

Preamble

Methods for automatization of radiotherapy treatment 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 le co-encadrement 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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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 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 treatment planning

Keywords: Cancer, Radiotherapy, Digital Health, Adaptive 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 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.

Acknowledgments

During those three years, I often felt alone, but I eventually realized that I could not name people who supported me, not because there were too few, but because there were so many. This section is dedicated to all those who directly or indirectly contributed to this manuscript.

I want to express my deepest gratitude to my PhD directors for their unwavering support and invaluable guidance throughout this journey.

To Nikos Paragios, thank you for the network and opportunities you have opened for me. Your insight and encouragement have broadened my horizons and enriched my academic experience.

To Pascal Fenoglietto, your guidance has been indispensable. Your thoughtful advice and attention to detail have steered me through the complexities of this work, and I sincerely appreciate your dedication to my progress.

To Paul-Henry Cournède, you have been more than a supervisor; you are a model of excellence in research and leadership. I am immensely grateful for inspiring me to reach new heights.

I would like to thank the TheraPanacea team, these numerous individuals who have contributed to my PhD journey in various ways:

To Alexandre Cafaro, for our exchanges on research. Sharing our experiences has been a source of motivation.

To Alexis Benichoux, for valuable insights into AI engineering practices.

To Alexis Bombezin-Domino, for sharing interesting facts e.g.: about military aviation.

To Amaury Leroy, for insightful discussions about PhD life and post-PhD life plans.

To Anne Walrafen, for sharing extensive knowledge about radiotherapy.

To Anothkanth Mahendran, for maintaining and updating specialized software, essential to my research.

To Audrey Duran, for maintaining nice colleague relationship despite the physical distance.

To Ayoub Oumani, for showing great skills on the soccer field during our 5v5 after-work matches.

To Baris Ungun, for fascinating discussions about unconventional scientific topics, like color theory.

To Basile Bertrand, for making ESTRO conference an enjoyable and memorable experience. Should I express my gratitude for sending me to ASTRO instead of attending yourself?

To Carlos Santos-Garcia, for being a true friend across multiple domains - from climbing to soccer, from AI discussions to board games.

To Catherine Martineau-Huynh, for showing genuine care for employees, and keeping us on our toes with unexpected questions.

To Claire Diaz, for bringing joy and enthusiasm to after-works and conferences.

To Clemence Gueguen, for the privilege of knowing you as both student and colleague. Many of us thank you for organizing memorable company events.

To Despina Ioannidou, for managing internal ~~gossips~~ communications with grace and discretion.

To Edouard Delasalles, for enlightening discussions about AI techniques.

To Elie Mangin, for leading me at the Centrale Night'N'Day race, and being a worthy baby-football opponent, and a great colleague.

To Ethan Corcos, for engaging scientific exchanges, and showing me cool figures.

To Eugenie Ullmann, for being a great colleague.

To Giorgi Benashvili, for resolving all my technical issues promptly and efficiently; you are a lightning bolt of efficiency.

To Gizem Temiz, for the gentle push toward abstract submissions, contributing to my academic growth.

To Jacob Buatti, for being an outstanding volleyball player and bringing athletic spirit to TheraPanacea.

To Jules Potel, for enriching scientific discussions.

To Lhassa Macke, for bringing energy and liveliness to the clinical room.

To Lisa Letournel, for sharing Catherine's front desk office, and maintaining a nice atmosphere.

To Lorenzo Colombo, for animating the clinical office room with complains, and successfully organizing the last company event.

To Louis Ducamp, for enlightening discussions about AI applications in healthcare.

To Léo Hardi, for patiently answering my database questions, no matter how basic they seemed.

To Mathilde Ravier, for meaningful conversations about company life and being a reliable running companion.

To Niels Pichon, for productive exchanges about development of AI tools.

To Norbert Bus, for an inspiring performance at Advent of Code.

To Olivier Teboul, for exemplary leadership of the scientific team.

To Quentin Spinat, for being an excellent climbing partner, providing much-needed breaks from work.

To Rafael Marini Silva, for providing invaluable guidance.

To Rafael Roblin, for engaging technology discussions and creative problem-solving during team building events.

To Rémi Vauclin, for stimulating scientific discussions.

To Sami Romdhani, for leading the AI team, and letting me participate to interesting meetings.

To Samia Achour, for expertize coordinating conferences, facilitating valuable networking.

To Sanmady Kandiban, for being a great colleague.

To Sofia Broome, for showing genuine interest in my work, and always having interesting questions.

To Sofiane Horache, for discussions on AI that helped shape my research.

To Sonia Martinot, for being an excellent DSBA co-teacher and sharing PhD life experiences.

To Tessa Kolb, for patiently guiding me through ASTRO demonstrations and enhancing my technical understanding.

To Thaïs Roque, for bringing a bit of Oxford experience to TheraPanacea.

To Vincent Luc, for making SFPM conference a valuable experience.

I would like to extend my heartfelt gratitude to my colleagues and friends from the MICS laboratory, whose presence and support have enriched the past three years in countless ways:

To Aaron Mamann, for our endless and enriching life discussions that often provided unneeded breaks, but relieved from academic pressures.

To Antonin Della Noce, for our engaging discussions about mathematics that challenged my thinking.

To Brice Hannebicque, for our enlightening discussions about teaching strategies.

To Céline Hudelot, thank you for trusting me to be your teaching assistant for computer vision and for advertising my enigmas, which has contributed to making them part of our lab culture.

To Fabienne Brosse, for expertly managing the administrative aspects of the lab and (most notably) for organizing our summer and Christmas parties.

To Félicie Giraud-Sauveur, for being my desk mate and creating an enjoyable environment.

To Gabriel Claret, for his incredible devotion to the lab life.

To Guillaume Joslin, for helping out with the computing resources. I do **not** thank you for hacking my enigmas!

To Gurvan Hermange, whose perspectives on PhD experience have helped me better understand the academic ecosystem.

To Hakim Benkirane, for our discussions about the latest developments in AI.

To Imane Chraki, for her contribution to lab life and the fun times we shared at the autumn school in Porto.

To Inès Mallevall, for creating a laboratory sportive life.

To Jun Zhu, whose exemplary work ethic has been truly inspiring. Thank you for always keeping me company during lunch!

To Konstantinos Florakis, for your endless enthusiasm for mathematical discussions.

To Laura Vuduc, for being a wonderful companion on our bus rides to CentraleSupélec, and for being an exceptional colleague throughout our PhD journey.

To Leo Filioux, for our enlightening discussions about teaching.

To Leo Milecky, for your sage advice on publication strategy and those memorable spike ball victories.

To Lily Monnier, for collaborating with me in teaching reinforcement learning, for being part of the autumn school in Porto team, and for our mutual encouragements during the PhD.

To Mahmoud Bentriou, for sharing your expertise on publication.

To Malek Ben Salah, for being a central member of the biomathematics team; I hear you will take over the annual BBQs.

To Manon Ramaroson, for volunteering to take over the enigmas for lab days, with Margherita.

To Margherita Bruno, for being a great member of the biomathematics team; I hear you will take over the enigmas for lab days.

To Maria Vakalopoulou, for organizing the Biomath seminars, which have been an incredible source of inspiration and knowledge.

To Marin Scalbert, for your intermittent yet enjoyable appearances at the lab.

To Marine Tesson, for her support with high school internship. It is always a pleasure to work with you.

To Othmane Laousy, for his insights about reinforcement learning (among others).

To Quentin Blampey, for his contribution to the lab, and for challenging during the climbing after-works.

To Romain Lhotte, for consistently challenging my coding and pushing me to excel. Teaching courses together has been an invaluable learning experience.

To Stergios Christodoulidis, for allowing me to teach reinforcement learning. His involvement in the autumn school in Porto have greatly enriched my academic journey.

To Sylvain Lannuzel, for his perspectives on PhD life and willingness to share his experience.

To Vessna Lukic, for our varied life discussions. Your ability to balance research with life's other aspects is genuinely inspiring.

To Vincent Mousseau, for validating my "heures de formation"¹.

To Véronique Letort, thank you for providing teaching opportunities, and valuable advice.

To Wassila Ouerdane, for providing the opportunity to teach NLP.

To Yoann Pradat, for our stimulating discussions about science and the intricacies of academic publishing.

Beyond the walls of MICS and Therapanacea, I've been fortunate to share this doctoral journey with fellow PhD candidates and friends. I would like to express my gratitude to the following individuals for their friendship, support, and challenges:

To Aiden Manley, for being not just a flatmate but a true friend, making our shared living space a home during this academic journey.

To Amaury Ajasse, for being a great partner, both in sports and theater.

To Arthur Vervaet, for your unwavering friendship, for consistently pushing my limits at the climbing gym, and for our thoughtful discussions about career trajectories and aspirations.

To Axel Kerbec, for our stimulating mathematical discussions and for our mutual drive to challenge each other intellectually, pushing us both to grow and excel.

¹even oenology was accepted

To Camille Béhar, for your friendship and for the humbling reminder that unlike my path in computer science, you will become a "real" medical doctor, bringing perspective to our different journeys in academia.

To Caroline Bouat, for maintaining our friendship through the years, and pursuing together a scientific PhD.

To Jeanne Redaud, for being an exceptional friend and confidante, sharing the unique challenges and triumphs of PhD life at L2S, making this journey feel less solitary.

To Landry Duguet, for our enduring friendship and the remarkable parallel journey we've shared in our scientific careers.

To Marie Girodengo, for sharing the unique experiences and concerns of PhD life, making this challenging journey more manageable.

To Pierre Houdouin, for our engaging climbing sessions that provided much-needed breaks from research, and for our meaningful discussions about PhD progress and milestones at L2S.

I've been fortunate to have friends outside academia whose insights, support, and contributions have enriched both this manuscript and my understanding of its broader impact.

To Axel Arno, for the hours we spent talking about mathematics, and creating/testing problems.

To Enea Sharxhi, for the countless hours spent mutually challenging each other with mathematical problems, often pushing the limits of our understanding and problem-solving abilities.

To Erwan Le Guennec, for sharing great climbing sessions.

To Julien Bruyninckx, for ensuring I maintained a balanced life beyond science while engaging in fascinating discussions about mathematics, quantum computing, and AI.

To Justin Cuzin, for our laughs and tears while teaching together.

To Louis Lhotte, for our engaging discussions about career, and being a great employee.

To Maxime Dufour, for forming an extraordinary hackathon team with Romain and Arthur, where our combined creativity led to innovative solutions and memorable coding adventures.

To Mélanie Kojaartinian, for her careful review and insightful feedback on the background chapter, contributing to its clarity and accessibility.

To Oscar Valdini, for our thoughtful discussions about career paths and possibilities.

To Roderick Rens, for being one of my longest-standing mathematician friend.

To Thomas Heyen-Dube, for sharing invaluable life wisdom and unwavering support.

Despite already having several doctors in our family tree, I somehow found myself trying to add another branch to this academic legacy. This journey would not have been possible without the unwavering support of my family, who have been my foundation throughout this adventure.

To my grandparents (Jean-Bernard, Marie-Paule, Maxime, Maguy), whose pride in their grandchildren's achievements has always been a source of motivation.

To my uncles (François, Philippe, Sylvain, Davi) and aunts (Anne, Vinciane), for showing genuine interest in my research even when I struggled to explain it in family-friendly terms.

To my cousins (Camille, Clément, Nathan, Louis, Victor, Jules, Mark, Mathilde, Adam, Jean, Matthis, Maryline, Julia, Hugo, Gabriel, Cécile, Lucie), for bringing laughter and perspective to our family gatherings.

To my parents (Pierre, Yollaine), who have supported every decision in my academic journey, never questioning my choice to pursue yet another family doctorate.

To my siblings (Marie, Emmanuel), who have masterfully balanced supporting my academic endeavors while keeping my ego in check through well-timed teasing.

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 his-

toriques 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, *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", 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 Paragios. *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, 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