The healthcare industry plays a critical role in saving lives every day. As a result, researchers, physicians, and experts are constantly working to find new ways to address illnesses and disabilities. In addition, technological advancements, especially in artificial intelligence and machine learning, have helped the scientific community design and propose advanced diagnostic tools to help physicians make crucial patient care decisions. These tools allow researchers to analyze vast amounts of data in new ways, often in real-time, for various purposes, such as detecting patterns behind illnesses, analyzing signals and detecting potential cancer from images.

In this context, this work was dedicated to the study of the Melanoma Image Binary Classification Problem (MIBCP), mainly by analyzing and proposing solutions to addressing the open issues in this field that did not allow a massive utilization of computer-aided diagnostic systems for early diagnosis. In particular, this work focuses on the resolution of the problems that may be behind high-performance automatic prediction models: the need to minimize risk situations, even by accepting lower overall performance; the opportunity to use clinical images instead of instrumental images in early diagnosis; the need able doctors to evaluate how the automatic prediction models learn and choose the results, rather than blindly relying only on the statistical values that can be calculated by analyzing the performance of the system on training, validation and test tests; the need for a scalable architecture specialized in allowing the refinement of prediction models in a fast and accessible way to non-experts.

The results reported aim to help increase trust in the automatic system that can be implemented thanks to deep learning, in particular by showing these systems' advantages, limitations and disadvantages and providing tools that show the potential to overcome these limitations. Also, this work aims to improve Melanoma early detection, which is now a limiting factor for first-line therapies in this tumour pathology.

Il settore sanitario svolge un ruolo fondamentale nel salvare vite ogni giorno. Di conseguenza, ricercatori, medici ed esperti lavorano costantemente per trovare nuovi modi per affrontare malattie e disabilità. Inoltre, i progressi tecnologici, in particolare nell'intelligenza artificiale e nell'apprendimento automatico, hanno aiutato la comunità scientifica a progettare e proporre strumenti diagnostici avanzati per aiutare i medici a prendere decisioni cruciali sulla cura del paziente. Questi strumenti consentono ai ricercatori di analizzare grandi quantità di dati in modi nuovi, spesso in tempo reale, per vari scopi, come rilevare modelli dietro malattie, analizzare segnali e rilevare potenziali tumori dalle immagini. In questo contesto, questo lavoro è stato dedicato allo studio del Melanoma Image Binary Classification Problem (MIBCP), principalmente analizzando e proponendo soluzioni per affrontare le questioni aperte in questo campo che non hanno consentito un utilizzo massiccio di sistemi diagnostici assistiti da computer per la diagnosi precoce. In particolare, questo lavoro si concentra sulla risoluzione dei problemi che possono essere alla base di modelli di previsione automatica ad alte prestazioni: la necessità di minimizzare le situazioni di rischio, anche accettando prestazioni complessive inferiori; l'opportunità di utilizzare immagini cliniche invece di immagini strumentali nella diagnosi precoce; la necessità di medici in grado di valutare come i modelli di previsione automatica apprendono e scelgono i risultati, piuttosto che affidarsi ciecamente solo ai valori statistici che possono essere calcolati analizzando le prestazioni del sistema su traning, validation e test set; la necessità di un'architettura scalabile specializzata nel consentire l'affinamento dei modelli di previsione in modo rapido e accessibile ai non esperti. I risultati riportati mirano ad aumentare la fiducia nel sistema automatico che può essere implementato grazie al deep learning, in particolare mostrando vantaggi, limiti e svantaggi di questi sistemi e fornendo strumenti che mostrano il potenziale per superare questi limiti. Inoltre, questo lavoro mira a migliorare la diagnosi precoce del melanoma, che ora è un fattore limitante per le terapie di prima linea in questa patologia tumorale.

## CONTENTS

1	Intro	oduction 1
	1.1	Overview 1
	1.2	Open Challenges 4
	1.3	Contribution of This Thesis 6
	1.4	Organization of the Thesis 7
2	Bacl	sground 9
	2.1	Melanoma 9
	2.2	Melanoma Assessment and Visual inspection 11
		2.2.1 Dermoscopic and Histological Inspection 14
		2.2.2 Lymph Node Mapping 16
		2.2.3 Computer Tomography 17
		2.2.4 Positron Emission Tomography 18
		2.2.5 Magnetic Resonance Image 20
		2.2.6 Standard blood chemistry tests 21
	2.3	State of the art and related works 22
	2.4	Machine Learning and Deep Learning 23
		2.4.1 Underfitting and Overfitting 24
		2.4.2 Training methodologies 25
	2.5	Evaluation of melanoma classification 33
		2.5.1 Explainable AI - XIA 34
		2.5.2 Local Interpretable Model-Agnostic Expla-
		nations (LIME) 35
3	Incr	easing trust in CAD using FNR minimization and
	XIA	37
	3.1	Background 37
	3.2	Methods 39
		3.2.1 Dataset preparation 39
		3.2.2 Image improvement method 41
		3.2.3 Image segmentation method 41
		3.2.4 CNN refactoring and evaluation 42
		3.2.5 XIA analysis 44
	3.3	Results and Discussion 45
	3.4	Conclusion 48
4	Gen	etic Algorithms for Melanoma Classification 53
	1 T	Idea 54

	4.2	Genet	ic Algorithms on Clinical Image 56
		4.2.1	Dataset 57
		4.2.2	Materials and Method 57
		4.2.3	Results and Discussion 59
		4.2.4	Conclusion 61
	4.3	Geneti	c Algorithms on Dermoscopic Images 62
		4.3.1	Dataset 62
		4.3.2	Pre-processing 63
		4.3.3	Training, Validation and Test sets 65
		4.3.4	
		4.3.5	GA definition 66
		4.3.6	Experiments Setup 69
		4.3.7	Results and Discussion 71
		4.3.8	Comparison with the literature 74
		4.3.9	Conclusion 75
5	AC	loud A	pproach for Melanoma Detection 77
5.1 Background and considered issues 77			
	5.2	Propos	sed method 78
	5.3	Used 1	Networks 80
		5.3.1	MED-NODE dataset and Pre-Processing 81
	5.4	Result	s 82
		5.4.1	Results for the transfer learning reliability
			evaluation 82
		5.4.2	Results for the impact of the three-layers
			architecture 83
	5.5	Conclu	usion 86
6	Con	clusion	s 87
6.1 Summary 87			ary 87
		6.1.1	Changing the POV regarding CAD perfor-
			mances 87
		6.1.2	The potential contribute of the clinical im-
			ages 89
		6.1.3	Addressing the intra-class/extra-class issue
			with the continuous retraining 90
	6.2	Future	e Works 91
	D:1.1		

Bibliography 93

# LIST OF FIGURES

Figure 2.1	Stages of Melanoma. 11		
Figure 2.2	Several examples of neavus and melanoma		
118410 2.2	images. 14		
Figure 2.3	Example of simple naevus with similar		
0 9	colour, thickness and diameter. 15		
Figure 2.4	Example of clinical and dermoscopic im-		
0 1	age. 15		
Figure 2.5	Sentinel lymph node. 17		
Figure 2.6	Melanoma metastasi in the liver.		
Figure 2.7	Melanoma PET scan. 20		
Figure 2.8	Melanoma metastases detect by MRI [29].	21	
Figure 2.9	A summary of the sierological prognostic		
0	markers for cutaneous Melanoma. 22		
Figure 3.1	Images of Naevi before and after applica-		
0 0	tion are shown from top to bottom. Specif-		
	ically in the upper part the images before		
	the application where you can also see the		
	skin while in the lower part the images		
	after the segmentation. 42		
Figure 3.2	Images of Melanoma before and after ap-		
0	plication are shown from top to bottom.		
	Specifically in the upper part the images		
	before the application where you can also		
see the skin while in the lower part t			
	images after the segmentation. 43		
Figure 3.3	The InceptionV3 prediction explained by		
	LIME. 45		
Figure 3.4	The global performances of the CNN on		
	the four datasets. 48		
Figure 3.5	Comparison of SN and SP for the INA e		
	IA datasets. 51		
Figure 3.6	Comparison of SN and SP for the NINA e		
	NIA datasets. 51		
Figure 4.1	GACNN performance over 100 iterations.	61	

Figure 4.2	The image segmentation process. 65
Figure 4.3	An overview of the experiment environ-
	ment architecture. 70
Figure 4.4	Trend of death ratio over the 11 itera-
	tions. 71
Figure 4.5	Structure of the best network in the last
	iteration. 73
Figure 4.6	Confusion matrix of the best NN in the
	11 <sup>th</sup> iteration. 73
Figure 5.1	General operation of the three layers ar-
	chitecture for melanoma detection. 80
Figure 5.2	Several SDs values computed for all net-
	works. 84

# LIST OF TABLES

Table 3.1 The global performances of the CNNs on the INA and IA datasets are reported. In addition, image improvement techniques are active. 46  Table 3.2 The global performances of the CNNs on the NINA and NIA datasets are reported. In addition, image improvement techniques are not active. 47  Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
addition, image improvement techniques are active. 46  Table 3.2 The global performances of the CNNs on the NINA and NIA datasets are reported. In addition, image improvement techniques are not active. 47  Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
Table 3.2 The global performances of the CNNs on the NINA and NIA datasets are reported. In addition, image improvement techniques are not active.  Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
Table 3.2 The global performances of the CNNs on the NINA and NIA datasets are reported. In addition, image improvement techniques are not active.  Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
on the NINA and NIA datasets are reported. In addition, image improvement techniques are not active.  Table 3.3  The FNR and the other metrics of the CNNs on the IA and INA datasets are
ported. In addition, image improvement techniques are not active. 47  Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
Table 3.3 The FNR and the other metrics of the CNNs on the IA and INA datasets are
CNNs on the IA and INA datasets are
THE RESIDENCE OF THE SECOND PROPERTY OF THE PR
to 1. The impact income to 1.
reported. The image improvement tech-
niques are active. 49
Table 3.4 The FNR and the other metrics of the
CNNs on the NINA and NIA datasets are
reported. The image improvement tech-
niques are active. 50
Table 4.1 Performance of AlexNet on the MED-NODE
dataset. 60

Table 4.2	Work Environment 70			
Table 4.3	Evolution during the iterations 72			
Table 4.4	Experiments results 74			
Table 4.5	Reference literature 75			
Table 5.1	Performance on MED-NODE dataset for			
	ACCs with Otsu segmentation and with			
	and without data augmentation 82			
Table 5.2	Performance on MED-NODE dataset for			
	ACCs without Otsu segmentation and with			
	and without data augmentation 83			
Table 5.3	Performance on MED-NODE with Otsu			
	segmentation and with and without data			
	augmentation 8 <sub>3</sub>			
Table 5.4	Performance on MED-NODE without Otsu			
	segmentation and with and without data			
	augmentation 8 <sub>4</sub>			
Table 5.5	Performance drop after 100 training steps			
	(related to Training and Validation steps) 85			
Table 5.6	Clock time (in seconds) measured for both			
	the experiments 85			

# LISTINGS

### ACRONYMS

#### 1.4 ORGANIZATION OF THE THESIS

After this Chapter Introduction, the thesis is divided as follows:

In Chapter 2, there is an overview of skin cancers, Melanoma and detection issues. In particular, it reports an overview of the scientific literature relating to melanoma detection problems using clinical images (MDCI). The Chapter begins with a review of some processes required for melanoma detection and ends with a description of the classification algorithms proposed in the literature to address these issues.

Chapter 3 illustrated the experimental results related to multiple CNN architectures trained on clinical images with and without segmentation and data augmentation in order to obtain the best model of CNN and for the minimization of False Negative Rate (FNR).

Chapter 4 presents an alternative way to use an extended version of GA to address the MDCI. In particular, the Chapter presents the experimental results obtained using GA (selection, mutation, merging and crossover) to perform the design of a CNN driven by the GA scoring function; the maximization of the prediction accuracy and the minimization of the FNR was used as scoring functions.

In Chapter 5, the contribution of the intra-class dissimilarities (ICD) and extra-class similarity (ECS) presence in melanoma images dataset in affect classification performance is reported;

then, a hybrid architecture design on the continuous re-training approach is presented and analyzed.

Finally, conclusions and future studies are followed in *Chapter* 6. This Chapter highlights the contributions proposed by these works and any future directions.