

Preamble

Méthodes pour l'automatisation de la dosimétrie en radiothérapie.

*Methods for automatization of radiotherapy
dosimetry.*

Thèse de doctorat de l'université Paris-Saclay

Spécialité de doctorat: Mathématiques & Intelligence Artificielle
École doctorale n° 573 Interfaces : matériaux, systèmes, usages, ED
INTERFACE

Graduate School: Sciences de l'Ingénierie et des Systèmes, SIS

Thèse préparée dans les unités de recherche **Radiothérapie** (Institut Régionale
du Cancer de Montpellier), **Advanced Research** (TheraPanacea), et
**Biomathématiques, MICS, Mathématiques et Informatique pour la
Complexité et les Systèmes** (Université Paris-Saclay, CentraleSupélec) , sous la
direction de **Nikos Paragios**, Professeur, et la co-direction de **Paul-Henry
Cournède**, Professeur

Thèse soutenue à Paris-Saclay, le 16 décembre 2024, par

Paul Raymond François DUBOIS

Composition du jury

Membres du jury avec voix délibérative

David AZRIA Professeur des universités - Praticien hospitalier, Faculté de Médecine de Montpellier-Nîmes	Président
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Titre: Méthodes pour l'automatisation de la dosimétrie en radiothérapie.

Mots clés: Mathématiques, Intelligence Artificielle, Radiothérapie

Résumé:

La dosimétrie en radiothérapie est essentielle pour garantir la précision et la sécurité des traitements contre le cancer. La complexité et la variabilité de la planification des traitements nécessitent des méthodologies avancées pour l'automatisation et l'optimisation. Cette thèse présente des approches novatrices visant à automatiser le processus de dosimétrie en radiothérapie.

Cette thèse commence par le développement d'un moteur de dosimétrie et une évaluation approfondie des algorithmes d'optimisation open-source existants pour la planification des traitements. Ensuite, ce manuscrit analyse les relations entre différentes doses. Cette analyse conduit à la proposition d'un cadre novateur pour l'optimisation multi-objectif et la sélection robuste de plans à l'aide de la théorie des graphes.

Afin de réduire davantage le temps nécessaire pour la planification en radiothérapie, la thèse explore l'application de l'apprentissage par renforcement pour l'optimisation des doses. Le système proposé réalise la dosimétrie pour de nou-

veaux patients en exploitant les données de dose des patients traités dans le passé. Cette méthode entièrement automatisée peut s'adapter aux pratiques de différentes cliniques, réduisant ainsi le besoin d'ajustements manuels et facilitant son adoption en pratique.

De plus, la thèse examine l'utilisation de l'apprentissage profond pour la prédiction des doses, en proposant une série de modèles guidés par des Histogrammes Dose-Volume (DVH) cibles. Ce guidage orientation permet l'incorporation de directives lors de la génération de doses par les modèles. En outre, cette technique permet d'entraîner un seul modèle capable de s'adapter, plutôt qu'un modèle pour chaque clinique.

Les contributions de cette thèse présentent des avancées dans la dosimétrie en radiothérapie, ouvrant la voie au développement d'un système de planification de traitement entièrement automatisé, s'adaptant aux contraintes cliniques. Ces innovations pourraient améliorer les flux de travail cliniques, en réduisant l'intervention humaine à un minimum, rendant la radiothérapie plus efficiente.

Title: Methods for automatization of radiotherapy dosimetry.

Keywords: Mathematics, Artificial Intelligence, Radiotherapy

Abstract:

Radiotherapy dosimetry is critical in ensuring the precision and safety of cancer treatments. The complexity and variability of treatment planning necessitate advanced methodologies for automation and optimization. This thesis introduces novel approaches aimed at automating the radiotherapy dosimetry process.

The research begins with developing a dosimetry engine, and comprehensively evaluating existing open-source optimization algorithms for treatment planning. Then, this thesis analyzes the relationships between different treatment plans. This analysis leads to the proposal of a novel framework for multi-objective optimization and robust plan selection using graph theory.

To further reduce the time required for radiotherapy planning, the thesis explores the application of reinforcement learning for dose optimization. The proposed sys-

tem performs dosimetry for new patients by leveraging dose data from past patients. This fully automated method can adapt to clinical dependencies, reducing the need for manual fine-tuning and easing its adoption in practice.

In addition, the thesis investigates the use of deep learning for dose prediction, proposing a series of models guided by target Dose Volume Histograms (DVH). This guidance facilitates the incorporation of guidelines into the deep-generated doses. Moreover, it allows a single model to be trained instead of one for each clinic.

The contributions of this thesis represent advancements in radiotherapy dosimetry, paving the way for the development of a fully automated, clinically dependent treatment planning system designed to operate with minimal human intervention. These innovations could enhance clinical workflows, making radiotherapy more efficient.

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¹even oenology was accepted

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List of contributions

Publication

Full-length Article

- "Radiotherapy dose optimization via clinical knowledge based reinforcement learning", Paul Dubois, Paul-Henry Cournède, Nikos Paragios, and Pascal Fenoglietto, *Artificial Intelligence in Medicine* (AIME), 2024

Full-length Presentation

- "Dose Volume Histograms Guided Deep Dose Predictions", Paul-Henry Cournède Nikos Paragios Paul Dubois, Carlos Santos Garcia and Pascal Fenoglietto, *Société Française de Physique Médicale* (SFPM), 2024, Dijon, France
- "Radiotherapy dose optimization via clinical knowledge based reinforcement learning", Paul Dubois, Paul-Henry Cournède, Nikos Paragios, and Pascal Fenoglietto, *Artificial Intelligence in Medicine* (AIME), 2024, Salt Lake City, Utha, USA

Poster Presentation

- "A Novel Framework for Multi-Objective Optimization and Robust Plan Selection Using Graph Theory", Paul Dubois, Carlos Santos Garcia, Paul-Henry Cournède, Nikos Paragios, and Pascal Fenoglietto, *Société Française de Physique Médicale* (SFPM), 2024, Dijon, France
- "Clinically Dependent Fully Automatic Treatment Planning System", Paul Dubois, Pascal Fenoglietto, Paul-Henry Cournède, and Nikos Paragios. *American Society for Radiation Oncology* (ASTRO), 2024, Dijon, France
- "Attention mechanism on dose-volume histograms for deep dose predictions", Paul-Henry Cournède Pascal Fenoglietto Paul Dubois, Nikos Paragios, *Société Française de Radio Oncologie* (SFRO), 2024, Paris, France

ArXiv

- "Radiotherapy Dosimetry: A Review on Open-Source Optimizer", Paul Dubois, *arXiv*, 2023

Teaching

Lectures

- Mathematics Refresher, DSBA 2nd year master students, ESSEC (2021, 2023, 2024)
- Deep Learning and NLP, Engineering 3rd year master students, CentraleSupélec (2023, 2024)

Teaching Assistant

- High-school students internship Co-supervision (June 2024)
- Reinforcement Learning (Winter 2024)
- Algorithmes et Complexité (Winter 2022-2023, Winter 2023-2024)
- Systèmes d'Information et Programmation (Autumn 2023)
- Natural Language Processing (Winter 2022)
- Reconnaissance Visuelle (Spring 2022)
- Coding Weeks (Autumn 2021, Autumn 2022)
- Optimisation (Autumn 2021)

Others

- SFPM: Participation to the contest "My PhD in 180 seconds" (June 2024)
- Artificial Intelligence and Philosophy "discussion", Association Cinéma et Culture Auterive (May 2024)
- Weekly Seminar, β iomathematics - MICS - CentraleSupélec: "DVH guided deep dose prediction" (May 2024)
- Popular Science Talk, Info@Lèze: "Intelligences Artificielles Génératives" (January 2024)
- Christmas Day Seminar, MICS - CentraleSupélec: "Do you understand where your models live?" (December 2023)
- Weekly Seminar, β iomathematics - MICS - CentraleSupélec: "Introduction to treatment planning in radiotherapy" (December 2023)

- Popular Science Talk, Info@Lèze: "Intelligences Artificielles: Mythes et Réalités" (July 2023)
- ISEP Scientific Day Presentation: "Automatic Dose Optimization for Radiotherapy" (June 2023)
- ISEP Panic Night Tutorial: "Solving Nim's Game: Genetic Algorithm Approach" (January 2023)
- Popular Science Talk, Info@Lèze: "Comment envoyer un secret avec un haut-parleur?" (September 2022)
- Presentation to police scientific research team, Fort de Issy-les-Moulineaux "Intelligences artificielles pour une reconnaissance vocale sécurisée" (June 2022)
- High School Workshop, Info@Lèze: "Genetic Algorithms" (June 2022)
- Pint of Science Talk: "I.A.: Generator vs Discriminator" (May 2022)
- High School Workshop, Info@Lèze: "Math on Mars" (May 2022)
- High School Workshop, Info@Lèze: "Math with Jupyter" (May 2022)

Formations

- BIP – Advanced Processing of Biomedical Signals and Images (October - November 2024)
- SaclAI School - Deep Learning and Signal Processing (February - March 2024)
- Interfaces Doctoral School Day (March 2024)
- Interfaces Back to School Day 2022 (January 2023)
- Climate Workshop and Engineering Sustainability (May 2024)
- Oenology (February - May 2023)
- Ruche user introduction (March 2024)
- Writing skills in Science "ADVANCED" (May - July 2022)
- AI 4 Health (January 2022)
- Theatrical techniques for pedagogy (February - March 2024)

List of acronyms

AAPM American **A**ssociation of **P**hysicists in **M**edicine

AI Artificial **I**ntelligence

AIME Artificial **I**ntelligence in **M**edecine (formerly **A**rtificial **I**ntelligence in **M**edecine Europe)

API Application **P**rogramming **I**nterface

ARIR Adaptive **R**easoning in **R**adiotherapy

ASTRO American **S**ociety for **R**adiation **O**ncology

BER Base **E**xcision **R**epair

BOO Beam **O**rientation **O**ptimization

CBCT Cone **B**eam **C**omputed **T**omography

CDF Cumulative **D**istribution **F**unction

CNN Convolutional **N**eural **N**etwork

CT Computed **T**omography

CTV Clinical **T**arget **V**olume

DAFT Direct **A**ffine **F**eature **T**ransforms

DAO Direct **A**perture **O**ptimization

DKFZ Deutsches **K**rebsforschungs**z**entrum (German Cancer Research Center)

DL Deep **L**earning

DSB Double-**S**trand **B**reak

DVH Dose-**V**olume **H**istogram

ESTRO European **S**ociety for **R**adiotherapy and **O**ncology

FMO Fluence Map Optimization

Gy Gray

ICRU International Commission on Radiation Units and Measurements

IMRT Intensity Modulated Radiotherapy

KBP Knowledge-Based Planning

KBRP Knowledge-Based Radiotherapy Planning

LINAC Linear Accelerator

LS Leaf Sequencing

MAE Mean Absolute Error

MCO Multi-Criteria Optimization

ML Machine Learning

MLC Multi-Leaf Collimator

MMR Mismatch Repair

MRI Magnetic Resonance Imaging

MSE Mean Squared Error

NER Nucleotide Excision Repair

NTCP Normal Tissue Complication Probability

OAR Organ at Risk

PCA Principal Component Analysis

PTV Principal Target Volume

RL Reinforcement Learning

RNN Recurrent Neural Network

RNS Reactive Nitrogen Species

ROS Reactive Oxygen Species

RT Radiotherapy

SFPM Société Française de Physique Médicale

SFRO Société Française de Radiothérapie Oncologique

SSB Single-**S**trand **B**reak

TCP Tumor **C**ontrol **P**robability

TLR Toll-**L**ike **R**eceptor

TPS Treatment **P**lanning **S**ystem

VMAT Volumetric **M**odulated **A**rc **T**herapy

WHO World **H**ealth **O**rganization

Bibliography