

Méthodes pour l'automatisation de la dosimetrie pour les traitements radiothérapiques.

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 Président ou Présidente Rapporteur & Examinateur / trice

Rapporteur & Examinateur / trice

Examinateur ou Examinatrice

Examinateur ou Examinatrice



Titre: Méthodes pour l'automatisation de la dosimetrie pour les traitements radiothérapiques.

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, consectetuer 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, consectetuer adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetuer 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	. 26
	2.2 Machines	. 26
	2.3 Irradiations techniques	. 26
	2.4 Treatment Planning Systems	. 26
	2.5 Dosimetry steps	. 26
	2.6 Simulation	. 27
3	Dosimetry Optimization	29
	3.1 Optim engine: classic and dose mimicking	. 30
	3.2 relation between optim doses (distance and network)	
	3.3 ESTRO (novel approach with graph theory)	. 30
4	Automation: Classical Approach	31
	4.1 RL + classic optim algo (AIME / ASTRO)	. 32
5	Automation: Deep Dose	33
	5.1 DVH guided deep dose $+$ dose mimicking algo (SFPM / SFRO)	. 34
6	Conclusion	35
7	Perspectives	37

Introduction

Abstract

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetuer 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.

1.1.1	luction to Cancer
1.1.1	Cells proliferating
	•
	DNA messed up
	variety of cancer
	some safe
	some not safe
1.1.2	who is concerned?
1.1.3	risk factors
	environment impacts the probability of getting cancer
	living habits as well
	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 blog vessels to get nutriments
	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
110	
1.1.6	4 cancer conditions
	mutation
	epigenetic reprogramming
	inflammatory context
	disruption of microbiota
1.1.7	phases of cancer
	initiation
	promotion
	$tumorigenesis + neoangiogenesis \dots $
	evolution (local, regional, metastasis)
1.1.8	cancer classification:
	tumor, node, mestastasis
	stages classification:
	stages classification:
	stages classification:

		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	Introd		19
	1.2.1	optimization def	19
	1.2.2		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	
	1.2.6		20
	1.2.7		20
	1.2.8	feasibility	20
	1.2.9	existance	
	1.2.10	optim algos	
		1st order	
		gradient descent	
			20
		quasi-newton methods	20
		2nd order	20
			20
			20
			20
		heuristics	20
	1.2.11		21
		multi-objective optimization	21
1.3		uction to Artificial Intelligence	
	1.3.1	quick def	
	1.3.2	general idea	
	1.3.3	common architectures	
		FC	21
			21
			21
			21
		transformers	21
	1.3.4	Classic AI vs Learning AI	21
	1.3.5	e de la companya de	21
	1.3.6	· · · · · · · · · · · · · · · · · · ·	21
	1.3.7	* *	21
		9 1-	$\frac{1}{21}$
		±	$\frac{1}{21}$
		•	$\frac{1}{21}$
			$\frac{1}{21}$
	1.3.8	į	$\frac{1}{21}$
			 21

	regression	21
	classification	21
	partitioning	
	dimension reduction	
	generative AI	21
	images => training is difficult	
	text	
1.3.9	recent progress	
	computer vision	
	playing games	
	image generation	
	text generation	
	<u> </u>	
	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 blog vessels to get nutriments

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, mestastasis

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

brute force

 ${\bf heuristics}$

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	$\max(f) <=> \min(-f) \ \text{hence only min}$					
1.2.7	notion of local vs global min					
1.2.8	feasibility					
1.2.9	existance					
1.2.10	optim algos					
1st ord	er					
gradien	gradient descent					
line search						
quasi-n	ewton methods					
2nd order						
newton's method						
$0 m th \ ord$	er					

- 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

 \mathbf{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, consectetuer adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetuer 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	Patien	t Path
	2.1.1	Detection / diagnostic
	2.1.2	RT Prescription
	2.1.3	CT scan
	2.1.4	Contouring
	2.1.5	Treatment Planning
	2.1.6	Irradiation Sessions
	2.1.7	Follow-up
2.2	Machir	nes
	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	Irradia	tions techniques
	2.3.1	IMRT
		Step and Shoot
		Sliding Window
	2.3.2	VMAT
2.4		nent Planning Systems
2.1	2.4.1	Manufacturer
	2.1.1	Eclipse (Varian)
		ONE Planning (Elekta)
		Precision (Accuray)
	2.4.2	Non-manufacturer
	2.4.2	RayStation (RaySearch)
		matRad (German Cancer Research Center - DKFZ)
		AutoPlan (TheraPanacea - coming soon)
2.5	Dogim	etry steps
۷.5	Dosim	Challenges
	2.5.1	BOO
	$\frac{2.5.1}{2.5.2}$	
0.0	2.5.3	LF
2.6	Simula	${ m tion}$

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 Treatment Planning
- 2.1.6 Irradiation Sessions
- 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 Treatment Planning Systems

2.4.1 Manufacturer

Eclipse (Varian)

ONE | Planning (Elekta)

Precision (Accuray)

2.4.2 Non-manufacturer

RayStation (RaySearch)

matRad (German Cancer Research Center - DKFZ)

AutoPlan (TheraPanacea - coming soon)

2.5 Dosimetry steps

Challenges

2.6. SIMULATION 27

- 2.5.1 BOO
- 2.5.2 FMO
- 2.5.3 LF
- 2.6 Simulation

Dosimetry Optimization

Abstract

3.3

3.1 3.2 3.3	Optim engine: classic and dose mimicking	30			
3.1	Optim engine: classic and dose mimicking				
3.2 relation between optim doses (distance and network)					

ESTRO (novel approach with graph theory)

Automation: Classical Approach

Abstract

	$CHAPTER \ 4.$	AUTOMATION: CLASSICAL APPROACH
4.1	RL + classic optim algo (AIME / ASTRO)	

$4.1 \quad \mathrm{RL} + \mathrm{classic} \; \mathrm{optim} \; \mathrm{algo} \; (\mathrm{AIME} \; / \; \mathrm{ASTRO})$

32

Automation: Deep Dose

Abstract

	CHAPTER 5. AUTOMATION: DEEP DOS	SE
5.1	DVH guided deep dose + dose mimicking algo (SFPM / SFRO)	34

5.1 DVH guided deep dose + dose mimicking algo (SFPM / SFRO)

34

Conclusion

Perspectives