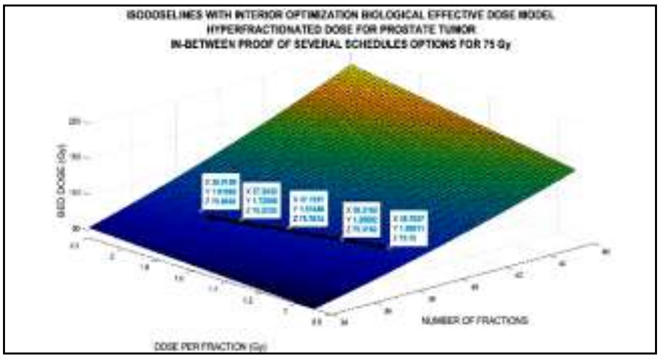

Figure 2.- In this image the Isodoseline fundamentals for IO calculations are demonstrated into a 3D surface with five examples of fixed BED dose along the 75 Gy Isodoseline All intermediate values are marked in-between the Isodoseline for 75 Gy. The practical TPO usage emerges from the figure.

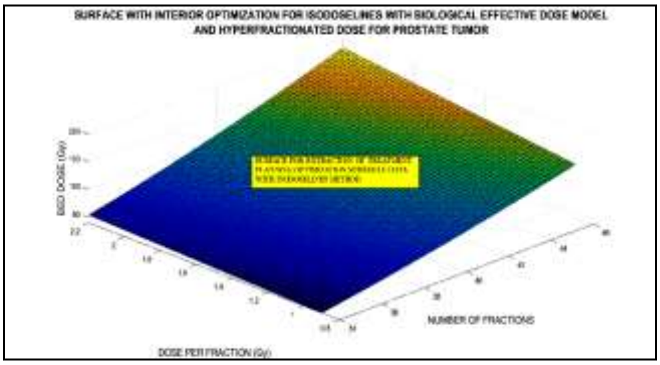

Figure 3.- Isodoselines for a series of BED doses. The Isodoselines can be set *ad libitum* within the IO surfactal plot. Pattern intervals for plotting were taken from PMO but with ***in vivo*** parameters. Every BED total dose can be

traced/fixed along any Isodoseline, while (**k**) and (**d**) parameters vary when cursor is moved along this Isodoseline, as in previous Figs. 4,5.

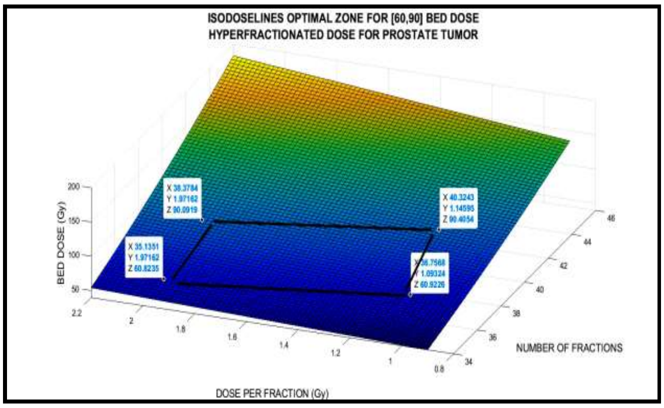

Figure 4.- The Isodoseline fundamentals for IO calculations within interval of total BED dose [60,90]. In this area the planner can select any convenient choice for the patient treatment. Enhanced in Appendix.

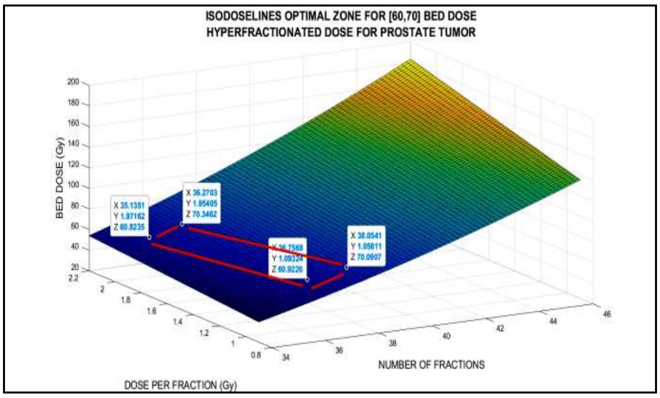

Figure 5.- The Isodoseline fundamentals for IO calculations within interval of total BED dose [60,70]. In this area the planner can select any convenient choice for the patient treatment. Enhanced in Appendix.

IV. RADIOTHERAPY MEDICAL PHYSICS APPLICATIONS

Table 3, modified/improved from [100], shows radiotherapy applications for RT treatment based on biological models, and specifically also for this study. Medical physics principal applications for radiotherapy TPO are explained briefly.

Table 3.- Briefing of radiotherapy and radioprotection applications derived from imaging results.

3D ISODOSELINES RADIOTHERAPY TREATMENT PLANNING OPTIMIZATION APPLICATIONS BRIEF		
APPLICATION	**MEDICAL PHYSICS FIELD**	**ISODOSELINES FOR TPO**
Optimal Dose Fractions Magnitude	Patient Treatment Precision	Increase TCP, TCCP, and possible decrease of NTCP
Optimal Dose Fractions	Patient Treatment Precision	Increase TCP, TCCP, and possible decrease of NTCP
Planner Selection of Optimal Dose and number of Fractions	Patient Treatment Schedule Precision	Increase TCP, TCCP, and possible decrease of NTCP
Post-RT Treatment Survival time	Optimization Time Schedule	Better life-quality for patient. Increase of Survival Time
Biological Models Research	Improvements in research and applications	Improvements LINAC Software And Imaging guided RT Treatment. Improvements in Gamma-Knife, and Cyber-Knife
NTCP Models	Possible applications also	Decrease of Side-Effects at OARs

V. DISCUSSION AND CONCLUSIONS

The objective of the study was to get a series of 3D Isodoselines charts to evidence and verify the results from [98,100] in prostate cancer hyperfractionated RT treatment with BED-LQ model and ***in vivo*** parameters. An improved and rather difficult software for 3D Interior Optimization to determine optimal surfaces and Isodoselines was constructed. All imaging processing results comfirm the previous studies [98,100].

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.

Succintly, an extensive prostate cancer constrained RT-BED hyperfractionation model with 3D imaging processing and ***in vivo*** data was performed with Isodoselines software engineering work. Isodoselines constitute a practical result for BED RT accurate planning. Applications for hyperfractionated dose delivery in prostate tumors and radiation therapy optimal TPO in general arise from all the study.

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SCIENTIFIC ETHIC STANDARDS

Formulas applied/included are from previous prostate article with in vitro data. Model is a modification from several authors, based also on [20,24,25,83,88,89] 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 [20,87,88] 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 [38,43-45]. References [38,43,44,45]: '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, algorithm, proposition or theorem is 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: in at least one article of theses series, it was written by mistake that radiation is previous to surger. That is a mistake, for cancer treatment, surgery, when possible, is previous to radiation]. 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, religious, religious-similar, non-scientific theories, personal opinions, political ideas, or economical influences. When anything is taken from a source, it is adequately recognized. Ideas and some text expressions/sentences from previous publications were emphasized due to a clarification aim [38, 43-45].

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 computational-engineering/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 in Radioprotection Low Energies Dosimetry [1985]). He studied always in public-educational institutions, was football player 1972-78 (defender and midfielder) and as Physician, supports healthy life and all sports activities. 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. His constant service to the International Scientific Community and Estonian technological progress (2016-present) commenced in 1985 with publications in Medical Physics, with further specialization in optimization methods in 1997 at Finland—at the moment approximately 100 recognized publications with approximately 62 DOI papers. His main branch is Computational-mathematical Nonlinear/Inverse Methods Optimization. Casesnoves best-achievements are the Numerical Reuleaux Method in dynamics and nonlinear-optimization [books 2019-2020], The series of Radiotherapy Improvements for AAA superposition-convolution model, the Graphical and Interior Optimization Methods [2016-8], the new Computational Dissection-Anatomical Method, [2020], invention of Forensic Robotics [2020-2021], and Molecular Effect Model for High Temperature Superconductors [2020]. Dr Casesnoves scientific service since 2016 to the Free and Independent Republic of Estonia for technological development (and also at Riga technical University, Power Electrical and Electronics Department) is about 37 physics-engineering articles, two books series, and 1 industrial radiotherapy project associated to Europe Union EIT Health Program (Tartu University, 2017). Treatment planning Optimization Invention of Isodoselines was created in July 2023

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APPENDIX

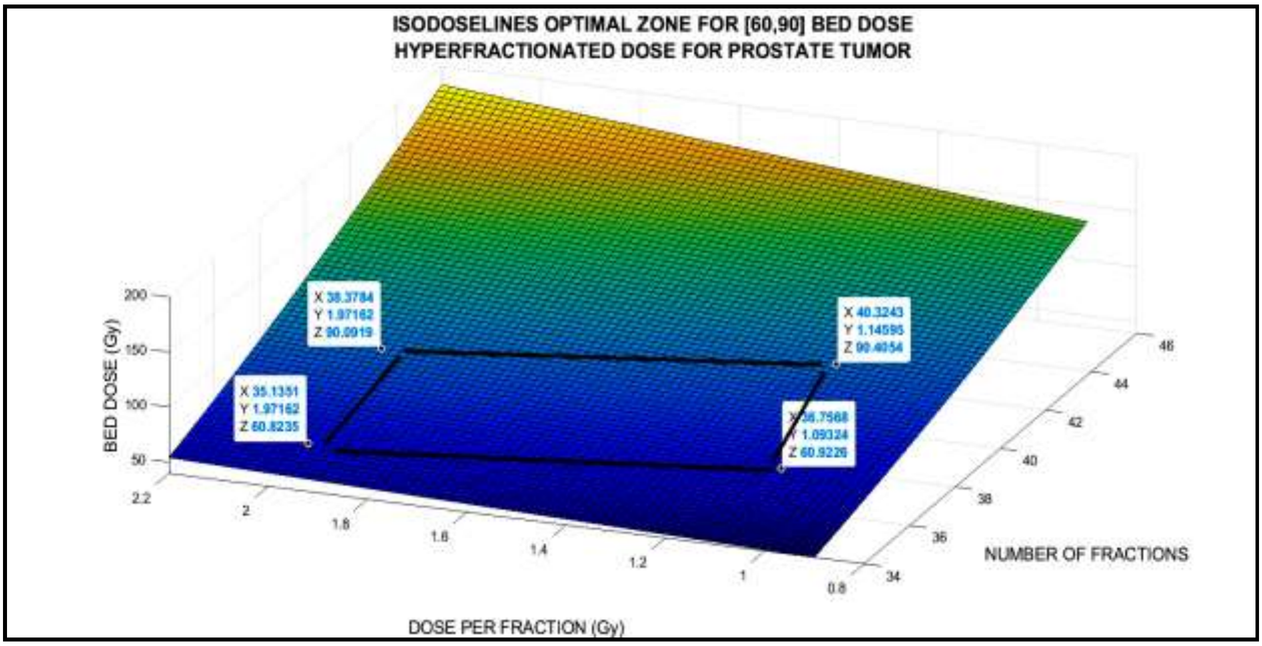

Figure 4 [Enhanced].- The Isodoseline fundamentals for IO calculations within interval of total BED dose [60,90]. In this area the planner can select any convenient choice for the patient treatment.

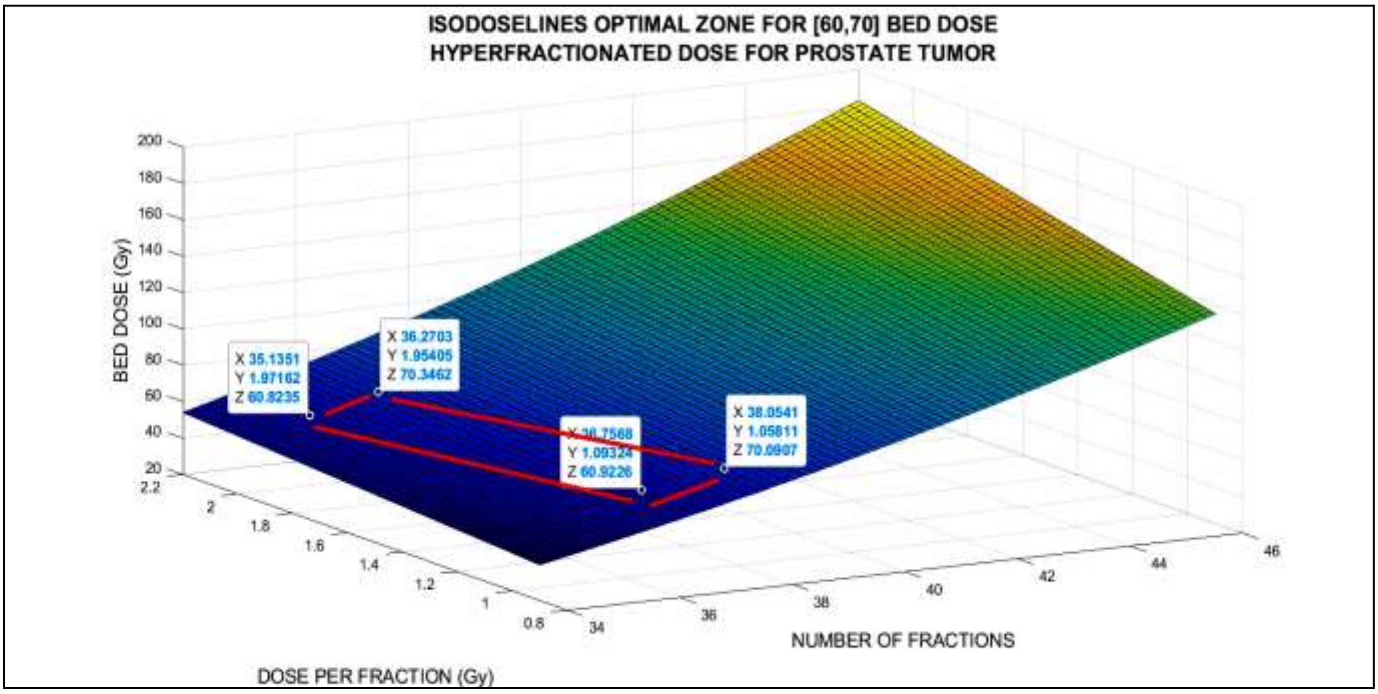

Figure 5 [Enhanced].- The Isodoseline fundamentals for IO calculations within interval of total BED dose [60,70]. In this area the planner can select any convenient choice for the patient treatment.