

Méthodes pour l'automatisation de la dosimétrie pour les traitements radiothérapeutiques.

*Methods for automatization of the dosimetry for radiotherapy
treatments.*

Thèse de doctorat de l'université Paris-Saclay

Spécialité de doctorat: ...

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 **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 JJ mois AAAA, par

Paul Raymond François DUBOIS

Composition du jury

Membres du jury avec voix délibérative

Prénom NOM
Titre, Affiliation
Prénom NOM
Titre, Affiliation
Prénom NOM
Titre, Affiliation
Prénom NOM
Titre, Affiliation
Prénom NOM
Titre, Affiliation

Président ou Présidente

Rapporteur & Examineur / trice

Rapporteur & Examineur / trice

Examineur ou Examinatrice

Examineur ou Examinatrice

Titre: Méthodes pour l'automatisation de la dosimétrie pour les traitements radiothérapeutiques.

Mots clés: Mathématiques, Intelligence Artificielle, Radiothérapie

Résumé: Nulla malesuada porttitor diam. Donec felis erat, congue non, volutpat at, tincidunt tristique, libero. Vivamus viverra fermentum felis. Donec nonummy pellentesque ante. Phasellus adipiscing semper elit. Proin fermentum massa ac quam. Sed diam turpis, molestie vitae, placerat a, molestie nec, leo. Maecenas lacinia. Nam ipsum ligula, eleifend at, accumsan nec, suscipit a, ipsum. Morbi blandit ligula feugiat magna. Nunc eleifend consequat lorem. Sed lacinia nulla vitae enim. Pellentesque tincidunt purus vel magna. Integer non enim. Praesent euismod nunc eu purus. Donec bibendum quam in tellus. Nullam cursus pulvinar lectus. Donec et mi.

Nam vulputate metus eu enim. Vestibulum pellentesque felis eu massa.

Quisque ullamcorper placerat ipsum. Cras nibh. Morbi vel justo vitae lacus tincidunt ultrices. Lorem ipsum dolor sit amet, consectetur adipiscing elit. In hac habitasse platea dictumst. Integer tempus convallis augue. Etiam facilisis. Nunc elementum fermentum wisi. Aenean placerat. Ut imperdiet, enim sed gravida sollicitudin, felis odio placerat quam, ac pulvinar elit purus eget enim. Nunc vitae tortor. Proin tempus nibh sit amet nisl. Vivamus quis tortor vitae risus porta vehicula.

Title: Methods for automatization of the dosimetry for radiotherapy treatments.

Keywords: Mathematics, Artificial Intelligence, Radiotherapy

Abstract: Lorem ipsum dolor sit amet, consectetur adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetur id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor

semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.

Nam dui ligula, fringilla a, euismod sodales, sollicitudin vel, wisi. Morbi auctor lorem non justo. Nam lacus libero, pretium at, lobortis vitae, ultricies et, tellus. Donec aliquet, tortor sed accumsan bibendum, erat ligula aliquet magna, vitae ornare odio metus a mi. Morbi ac orci et nisl hendrerit mollis. Suspendisse ut massa. Cras nec ante. Pellentesque a nulla. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Aliquam tincidunt urna. Nulla ullamcorper vestibulum turpis. Pellentesque cursus luctus mauris.

Acknowledgments

A PhD is more than just hard work; it thrives on mentorship, collaboration, and unwavering support.
[...]

List of Contributions

- Teaching: *Consistency and Reproducibility of Grades in Higher Education: A Case Study in Deep Learning* *replace icon*
- ArXiv: Radiotherapy Dosimetry: A Review on Open-Source Optimizer
- ESTRO: A Novel Framework for Multi-Objective Optimization and Robust Plan Selection Using Graph Theory
- SFPM: Dose Volume Histograms Guided Deep Dose Predictions
- AIME: Radiotherapy Dose Optimization via Clinical Knowledge Based Reinforcement Learning (full paper coming soon)
- ASTRO: Clinically Dependent Fully Automatic Treatment Planning System
- SFRO: Attention Mechanism on Dose-Volume Histograms for Deep Dose Predictions

List of Figures

List of Tables

Contents

1	Introduction	13
1.1	Introduction to Cancer	17
1.2	Introduction to Mathematical Optimization	19
1.3	Introduction to Artificial Intelligence	21
2	Radiotherapy	23
2.1	Patient Path	25
2.2	Machines	25
2.3	Irradiations techniques	25
2.4	Dosimetry steps	25

Introduction

Abstract

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetur id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.

Nam dui ligula, fringilla a, euismod sodales, sollicitudin vel, wisi. Morbi auctor lorem non justo. Nam lacus libero, pretium at, lobortis vitae, ultricies et, tellus. Donec aliquet, tortor sed accumsan bibendum, erat ligula aliquet magna, vitae ornare odio metus a mi. Morbi ac orci et nisl hendrerit mollis. Suspendisse ut massa. Cras nec ante. Pellentesque a nulla. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Aliquam tincidunt urna. Nulla ullamcorper vestibulum turpis. Pellentesque cursus luctus mauris.

1.1	Introduction to Cancer	17
1.1.1	what is cancer?	17
	Cells proliferating	17
	DNA messed up	17
	variety of cancer	17
	some safe	17
	some not safe	17
1.1.2	who is concerned?	17
1.1.3	risk factors	17
	environment impacts the probability of getting cancer	17
	living habits as well	17
	genetic impacts as well (e.g. "cancer gene")	18
1.1.4	possible treatments	18
	surgery	18
	RT	18
	chemotherapy	18
	combination	18
1.1.5	10 cancer markers	18
	cell proliferation	18
	reprogram cellular metabolism	18
	stop cell growth arrest	18
	evade apoptosis	18
	escape immune system	18
	ability to undergo a sufficient number of successive cell cycles of growth and division to generate macroscopic tumors	18
	create new blood vessels to get nutrients	18
	allow cell escape and metastasis formation	18
	change cellular response phenotypic via plasticity	18
	senescence	18
	cancer can be considered as a living thing on its own	18
	beyond the cellular level, impacting tissues	18
1.1.6	4 cancer conditions	18
	mutation	18
	epigenetic reprogramming	18
	inflammatory context	18
	disruption of microbiota	18
1.1.7	phases of cancer	18
	initiation	18
	promotion	18
	tumorigenesis + neoangiogenesis	18
	evolution (local, regional, metastasis)	18
1.1.8	cancer classification:	18
	tumor, node, metastasis	18
	stages classification:	18
	stage 0 which corresponds to a so-called in situ tumor	18
	stage 1 which corresponds to a single, small tumor	19
	stage 2 which corresponds to a larger local volume	19
	stage 3 which corresponds to invasion of the lymph nodes or surrounding tissues	19

	stage 4 which corresponds to a wider extension in the body in the form of metastases	19
1.1.9	cancer causes	19
	environment	19
	inherited mutations	19
	mistake in DNA copy	19
1.1.10	personalized treatments	19
	revolution	19
	rapid advances	19
	help of mathematics	19
	help of AI	19
1.2	Introduction to Mathematical Optimization	19
1.2.1	optimization def	19
1.2.2	in math: more precisely	19
1.2.3	notion of allowed set	20
1.2.4	discrete vs continuous optim	20
1.2.5	many real-world and theoretical problems may be modeled in continuous general framework	20
1.2.6	$\max(f) \iff \min(-f)$ hence only min	20
1.2.7	notion of local vs global min	20
1.2.8	feasibility	20
1.2.9	existence	20
1.2.10	optim algos	20
	1st order	20
	gradient descent	20
	line search	20
	quasi-newton methods	20
	2nd order	20
	newton's method	20
	0th order	20
	brute force	20
	heuristics	20
1.2.11	least squares	21
1.2.12	multi-objective optimization	21
1.3	Introduction to Artificial Intelligence	21
1.3.1	quick def	21
1.3.2	general idea	21
1.3.3	common architectures	21
	FC	21
	MLP	21
	CNN	21
	RNN	21
	transformers	21
1.3.4	Classic AI vs Learning AI	21
1.3.5	Machine learning vs Artificial Intelligence vs Deep Learning	21
1.3.6	applications	21
1.3.7	learning types	21
	supervised	21
	un-supervised	21
	self-supervised	21
	reinforcement / semi-supervised	21
1.3.8	tasks	21
	classical tasks	21

	regression	21
	classification	21
	partitioning	21
	dimension reduction	21
	generative AI	21
	images => training is difficult	21
	text	21
1.3.9	recent progress	22
	computer vision	22
	playing games	22
	image generation	22
	text generation	22
	healthcare	22

1.1 Introduction to Cancer

1.1.1 what is cancer?

Cells proliferating

DNA messed up

variety of cancer

some safe

(e.g.: mole/freckle)

some not safe

worse make the human die

1.1.2 who is concerned?

more and more ppl

1.1.3 risk factors

environment impacts the probability of getting cancer

(e.g.: UV exposure)

living habits as well

(e.g.: smooking)

genetic impacts as well (e.g. "cancer gene")

1.1.4 possible treatments

surgery

RT

chemotherapy

combination

1.1.5 10 cancer markers

cell proliferation

reprogram cellular metabolism

stop cell growth arrest

evade apoptosis

escape immune system

ability to undergo a sufficient number of successive cell cycles of growth and division to generate macroscopic tumors

create new blood vessels to get nutrients

allow cell escape and metastasis formation

change cellular response phenotypic via plasticity

senescence

cancer can be considered as a living thing on its own

beyond the cellular level, impacting tissues

1.1.6 4 cancer conditions

mutation

epigenetic reprogramming

inflammatory context

disruption of microbiota

1.1.7 phases of cancer

initiation

promotion

tumorigenesis + neoangiogenesis

evolution (local, regional, metastasis)

1.1.8 cancer classification:

tumor, node, metastasis

stages classification:

stage 0 which corresponds to a so-called in situ tumor

stage 1 which corresponds to a single, small tumor

stage 2 which corresponds to a larger local volume

stage 3 which corresponds to invasion of the lymph nodes or surrounding tissues

stage 4 which corresponds to a wider extension in the body in the form of metastases

1.1.9 cancer causes

various reasons why

environment

inherited mutations

mistake in DNA copy

1.1.10 personalized treatments

revolution

rapid advances

help of mathematics

help of AI

1.2 Introduction to Mathematical Optimization

1.2.1 optimization def

selection of a best element, with regard to some criteria

1.2.2 in math: more precisely

optimization problem consists of maximizing or minimizing a real function by systematically choosing input

1.2.3 notion of allowed set

1.2.4 discrete vs continuous optim

1.2.5 many real-world and theoretical problems may be modeled in continuous general framework

1.2.6 $\max(f) \Leftrightarrow \min(-f)$ hence only min

1.2.7 notion of local vs global min

1.2.8 feasibility

1.2.9 existence

1.2.10 optim algos

1st order

gradient descent

line search

quasi-newton methods

2nd order

newton's method

0th order

brute force

heuristics

1.2.11 least squares

1.2.12 multi-objective optimization

1.3 Introduction to Artificial Intelligence

1.3.1 quick def

1.3.2 general idea

1.3.3 common architectures

FC

MLP

CNN

RNN

transformers

1.3.4 Classic AI vs Learning AI

1.3.5 Machine learning vs Artificial Intelligence vs Deep Learning

1.3.6 applications

1.3.7 learning types

supervised

un-supervised

self-supervised

reinforcement / semi-supervised

1.3.8 tasks

classical tasks

regression

classification

partitioning

dimension reduction

generative AI

images => training is difficult

text

1.3.9 recent progress**computer vision****playing games**

(a way to assess intelligence)

image generation**text generation****healthcare**

Radiotherapy

Abstract

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetur id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.

Nam dui ligula, fringilla a, euismod sodales, sollicitudin vel, wisi. Morbi auctor lorem non justo. Nam lacus libero, pretium at, lobortis vitae, ultricies et, tellus. Donec aliquet, tortor sed accumsan bibendum, erat ligula aliquet magna, vitae ornare odio metus a mi. Morbi ac orci et nisl hendrerit mollis. Suspendisse ut massa. Cras nec ante. Pellentesque a nulla. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Aliquam tincidunt urna. Nulla ullamcorper vestibulum turpis. Pellentesque cursus luctus mauris.

2.1	Patient Path	25
2.1.1	Detection / diagnostic	25
2.1.2	RT Prescription	25
2.1.3	CT scan	25
2.1.4	Contouring	25
2.1.5	Dosimetry	25
2.1.6	Treatment	25
2.1.7	Follow-up	25
2.2	Machines	25
2.2.1	Molds / 3D-RT	25
2.2.2	MLC-LINAC	25
2.2.3	Tomotherapy	25
2.2.4	CyberKnife	25
2.2.5	Brachytherapy	25
2.3	Irradiations techniques	25
2.3.1	IMRT	25
	Step and Shoot	25
	Sliding Window	25
2.3.2	VMAT	25
2.4	Dosimetry steps	25
	Challenges	25
2.4.1	BOO	25
2.4.2	FMO	25
2.4.3	LF	25

2.1 Patient Path

2.1.1 Detection / diagnostic

2.1.2 RT Prescription

2.1.3 CT scan

2.1.4 Contouring

2.1.5 Dosimetry

2.1.6 Treatment

2.1.7 Follow-up

2.2 Machines

2.2.1 Molds / 3D-RT

2.2.2 MLC-LINAC

2.2.3 Tomotherapy

2.2.4 CyberKnife

2.2.5 Brachytherapy

2.3 Irradiations techniques

2.3.1 IMRT

Step and Shoot

Sliding Window

2.3.2 VMAT

2.4 Dosimetry steps

Challenges

2.4.1 BOO

2.4.2 FMO

2.4.3 LF