3rd Cuneo City ImmunoTherapy Conference (CCITC)

Immunotherapy in Hematological Malignancies 2023

CUNEO
May 18-20, 2023
Spazio incontri Fondazione CRC

“Machine learning and artificial intelligence in immune-mediated diseases”

Alessandro Tonacci (CNR-IFC, Pisa)

Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo, Italy
and Centro Interdipartimentale di Ricerca in Biologia Molecolare (CIRBM), Torino, Italy

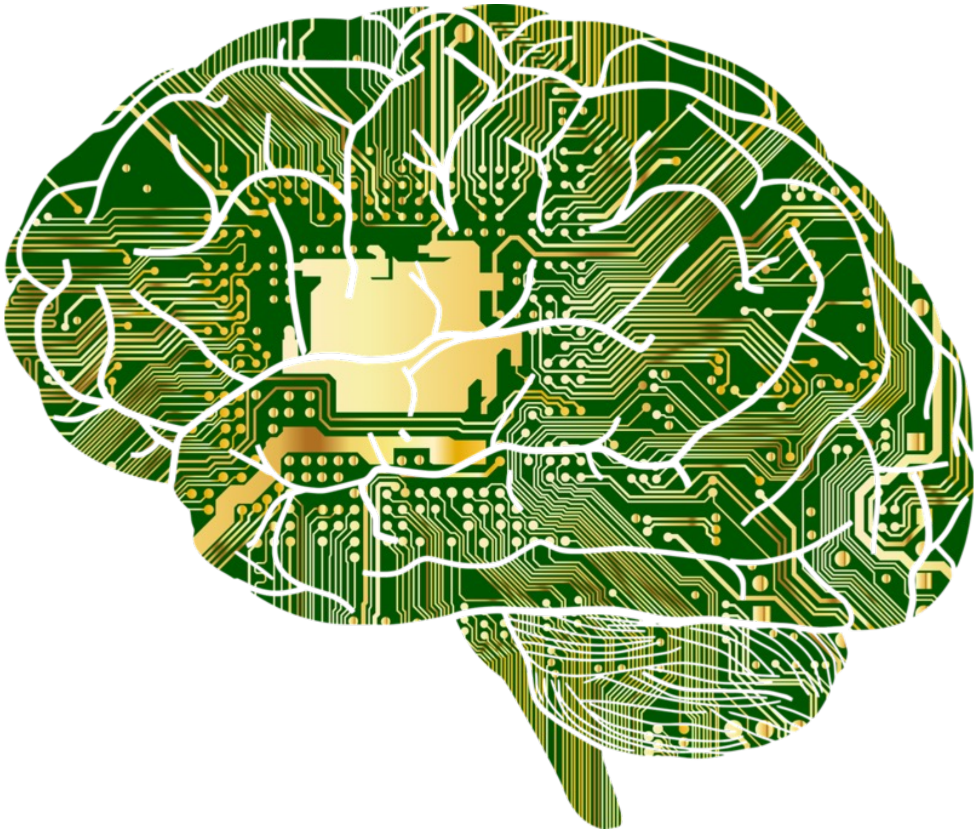
DICHIARAZIONE

Relatore: ALESSANDRO TONACCI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Consulenza ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazione ad Advisory Board (**NIENTE DA DICHIARARE**)
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Altro

INTRODUCTION

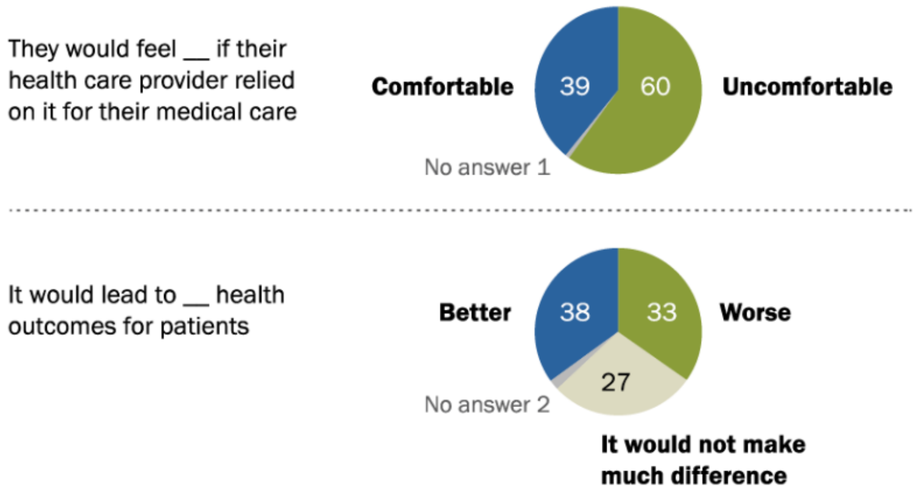


«Machine Learning can help process medical data and give medical professionals important insights, improving health outcomes and patient experiences.» (IBM)

…NOT WITHOUT RISKS…

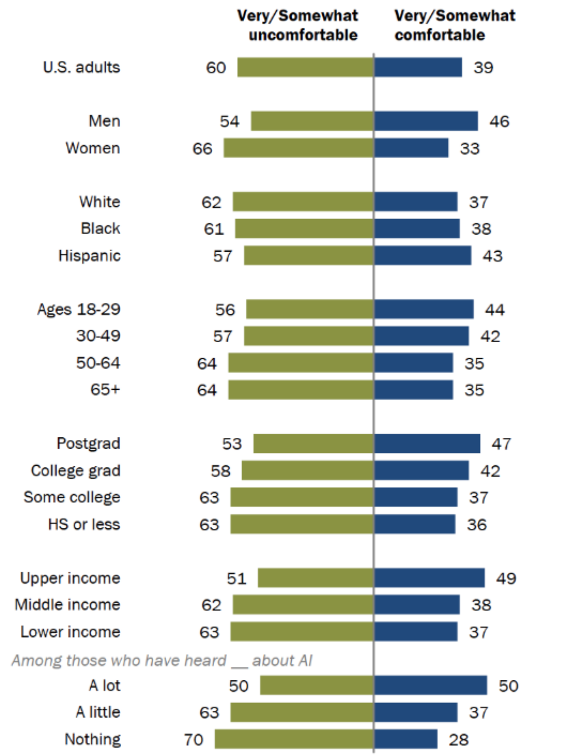
Fewer than half in U.S. expect artificial intelligence in health and medicine to improve patient outcomes

% of U.S. adults who say that thinking about the use of artificial intelligence in health and medicine to do things like diagnose disease and recommend treatments …



Source: Survey conducted Dec. 12-18, 2022.
"60% of Americans Would Be Uncomfortable With Provider Relying on AI in Their Own Health Care"

PEW RESEARCH CENTER



Note: Respondents who did not give an answer are not shown. White and Black adults include those who report being only one race and are not Hispanic. Hispanics are of any race. Family income tiers are based on adjusted 2021 earnings.
Source: Survey conducted Dec. 12-18, 2022.
"60% of Americans Would Be Uncomfortable With Provider Relying on AI in Their Own Health Care"

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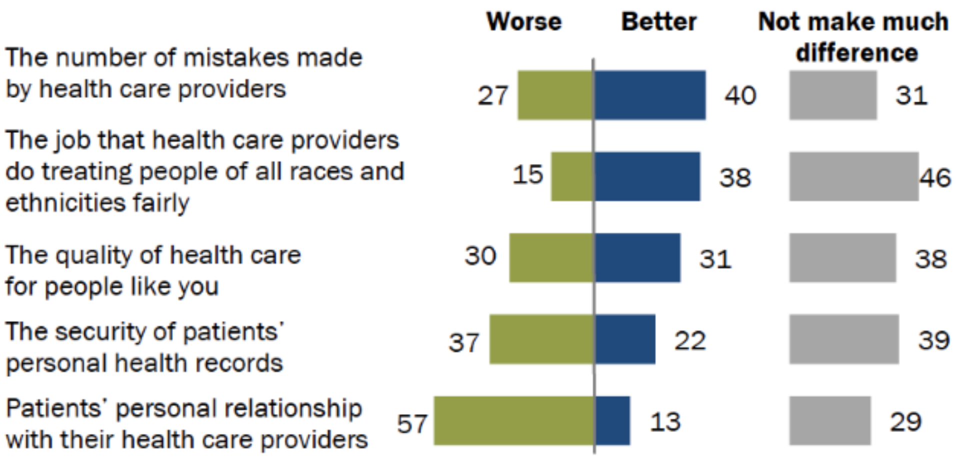
…WHICH ONES?

Americans tilt positive on AI's ability to reduce medical errors; greater concern around data security, patient-provider relationships

% of U.S. adults who say the use of artificial intelligence in health and medicine to do things like diagnose diseases and recommend treatments would make each of the following …



Note: Respondents who did not give an answer are not shown.
Source: Survey conducted Dec. 12-18, 2022.
"60% of Americans Would Be Uncomfortable With Provider Relying on AI in Their Own Health Care"

PEW RESEARCH CENTER

Sample sizes and margins of error, ATP Wave 119

	Unweighted sample size	Margins of error in percentage points
U.S. adults	11,004	+/- 1.4
Men	4,884	+/- 2.2
Women	5,993	+/- 1.8
Ages 18-29	930	+/- 4.3
30-49	3,514	+/- 2.4
50-64	3,157	+/- 2.5
65+	3,367	+/- 2.5
Postgraduate	2,503	+/- 2.6
College grad	2,918	+/- 2.4
Some college	3,523	+/- 2.4
HS or less	2,029	+/- 3.0
Upper income	2,625	+/- 2.6
Middle income	5,233	+/- 2.0
Lower income	2,283	+/- 3.2

Note: The margins of error are reported at the 95% level of confidence and are calculated by taking into account the average design effect for each subgroup. Family income tiers are based on adjusted 2021 earnings.
Source: Survey conducted Dec. 12-18, 2022.
"60% of Americans Would Be Uncomfortable with Provider Relying on AI in Their Own Health Care"

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…KNOWING IS HALF THE BATTLE

EDITORIAL

CMJ

Croat Med J. 2023;64:1-3
https://doi.org/10.3325/cmj.2023.64.1

Opportunities and risks of ChatGPT in medicine, science, and academic publishing: a modern Promethean dilemma

Jan Homolak[1,2]

[1]Department of Pharmacology, University of Zagreb School of Medicine, Zagreb, Croatia

[2]Croatian Institute for Brain Research, University of Zagreb School of Medicine, Zagreb, Croatia

Jan.homolak@mef.hr

- *AI has a tremendous potential to revolutionize health care and make it more efficient by improving diagnostics, detecting medical errors, and reducing the burden of paperwork; however, chances are it will never replace physicians.*
- *The probability of automating the jobs of physicians and surgeons is 0.42%*
    - *Algorithms perform relatively well on knowledge-based tests despite the lack of domain-specific training; […] However, they are notoriously bad at context and nuance – two things critical for safe and effective patient care, which requires the implementation of medical knowledge, concepts, and principles in real-world settings.*
- *Training a model requires a tremendous amount of (high-quality) data, and current algorithms are often trained on biased data sets*
- *Other ethical issues are related to the legal framework. For example, it remains to be determined who is to blame when an AI physician makes an inevitable mistake.*

…BUT STAY AWARE…

'The Godfather of A.I.' Leaves Google and Warns of Danger Ahead

For half a century, Geoffrey Hinton nurtured the technology at the heart of chatbots like ChatGPT. Now he worries it will cause serious harm.

Future of Life   Our mission   Cause areas   Our work   About us

Home › Pause Giant AI Experiments: An Open Letter

← All Open Letters

Pause Giant AI Experiments: An Open Letter

We call on all AI labs to immediately pause for at least 6 months the training of AI systems more powerful than GPT-4.

Signatures
27565

Add your signature

PUBLISHED
March 22, 2023

Yoshua Bengio, Founder and Scientific Director at Mila, Turing Prize winner and professor at University of Montreal

Stuart Russell, Berkeley, Professor of Computer Science, director of the Center for Intelligent Systems, and co-author of the standard textbook "Artificial Intelligence: a Modern Approach"

Bart Selman, Cornell, Professor of Computer Science, past president of AAAI

Elon Musk, CEO of SpaceX, Tesla & Twitter

Steve Wozniak, Co-founder, Apple

Yuval Noah Harari, Author and Professor, Hebrew University of Jerusalem.

Emad Mostaque, CEO, Stability AI

Andrew Yang, Forward Party, Co-Chair, Presidential Candidate 2020, NYT Bestselling Author, Presidential Ambassador of Global Entrepreneurship

John J Hopfield, Princeton University, Professor Emeritus, inventor of associative neural networks

Valerie Pisano, President & CEO, MILA

Connor Leahy, CEO, Conjecture

Jaan Tallinn, Co-Founder of Skype, Centre for the Study of Existential Risk, Future of Life Institute

Evan Sharp, Co-Founder, Pinterest

Chris Larsen, Co-Founder, Ripple

Craig Peters, Getty Images, CEO

Association for the Advancement of Artificial Intelligence

Working together on our future with AI

April 5, 2023

Francesca Rossi, IBM (AAAI President, 2022-2024)

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Bart Selman, Cornell University (AAAI President, 2020-2022)

Yolanda Gil, University of Southern California (AAAI President, 2018-2020)

Subbarao Kambhampati, Arizona State University (AAAI President, 2016-2018)

Thomas Dietterich, Oregon State University (AAAI President, 2014-2016)

Manuela Veloso, JPMC AI Research (AAAI President, 2012-2014)

Henry Kautz, University of Rochester (AAAI President, 2010-2012)

Martha Pollack (AAAI President, 2009-2010)

Eric Horvitz, Microsoft (AAAI President, 2007-2009)

Alan Mackworth, University of British Columbia (AAAI President, 2005-2007)

Ron Brachman, Cornell University (AAAI President, 2003-2005)

Tom Mitchell, Carnegie Mellon University (AAAI President, 2001-2003)

Bruce Buchanan, University of Pittsburgh (AAAI President,1999-2001)

Randall Davis, MIT (AAAI President, 1995-1997)

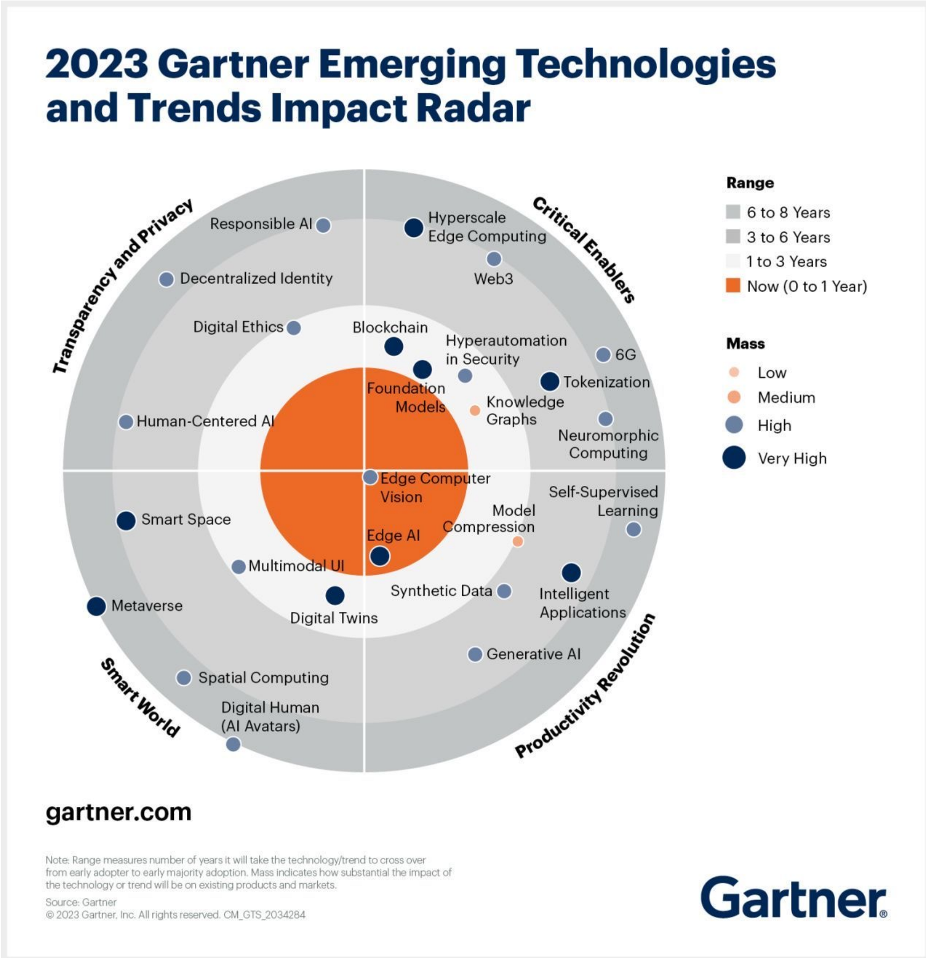
Barbara Grosz, Harvard University (AAAI President 1993-1995)

Patrick Hayes (AAAI President, 1991-1993)

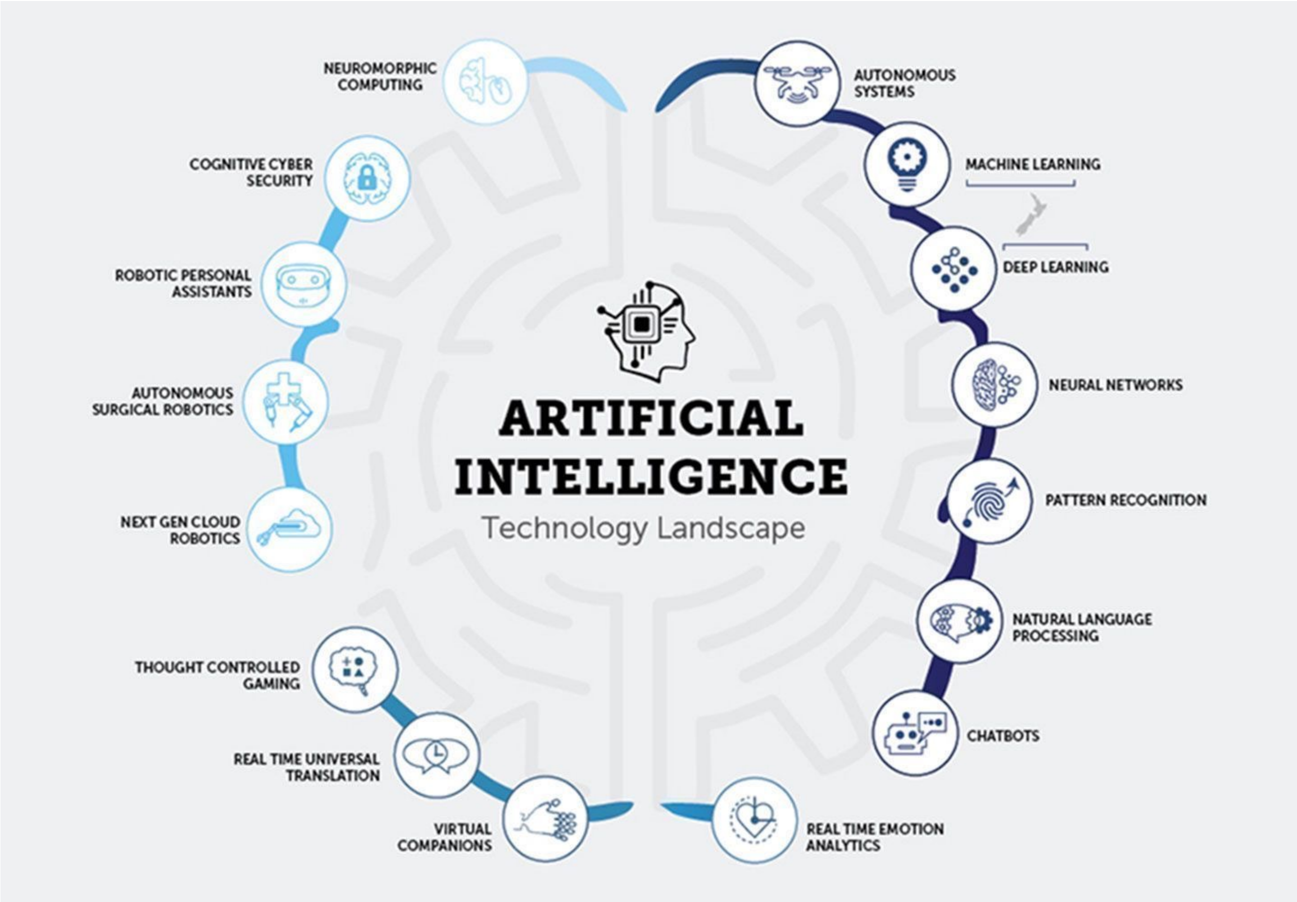
Raj Reddy, Carnegie Mellon University (AAAI President, 1987-1989)

Ed Feigenbaum, Stanford University (AAAI President, 1980-1981)

AI IN THE NEXT FUTURE

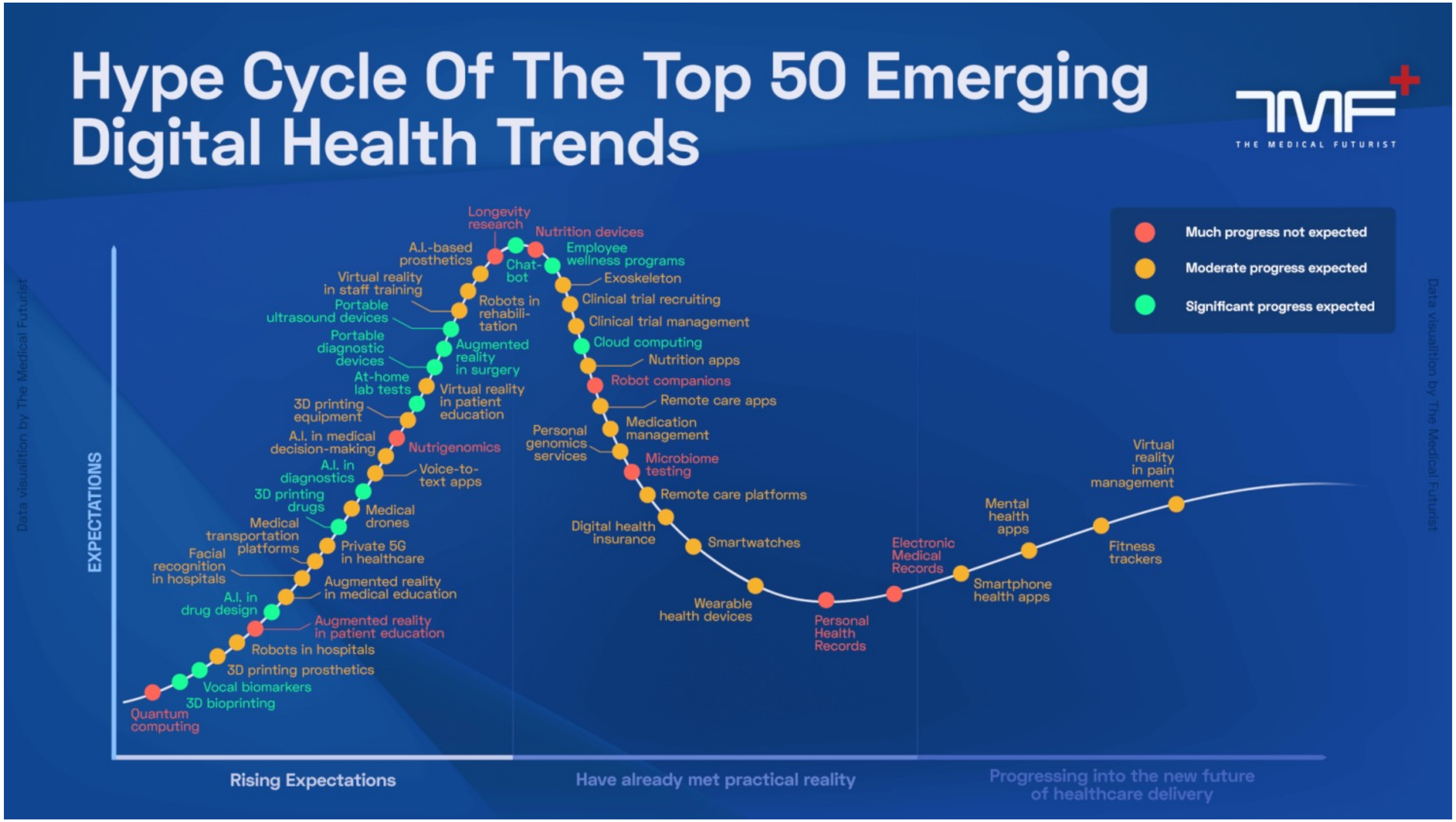


AI IN THE NEXT FUTURE



Artificial Intelligence Market Share, Size, Trends, Industry Analysis Report, By Solution (Hardware, Software, Services); By Technology (Deep Learning, Machine Learning, Natural Language Processing, Machine Vision); By End-Use; By Region; Segment Forecast 2022 - 2030

AI IN MEDICINE

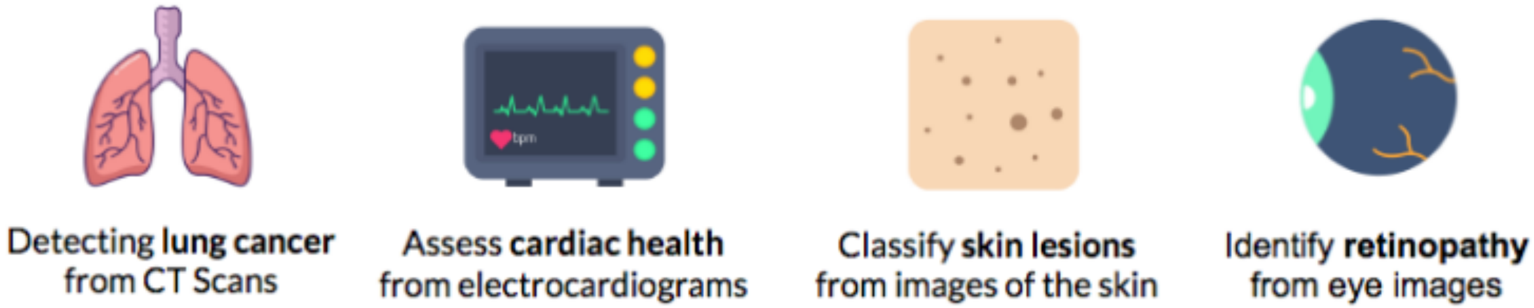


AI IN MEDICINE: APPLICATIONS

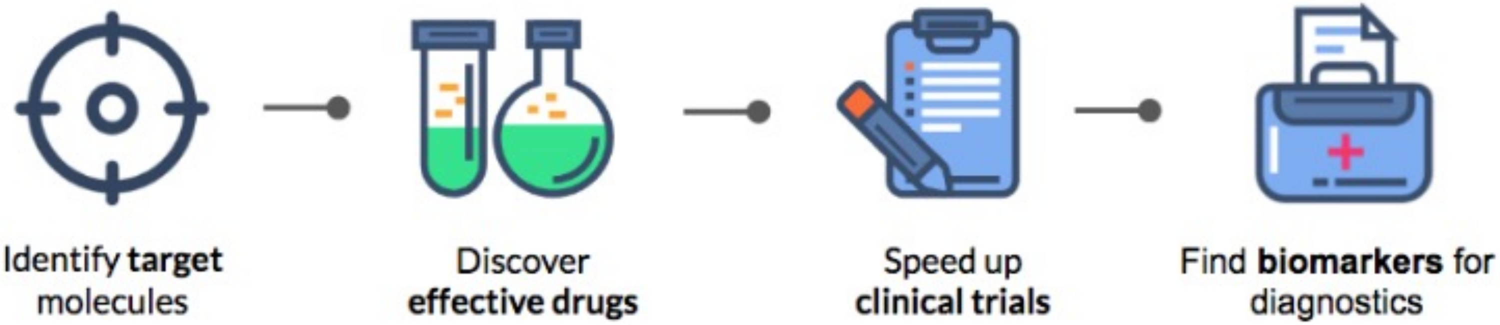
1. Diseases' diagnosis
2. Drugs development
3. Therapy personalization
4. Gene editing improvement

AI IN MEDICINE: APPLICATIONS

Diseases' diagnosis



Drugs development



Therapy personalization

Same therapies lead to different results on different patients

↓

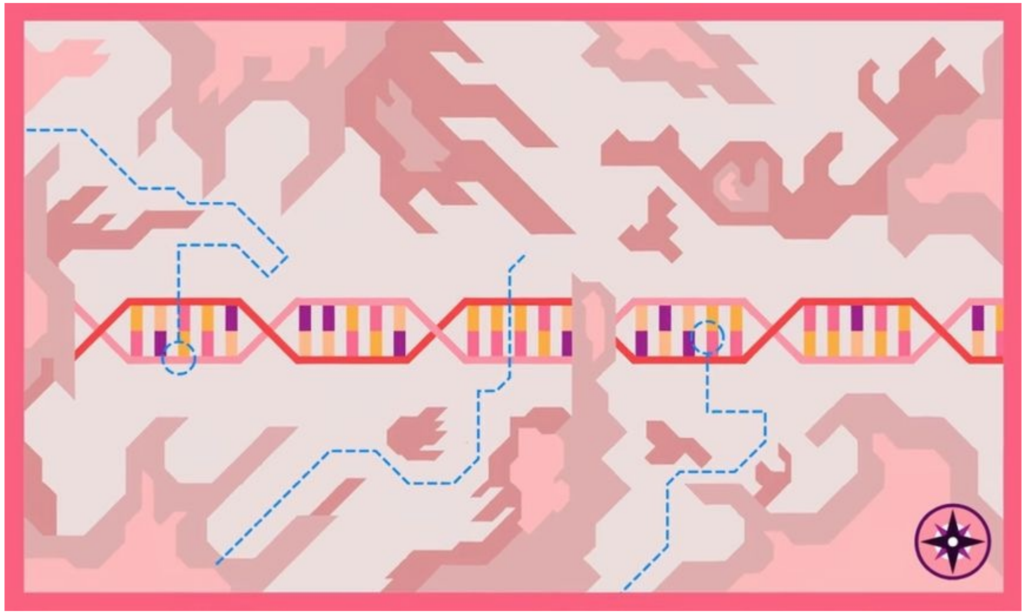
ML can help finding patients' characteristics explaining such different results

↓

Intelligent Tools can cluster patients based on the expected outcome, supporting the clinician defining proper treatments

Gene editing improvement

ML can predict interactions driver-target and off-target effects in specific short-guide RNAs (sgRNA), making the development of RNA guides quicker for each human DNA region

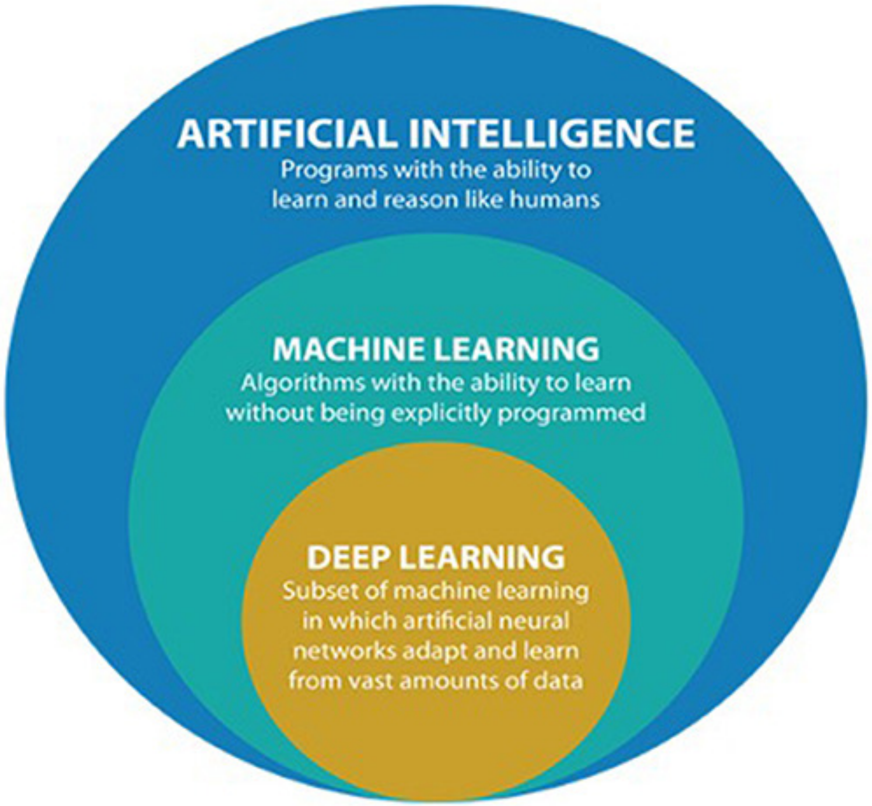


AI IN MEDICINE

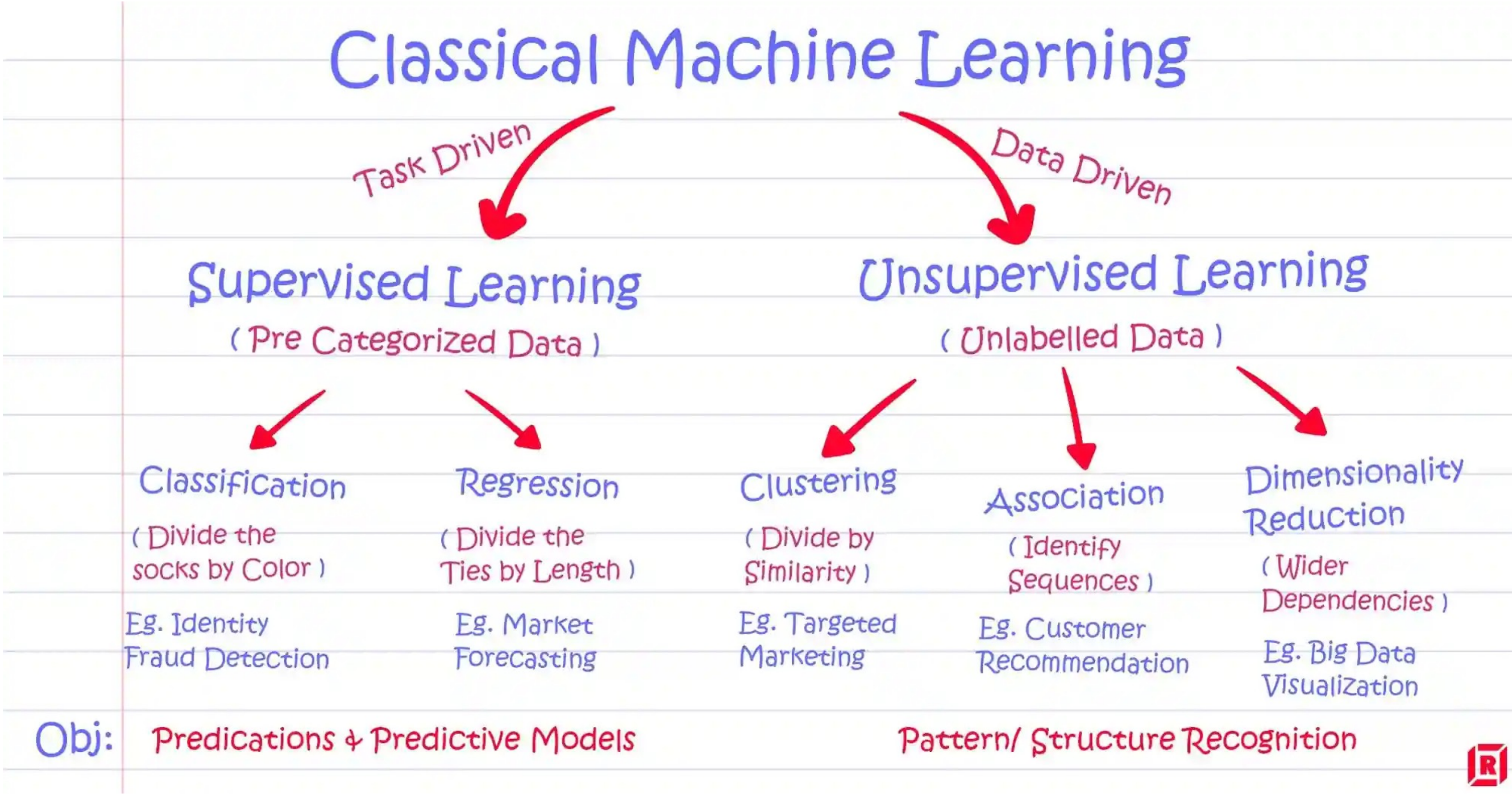
REVIEW article
Front. Med., 30 August 2021
Sec. Ophthalmology
Volume 8 - 2021 | https://doi.org/10.3389/fmed.2021.710329

The Impact of Artificial Intelligence and Deep Learning in Eye Diseases: A Review

Raffaele Nuzzi*, Giacomo Boscia, Paola Marolo and Federico Ricardi



MACHINE LEARNING AT A GLANCE



https://www.labellerr.com/blog/supervised-vs-unsupervised-learning-whats-the-difference/

ML IN IMMUNE-MEDIATED DISEASES

Open Access Article

A Machine Learning Application to Predict Early Lung Involvement in Scleroderma: A Feasibility Evaluation

by Giuseppe Murdaca [1], Simone Caprioli [2], Alessandro Tonacci [3,*], Lucia Billeci [3], Monica Greco [1], Simone Negrini [1], Giuseppe Cittadini [2], Patrizia Zentilin [4], Elvira Ventura Spagnolo [5] and Sebastiano Gangemi [6]

1 Department of Internal Medicine, Scleroderma Unit, Clinical Immunology Unit, University of Genoa, 16143 Genoa, Italy
2 Radiology Unit, IRCCS Policlinico San Martino, 16132 Genoa, Italy
3 Clinical Physiology Institute, National Research Council of Italy (IFC-CNR), 56124 Pisa, Italy
4 Department of Internal Medicine, Gastroenterology Unit, University of Genoa, 16143 Genoa, Italy
5 Section of Legal Medicine, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Via del Vespro, 129, 90127 Palermo, Italy
6 Department of Clinical and Experimental Medicine, School and Operative Unit of Allergy and Clinical Immunology, University of Messina, 98122 Messina, Italy
* Author to whom correspondence should be addressed.

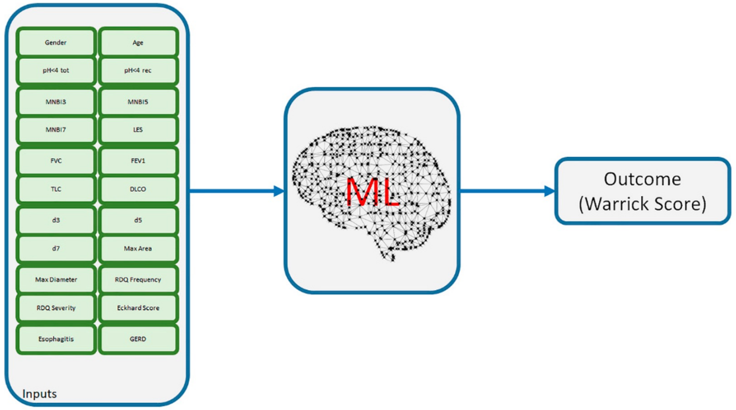
Diagnostics **2021**, *11*(10), 1880; https://doi.org/10.3390/diagnostics11101880

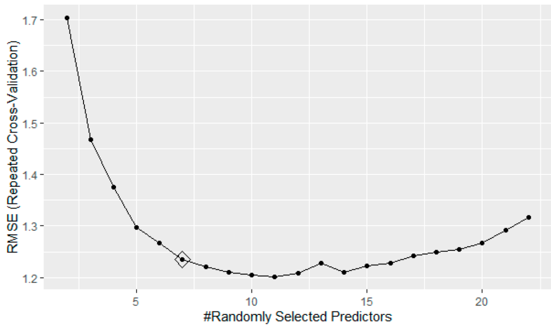
Received: 24 August 2021 / Revised: 1 October 2021 / Accepted: 9 October 2021 / Published: 12 October 2021

(This article belongs to the Special Issue Advances in Identification and Management of Systemic Sclerosis)

Classifier	Hyper-Parameter(s)	Hyper-Parameter(s) Value(s) Range	Hyper-Parameter(s) Optimal Value(s)	RMSE		R-Squared	
				Test Set	Training Set	Test Set	Training Set
LASSO	fraction	0–1	0.718	4.091	4.074	4.102	4.095
RIDGE	lambda	0–1	0.012	4.090	4.013	4.111	4.042
Elastic net	fraction, lambda	0–1	0.765 (fraction), 0 (lambda)	4.074	4.033	4.121	4.123
CART	cp	0–1	0.004	2.169	2.264	7.810	7.533
Random forest	mtry	1–22	7	0.810	0.425	0.619	0.485

Classifier	Time Elapsed (s)	Memory Used (MB)	Number of Variables
LASSO	34.09	0.303	20
RIDGE	655.06	11.5	2
Elastic net	108.14	11.6	20
CART	143.92	1.49	9
Random forest	1422.39	5.99	7





(i) total lung capacity (TLC)
(ii) mean nocturnal basal impedance at 3 cm (MNBI3)
(iii) diffusing capacity for carbon monoxide (DLCO)
(iv) forced expiratory volume in the first second (FEV1)
(v) forced vital capacity (FVC)
(vi) mean nocturnal basal impedance at 5 cm (MNBI5)
(vii) mean nocturnal basal impedance at 7 cm (MNBI7)

ML IN IMMUNE-MEDIATED DISEASES

Autoimmunity Reviews 21 (2022) 103105

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Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

A machine learning analysis to predict the response to intravenous and subcutaneous immunoglobulin in inflammatory myopathies. A proposal for a future multi-omics approach in autoimmune diseases

Maria Giovanna Danieli [a,b,*], Alessandro Tonacci [c], Alberto Paladini [d], Eleonora Longhi [e], Gianluca Moroncini [a,d], Alessandro Allegra [f], Francesco Sansone [c], Sebastiano Gangemi [g,*]

	n	%
Age at diagnosis (years), median (min–max)	53 (18–86)	
Gender: Females	41	80
Type of myositis		
PM	17	33
DM	18	35
ASS	9	18
IMNM	7	14
Autoantibodies positivity: (negative in 9 pts)		
Antinuclear antibodies	14	27
Anti-SRP	5	10
Anti-HMGCR	2	4
Anti-Jo1	8	16
Anti-Mi-2	5	10
Anti-MDA-5	1	2
Anti-TIF1, EJ, NXP2 (each)	3	6
Anti-myositis-associated autoantibodies (SSA, SSB, RNP)	12	23
Organ involvement		
Interstitial lung disease	20	40
Clinically overt heart involvement	18	35
Dysphagia	27	53
Arthritis	15	29
Course of disease		
Monocyclic	13	25
Polycyclic	15	29
Chronic continuous	23	45
Median follow-up period (min–max)	113 (12–310)	
(From treatment start to the last visit; months)		

Table 3
Root Mean Squared Error performances of the different models and approaches for the regression task estimating the muscle strength as evaluated by MMT8 score at follow-up as the outcome variable. LASSO, Least Absolute Shrinkage and Selection Operator; RIDGE, Ridge regression; E-NET, Elastic Net; CART, Classification and Regression Trees; RF, Random Forest.

Method	Train/Test 80/20	Train/Test 80/20 + 1× Aug	Train/Test 80/20 + 2× Aug	Train/Test 70/30 + 1× Aug	Train/Test 70/30 + 2× Aug
LASSO	3.939	3.878	3.847	6.137	6.166
RIDGE	5.052	4.100	4.411	5.238	5.107
E-NET	3.301	3.713	3.968	5.958	6.013
CART	4.935	4.523	4.470	4.341	4.313
RF	4.015	4.213	4.100	4.438	5.455

(at baseline):
i) MMT8 score
ii) presence of dysphagia
iii) MITAX score
iv) presence of skin disorders

Table 5
Accuracy performances of the different models and approaches for the classification task estimating the therapy outcome as the outcome variable. CART, Classification and Regression Trees; RF, Random Forest.

Method	Train/Test 80/20	Train/Test 80/20 + 1× Aug	Train/Test 80/20 + 2× Aug	Train/Test 70/30 + 1× Aug	Train/Test 70/30 + 2× Aug
CART	66.7	88.9	88.9	69.2	69.2
RF	66.7	88.9	88.9	69.2	69.2

Therapy outcome:
i) complete response
ii) Partial response
iii) no response

The type of disease progress (monocyclic, polycyclic,continuous) was the most important feature employed by the model

ML IN IMMUNE-MEDIATED DISEASES

Autoimmunity Reviews xxx (xxxx) 103353

Contents lists available at ScienceDirect

Autoimmunity Reviews

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A machine learning analysis to evaluate the outcome measures in inflammatory myopathies

Maria Giovanna Danieli[a,b,*], Alberto Paladini[c], Eleonora Longhi[d], Alessandro Tonacci[e,1], Sebastiano Gangemi[f,1]

	n	%
Age at diagnosis (years), median (min–max)	53 (18–86)	
Gender: Females	76	73
Type of myositis		
PM	33	34
DM	53	49
ASS	9	8
IMNM	8	7.7
Autoantibodies positivity: (negative in 20 pts)		
Antinuclear antibodies	21	20
Anti-SRP	6	4.8
Anti-HMGCR	2	1.9
Anti-Jo1	8	7.7
Anti-Mi-2	5	4.8
Anti-TIF1	3	2.9
Anti-MDA-5	2	1.9
Anti-EJ, NXP2 (each)	3	2.9
Anti-myositis-associated autoantibodies (SSA, SSB, RNP, etc)	23	22.3
Organ involvement		
Interstitial lung disease	42	40.7
Clinically overt heart involvement	28	27.1
Dysphagia	59	57.2
Arthritis	33	32.0
Course of disease		
Monocyclic	28	27.1
Polycyclic	27	26.2
Chronic continuous	48	46.6
Mean follow-up period (min–max) (From treatment start to the last visit; years)	10 (1–28)	

Table 9
Summary of the data obtained by Machine Learning analysis.

Predicted follow-up indexes		Machine Learning model Analysis	First most predictive variable	Second most predictive variable	Third most predictive variable
ACTIVITY INDEX	MITAX	Linear SVM	RP-ILD at the onset	Skin involvement	
	MMT8	CART	MMT8 baseline	MITAX baseline	MMT8 baseline
DAMAGE INDEX	MDI	RBF SVM	MITAX baseline	HAQ-DI baseline	Age at the diagnosis
	HAQ-DI	Linear SVM	Health status at last visit	MDI baseline	

Table 8
Performances of the best models in predicting the different outcomes as the percentage error with respect to the mean outcome value.

Outcome	MITAX score	MDI index	HAQ-DI score	MMT8 score	Immunosuppressant use
% Error	6.9%	5.16%	7.39%	0.6%	10.5%

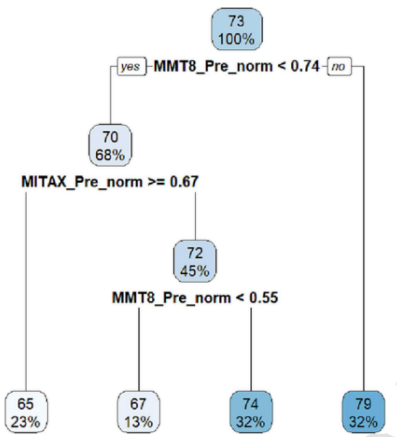

Fig. 1. CART for predicting the MMT8 score at follow-up.

CONCLUSIONS

- AI useful in the medical world, taking care of the several threats (ethics, privacy, etc.)
- Supporting statistics to solve complex, non-linear problems
    - Diagnostic support
    - Therapy personalization – towards «p4 medicine»
    - Discovering new biomarkers
        - Lower costs, low obtrusiveness, higher diagnostic accuracy, (possibly) less mistakes

Alessandro Tonacci
(IFC-CNR, SIIT Group)

alessandro.tonacci@cnr.it

SIIT Group:

Francesco Sansone
Gianluca Diodato
Loris Giunta
Patrizia Landi
Francesco Napoli
Anna Paola Pala
Luca Pisani
Domenico Profumo
Maria Cristina Scudellari
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3rd Cuneo City ImmunoTherapy Conference (CCITC)
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Thank You!
Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo, Italy
and Centro Interdipartimentale di Ricerca in Biologia Molecolare (CIRBM), Torino, Italy