Preamble

Methods for automatization of radiotherapy treatmrent planning

Méthodes pour l'automatisation de la planification de traitements en radiothérapie

Thèse de doctorat de l'université Paris-Saclay

École doctorale n° 573 Interfaces: matériaux, systèmes, usages
Spécialité de doctorat: Mathématiques Appliquées
Graduate School: Sciences de l'Ingénierie et des Systèmes
Référent: CentraleSupélec

Thèse préparée dans les unités de recherche **Radiothérapie** (Institut Régional du Cancer de Montpellier), **Advanced Research** (TheraPanacea), et **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

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Composition du jury

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THESE DE DOCTORAT

NNT : 2024UPAST189

ÉCOLE DOCTORALE
Interfaces:
matériaux, systèmes, usages

Titre: Méthodes pour l'automatisation de la planification de traitements en radiothérapie

Mots clés: Cancer, Radiothérapie, Santé Digitale, Traitement Adaptatif, Intelligence Artificielle, Apprentissage Profond

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 nouveaux 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 treatmrent planning

Keywords: Cancer, Radiotherapy, Digital Health, Adaptative Treatment, Artificial Intelligence, Deep Learning

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 plannification. 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 system 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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[1] even oenology was accepted

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Synthèse

Le cancer constitue l'une des principales causes de mortalité dans le monde, en particulier dans les pays les plus développés. Le cancer est caractérisé par la prolifération incontrôlée et anormales de cellules. Ces cellules cancéreuses envahissent les tissus voisins et peuvent se propager à d'autres parties du corps (un processus appelé métastase). Avec une incidence croissante liée au vieillissement de la population et aux facteurs environnementaux, le cancer représente un défi majeur pour la santé publique.

Pour lutter contre cette maladie, trois principales approches thérapeutiques sont utilisées: la chirurgie, la chimiothérapie et la radiothérapie. La chirurgie est le traitement de choix les cancers localisés, permettant une ablation physique des tumeurs. La chimiothérapie utilise des agents chimiques pour détruire les cellules cancéreuses, mais elle affecte aussi les cellules saines, entraînant des effets secondaires significatifs. La radiothérapie repose sur l'utilisation de rayonnements ionisants pour cibler et détruire les cellules tumorales, avec un impact plus ciblé que la chimiothérapie.

La dosimétrie en radiothérapie joue un rôle central dans la prise en charge des cancers, où l'objectif est de maximiser l'efficacité thérapeutique tout en minimisant les effets indésirables sur les tissus sains. La complexité croissante des techniques de planification et la variabilité des cas cliniques nécessitent des approches avancées pour automatiser et optimiser ces processus. Cette thèse explore plusieurs méthodologies innovantes pour améliorer la dosimétrie, avec pour ambition long terme de créer un système de planification entièrement automatisé et adaptable aux contraintes cliniques.

Dans un premier temps, la thèse présente le développement d'un moteur de dosimétrie performant, accompagné d'une évaluation exhaustive des algorithmes d'optimisation open-source existants. Ces travaux initiaux permettent d'identifier les limites et opportunités pour l'amélioration des systèmes actuels. Une analyse approfondie des relations entre différentes doses conduit à l'élaboration d'un cadre novateur pour l'optimisation multi-objectif et la sélection robuste de plans, basé sur les concepts de la théorie des graphes. Ce cadre simplifie la gestion des compromis entre objectifs cliniques concurrents, tout en garantissant la qualité et la sécurité des traitements.

Pour répondre au défi du temps de planification, la thèse se penche sur l'apprentissage par renforcement comme levier d'accélération. Le système proposé utilise les données historiques de patients pour optimiser les plans de nouveaux cas, apprenant à reproduire des stratégies efficaces et adaptées aux spécificités cliniques. Cette approche réduit considérablement le besoin d'ajustements manuels, rendant le processus plus rapide et plus homogène.

Par ailleurs, la thèse explore l'application de l'apprentissage profond pour prédire les distributions de dose, en s'appuyant sur des Histogrammes Dose-Volume (DVH) cibles. Ce guidage structuré permet non seulement d'incorporer les directives cliniques dans la prédiction, mais aussi de créer un modèle unique capable de s'adapter aux pratiques variées des cliniques. Cette innovation évite le besoin de développer un modèle spécifique pour chaque centre, facilitant l'adoption de la méthode dans des environnements diversifiés.

Enfin, les contributions de cette thèse marquent une avancée significative vers la création d'un système de dosimétrie entièrement automatisé, intégré et adaptable. Ces approches réduisent l'intervention humaine à son strict minimum, optimisent les flux de travail cliniques, et ouvrent la voie à une radiothérapie plus efficiente. Ces innovations s'inscrivent dans une perspective d'amélioration continue des soins oncologiques, offrant une meilleure accessibilité et standardisation des traitements.

Cette thèse jette les bases d'un écosystème automatisé et intelligent pour la dosimétrie en radiothérapie, au service des patients et des cliniciens.

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, *Artifcial 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, *Artifcial 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", Dubois, Paul and Paragios, Nikos and Cournède, Paul-Henry and Temiz, Gizem and Marini-Silva, Rafael and Bus, Norbert and Fenoglietto, Pascal *European Society for Radiotherapy and Oncology* (ESTRO), 2024, Glasgow, UK

- "Clinically Dependent Fully Automatic Treatment Planning System", Paul Dubois, Pascal Fenoglietto, Paul-Henry Cournède, and Nikos Paragyos. *American Society for Radiation Oncology* (ASTRO), 2024, Washington DC, USA

- "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, βiomathematics - 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, βiomathematics - 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 **A**merican **A**ssociation of **P**hysicists in **M**edicine

AI **A**rtificial **I**ntelligence

AIME **A**rtificial **I**ntelligence in **Me**decine (formely **A**rtificial **I**ntelligence in **M**edecine **E**urope)

API **A**pplication **P**rogramming **I**nterface

ARIR **A**daptive **R**easoning **i**n **R**adiotherapy

ASTRO **A**merican **S**ocie**t**y for **R**adiation **O**ncology

BER **B**ase **E**xcision **R**epair

BOO **B**eam **O**rientation **O**ptimization

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

CDF **C**umulative **D**istribution **F**unction

CNN **C**onvolutional **N**eural **N**etwork

CT **C**omputed **T**omography

CTV **C**linical **T**arget **V**olume

DAFT **D**irect **A**ffine **F**eature **T**ransforms

DAO **D**irect **A**perture **O**ptimization

DKFZ **D**eutsches **K**rebs**f**orschungs**z**entrum (German Cancer Research Center)

DL **D**eep **L**earning

DSB **D**ouble-**S**trand **B**reak

DVH **D**ose-**V**olume **H**istogram

ESTRO **E**uropean **S**ocie**t**y for **R**adiotherapy and **O**ncology

FMO **F**luence **M**ap **O**ptimization

Gy **G**ra**y**

ICRU **I**nternational **C**ommission on **R**adiation **U**nits and Measurements

IMRT **I**ntensity **M**odulated **R**adio**t**herapy

KBP **K**nowledge-**B**ased **P**lanning

KBRP **K**nowledge-**B**ased **R**adiotherapy **P**lanning

LINAC **Lin**ear **Ac**celerator

LS **L**eaf **S**equencing

MAE **M**ean **A**bsolute **E**rror

MCO **M**ulti-**C**riteria **O**ptimization

ML **M**achine **L**earning

MLC **M**ulti-**L**eaf **C**ollimator

MMR **M**is**m**atch **R**epair

MRI **M**agnetic **R**esonance **I**maging

MSE **M**ean **S**quared **E**rror

NER **N**ucleotide **E**xcision **R**epair

NTCP **N**ormal **T**issue **C**omplication **P**robability

OAR **O**rgan **a**t **R**isk

PCA **P**rincipal **C**omponent **A**nalysis

PTV **P**rincipal **T**arget **V**olume

RL **R**einforcement **L**earning

RNN **R**ecurrent **N**eural **N**etwork

RNS **R**eactive **N**itrogen **S**pecies

ROS **R**eactive **O**xygen **S**pecies

RT **R**adio**t**herapy

SFPM **S**ociété **F**rançaise de **P**hysique **M**édicale

SFRO **S**ociété **F**rançaise de **R**adiothérapie **O**ncologique

SSB **S**ingle-**S**trand **B**reak

TCP **T**umor **C**ontrol **P**robability

TLR **T**oll-**L**ike **R**eceptor

TPS **T**reatment **P**lanning **S**ystem

VMAT **V**olumetric **M**odulated **A**rc **T**herapy

WHO **W**orld **H**ealth **O**rganization

Bibliography