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Metaheuristic-Driven Deep Learning Framework for Optimizing Radiotherapeutic Planning

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ABSTRACT

Introduction: Humans are the utmost creatures living on this planet; besides being able to express their thoughts and feelings, they possess cognitive and behavioural intricacies. Further, they have immunity which allows them to fight disease-causing germs. Still, it seldom happens that the immunity of humans fails to fight against pathogens, as in the case of cancer, thus requiring interference from foreign influence.

Objectives: Radiotherapeutic Planning is an important aspect that aids cancer treatment by optimizing the choice of dosage and beam orientation. This research aims to propose a novel methodology to deal with this problem by employing Artificial Intelligence, thereby improving the efficiency of Radiotherapeutic Planning.

Methods: A Residual Network (ResNet) is used to identify the mapping between the anatomy of the patient and the therapeutic variables. The ResNet, trained with a relatively small dataset of nearly 15 subjects, showed better performance compared to state-of-the-art approaches using large datasets. Additionally, the neuronal parameters of the ResNet were concurrently updated using Particle Swarm Optimization (PSO) and Grey Wolf Optimization (GWO). The proposed methodology and its variants were compared to Columnar Generation-based Optimization and a standard Convolutional Neural Network (CNN).

Results: The results suggested that the Column Generation (CG) method produced outcomes are similar to those generated by the ResNet and its variants optimized via PSO and GWO.

Conclusion: From the experiments presented, it is evident that the performance analysis shows that Deep Learning-based therapeutic paradigms are comparable to Column Generation Optimization in Radiotherapeutic Planning.
Keywords: Radiotherapy, Optimization, Residual Network, Lung Cancer.

1. INTRODUCTION

Cancer is a broad category of disorders caused by abnormal cells that proliferate quickly and have the potential to spread to other organs and tissues. Tumours may be inferred from these cells' fast growth. They might also interfere with the body's normal processes. One of the main causes of death worldwide is cancer. As per the World Health Organization (WHO), about 1 in 6 fatalities in 2020 were related to cancer. Every day, experts put in a lot of effort to try out novel cancer treatments. External Beam Radiation Therapy (EBRT) (Moghaddam et al., 2024) is one of the prominent approaches to fight against cancer cells. It involves making use of High Energy Radiation to suppress (or kill) the cancerous cells, while preventing the adjacent cells from getting damaged. The radiation cannot distinguish between the cancerous and healthy cells, thus making the treatment more vulnerable to radiation numbness (Jaeckle KA, 2010). To efficiently conduct radiotherapy, the therapeutic parameters, Dosage, and Orientation must be chosen optimally, such that the effect of the radiation on the cancerous cells can be maximized while minimizing the effect on its' adjacent healthy cells.

Traditionally, the choice of these parameters is made randomly using the hit and trial (trial-n-error) method, but the risk factor involved in this method is significantly high; thus, urging the need for efficient Radiotherapy Planning. The basis for these advancements was laid by the innovations in the Biomedical field,

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as in the development of advanced medical imaging techniques, like Magnetic Resonance Imaging (MRI) (Kamagata et al.,2024), Computed Tomography (CT) Scan Cross III et al. (2024), etc, that besides precisely locating the tumour insists several therapeutic planning processes that help the radiologists eradicate the cancer cells. Intensity-modulated radiation therapy (IMRT) (Budrukkar et al., 2024) and Volumetric-modulated radiation therapy (VMRT) (Ogata et al.,2024) are some of the sophisticated radiotherapeutic planning algorithms. In the existing literature, and in recent times, several works have been contributed that adversely support the Radiotherapeutic Planning.

Ruysscher et al. in their contribution, "Radiotherapy toxicity" (De Ruysscher et al., 2019) presents the maliciousness and the adversities related to External Beam Radiotherapy. Schwarz et al. discuss the limitations of radiotherapy for the cure of osteosarcoma in their work, "The Role of Radiotherapy in Oseosarcoma" (Schwarz et al., 2010). Li, Wu, and Ma, in their contribution, "Artificial intelligence in radiotherapy" by Li et al. (2022) review the recent intervention of Artificial intelligence in radiotherapy due to the presence of big datasets associated with Medical Domains. Rebelo et al. devised a virtual assistant using IBM Watson to explain the radiation treatment procedure in their work, "Learning the Treatment Process in Radiotherapy Using an Artificial Intelligence-Assisted Chatbot: Development Study", Rebelo et al. (2022). In the last few decades, the spine of Machine Intelligence got no chills, and thus, now it has captured almost every domain of science, technology, management, and engineering. Initially, it evolved as a hidden set of rules, (simple if-else statements), but later it transformed into mathematical algorithms that can learn those rules on their own, and then mimic the neuronal firing patterns of the brain to memorize, and model the observations, not only numerically, but also visually.

This research instincts the optimal parameter choice (dosage, and orientation) for therapeutic planning. But, unlike the traditional error and trial mechanism, a Residual Network, is employed that attempts to model the neuronal parameters (weights, and biases) using optimization algorithms like Particle Swarm Optimization, Grey Wolf Optimization, in such a way that it optimizes the damage to the affected, cancerous cells. For the provenance of its efficiency, the proposed model is compared with its' primitives, subjective to a dataset from 10 subjects with lung cancer.

2. PRELIMINARIES

This section elaborates the necessary preliminaries for the research, beginning with the Problem Statement, rolling with the formal definition as an Optimization Problem, the fundamentals of the Resnet Modularity, and the optimization techniques employed in the research.

2.1 Problem Statement

The objective of this research is the fulfillment of the Fluence Map Optimization Problem (refer Equation 1 (Ramesh et al., 2024), minimization of the erratic influence,

$$\min_{p_1,p_2} \varphi(p_2) \tag{1}$$

subject to the KKT Conditions,

$$p_2 = \sum_{\beta\in B} \begin{pmatrix} \delta_{\beta,\sigma_1} \\ \delta_{\beta,\sigma_2} \\ \vdots \\ \delta_{\beta,\sigma_n} \end{pmatrix} \cdot p_{1\beta}$$

Here $p_{1\beta} \geq 0 \forall \beta \in B$, with p_1, p_2 being the parameters, and δ_{β,σ_i} corresponds to the σ_i^{th} structure for the β^{th} beam. Further, the target function, $\varphi(p_2)$ is
as in Equation 2

$$\varphi(p_2) = \varphi \begin{pmatrix} p_{2\sigma} = \sigma_1 \\ p_{2\sigma=\sigma_2} \\ \vdots \\ p_{2\sigma=\sigma_n} \end{pmatrix} = \sum_{\sigma\in S} \frac{\mathbf{w}_\sigma}{2}^2 \cdot \left\| p_{2_\sigma} - \pi_\sigma \right\|_2^2 \tag{2}$$

with σ being the Structural Iterator, and S as the complete set under consideration. $\mathbf{w}_\sigma$, and π_σ are the user defined weight structure, and the corresponding prescribed dosage respectively.

2.2 Residual Neural Network

A Residual Neural Network (Katsman et al. 2024) is a groundbreaking deep learning model where the weight layers use the layer inputs as a basis for understanding residual functions. ResNet operates akin to a highway

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network, where its gates are opened by considerably positive bias weights (Dutta et al., 2023a). Deep learning models with hundreds or thousands of layers can now train faster and approach higher accuracy as they progress (Kanti Kumar et al.2023). Identity skip connections also referred to as "residual connections" -were also used by the original LSTM network by Neelima et al. (2023) and transformer models by Vaswani et al. (2017).

Consider a sub network with a specific number of stacked layers in a multi-layer neural network model (Voumik et al., 2023). Indicate that this sub network's underlying function is $\mathscr{H}(x), x$ serving as the subnetwork's input. Re-parameterizing this subnetwork through residual learning allows the parameter layers to reflect a "residual function", $\mathscr{F}(x) = \mathscr{H}(x) - x$. This subnetwork's output, y, is then as in Equation 3

$$y = \mathscr{F}(x) + x \qquad (3)$$

Figure 1 gives a pictorial demonstration of the Skip Connection in a Residual Neural Network. Algorithm 1 gives an exemplary Pseudo code for the ResNet Architecture.

2.3 Optimization

The subsection discusses the optimization techniques (Dutta et al., 2023b) invoked in the context of the research carried out.

2.3.1 Column Generation

Column Generation, abbreviated as CG, is an approximation based iterative optimization problem (Ozcan et al., 2024) that involves choosing a restrictive subset from the entire set of beams for therapeutic action. Iteratively, it keeps on incrementing the count of the beams taken into action and restricts only

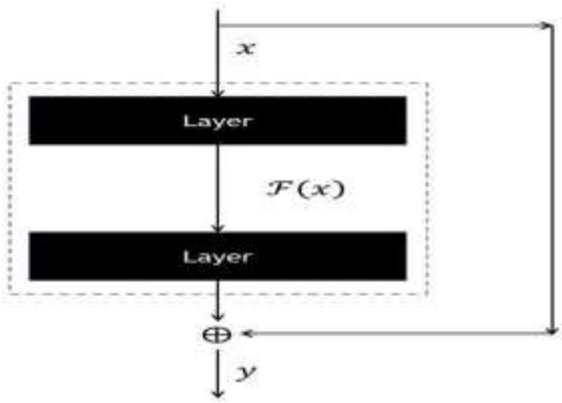

Fig. 1 A Residual Block with x as input, $\mathscr{F}(x)$ as the residual function, and y as the output. As per Equation 3, $y = \mathscr{F}(x) + x$

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Algorithm 1 ResNet Architecture
function RESIDUALBlocK ($\mathbf{x}, \mathbf{W}_1, \mathbf{W}_2$)
$\mathbf{y} \leftarrow \operatorname{ReLU}(\mathbf{x} * \mathbf{W}_1 + \mathbf{b}_1)$ ▹ First Convolution
$\mathbf{y} \leftarrow \operatorname{ReLU}(\mathbf{y} * \mathbf{W}_2 + \mathbf{b}_2)$ ▹ Second Convolution
output $\leftarrow \mathbf{x} + \mathbf{y}$ ▹ Skip Connection
return output
end function
function RESNET(input_shape, num_classes)
$\mathbf{X} \leftarrow$ Input(input_shape) Input Data
$\mathbf{X} \leftarrow$ Conv 2D($\mathbf{X}, \mathbf{W}_0$, stride $= 2$) ▹ Initial Convolution
$\mathbf{X} \leftarrow$ BatchNormalization($\mathbf{X}$) ▹ Batch Normalization
$\mathbf{X} \leftarrow$ MaxPooling2D(X, pool_size $= 3$, stride $= 2$) ▹ Max Pooling
$\mathbf{X} \leftarrow$ ResidualBlock ($\mathbf{X}, \mathbf{W}_1, \mathbf{W}_2$) ▹ Residual Block
$\mathbf{X} \leftarrow$ ResidualBlock ($\mathbf{X}, \mathbf{W}_3, \mathbf{W}_4$)
$\mathbf{X} \leftarrow$ ResidualBlock ($\mathbf{X}, \mathbf{W}_5, \mathbf{W}_6$)
$\mathbf{X} \leftarrow$ ResidualBlock ($\mathbf{X}, \mathbf{W}_7, \mathbf{W}_8$)
$\mathbf{X} \leftarrow$ AveragePooling2D ($\mathbf{X}$, pool_size $= 7$) ▹ Global Average Pooling
$\mathbf{X} \leftarrow$ Flatten ($\mathbf{X}$) ▹ Flatten
$\mathbf{Y} \leftarrow$ Softmax ($\mathbf{X} * \mathbf{W}_{\text{out}} + \mathbf{b}_{\text{out}}$) ▹ Output Layer
model $\leftarrow$ Model(Input(input_shape) , $\mathbf{Y}$) ▹ Construct Model
return model
end function

those, which cause maximum optimization (minimization in our case) of the objective function, as presented in Equation 1. The stopping condition being,

1. Cardinality of the subset equals that of the entire set, $|\beta^*| = n$
2. Optimality of $\varphi(p_2)$ is achieved.

2.3.2 Particle Swarm Optimization

A potent metaheuristic optimization technique, Particle Swarm Optimization (PSO) (Suriyan and Nagarajan., 2024) was created in response to findings about swarm behavior in natural environments, like fish and bird schools. PSO simulates a basic social system. Originally, the PSO algorithm was intended to graphically depict a flock of birds' delicate, chaotic choreography. In nature, any location that falls within the bird's field of vision is limited. However, only in the presence of multiple birds can a swarm of birds be aware of the larger surface of a fitness function. The PSO's mathematical assimilation is as follows,

1. In particle swarm optimization, every particle has a position, velocity, and fitness value.
2. The best local fitness value and the corresponding position are kept on track.
3. A track is kept similarly for the global fitness value and the corresponding position.

Algorithm 2 gives a pseudo code for the Particle Swarm Optimization (PSO).

Algorithm 2 Particle Swarm Optimization (PSO)
Initialize population of particles X with random positions and velocities
Initialize personal best positions P_{best} of each particle as their current positions
Initialize global best position G_{best} as the position of the particle with the best fitness value in X
while termination criterion not met do
for each particle i in X do
Evaluate fitness of particle i
if current position of i is better than $P_{\text{best}}[i]$ then
Update $P_{\text{best}}[i]$ to the current position of i
end if
if the fitness of current position of i is better than the fitness of G_{best} then
Update G_{best} to current position of i
end if
end for
for each particle i in X do
Update velocity of particle i as in Equation *4*
Update position of particle i as in Equation *6*
end for
end while

Equations for velocity and position update:

$$\mathbf{v}_i^{t+1} = \omega \mathbf{v}_i^t + c_1 r_1 (\mathbf{P}_{\text{best}}[i] - \mathbf{x}_i^t) + c_2 r_2 (\mathbf{G}_{\text{best}} - \mathbf{x}_i^t) \quad (4)$$

$$\mathbf{x}_i^{t+1} = \mathbf{x}_i^t + \mathbf{v}_i^{t+1} \quad (5)$$

where,

- $\mathbf{x}_i^t$ is the position of particle i at iteration t,
- $\mathbf{v}_i^t$ is the velocity of particle i at iteration t,
- $\mathbf{P}_{\text{best}}[i]$ is the personal best position of particle i,
- $\mathbf{G}_{\text{best}}$ is the global best position,
- ω is the inertia weight,
- c_1 and c_2 are acceleration coefficients,
- r_1 and r_2 are random numbers in the range[0,1].

2.3.3 Grey Wolf Optimization

The Grey Wolf Optimizer (GWO) (Liu et al., 2024) is an algorithm based on population-based meta-heuristics that mimics the hunting strategy and leadership structure of real-world grey wolves. Algorithm 3 gives a pseudo code for the Grey Wolf Optimizer (GWO).

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Algorithm 3 Grey Wolf Optimization (GWO)
Initialize a population of grey wolves X with random positions
Initialize positions of alpha, beta, and delta wolves A, B and D
while termination criterion not met do
for each grey wolf x_i in X do
Calculate fitness of x_i
end for
Update positions of alpha, beta, and delta wolves A, B and D
for each grey wolf x_i in X do
Update position of x_i as in Equation 6
end for
end while

The equation for position update:

$$\mathbf{x}_i^{t+1} = \frac{1}{2}(\mathbf{A} + \mathbf{x}_i^t) - \frac{\mathbf{D}}{\sqrt{1 + \left(\frac{t}{T}\right)^2}} \tag{6}$$

where,

- $\mathbf{x}_i^t$ is the position of grey wolf i at iteration t,
- A is the position of the alpha wolf,
- **D** is the position of the delta wolf,
- t is the current iteration,
- T is the maximum number of iterations.

3. METHODOLOGY

There are several parameters in therapeutic planning that affect the quality of the treatment. The methodology, hereby employed for the Radio therapeutic Treatment of Cancer builds on the parameters like dosage, the anatomy of the patient, the beam orientation, etc. The Column Generation based Optimization (as discussed in segment 2.3.1) is a primitive, and hereby serves as a ground truth for the Residual Network, thereby steadily modifying the randomized weights and biases of the Residual Network, following the validation using a loss function, and therefore performing Back propagation for the same. The prime parameters of interest for this research are a) Dosage b) Beam Orientation. Generally, the ResNet Modality is of substantially longer layers sandwiched one after another, for e.g. ResNet-50, ResNet 100, etc. The intricacies of the ResNet Modality are similar to that of the Convolutional Neural Network, as discussed in the research, "Optimization Strategies for Beam Direction and Dose Distribution Selection in Radiotherapy Planning" by Keshav Kumar K. et al.(2023). The ResNet modality consists of a collection of $k \times k$ Convolution Layers (Dutta et al., 2023c) with Skip Connection, and some pooling layers, as discussed in Section 2.2. In the Convolutional Neural Network, while there was plain conjugation of the layers, the Residual Neural Network involved conjugation of the skip connections too.

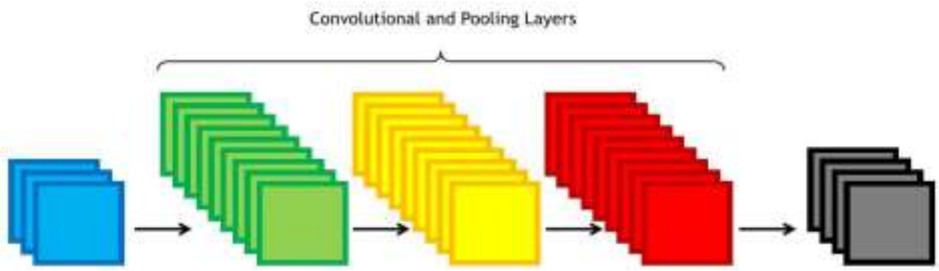

Fig. 2 Architectural view of the Convolutional Neural Network. The elements in blue correspond to the Input Layers, and those in Grey corresponds to that of the Output Layer.

Figure 4 presents the architectural view of the Proposed Model.

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4. EXPERIMENTAL SETUP

To evaluate the efficiency of the methodology using ResNet Architecture, it is subjected to a real-time dataset (Subsection 4.1) and is compared using the metrics presented in Subsection 4.2. The comparative tabulation is presented in Subsection 4.3.

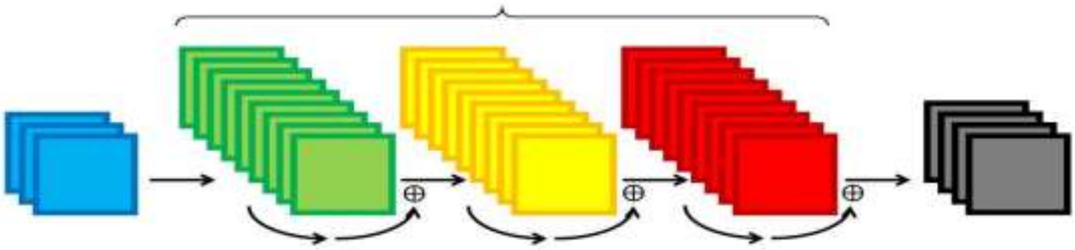

Fig. 3 Architectural view of the Residual Neural Network. The elements in blue correspond to the Input Layers, and those in Grey corresponds to that of the Output Layer. The skip connections are connected by the arithmetic addition operation, ⊕.

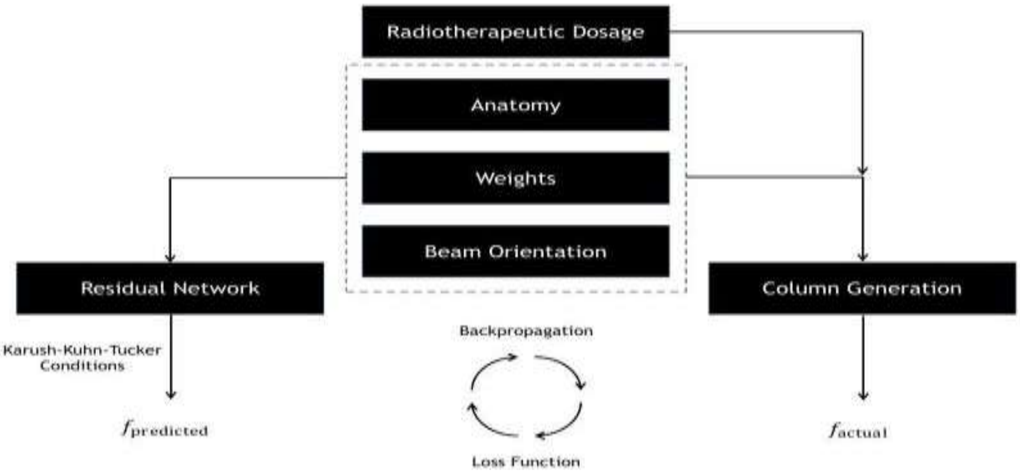

Fig. 4 Architectural view of the Methodology used for Radio therapeutic Planning. Based on the several parameters that influence the therapeutic action, like the Anatomy of the Patient, Beam Orientation, Dosage, etc., the Column Generation Optimization (refer to segment 2.3.1) generates the actual (optimal) fitness value of the beam orientations following the training samples. Besides, the Residual Network is used to generate a predicted fitness of the orientations, the variance in the actual and the predicted orientation leads to a loss, which is further used to tune the weights and biases of the network, by Backpropagation.

4.1 Data

For this research, we considered data from 10 subjects, suspended to Lung Cancer, with 3 target volumes, Esophagus, Heart, and Spinal Cord. The data was augmented by the Auto-Augmentation technique, AugMix, as contributed in the work, "AugMix: A Simple Data Processing Method to Improve Robustness and Uncertainty" by Hendrycks et al., 2019. Further, the data was split using a 80-20 split to segregate into Training and Testing Samples that serve as input for the Residual Network. The dataset can be availed by reaching out to the author in correspondence.

4.2 Metrics

To evaluate, and thereby compare the models, the following metrics are used.

1. $\mathfrak{D}^{TV}{}_{98}$, dosage corresponding to 98% acceptance by the Target Volumes.
2. $\mathfrak{D}^{TV}$ 99 , dosage corresponding to 99% acceptance by the Target Volumes.
3. $\mathfrak{D}^{TV}{}_{max}$, dosage corresponding to maximum acceptance by the Target Volumes.
4. $\mathfrak{H}^{TV}$, the Target Volumes' Homogeneity. It is computed mathematically as in Equation 7.

$$\mathfrak{H}^{TV} = \frac{\mathfrak{D}^{TV}{}_{2} - \mathfrak{D}^{TV}{}_{98}}{\mathfrak{D}^{TV}{}_{50}} \quad (7)$$

where, $\mathfrak{D}^{TV}{}_{i}$, is the dosage corresponding to *i*% acceptance by the Target Volumes.

5. $\mathfrak{V}_{conformation}$, Van't Riet Conformation Number, that is computed mathematically as in Equation 8.

$$\mathfrak{V}_{conformation} = \frac{(V \cap V_{100\%\ isodose})^2}{V \cdot V_{100\%\ isodose}} \quad (8)$$

where, $V_{100\%\ isodose}$ corresponds to the volume of isodosage, accepting 100% dosage.

6. $\mathfrak{R}_{50}$, is computed mathematically as in Equation 9 .

$$\mathfrak{R}_{50} = \frac{V_{50\%\ isodose}}{V} \quad (9)$$

where, $V_{50\%\ isodose}$ corresponds to the volume of isodosage, accepting 50% dosage.

4.3 Results

The proposed methodology (refer to Section 3) and its' variants optimized using Particle Swarm Optimization (PSO), and Grey Wolf Optimization (GWO) are compared to that of the performance of Columnar Generation based Optimization, and that with a Convolutional Neural Network (CNN). The results are tabulated in the Table 1. It is evident from the table that the results suggested by the CG, are similar to those of generated using ResNet and its' variants.

5. DISCUSSION

One of the main causes of death in the globe is cancer. Globally, there were 9.5 million cancer-related deaths and 18.1 million new cases in 2018. It is anticipated that by 2040, there would be 29.5 million new instances of cancer annually, and 16.4 million cancer-related deaths.

Table 1 Comparative performance analysis of ResNet, and its' variants with Column Generation as per the metrics discussed in Subsection 4.2.

Metrics	Models				
	Column Generation	CNN	ResNet	ResNet - PSO	ResNet – GWO
$\mathfrak{D}^{TV}98$	0.8645	0.8441	0.8645	0.8843	0.8645
	(0.031)	(0.028)	(0.033)	(0.030)	(0.033)
$\mathfrak{D}^{TV}99$	0.8298	0.8235	0.8137	0.8331	0.8295
	(0.026)	(0.033)	(0.015)	(0.017)	(0.015)
$\mathfrak{D}^{TV}max$	0.8351	0.8052	0.8335	0.8142	0.8354
	(0.027)	(0.098)	(0.028)	(0.026)	(0.026)
$\mathcal{H}^{TV}$	0.0094	0.0089	0.0092	0.0095	0.0093
	(0.001)	(0.012)	(0.018)	(0.001)	(0.015)
$\mathcal{V}_{conformation}$	0.7368	0.7484	0.7384	0.7234	0.7364
	(0.034)	(0.019)	(0.026)	(0.015)	(0.0042)
$\mathfrak{R}_{50}$	3.6527	3.3528	3.5472	3.6418	3.6518
	(0.528)	(0.444)	(0.483)	(0.502)	(0.486)

To alter the rising death toll, there needs to be a well fledged and defensive mechanism that can counter the cancerous cells. Scientists from several domains like Chemistry, Biology, etc., are coming up with their own methodology to deal with this menace. In recent times, and especially post Covid-19 pandemic, we have witnessed (in fact are witnessing) the fourth industrial revolution that comes in hand of the Artificial Intelligence. Machine Intelligence, and Deep Learning are finding its' application today in almost every domain of science, technology, management, and engineering. Several works in the past few decades have been done of the efficient use of the machine intelligence in radiotherapeutic planning, and thereby countering cancerous germs. Beam Based Radiotherapy includes making use of radiation and pointing the beam of the radiation towards the targeted (cancerous) cells to kill the harmful germs. Now, the choice of the influential parameters adversely affects the treatment quality. The problem is mathematically thought of an optimization problem with a well defined set of KKT Conditions for the constraints, and to solve the same, several propositions have been tried. To date, the Column Generation based Optimization strategy is known to perform the best. The work proposed in the manuscript employs making use of a Residual Neural Network along with the famous Particle Swarm Optimization and Grey Wolf Optimization as the important preliminaries. Though the results as per the experimentations done in the research, signify the good accuracy of the Deep Learning based strategies, there exists some limitations to these paradigms, and especially, to begin with, its availability of the Data. Medical Data is always scarce than any data on any other domains and it won't be wrong to say that Data is the sole fuel of any Intelligent Learner. Another limitation is the requirement for stronger computes to process these data.

6. CONCLUSION

This study delineates the efficiency of the radiotherapeutic action. It thus enacts the optimal parametric choice that leads to a patient receiving radiation suffering from minimal adjacency loss and therefore optimizes the treatment planning. Besides the quite efficient Column Generation Optimization Technique, some novel deep learning-based action strategies for example, Convolutional Neural Networks and residual Neural Networks, have been studied along with some well-established optimization techniques as a support for its' variants; for instance, hereby in the research, the famous Particle Swarm Optimization, and the Grey Wolf Optimization is used along with the ResNet Architecture. From the experiments carried out and thus presented in the manuscript, it is evident that the performance analysis presents the similarity of Deep Learning-based therapeutic paradigms to that of Column Generation Optimization.

Scopes of future research include making use of state-of-the-art techniques like the Transformer models, for the choice of parameters. In recent times, Transformers have been proven to perform better than many primitives that lead the performance in their domain, for example, in Scientific Machine Learning, only a few years ago, the Probabilistic Models were at a great high, but now, it's getting actively replaced by that of the Transformer.

Conflict of interest: The authors declare no conflict of interest.

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