



XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

 Associazione Italiana
Radioterapia e Oncologia clinica

 Società Italiana di Radiobiologia

 Associazione
Italiana
Radioterapia
e Oncologia
clinica




XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

MACHINE LEARNING BASED MODELS OF RADIOTHERAPY-INDUCED SKIN INDURATION FOR BREAST CANCER PATIENTS.

E La Rocca, A Cicchetti, M C De Santis, P Seibold, D Azria, D De Ruysscher, R Valdagni, A M Dunning, R Elliott, S Gutiérrez, M Lambrecht, E Sperk, T Rancati, T Rattay, B Rosenstein, C Talbot, A Vega, L Veldeman, A Webb, J Chang-Claude, C West



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

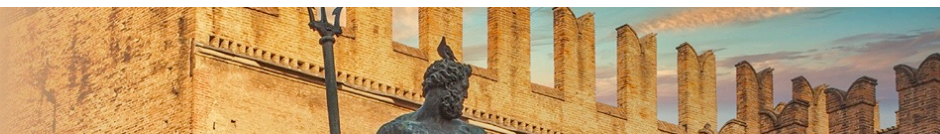


Associazione Italiana
Radioterapia e Oncologia clinica



Società Italiana di Radiobiologia





DICHIARAZIONE

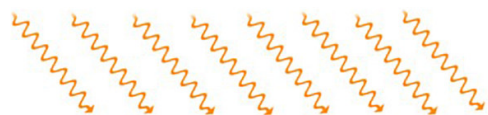
Relatore: Eliana La Rocca

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



Ionizing radiation side effects

Acute effects

Erythema
Dermatitis
Hyperpigmentation
Mucositis
Cystitis

Chronic effects

Fibrosis
Skin atrophy
Ulceration
Telangiectasia

"not all patients react the same way to radiotherapy"

patients with
identical tumor
characteristics
(location,
pathology, size,
stage)

+

same
treatment
schedule

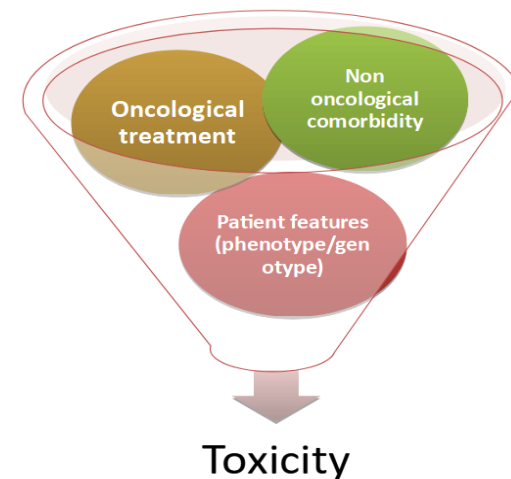
=

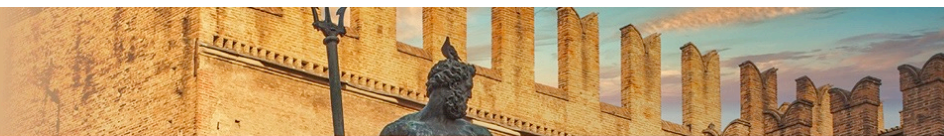
some will be cured
and some will not

some will suffer
toxicity effects
and
some will not

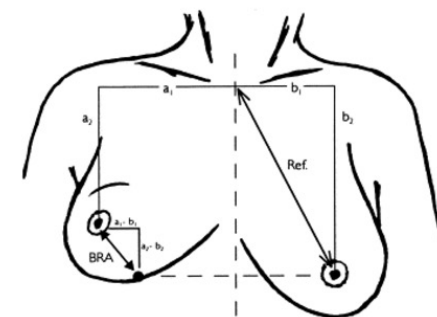
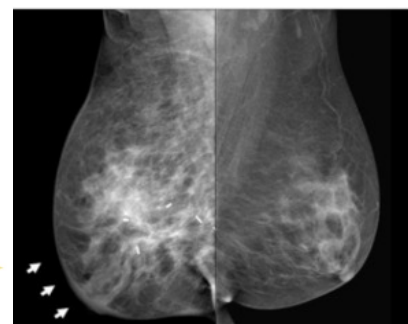
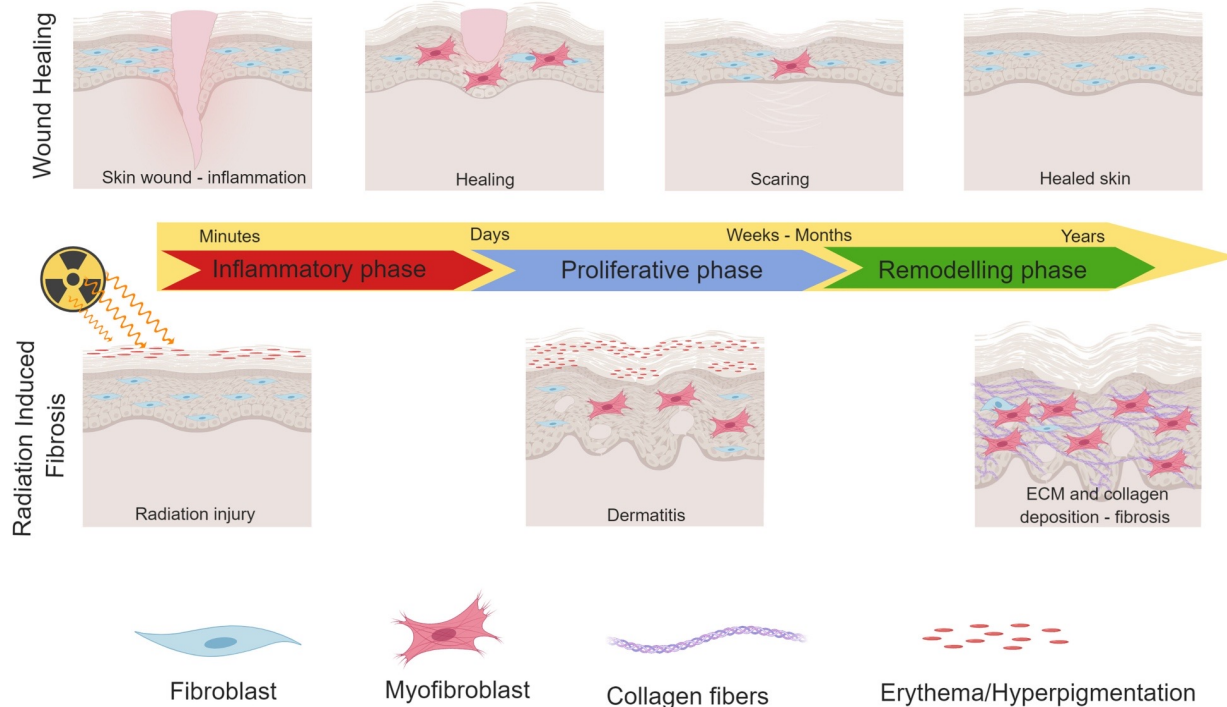


Courtesy of Prof. Riccardo Valdagni





Fibrosis and skin induration



Rad-Precise pts



Modeling

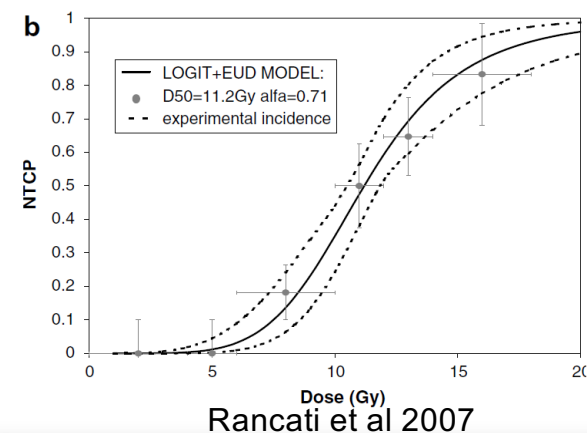
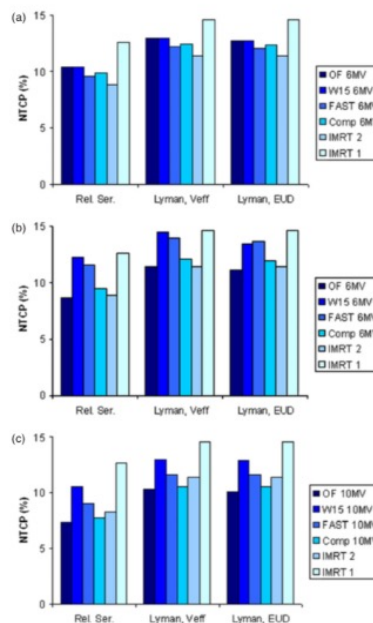
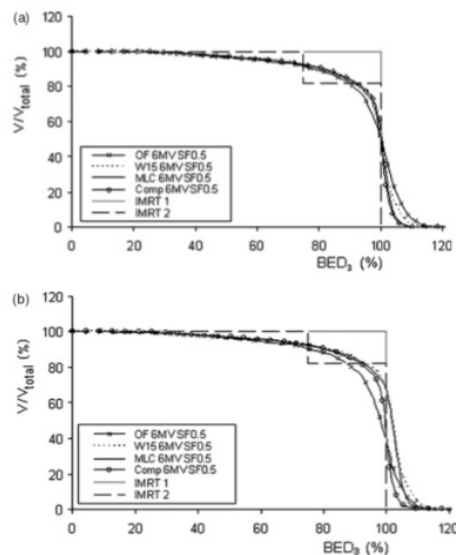
IOP Publishing
Phys. Med. Biol. 52 (2007) 1831–1843

PHYSICS IN MEDICINE AND BIOLOGY
doi:10.1088/0031-9155/52/7/005

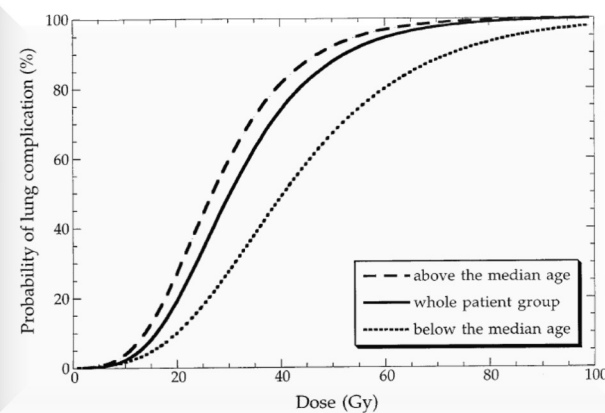
Normal tissue complication probability modelling of tissue fibrosis following breast radiotherapy

M A R Alexander, W A Brooks and S W Blake

Medical Physics Department, Royal Devon & Exeter Hospital NHS Foundation Trust, Barrack Road, Exeter, Devon, EX2 5DW, UK



Rancati et al 2007



Gagliardi et al 2000



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI



Associazione Italiana
Radioterapia e Oncologia clinica



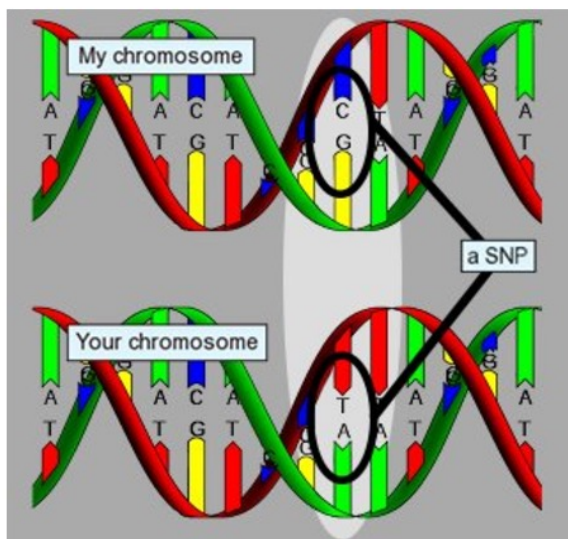
Società Italiana di Radiobiologia



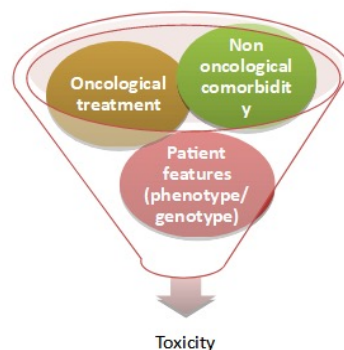
BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

Single-nucleotide Polymorphisms

Radiogenomics is used to refer to the study of genetic variation associated with response to RT.

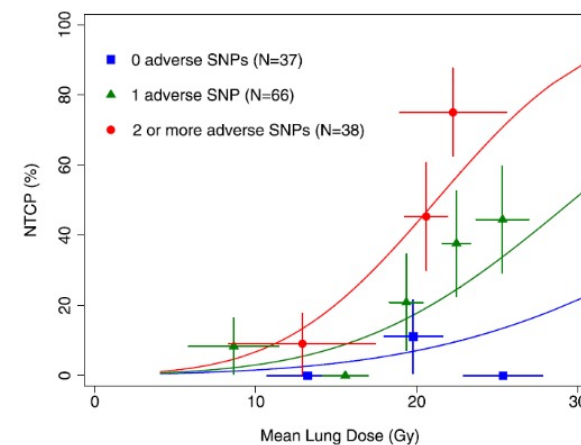


Genetic variation Single nucleotide polymorphisms SNP is studied in relation to a cancer patient's risk of developing toxicity following RT.



Incorporating Single-nucleotide Polymorphisms Into the Lyman Model to Improve Prediction of Radiation Pneumonitis

Susan L. Tucker, PhD,* Minghuan Li, MD, PhD,^{||} Ting Xu, MD,[†] Daniel Gomez, MD,[‡] Xianglin Yuan, MD, PhD,[§] Jinming Yu, MD, PhD,^{||} Zhensheng Liu, MD, PhD,[‡] Ming Yin, MD,[§] Xiaoxiang Guan, MD, PhD,[†] Li-E Wang, MD,[‡] Qingyi Wei, MD, PhD,[‡] Radhe Mohan, PhD,[§] Yevgeniy Vinogradskiy, PhD,** Mary Martel, PhD,[§] and Zhongxing Liao, MD[†]



AIRO2022

XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

Radioterapia di precisione per un'oncologia innovativa e sostenibile

REQUIRE

Validating Predictive Models and Biomarkers of
Radiotherapy Toxicity to Reduce Side-Effects and Improve
Quality of Life in Cancer Survivors



- epidemiology data
- treatment data
- side-effect
- quality of life data (before, after treatment, 1 yr ,2 yr)
- centralised database and biobank

Funded from the European Union's 7th Framework
Programme for research, technological development and
demonstration under grant agreement no. 601826.

Funded by the ERA PerMed Network, 1st Joint Transnational Call for Proposals (2018),
Reference Number: ERAPERMED2018-244.



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI



Associazione Italiana
Radioterapia e Oncologia clinica



Società Italiana di Radiobiologia



BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

Radiotherapy and Oncology 138 (2019) 59–67



Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Original Article

**REQUIRE: A prospective multicentre cohort study of patients undergoing
radiotherapy for breast, lung or prostate cancer**



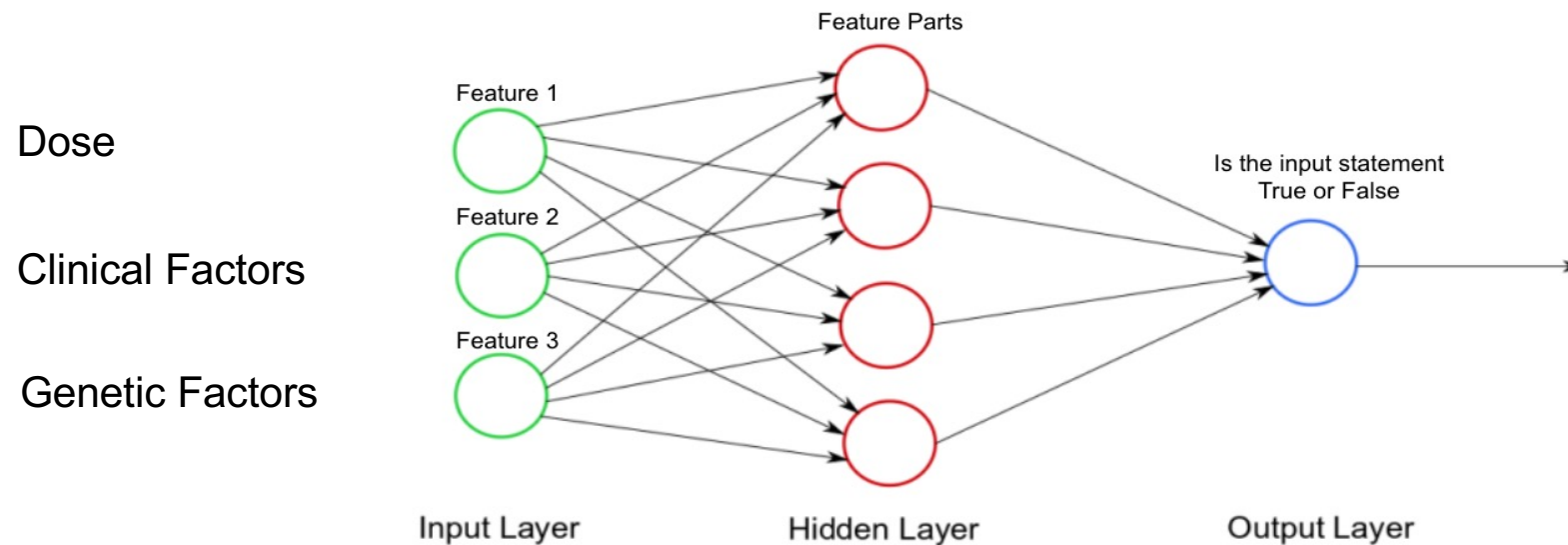
Petra Seibold^{a,1,*}, Adam Webb^{b,1}, Miguel E. Aguado-Barrera^{c,d}, David Azria^e, Celine Bourcier^e,
Muriel Brengues^f, Erik Briens^g, Renée Bultjink^h, Patricia Calvo-Crespoⁱ, Ana Carballo^j,
Ananya Choudhury^j, Alessandro Cicchetti^k, Johannes Claßen^l, Elena Delmastro^m, Alison M. Dunningⁿ,
Rebecca M. Elliott^l, Laura Fachal^o, Marie-Pierre Farcy-Jacquet^o, Pietro Gabriele^m, Elisabetta Garibaldi^m,
Antonio Gómez-Caamaño^{d,i}, Sara Gutiérrez-Enríquez^o, Daniel S. Higginson^q, Kerstie Johnson^r,
Ramón Lobato-Busto^s, Meritxell Mollà^{t,2}, Anusha Müller^a, Debbie Payne^u, Paula Peleteiro^l,
Giselle Post^h, Tiziana Rancati^k, Tim Rattay^f, Victoria Reyes^t, Barry S. Rosenstein^v, Dirk De Ruyscher^{w,x},
Maria Carmen De Santis^y, Jörg Schäfer^z, Thomas Schnabel^{aa}, Elena Sperk^{ab}, R. Paul Symonds^r,
Hilary Stobart^{ac}, Begoña Taboada-Valladares^l, Christopher J. Talbot^r, Riccardo Valdagni^{ky,ad},
Ana Vega^{c,d,ae}, Liv Veldeman^{h,af}, Tim Ward^{ag}, Christian Weißenberger^{ah}, Catharine M.L. West^{j,3},
Jenny Chang-Claude^{a,ai,3}, REQUIRE consortium⁴

- ❖ validate published biomarkers of
radiosensitivity
- ❖ validate clinical predictors of RT toxicity
- ❖ incorporate biomarker data in trials
- ❖ provide a resource for dissemination and
exploitation to the RT community.

AIM

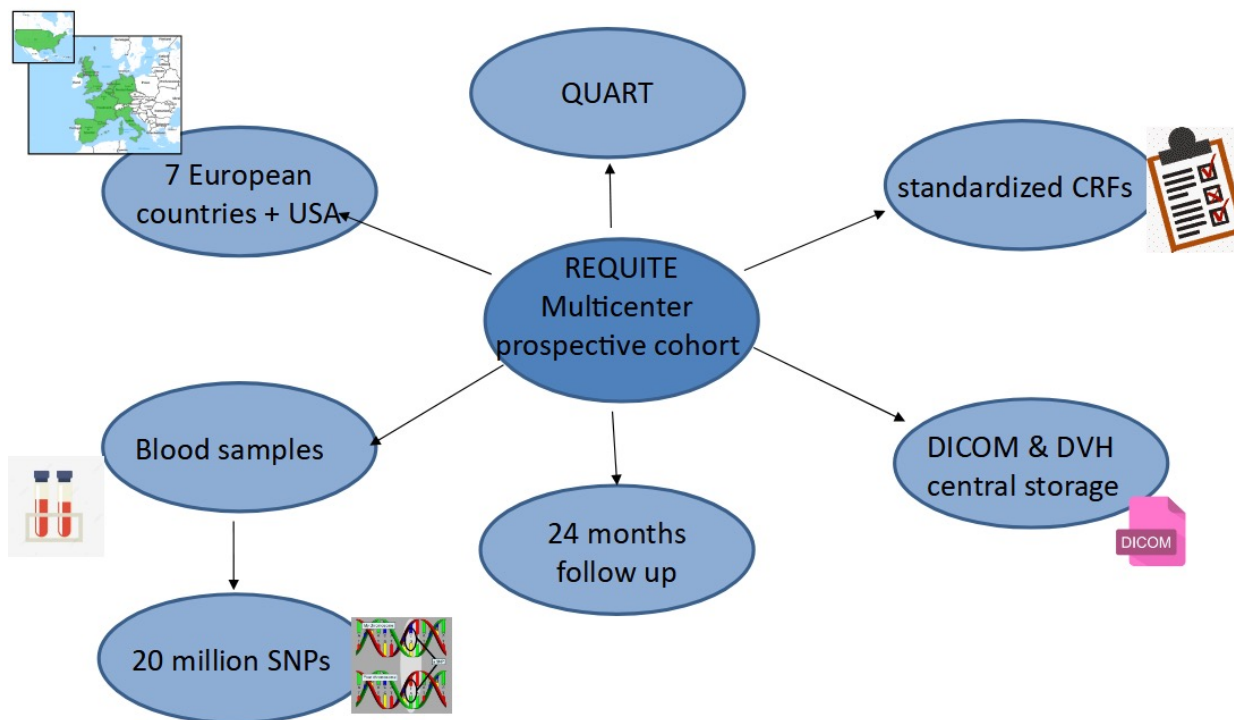


Develop predictive models for late skin induration/fibrosis after RT using machine learning approach.



MATERIAL AND METHODS

Study population and data collect



REQUITE

Validating Predictive Models and Biomarkers of
Radiotherapy Toxicity to Reduce Side-Effects and Improve
Quality of Life in Cancer Survivors



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI



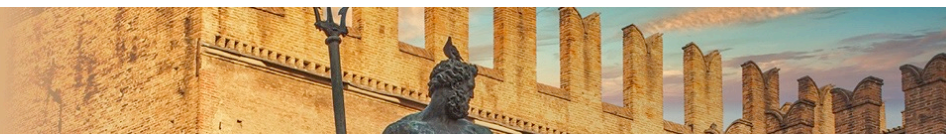
Associazione Italiana
Radioterapia e Oncologia clinica



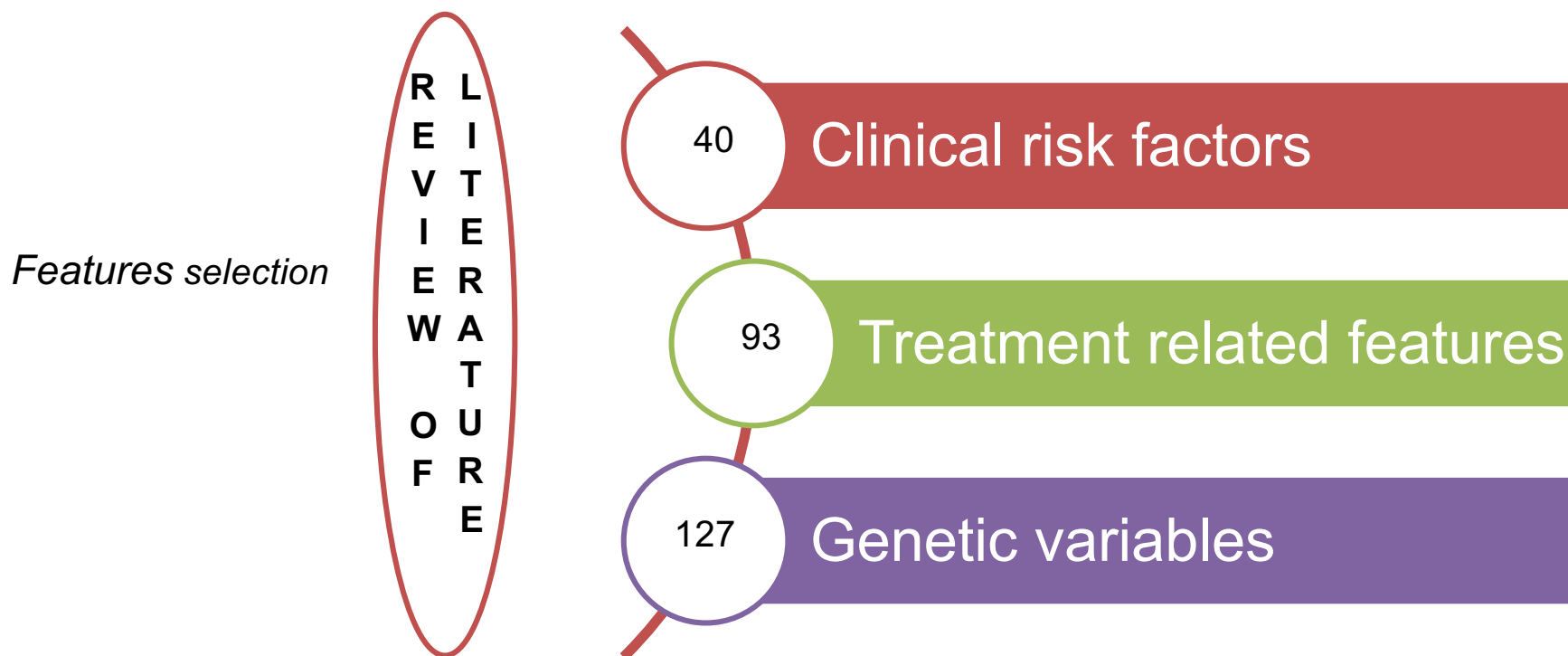
Società Italiana di Radiobiologia



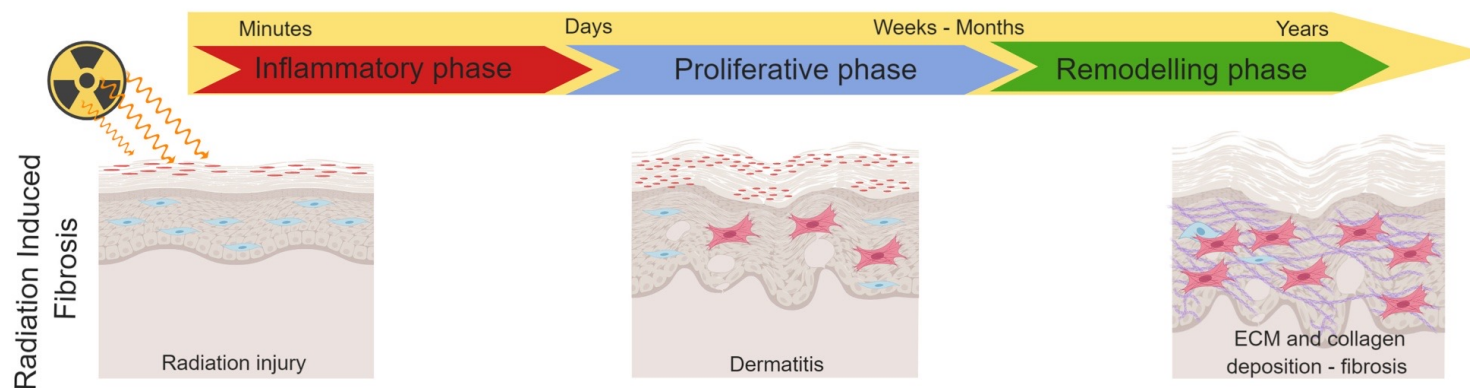
BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI



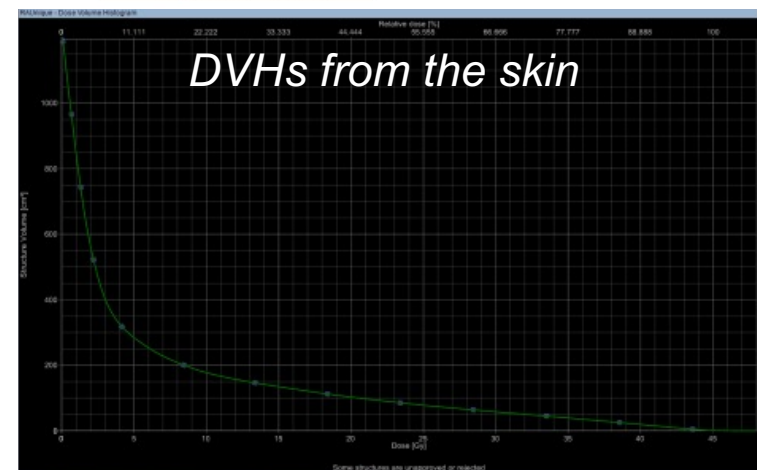
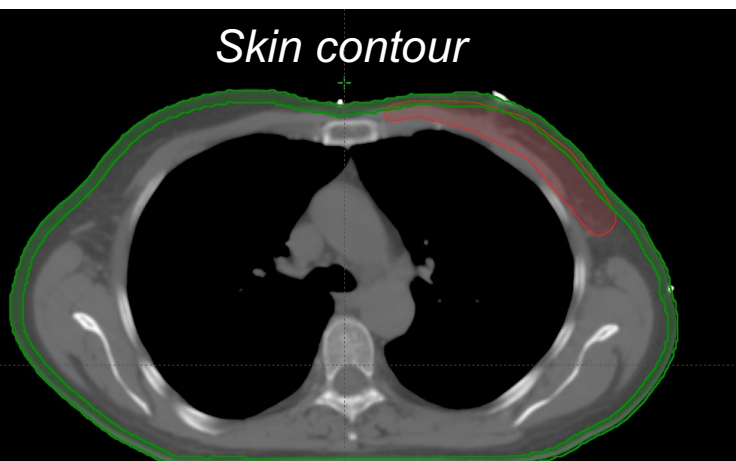
MATERIAL AND METHODS

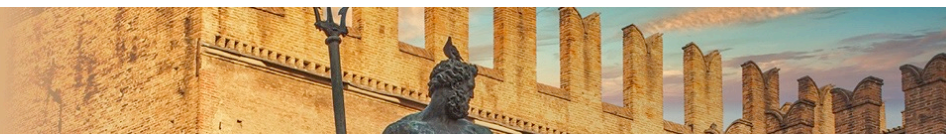


MATERIAL AND METHODS



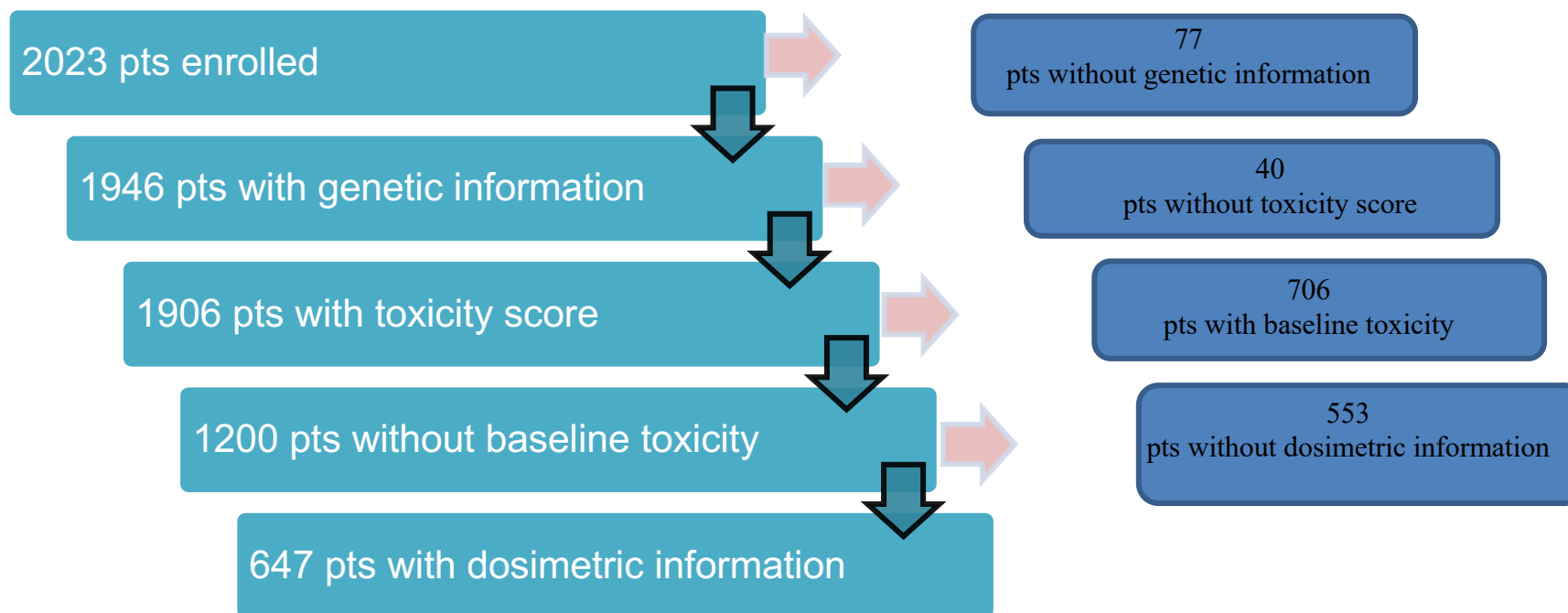
Skin contour



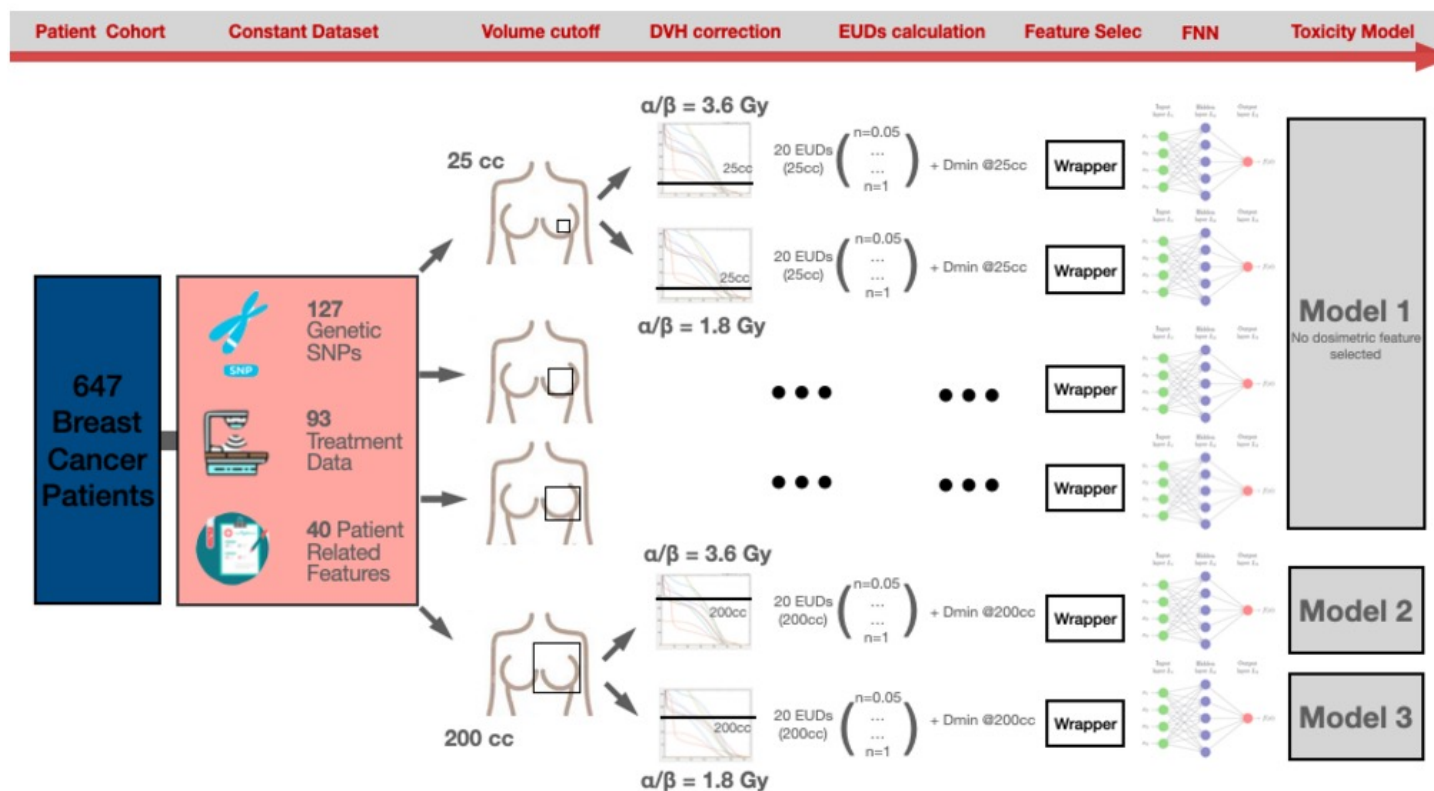
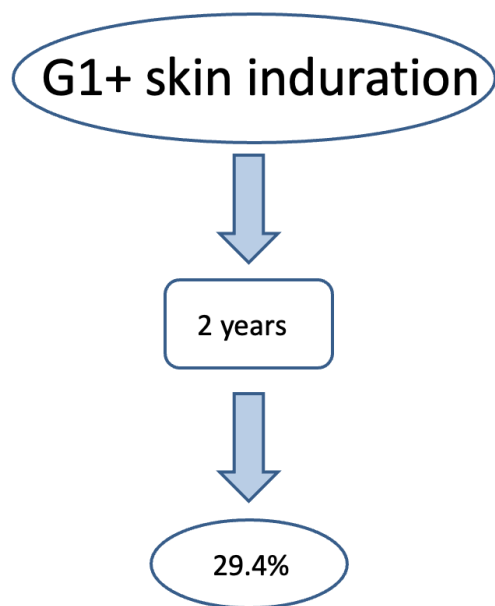


RESULTS

Consort Diagram



Machine learning



Machine learning

Common Features

Genetic Panel

- rs12611088
- rs3213235
- rs1875976
- rs3957336
- rs7791642
- rs1466338

Treatment Features

- Breast CT Volume
- Boost
- Treated Position
- Electron Boost Dose (Gy)
- Photon Energy (MV)
- Aromatase Inhibitor X

Patient factors

- Antidepressant V
- Menopausal status

Model 1
+RT Technique
+Boost diameter (cm)

True Class	Predicted Class	
	0	1
0	394	63
1	43	147

Acc. = 84%
Sens. = 77%
Spec. = 86%

Model 2

+RT Technique
+ Hotspot Quadrant
+ Dmin @200cc

for Skin Sub-DVH of 200 cc
a/b = 3.6 Gy

True Class	Predicted Class	
	0	1
0	405	52
1	51	139

Acc. = 84%
Sens. = 73%
Spec. = 89%

Model 3

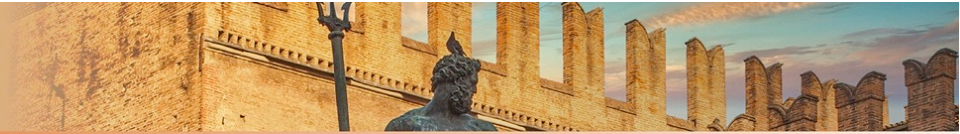
+ EUD (n=0.5)
+Dmin @ 200cc

for Skin Sub-DVH of 200 cc
a/b = 1.8 Gy

True Class	Predicted Class	
	0	1
0	420	37
1	60	130

Acc. = 85%
Sens. = 68%
Spec. = 90%





CONCLUSIONS

Use of ANN models and which one using depends on the clinical intention :

- ❖ Model 1 high sensitivity → to identify low-risk patients → escalation dose
- ❖ Model 2 and 3 high specificity → to identify high-risk patients → de-escalation

In the scenario where RT utilization was increased patients with pT1-2pN1 (1-3 positive lymph nodes), the use of predictive models of toxicity could be helpful to personalize the treatment by evaluating the risk/benefit ratio.

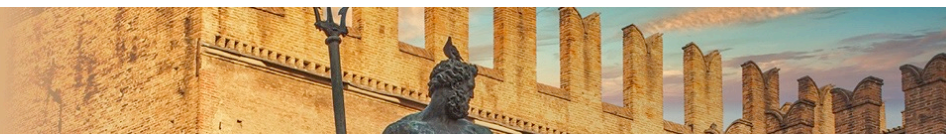
Personalized Medicine



AIRO2022

XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

Radioterapia di precisione per un'oncologia innovativa e sostenibile



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

REQUIRE

Validating Predictive Models and Biomarkers of
Radiotherapy Toxicity to Reduce Side-Effects and Improve
Quality of Life in Cancer Survivors



ERA PerMed



Associazione Italiana
Radioterapia e Oncologia clinica



Società Italiana di Radiobiologia



BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI