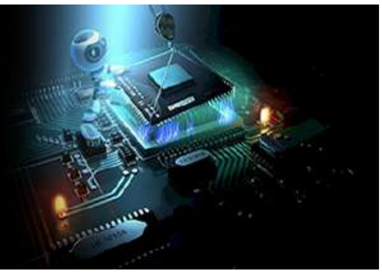
International Journal of Engineering in Computer Science



E-ISSN: 2663-3590
P-ISSN: 2663-3582
IJECS 2023; 5(1): 27-40
Received: 07-11-2022
Accepted: 22-12-2022

Francisco Casesnoves
Ph.D., Engineering, M.Sc. Physics-Mathematics, Physician. Independent Research Scientist, International Association of Advanced Materials, Sweden. Uniscience Global Scientific Member, Wyoming, USA

Correspondence
Francisco Casesnoves
Ph.D., Engineering, M.Sc. Physics-Mathematics, Physician. Independent Research Scientist, International Association of Advanced Materials, Sweden. Uniscience Global Scientific Member, Wyoming, USA

Radiotherapy additional genetic algorithm 2D Pareto-Multiobjective optimization of biological effective dose results for head and neck cancer advanced treatment

Francisco Casesnoves

DOI: https://doi.org/10.33545/26633582.2023.v5.i1a.86

Abstract
Additional-extensive graphical and numerical results for BED model (Biological Effective Dose) in Head and Neck tumors hyper fractionation TPO optimized with Pareto-Multiobjective (PMO) Genetic Algorithms (GA) software are presented. The mathematical GA is applied for two series of Pareto Functions. Artificial Intelligence (AI) with GA is applied on Radiotherapy Treatment Planning Optimization (TPO) is explained in brief. Series of findings comprise PMO imaging process sequences and numerical values of PMO Head and Neck cancer parameters. Further solutions prove PMO-GA BED model both with Pareto-Optimal Front detailed graphics, charts and numerical dose fractionation datasets. Improved and advanced RT Head and Neck cancer TPO, and tumors in general for Fractional-dose photon dose delivery are explained.

Keywords: Pareto-Multiobjective Optimization (PMO), Mathematical Methods (MM), Biological Models (BM), Radiation Therapy (RT), etc.

Introduction

In a recent study, Artificial Intelligence with Genetic Algorithms was applied on radiotherapy BED model for Head and Neck tumors [87, 88]. The objective of this research is further extend, explain, apply, and detail those previous results [87, 88].

For these objectives, Nonlinear GA-PMO engineering software was improved and designed in a number of programs for PMO-BED models, Figures 1-5, Tables 3-4. In [87, 88], a second model for $N_{Effective}$ (Effective Tumor Population Clonogens Number) was optimized with 3D Graphical optimization programs and imaging processing techniques [75, 85-88].

Therefore, innovation of this article is the extension and detail of previous results for easy learning and results confirmation. Thorough GA findings are presented both in 2D graphics and dataset. Numerical results and applications to improve head and neck tumor RT treatment are detailed in Tables 5-6.

Head and neck cancer pathology have very specific oncological, epidemiological, pathogenesis, and radiobiological characteristics [75-79, 83-88]. Additionally, those tumors are classified rationally in those strands because of a number of common anatomical-pathological characteristics. Namely, their onco-pathogenesis shows two main origins, external, which is the most important, and the internal.

The external media intake/contact from a group of substances have significant pathogenesis factors in the oncological origin of these cancers. These intakes could be toxic substances or biological ones, such as virus or bacteria. Among virus, for example, the Espstein-Barr one is linked to nasopharyngeal carcinoma pathogenesis, and Papillomavirus to Tonsillar carcinomas. That is, the head, thorax cavity and neck anatomical zones catch from air many of them from exterior media into the mouth nose, and lungs. Therefore tobacco influence is epidemiologically-statistically high. The oral cavity can accumulate tobacco and alcohol as oncogenetical factors. The high-temperature drinks that can damage the interior mucose of mouth and esophagus can also create oncological conditions/predisposition in these structures. The lungs could also take in materials that cause mesothelioma. Specific processed substances contained in food could cause oncogenesis phenomena in oral cavity, esophagus and stomach. External radiation sources show an important influence for thyroid cancer origin [83, 84]. Electromagnetic radiation constant and daily magnitude may have epidemiological influence in specific brain cancer tumors pathogenesis.

As an example of internal pathogenesis, the lymphomas, methastases from other regions, or neural-spinal cancers located on brain, neck and thorax constitute an important group.

Succintly, an extension of previous Nonlinear Pareto-Multiobjective GA optimization was performed for radiotherapy BED models in head and neck tumors [87, 88]. Applications for radiotherapy TPO and future improvements in RT are also presented.

Mathematical and Software Engineering Methods

Pareto-Multiobjective Optimization basic BED $_{Effective}$ model was set in software, [24]. Parameters intervals are detailed in Algorithm 1 [85-88]. Two different PMO optimization programming series are presented with different parameter intervals magnitudes, Tables 1-2. This BED model constitutes the fundamentals for fractionate radiotherapy, although there are variations among authors [20-25]. Formulation is based on previous studies computational software [1-21, 85-88]. The algorithm that was set, with Chebyshev L_1 norm, [Algorithm 1], reads.

$$\text{Chebyshev } L_1 \text{ Optimization for,}$$
$$BED_{Effective} = k\,d\left[1+\frac{d\times\beta}{\alpha}\right]-\ldots$$
$$\ldots-\frac{Ln(2)}{\alpha}\left[\frac{T_{Treatment}-T_{Delay}}{T_{Potential}}\right]; \quad (1)$$

Where

K. Dose fraction number for hyper fractionated.
RT protocol. [20-25].
Software pattern set [35, 45] Fractions.
D: Dose fraction for hyper fractionated
RT protocol [20-25].
Software pattern set [1, 2.2 II Gy.
A: Clonogen Head and Neck tumor
Radio sensitivity parameter [0.19, 0.61]. [20-25].
B: Clonogen Head and Neck tumor
Radio sensitivity parameter [0.0581]. [20-25].
$T_{Treatment}$: Total time for radiation dose delivered. Software pattern set [22, 55] days [20-25].
T_{Delay}: Total standard repopulation delays for RT. Software set [21] days. [20-25].
$T_{Potential}$: Total standard Head and Neck cancer potential repopulation factor.
Software pattern set [3.5, 4.5] days [20-25].

Algorithm 1 [Casesnoves, 2022]. Head and Neck PMO algorithm [1-21, 85-88] implemented in software. The intervals for optimization parameters in software are detailed. It is an improvement from a series of previous research in radiotherapy.

Bio models equations depend on several parameters experimentally determined. Some of them, specific for every type of cancer are N_0 and N $_{Effective}$ clonogens rates. Resulting Survival Rate, N_S is determined usually by exponential functions, statistical distributions [Binomial or Poisson], and two radiosensitivity key parameters. Namely, [α and β biological modelling parameters], whose magnitudes intervals can be experimentally calculated by *in vitro* or *in vivo* experimental. An Integral Equation Model (IEM) for TCCP, based on new Linear Quadratic Model and Statistical Binomial Distribution approximation was published in recent contributions [20, 75, 85-88]. Dataset and approximation intervals for head and neck cancer implemented into Equation1 model is shown in Tables 1-2, [20-25, 75, 85-88].

The programming method(s) applied for this research are based in a number of previous papers [1-20, 74]. For Genetic Algorithm PMO and N $_{Effective}$ modeling Equation1 implementation on 2D/3D programs. Tables 1-2 show the 2D GA programming method variations to obtain acceptable better calculations, and 2D Graphical Optimization processing images, error determinations, and get applied exactly the PMO-BED model. All those figures are implemented in Equation 1 formula for software.

Table 1: First GA optimization dataset. 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].

GENETIC ALGORITHM ARTIFICIAL INTELLIGENCE OPTIMIZATION PARAMETER INTERVAL FOR HEAD AND NECK TUMORS FIRST GA OPTIMIZATION		
PARAMETER	**MAGNITUDE INTERVAL**	**ADDITIONAL**
Dose fraction number	[32, 40]	Usual protocol in literature [1-21,74-86].
Dose fraction magnitude	[1.2,1.5] Gy	Usual protocol in literature [1-21,74-86]. Set with intervals according to different criteria.
$T_{Treatment}$ (total)	[22,52] Days	Usual protocol in literature [1-21,74-86]. Set with intervals according to different criteria. The RT treatment varies according to weekends breaks, secondary effects, patient circumstances, etc.
T_{Delay}	[20,30] Days	Usual protocol in literature [1-21,74-86]. Set with intervals according to different criteria.
$T_{Potential}$ α [Gy^{-1}] , β [Gy^{-2}] radiobiological parameters	[3.5, 4.5] Days [calculated from head and neck cancer experimental α = 0.40 ±0.21 Gy^{-1} , β= 0.0581 Gy^{-2}]	Usual protocol in literature [1-21,74-86]. Set with intervals according to different criteria.
Dose interval in Objective Function	47 Gy for Pareto F 1 function 55 Gy for Pareto F 2 function	Usual protocol in literature [1-21,74-86]. Set with two total dose Pareto Functions according to different criteria.

Table 2: The second simulations were done with approximate numerical-experimental data from several authors. $T_{Potential}$ is taken [3.5, 4.5] days.

GENETIC ALGORITHM ARTIFICIAL INTELLIGENCE OPTIMIZATION PARAMETER INTERVAL FOR HEAD AND NECK TUMORS SECOND GA OPTIMIZATION		
PARAMETER	**MAGNITUDE INTERVAL**	**ADDITIONAL**
Dose fraction number	[35, 50]	Usual protocol in literature [1-21,74-88].
Dose fraction magnitude	[1.2 , 2.0] Gy	Usual protocol in literature [1-21,74-88]. Set with intervals according to different criteria.
$T_{Treatment}$ (total)	[22,52] Days	Usual protocol in literature [1-21,74-88]. Set with intervals according to different criteria. The RT treatment varies according to weekends breaks, secondary effects, patient circumstances, etc.
T_{Delay}	[20,30] Days	Usual protocol in literature [1-21,74-88]. Set with intervals according to different criteria.
$T_{Potential}$ α [Gy^{-1}] , β [Gy^{-2}] radiobiological parameters	[3.5, 4.5] Days [calculated from head and neck cancer experimental α = 0.40 ±0.21 Gy^{-1} , β= 0.0581 Gy^{-2}]	Usual protocol in literature [1-21,74-88]. Set with intervals according to different criteria.
Dose interval in Objective Function	35 Gy for Pareto F 1 function 50 Gy for Pareto F 2 function	Usual protocol in literature [1-21,74-88]. Set with two total dose Pareto Functions according to different criteria.

Table 2: The second simulations were done with approximate numerical-experimental data from several authors. $T_{Potential}$ is taken [3.5, 4.5] days

Results

Figures 1-5 show PMO results. Tables 3-4 present details of both numerical PMO optimization results. The most important to validate the results are those ones that show the Pareto Front. Average distance among generation individuals, stopping criteria, are also important. The other details are complementary and shown in additional 2D charts for first and second PMO optimization. Maximum number of generations selected was 300-800. Score histograms also prove the validity of the software and PMO done. Running time for both processes is about 2-4 minutes.

Numerical results, Tables 3-4, resume for PMO in BED model. Dose fraction magnitude should be less than 2 Gy approximately [19-21, 75, 85-88].

PMO-GA Imaging Processing First Optimization Results

First optimization results are shown in Figures 1-2, Table 1. Pareto function 2 results are more accurate than Pareto function 1. Every chart of Artificial Intelligence GA is detailed with further explanations.

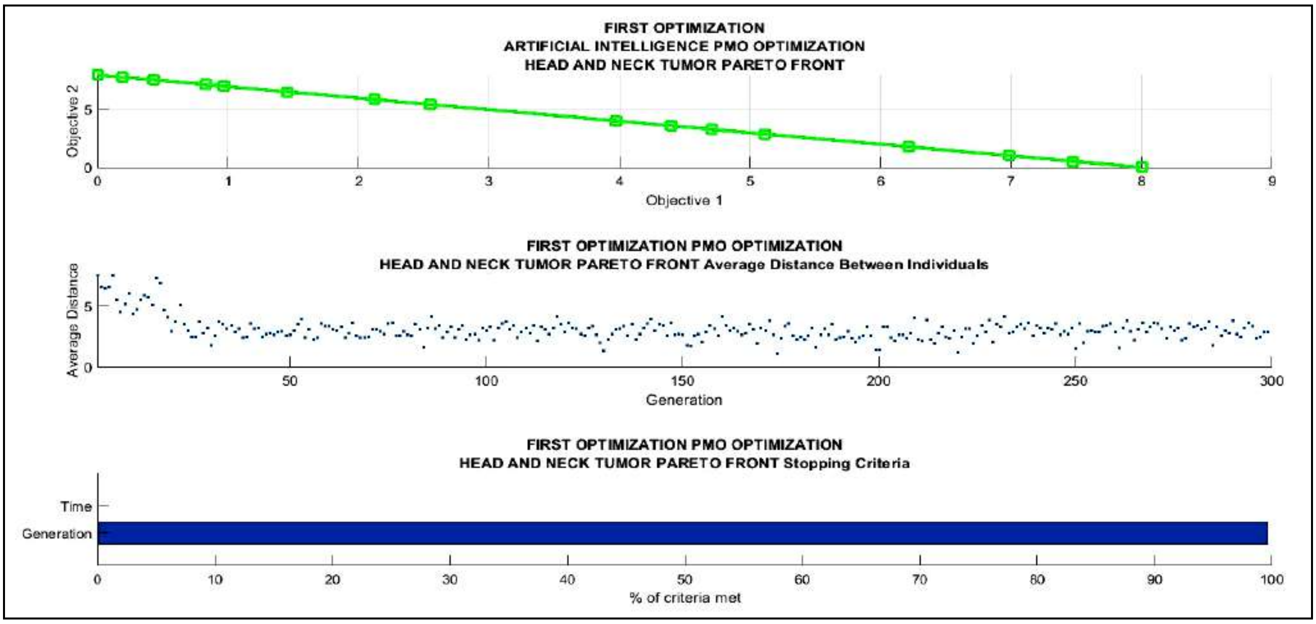


Fig 1: First optimization Multifunctional GA 2D graph. This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f 1 and f 2 show low residuals.

Therefore, results are acceptable in first optimization for function 1 and function 2. The number of points on the Pareto front was: 18. The number of generations was: 300. Enhanced in Appendix.

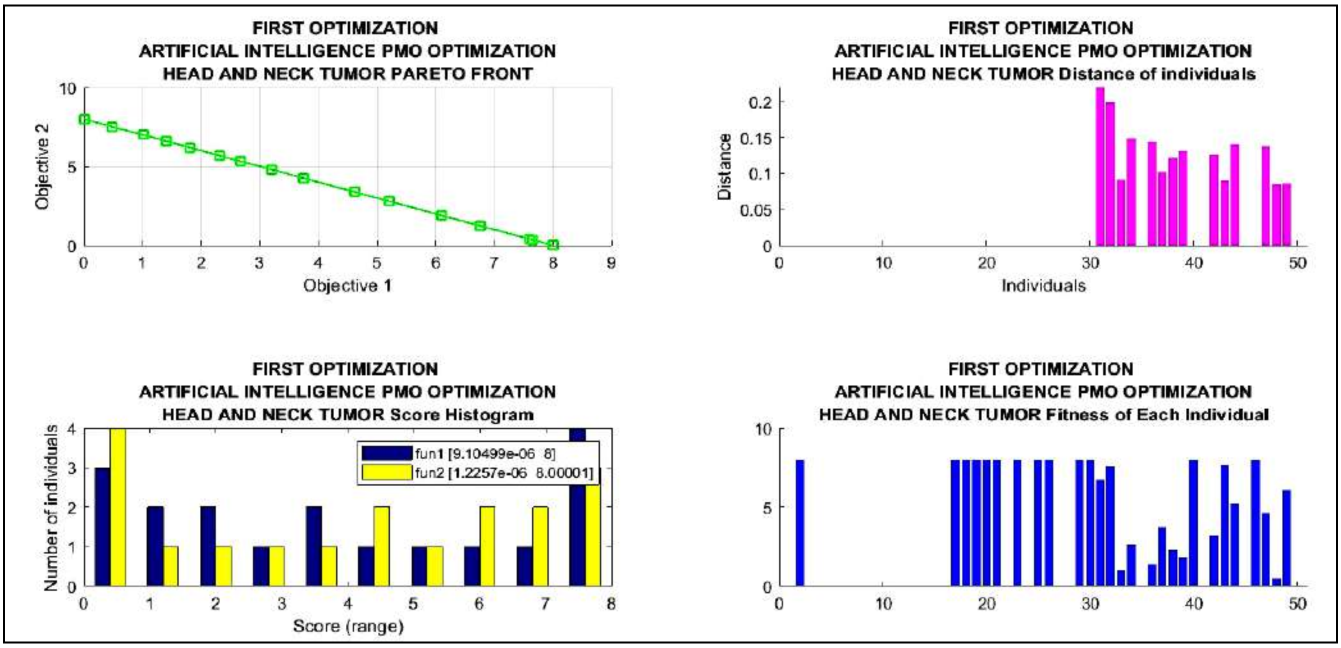


Fig 2: First optimization Multifunctional GA 2D graph. This is the complementary multifunctional graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f 1 and f 2 show low residuals. Therefore, results are acceptable in first optimization for function 1 and function 2. The number of points on the Pareto front was: 18. The number of generations was: 300.

PMO-GA Imaging Processing Second Optimization Results

Second optimization results are shown in Figures 4-6, Table 2. Pareto function 2 results be more accurate than Pareto function 1. Every chart of Artificial Intelligence GA is detailed with further explanations.

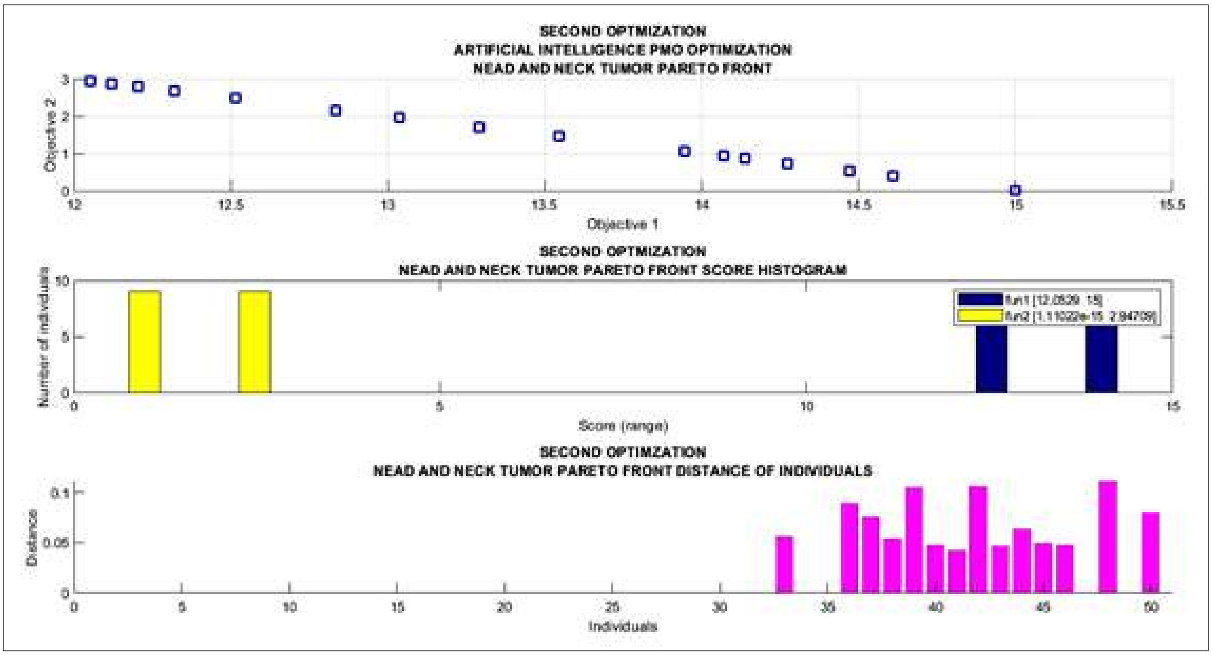


Fig 3: Second simulation. Multifunctional GA 2D graph. This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f 1 and f 2 show low residuals. Therefore, results are acceptable. The number of points on the Pareto front was: 18. The number of generations was: 300.

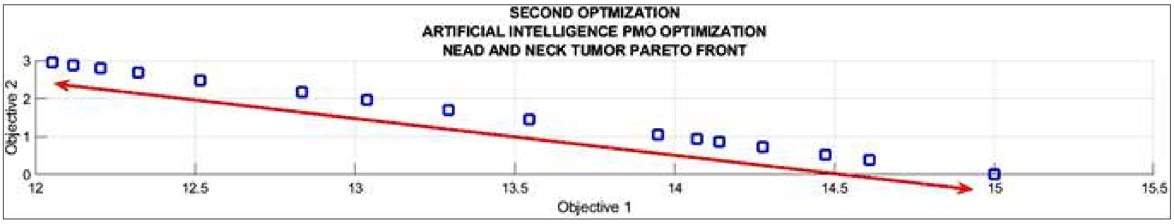


Fig 4: This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f1 and f2 show low residuals. Objective 2 is more accomplished. Therefore, results are acceptable. The number of points on the Pareto front was: 18. The number of generations was: 300. Enhanced in Appendix.

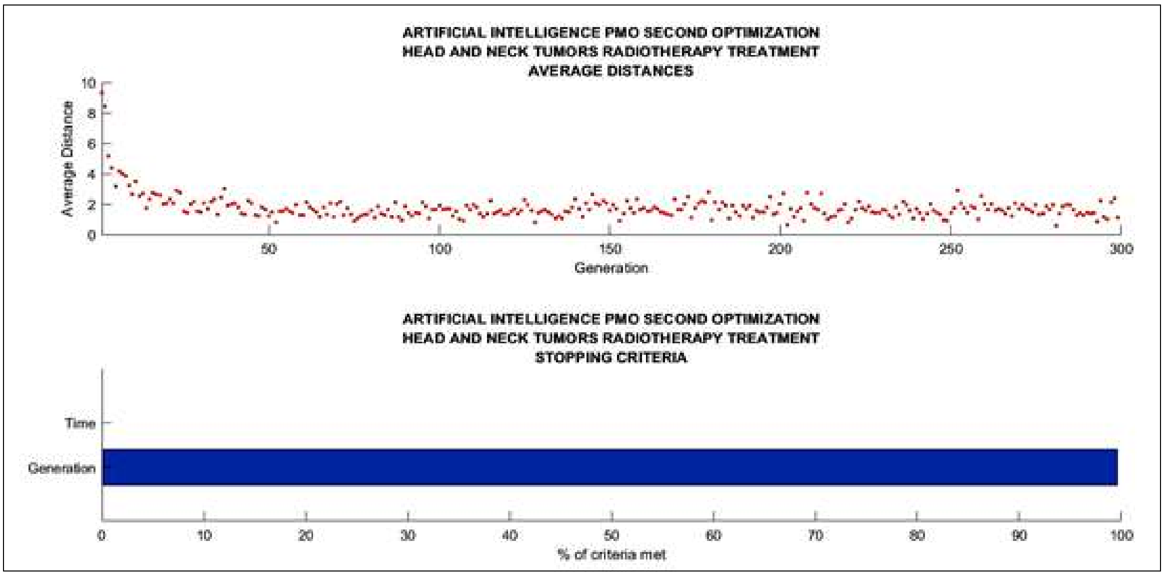


Fig 5: This is important complementary graph given by software when PMO is performed to check the optimization accuracy. Average Distances is an significant parameter. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both f 1 and f 2 show low average distances, less than 2. Therefore, results are acceptable. The number of points on the Pareto front was: 18. The number of generations was: 300.

PMO-GA Numerical Results

Examples of Numerical results resume for PMO in BED model are detailed in n Tables 3-4. Chebyshev norms were set for [55, 65] Gy interval. Dose fraction magnitude should be less than 2 Gy approximately. Numerical Results for model are developed and reviewed from the innovation from [20, 21, 75, 85-88].

Table 3: First simulation. Brief of PMO Artificial Intelligence with GA optimization numerical results in Head and Neck tumors for advanced TPO. Enhanced in Appendix.

BRIEF OF NUMERICAL FIRST PMO OPTIMIZATION RESULTS HEAD AND NECK BIOLOGICAL EFFECTIVE RADIOTHERAPY TREATMENT

Generation	Func-count	Pareto distance	Pareto spread
271	13550	0.0664648	0.233149
272	13600	0.0295673	0.123498
273	13650	0.0244215	0.0989167
274	13700	0.0424819	0.177761
275	13750	0.0179927	0.0802337
276	13800	0.0373533	0.158533
277	13850	0.0215619	0.091576
278	13900	0.0371236	0.135267
279	13950	0.0353069	0.133862
280	14000	0.0329375	0.114606
281	14050	0.0302815	0.112513
282	14100	0.0200634	0.081698
283	14150	0.0452573	0.183996
284	14200	0.0239752	0.100783
285	14250	0.023378	0.10136
286	14300	0.0466089	0.176541
287	14350	0.0571169	0.210486
288	14400	0.0350603	0.132537
289	14450	0.0168583	0.0738853
290	14500	0.0364302	0.14719
291	14550	0.0343554	0.148173
292	14600	0.0265149	0.108386
293	14650	0.0445348	0.173242
294	14700	0.018079	0.0786436
295	14750	0.0281023	0.117192
296	14800	0.0319461	0.122923
297	14850	0.0266535	0.10269
298	14900	0.0190131	0.0802516
299	14950	0.0195492	0.0867326
300	15000	0.0391879	0.150761

Optimization terminated: maximum number of generations exceeded.

population =

32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5508
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
32.6551	1.2549	25.4416
33.4949	1.3032	25.5279
36.3169	1.3043	26.5530
34.7218	1.3080	25.5166
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
34.9485	1.2867	25.4865
32.6925	1.2656	25.4444
35.6515	1.2953	25.8327
32.6551	1.2549	25.4337

Table 4: Second simulation. Brief of PMO Artificial Intelligence with GA optimization numerical results in Head and Neck tumors for advanced TPO. These numerical results are an example, the dataset got is much bigger

BRIEF OF NUMERICAL SECOND PMO OPTIMIZATION RESULTS HEAD AND NECK BIOLOGICAL EFFECTIVE RADIOTHERAPY TREATMENT

Generation	Func-count	Pareto distance	Pareto spread
271	13550	0.0264619	0.183624
272	13600	0.017658	0.128402
273	13650	0.0227234	0.15417
274	13700	0.0124722	0.0958928
275	13750	0.0215654	0.159534
276	13800	0.0153963	0.116006
277	13850	0.0294572	0.213636
278	13900	0.0318413	0.189485
279	13950	0.0176281	0.133355
280	14000	0.0214485	0.155889
281	14050	0.0307415	0.186141
282	14100	0.0176285	0.124615
283	14150	0.0357828	0.243373
284	14200	0.0144201	0.115587
285	14250	0.0150138	0.108402
286	14300	0.0203258	0.147338
287	14350	0.0224556	0.162609
288	14400	0.016788	0.116911
289	14450	0.00963603	0.0784907
290	14500	0.0108432	0.0803516

289	14450	0.00963603	0.0784907
290	14500	0.0108432	0.0803516
291	14550	0.0287958	0.205909
292	14600	0.0315205	0.205436
293	14650	0.0216337	0.147394
294	14700	0.0288101	0.209371
295	14750	0.0191258	0.12803
296	14800	0.010983	0.0858918
297	14850	0.0216991	0.136979
298	14900	0.0151757	0.0946424
299	14950	0.0256791	0.163865
300	15000	0.015325	0.106296

Optimization terminated: maximum number of generations exceeded.
The number of points on the Pareto front was: 18
The number of generations was : 300

population =

35.0000	1.2000	22.0000
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.2046	1.2294	23.3154
35.1347	1.2028	22.0698
35.3080	1.2236	23.1548
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.2739	1.2458	23.6035
35.2248	1.2465	23.0652
35.0000	1.2000	22.0000
35.1337	1.2028	22.0704
35.2062	1.2187	22.4697
35.3452	1.2473	23.6728
35.3432	1.2398	23.1952
35.3452	1.2473	23.6728
35.3452	1.2473	23.6728
35.0513	1.2010	22.1323
35.1628	1.2314	22.0871
35.2275	1.2412	22.5324
35.3112	1.2309	22.9631
35.2991	1.2168	23.0616
35.2047	1.2051	22.4210

Head and neck cancer radiotherapy physics applications

Table 5 presents brief of RT TPO methods and subsequent positive effects in patient cure and post-radiation life, head and neck tumors in BED modeling. Table 6 shows a resume of radiotherapy applications in head and neck tumors. Medical physics principal applications for radiotherapy TPO are explained briefly. Those prospective according to $N_{Effective}$ model applications are useful for radiotherapy research/applications on head and neck tumors and other types of cancer.

Table 5: Brief of RT TPO methods and subsequent positive effects in patient cure and post-radiation life. Those are justified also for the rise of head and neck tumor survival time and complete cure got by modern RT, IMRT, IMPT, Chemo and Immunotherapy advances. Enhanced in Appendix

$N_{Effective}$ MODEL FOR HEAD AND NECK TUMORS APPLICATIONS	
RT TPO METHOD IMPROVEMENTS	**DIRECT EFFECT**
Mathematical Improvements when N_{Eff} is implemented in Survival Fraction Models	With N_{Eff} Implementation TCP is numerically more accurate Without N_{Eff} TCP is falsely numerically higher With N_{Eff} Implementation NTCP is numerically more accurate Without N_{Eff} Implementation NTCP is falsely numerically lower
N_{Eff} Implementation in Survival Fraction Models	Dose Delivery Precision because it minimizes Clonogenes growth during radiotherapy Treatment Time, Maximum Effect/Maximum Tumor Control Probability [TCP]
N_{Eff} Implementation in Survival Fraction Models for exact calculation of NTCP instead N_0 . Then, TCP and NTCP are more efficacious.	Radioprotection OARs Dose Precision because it sets exact Clonogenes growth during radiotherapy Treatment Time, Maximum Effect/Maximum Normal Tissue Complications Probability [NTCP]
Optimization of Biological Models	Dose Delivery Precision, minimum dose/ maximum effect
Previous Photon-dose Optimization	Dose Delivery Precision to be implemented in BM, minimum dose/ maximum effect
Normal Tissue Complications Probability Models [NTCP]	Dose-Volume-Histogram Dose Delivery Precision to be implemented in BM, minimum dose at OARs
ON PATIENT EFFECTS	
OARs Radioprotection	Avoid Damage at any FSUs [Organ Funcional Subunits]
Radiation Therapy Secondary Effects	Hypo Fractionations decreases Radiation Undesirable Symptoms
Patient Life Quality	Not only Physical benefit but also Psychological for Patient

Table 6: Some radiotherapy and radioprotection for RT head and 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 $N_{Effective}$	Clinical improvements with BMs after research according to $N_{Effective}$	Inverse planning system set up on BMs according to $N_{Effective}$
LINAC OPTIMIZATION	Optimization of photon-dose for BMs	LINACs BMs Usage for IMRT, IMPT according to $N_{Effective}$	Exploration of new possibilities for $N_{Effective}$ models	Manufacturing adaptation of LINACs fro BMs according to $N_{Effective}$
Theoretical improvements for new models	Dosimetry improvements in accuracy according to radiobiology experimental $N_{Effective}$	From tumor survival clinical statistics advances in BMs according to $N_{Effective}$	According to $N_{Effective}$ new BMs research sources, both theory and clinical experimental trials	BMs got experimental evidences to be set on TPO according to $N_{Effective}$

Discussion and Conclusions

The objectives of the study were further and extensive results explanations from [87, 88]. Artificial intelligence with GA Pareto-Multiobjective method for head and neck tumors BED model was comprehensively developed.

The PMO-BED model results can be considered illustrative, Figures 1-5, Tables 3-4. Simulations were presented as objective of the research, computationally designed for head and neck tumors [82-88]. It was intended to set in software precise experimental constants [22, 81-88]. Therefore, 3D simulations could offer a realistic graphical and numerical dataset this type of cancers. Two different simulations with different constraints are shown and proven.

Advantages of this AI-GA model are the precision/ adaptability of the method. Inconvenient for the PMO-BED model are the rather longer running time compared to Inverse Least Squares optimization methods, 2-4 minutes.

Grosso modo, Pareto Multiobjective model was got applied for optimization of radiotherapy BED algorithm. The practical radiotherapy physics significance is an improved radiation therapy treatment for head and neck RT medical physics computational planning.

Scientific Ethics Standards

This article shows additional results that complement previous studies and contributions, recently [87-88]. All the images are new/improved and numerical results from former publications are extended and detailed. GA Artificial intelligence software was developed originally by Dr Casesnoves on September 2022. All initial modelling equations were developed from previous researcher's contributions [20-25, 87-88]. The N_S initial formulation and integral Tumor Control Cumulative Probability, (TCCP), were published in [20-25]. From those equations, all the mathematical development implementation is original from the author [1-21, 75]. This article has previous papers mathematical techniques, reviews with explanations, [1-21, 75], who's use was essential to make model numerical solutions and approximations. Equation 1 and $N_{\text{Effective}}$ model are developed and reviewed from [20, 21, 75, 85, 86-88], essential for study understanding. Some information of [20, 21, 75, 86-88] was presented for results clarification, e. g., Table 2. Tables 5-6 from [87, 88] were presented for results and applications further explaining. The number of Dr Casesnoves publications at references is intended also for reader's learning. This study was carried out, and their contents are done according to the European Union Technology and Science Ethics and International Scientific Ethics norms [38, 43-45]. This research was completely done by the author, the calculations, images, mathematical propositions and statements, reference citations, and text is original from the author. When a mathematical statement, proposition or theorem is presented, demonstration is always included. If any results inconsistency is found after publication, it is clarified in subsequent contributions. When a citation such as [Casesnoves, 'year'] appears, there is not vanity or intention to brag. The reason is to keep clearly the intellectual property. The article is exclusively scientific, without any commercial, institutional, academic, religious, religious-similar, non-scientific theories, personal opinions, friends and/or relatives favours, 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].

References

1. Casesnoves F. Radiotherapy Wedge Filter AAA Model 18 Mev-Dose Delivery 3D Simulations with several software systems for medical physics Applications. Applications. Biomed J Sci & Tech Res. 2022;40:5. DOI: 10.26717/BJSTR.2022.46.007337.
2. Casesnoves F. Mathematical Exact 3D Integral equation determination for radiotherapy wedge filter convolution factor with algorithms and numerical simulations. Journal of Numerical Analysis and Applied Mathematics. 2016;1(2):39-59. ISSN Online: 2381-7704.
3. Casesnoves F. Radiotherapy Conformal Wedge Computational Simulations, Optimization Algorithms, and Exact Limit Angle Approach. International Journal of Scientific Research in Science, Engineering and Technology (IJSRSET). 2015;1(2):353-362. Print ISSN: 2395-1990. Online ISSN: 2394-4099.
4. Casesnoves F. Improvements in simulations for radiotherapy wedge filter dose and AAA-Convolution Factor Algorithms. International Journal of Scientific Research in Science, Engineering and Technology (IJSRSET). 2019;6(4):194-219. Print ISSN: 2395-1990. Online ISSN : 2394-4099.
5. Casesnoves F. Exact/Approximated Geometrical Determinations of IMRT Photon pencil-beam path through alloy static wedges in radiotherapy using Anisothropic Analytic Algorithm (AAA). Peer-reviewed ASME Conference Paper. ASME 2011 International Mechanical Eng Congress. Denver. USA. IMECE2011-65435; c2011.
6. Casesnoves F. Geometrical Determinations of Limit angle (LA) related to maximum Pencil-Beam Divergence Angle in Radiotherapy Wedges. Peer-reviewed ASME Conference Paper. ASME 2012 International Mechanical Eng Congress. Houston. USA. IMECE2012-86638; c2012.
7. Casesnoves F. A Conformal Radiotherapy Wedge Filter Design. Computational and Mathematical Model/Simulation'. Peer-Reviewed Poster IEEE (Institute for Electrical and Electronics Engineers), Northeast Bioengineering Conference. Syracuse New York, USA. April 6th, 2013. Peer-Reviewed Poster Session on 6th April 2013. Sessions 1 and 3 with Poster Number 35. Page 15 of Conference Booklet Printed; c2013.
8. Casesnoves F. Mathematical and Geometrical Formulation/Analysis for Beam Limit Divergence Angle in Radiotherapy Wedges. Peer-Reviewed International Engineering Article. International Journal of Engineering and Innovative Technology (IJEIT). 2014;3:7. ISSN: 2277-3754. ISO 9001:2008 Certified.
9. Casesnoves F. Geometrical determinations of IMRT photon pencil-beam path in radiotherapy wedges and limit divergence angle with the Anisotropic Analytic Algorithm (AAA) Casesnoves, F. Peer- Reviewed scientific paper, both Print and online. International Journal of Cancer Therapy and Oncology. 2014;2(3):02031. DOI:10.14319/IJCTO.0203.1. Corpus ID: 460308.
10. Casesnoves F. Radiotherapy conformal wedge computational simulations and nonlinear optimization algorithms. Peer-reviewed Article, Special Double-Blind Peer-reviewed paper by International Scientific Board with contributed talk. Official Proceedings of Bio- and Medical Informatics and Cybernetics: BMIC 2014 in the context of the 18th Multi-conference on Systemics, Cybernetics and Informatics: WMSCI. 2014 July 15-18, Orlando, Florida, USA. ISBN: 978-1-941763-03-2 (Collection). ISBN: 978-1-941763-10-0.

2014;2:15-18.
11. Casesnoves F. Large-Scale Matlab Optimization Toolbox (MOT) Computing Methods in Radiotherapy Inverse Treatment Planning'. High Performance Computing Meeting. Nottingham University. Conference Poster; c2007.
12. Casesnoves F. A Computational radiotherapy optimization method for inverse planning with static wedges. High Performance Computing Conference. Nottingham University. Conference Poster; c2008.
13. Casesnoves F. Radiotherapy Conformal Wedge Computational Simulations, Optimization Algorithms, and Exact Limit Angle Approach. International Journal of Scientific Research in Science, Engineering and Technology. 2015;1:2. Print ISSN: 2395-1990, Online ISSN: 2394-4099.
14. Casesnoves F. Radiotherapy Standard/Conformal Wedge IMRT-Beamlet divergence angle limit exact method, mathematical formulation, and bioengineering applications. International article-poster. Published in proceedings of conference. 41st Annual Northeast Bioengineering Conference. Rensselaer Polytechnic Institute. Troy, New York USA; c2015 April. p. 17-19. DOI: 10.1109/NEBEC.2015.7117152. Corpus ID: 30285689.
15. Casesnoves F. Radiotherapy Standard/Conformal Wedge IMRT-Beamlet divergence angle limit exact method, mathematical formulation, and Bioengineering Applications. IEEE (Institute for Electrical and Electronics Engineers), International Article-Poster; c2015. http://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=7117152.
16. Casesnoves F. Abstract-Journal. 'Radiotherapy Standard/ Conformal Wedge IMRT-Beamlet Divergence Angle Limit Exact Method, Mathematical Formulation. International Conference on Significant Advances in Biomedical Engineering. 252nd OMICS International Conference. Francisco Casesnoves, J Bioengineer & Biomedical Sci. 2015;5:1. http://dx.doi.org/10.4172/2155-9538.S1.003.
17. Casesnoves F. Determination of absorbed doses in common radio diagnostic explorations. 5th National Meeting of Medical Physics. Madrid, Spain. September 1985. Treatment Planning; c2001.
18. Casesnoves F. Master Thesis in Medical Physics. Eastern Finland University. Radiotherapy Department of Kuopio University Hospital and Radiotherapy Physics Grouversity-Kuopio. Defense approved in 2001. Library of Eastern Finland University. Finland; c2001.
19. Casesnoves F. A Conformal Radiotherapy Wedge Filter Design. Computational and Mathematical Model/Simulation'. Peer-Reviewed Poster IEEE (Institute for Electrical and Electronics Engineers), Northeast Bioengineering Conference. Syracuse New York, USA. Presented in the Peer-Reviewed Poster Session on 6th April 2013. Sessions 1 and 3 with Poster Number 35. Page 15 of Conference Booklet; c2013 April 6th.
20. Casesnoves F. Radiotherapy biological tumor control probability integral equation model with analytic determination. International Journal of Mathematics and Computer Research. 2022;10(8):2840-2846. DOI: https://doi.org/10.47191/ijmcr/v10i10.01.
21. Casesnoves F. Radiotherapy Wedge Filter AAA Model 3D Simulations for 18 Mev 5 cm-Depth Dose with Medical Physics Applications", International Journal of Scientific Research in Computer Science, Engineering and Information Technology (IJSRCSEIT). 2022;8(1):261-274. www.ijsrcseit.com. ISSN: 2456-3307. DOI: https://doi.org/10.32628/CSEIT228141.
22. Walsh S. Radiobiological modelling in Radiation Oncology. Ph.D., Thesis. School of Physics. National University of Galway; c2011. http://hdl.handle.net/10379/3027.
23. Chapman D, Nahum A. Radiotherapy Treatment Planning, Linear-Quadratic Radiobiology. CRC Press; c2015. ISBN 9780367866433.
24. Mayles W, Nahum A. Rosenwald, J. Editors. Handbook of Radiotherapy Physics. Second Edition. CRC Press; c2015. ISBN 9780367192075. International Standard Book Number-13: 978-1-4987-2146-2.
25. Nahum A, Webb S. A model for calculating tumour control probability in radiotherapy including the effects of inhomogeneous distributions of dose and clonogenic cell density. Physics in Medicine and Biology. 1993;38(6):653-666 . ISSN 0031-9155.
26. Haydaroglu A, Ozyigit G. Principles and Practice of Modern Radiotherapy Techniques in Breast Cancer. Springer; c2013. DOI: 10.1007/978-1-4614-5116-7 .
27. Casesnoves F. Die numerische Reuleaux-Methode Rechnerische und dynamische Grundlagen mit Anwendungen (Erster Teil); c2019-20. ISBN-13: 978-620-0-89560-8, ISBN-10: 6200895600. Publishing House: Scientia Scripts; c2019-20.
28. Ulmer W, Harder D. Corrected Tables of the Area Integral I(z) for the Triple Gaussian Pencil Beam Model. Z Med Phys. 1997;7(3):192-193. DOI: https://doi.org/10.1016/S0939-3889(15)70255-2 .
29. Ulmer W, Harder D. A triple Gaussian pencil beam model for photon beam treatment planning. Med. Phys. 1995;5(1):25-30. DOI: 10.1016/S0939-3889(15)70758-0.
30. Ulmer W, Harder D. Applications of a triple Gaussian pencil beam model for photon beam treatment planning. Med Phys. 1996;6(2):68-74. https://doi.org/10.1016/S0939-3889(15)70784-1 .
31. Ma C, Lomax T. Proton and Carbon Ion Therapy. CRC Press; c2013. DOI: https://doi.org/10.1201/b13070.
32. Censor Y, Zenios S. Parallel Optimization: Theory, Algorithms and Applications'. UOP; c1997. DOI: 10.12694/SCPE.V3I4.207.Corpus ID: 19584334.
33. Ulmer W, Pyyry J, Kaissl W. A 3D photon superposition/convolution algorithm and its foundation on results of Monte Carlo calculations. Phys Med Biol; c2005, p. 50. DOI: 10.1088/0031-9155/50/8/010.
34. Ulmer W, Harder D. Applications of the triple Gaussian Photon Pencil Beam Model to irregular Fields, dynamical Collimators and circular Fields. Phys Med Biol; c1997. DOI: https://doi.org/10.1023/B:JORA.0000015192.56164.a5.
35. Haddad K, Anjak O, Yousef B. Neutron and high energy photon fluence estimation in CLINAC using gold activation foils. Reports of practical oncology and radiotherapy. 2019;24(1):41-46. DOI: 10.1016/j.rpor.2018.08.009.

36. Sievinen J, Waldemar U, Kaissl W. AAA Photon Dose Calculation Model in Eclipse™. Varian Medical Systems Report. Rad #7170A.
37. Vagena E, Stoulos S, Manolopoulou M. GEANT4 Simulations on Medical LINAC operation at 18MV: experimental validation based on activation foils. Radiation Physics and Chemistry; c2016. DOI:10.1016/j.radphyschem.2015.11.030.
38. Ethics for Researchers. EU Commission. Directorate-General for Research and Innovation. Science in society/Capacities FP7; c2013. https://data.europa.eu/doi/10.2777/7491.
39. Casesnoves F. Surgical Pathology I course class notes and clinical practice of Surgical Pathology Madrid Clinical Hospital [Professor Surgeon Dr Santiago Tamames Escobar]. 4th academic year course for graduation in Medicine and Surgery. Lessons and practice Breast Cancer Surgical and Medical Treatment. 1980-1981. Madrid Complutense University; c1981.
40. Tamames Escobar S. Cirugia/ Surgery: Aparato Digestivo. Aparato Circulatorio. Aparato Respiratorio/ Digestive System. Circulatory System. Respiratory System (Spanish Edition); c2000. ISBN: 10:8479034955. ISBN 13:9788479034955.
41. Silvia Formenti C, Sandra Demaria. Combining Radiotherapy and Cancer Immunotherapy: A Paradigm Shift Silvia C. Formenti, Sandra Demaria. J Natl Cancer Inst. 2013;105(4):256-265. DOI: 10.1093/jnci/djs629.
42. Numrich R. The computational energy spectrum of a program as it executes. Journal of Supercomputing; c2010. p. 52. DOI: 10.1007/s11227-009-0273-x.
43. European Commission, Directorate-General for Research. Unit L3. Governance and Ethics. European Research Area. Science and Society; c2021.
44. ALLEA. The European Code of Conduct for Research Integrity, Revised ed.; ALLEA: Berlin Brandenburg Academy of Sciences; c2017.
45. Good Research Practice. Swedish Research Council; c2017. ISBN: 978-91-7307-354-7.
46. Ulmer W, Schaffner B. Foundation of an analytical proton beamlet model for inclusion in a general proton dose calculation system. Radiation Physics and Chemistry. 2011;80(3):378-389. DOI: 10.1016/j.radphyschem.2010.10.006.
47. Sharma S. Beam modification devices in radiotherapy. Lecture at Radiotherapy Department, PGIMER. India; c2008.
48. Barrett Colls A. Practical Radiotherapy Planning. Fourth Edition. Hodder Arnold; c2009. ISBN 9780340927731.
49. Ahnesjö A, Saxner M, Trepp A. A pencil beam model for photon dose calculations. Med Phys; c1992. p. 263-273. DOI: 10.1118/1.596856.
50. Brahime A. Development of Radiation Therapy Optimization. Acta Oncologica. 2000;39:5. DOI: 10.1080/028418600750013267.
51. Bortfeld T, Hong T, Craft D, Carlsson F. Multicriteria Optimization in Intensity-Modulated Radiation Therapy Treatment Planning for Locally Advanced Cancer of the Pancreatic Head. International Journal of Radiation Oncology and Biology Physics. 2008;72:4. DOI: 10.1016/j.ijrobp.2008.07.015.
52. Brown B, cols. Clinician-led improvement in cancer care (CLICC) - testing a multifaceted implementation strategy to increase evidence-based prostate cancer care: phased randomised controlled trial - study protocol. Implementation Science. 2014;9(1):64. DOI: https://doi.org/10.1186/1748-5908-9-64.
53. Bortifield T. IMRT: a review and preview. Phys Med Biol. 2006;51(13):R363-R379. DOI: 10.1088/0031-9155/51/13/R21.
54. Censor Y. Mathematical Optimization for the Inverse problem of Intensity-Modulated Radiation Therapy. Laboratory Report, Department of Mathematics, University of Haifa, Israel; c1996.
55. Capizzello A, Tsekeris PG, Pakos EE, Papathanasopoulou V, Pitouli EJ. 'Adjuvant Chemo-Radiotherapy in Patients with Gastric Cancer. Indian Journal of Cancer. 2006;43:4. ISSN: 019-509X.
56. Tamer Dawod, Abdelrazek EM, Mostafa Elnaggar, Rehab Omar. Dose validation of physical wedged symmetric fields in artiste linear accelerator. International journal of medical physics, Clinical Engineering and Radiation Oncology. 2014;3(4):201-209. DOI: 10.4236/ijmpcero.2014.34026.
57. Do SY, David A, Bush Jerry D Slater. Comorbidity-adjusted survival in early-stage lung cancer patients treated with hypo fractioned proton therapy. Journal of Oncology; c2010. DOI: 10.1155/2010/251208.
58. Ehrgott M, Burjony M. Radiation Therapy Planning by Multicriteria Optimization. Department of Engineering Science. University of Auckland. New Zealand. Conference Paper; c1999.
59. Ezzel G. Genetic and geometric optimization of three-dimensional radiation therapy treatment planning. Med Phys. 1996;23(3):293-305. DOI: 10.1118/1.597660.
60. Effective Health Care. Number 13. Comparative Effectiveness of Therapies for Clinically Localized Prostate cancer. Bookshelf ID; c2008. NBK554842.
61. Hansen P. Rank-deficient and discrete ill-posed problems: Numerical aspects of linear inversion'. SIAM monographs on mathematical modelling and computation; c1998. ISBN-13: 978-0898714036.
62. Hashemiparast S, Fallahgoul H. Modified Gauss quadrature for ill-posed integral transform. International Journal of Mathematics and Computation. 2011;13:11. ISSN: 0974-570X.
63. Isa N. Evidence based radiation oncology with existing technology. Reports of practical oncology and radiotherapy. 2014;19(4):259-266. DOI: 10.1016/j.rpor.2013.09.002
64. Johansson KA, Mattsson S, Brahme A, Turesson I. Radiation Therapy Dose Delivery'. Acta Oncologica. 2003;42(2):85-91. DOI: 10.1080/02841860310004922.
65. Khanna P, Blais N, Gaudreau PO, Corrales-Rodriguez L. Immunotherapy Comes of Age in Lung Cancer, Clinical Lung Cancer; c2016. DOI: 10.1016/j.cllc.2016.06.006.
66. Kufer KH, Hamacher HW, Bortfeld T. A multicriteria optimization approach for inverse radiotherapy planning. University of Kaiserslautern, Germany; c2000. DOI: 10.1007/978-3-642-59758-9_10.
67. Kirsch A. An introduction to the Mathematical Theory of Inverse Problems. Springer Applied Mathematical Sciences; c1996. Series E-ISSN2196-968X.
68. Luenberger D. Linear and Nonlinear Programming (2nd ed.). Addison-Wesley; c1989. ISBN-13: 978-

3030854492.
69. Moczko J, Roszak A. Application of Mathematical Modeling in Survival Time Prediction for Females with Advanced Cervical cancer treated Radio-chemotherapy. Computational Methods in science and Technology. 2006;12(2):143-147.
DOI: 10.12921/cmst.2006.12.02.143-147
70. Ragaz J, Ivo Olivotto A, John Spinelli J, Norman Phillips, Stewart Jackson M, *et al*. Regional Radiation Therapy in Patients with High-risk Breast Cancer Receiving Adjuvant Chemotherapy: 20-Year Results of the Columbia Randomized Trial'. Journal of National Cancer Institute. 2005;97(2):116-126.
DOI: 10.1093/jnci/djh297.
71. Steuer R. Multiple Criteria Optimization: Theory, Computation and Application. Wiley; c1986.
https://doi.org/10.1002/oca.4660100109.
72. Spirou SV, Chui CS. A gradient inverse planning algorithm with dose-volume constraints. Med Phys. 1998;25:321-323. DOI: 10.1118/1.598202.
73. Das I. colls. Patterns of dose variability in radiation prescription of breast cancer. Radiotherapy and Oncology. 1997;44(1):83-89.
DOI: 10.1016/s0167-8140(97)00054-6
74. Casesnoves F. Practical Radiotherapy TPO course and practice with Cyber knife. Robotic simulations for breathing movements during radiotherapy treatment. Sigulda Radiotherapy Cyber knife Center. Latvia. Riga National Health Oncology Hospital Varian LINACs TPO practice/lessons several Varian LINACs. Riga Technical University Bioengineering Training-Course Nonlinear Life; c2018 Aug.
75. Casesnoves F. Radiotherapy Linear Quadratic Bio Model 3D Wedge Filter Dose Simulations for AAA Photon-Model [18 Mev, Z= 5, 15 cm] with Mathematical Method System. Biomed J Sci & Tech Res. 2022;46:2. BJSTR. MS.ID.007337.
DOI: 10.26717/BJSTR.2022.46.007337
76. Casesnoves F. Master in Philosophy Thesis at Medical Physics Department. Protection of the Patient in Routinary Radiological Explorations. Experimental Low Energies RX Dosimetry. Medicine Faculty. Madrid Completeness University; c1984. p. 85.
77. Casesnoves F. Ionization Chamber Low Energies Experimental Measurements for M-640 General Electric RX Tube with Radcheck ionization camera, Radcheck Beam Kilovolt meter and TLD dosimeters. Radiology Department practice and measurements. Madrid Central Defense Hospital. Medical Physics Department. Master in Philosophy Thesis. Medicine Faculty. Completeness University. Madrid; c1983-5.
78. Casesnoves F. Determination of Absorbed Doses in Routinary Radiological Explorations. Medical Physics Conference organized by Medical Physics Society Proceedings Printed. San Lorenzo del Escorial. Madrid. September; c1985.
79. Greening J. Fundamentals of Radiation Dosimetry. Taylor and Francis. Second Edition; c1985.
DOI: https://doi.org/10.1201/9780203755198.
80. International Commission of Radiation Protection. Bulletin 26th. The International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. Pergamon Press. Copyright © 1977 The International Commission on Radiological Protection; c1977.
81. Stanton P. Colls. Cell kinetics *in vivo* of human breast cancer. British Journal of Surgery. 1996;83(1):98-102.
DOI: https://doi.org/10.1002/bjs.1800830130 .
82. Hedman M, Bjork-Eriksson T, Brodin O, Toma-Dasu I. Predictive value of modelled tumour control probability based on individual measurements of *in vitro* radiosensitivity and potential doubling time. Br J Radiol. 2013;86:2013.0015.
DOI: 10.1259/bjr.20130015.
83. Fowler J. 21 years of Biologically Effective Dose. The British Journal of Radiology. 2010;83:554-568.
84. Marcu, L, al. Radiotherapy and Clinical Radiobiology of Head and Neck Cancer. Series in Medical Physics and Biomedical Engineering. CRC Press; c2018.
85. Casesnoves F. Radiotherapy 3D Isodose Simulations for Wedge Filter 18 Mev-Dose [z = 5, 15 cm] with AAA Model with Breast Cancer Applications. International Journal on Research Methodologies in Physics and Chemistry (IJRPC) ISSN: 2349-7963. 2022;9:2.
86. Garden A, Beadle B, Gunn G. Radiotherapy for Head and Neck Cancers. Fifth Edition. Wolters Kluwer; c2018.
87. Casesnoves F. Radiotherapy Genetic Algorithm Pareto-multiobjective optimization of biological effective dose and clonogens models for head and neck tumor advanced treatment. International Journal of Mathematics and Computer Research. ISSN: 2320-7167. Jan 2023;11(1):3156-3177.
DOI: 10.47191/ijmcr/v11i1.08.
88. Casesnoves F. Radiotherapy effective clonogens model graphical optimization approaching linear quadratic method for head and neck tumors. International Journal of Molecular Biology and Biochemistry. ISSN Print: 2664-6501. ISSN Online: 2664-651X. Impact Factor: RJIF 5.4. IJMBB. 2023;5(1):33-40.

Appendix

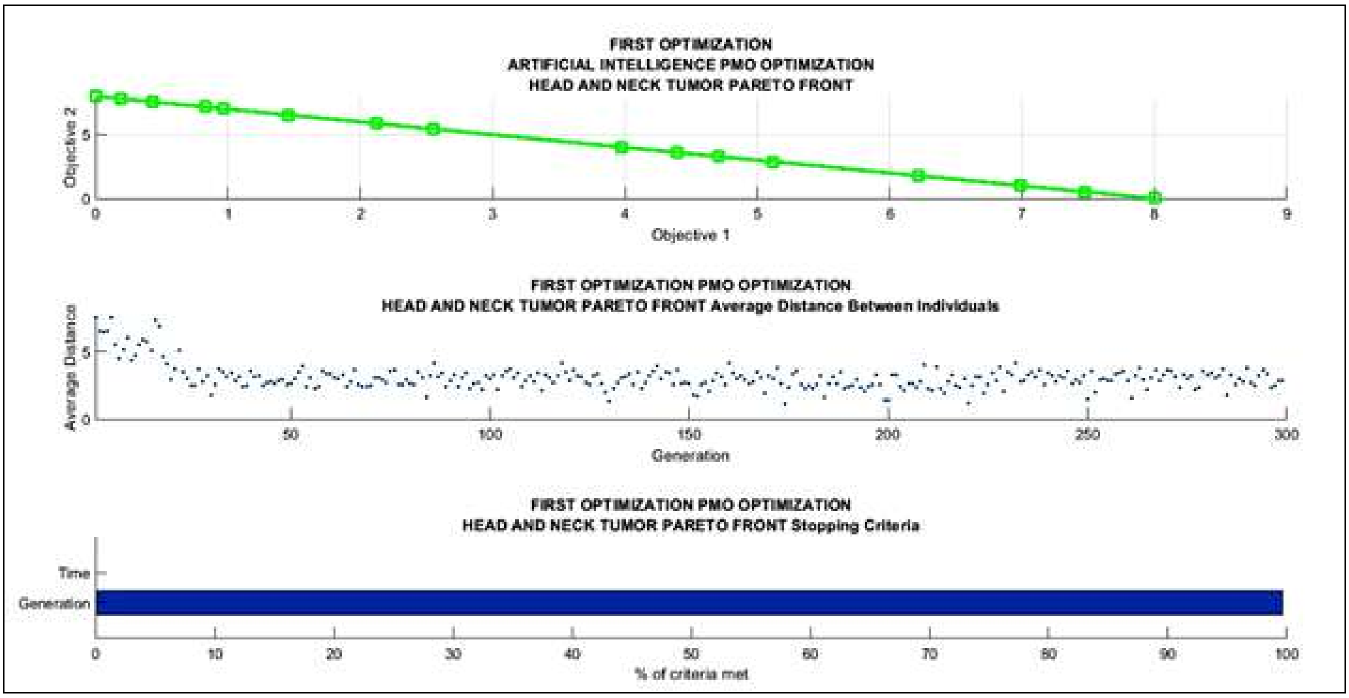


Fig 1: [Enhanced]-First optimization Multifunctional GA 2D graph. This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both F1 and F2 show low residuals. Therefore, results are acceptable in first optimization for function 1 and function 2. The number of points on the Pareto front was: 18. The number of generations was: 300.

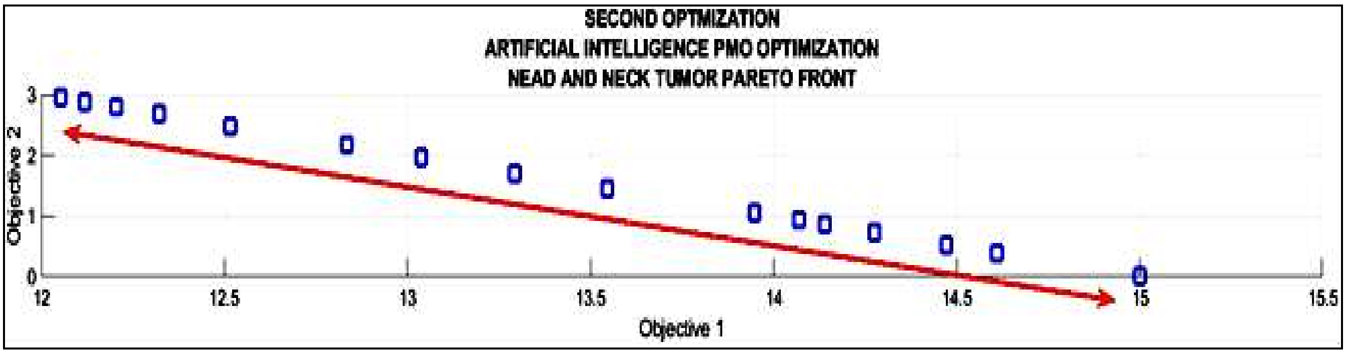


Fig 2: [Enhanced]-This is the most important graph given by software when PMO is performed to check the optimization accuracy. The fundamentals of Nonlinear PMO calculations are usually based on 2D PMO functions charts. In this study both F1 and F2 show low residuals. Objective 2 is more accomplished. Therefore, results are acceptable. The number of points on the Pareto front was: 18. The number of generations was: 300.

Table 1: [Enhanced]-First simulation. Brief of PMO Artificial Intelligence with GA optimization numerical results in Head and Neck tumors for advanced TPO.

BRIEF OF NUMERICAL FIRST PMO OPTIMIZATION RESULTS HEAD AND NECK BIOLOGICAL EFFECTIVE RADIOTHERAPY TREATMENT

Generation	Func-count	Pareto distance	Pareto spread
271	13550	0.0664648	0.233149
272	13600	0.0295673	0.123498
273	13650	0.0244215	0.0989167
274	13700	0.0424819	0.177761
275	13750	0.0179927	0.0802337
276	13800	0.0373533	0.158533
277	13850	0.0215619	0.091576
278	13900	0.0371236	0.135267
279	13950	0.0353069	0.133862
280	14000	0.0329375	0.114606
281	14050	0.0302815	0.112513
282	14100	0.0200634	0.081698
283	14150	0.0452573	0.183996
284	14200	0.0239752	0.100783
285	14250	0.023378	0.10136
286	14300	0.0466089	0.176541
287	14350	0.0571169	0.210486
288	14400	0.0350603	0.132537
289	14450	0.0168583	0.0738853
290	14500	0.0364302	0.14719
291	14550	0.0343554	0.148173
292	14600	0.0265149	0.108386
293	14650	0.0445348	0.173242
294	14700	0.018079	0.0786436
295	14750	0.0281023	0.117192
296	14800	0.0319461	0.122923
297	14850	0.0266535	0.10269
298	14900	0.0190131	0.0802516
299	14950	0.0195492	0.0867326
300	15000	0.0391879	0.150761

Optimization terminated: maximum number of generations exceeded.

population =

32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5489
36.3169	1.3119	26.5508
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
32.6551	1.2549	25.4416
33.4949	1.3032	25.5279
36.3169	1.3043	26.5530
34.7218	1.3080	25.5166
32.6551	1.2549	25.4416
36.3169	1.3119	26.5489
34.9485	1.2867	25.4865
32.6925	1.2656	25.4444
35.6515	1.2953	25.8327
32.6551	1.2549	25.4337