Personalised Radiotherapy: Organs at risk: How to individualise?

Dirk De Ruysscher, MD, PhD
Radiation Oncologist
University Hospitals Leuven/ KU Leuven
Leuven, Belgium

UZ Leuven | Herestraat 49 B - 3000 Leuven | www.uzleuven.be tel. +32 16 33 22 11 | UNIVERSITY HOSPITALS LEUVEN

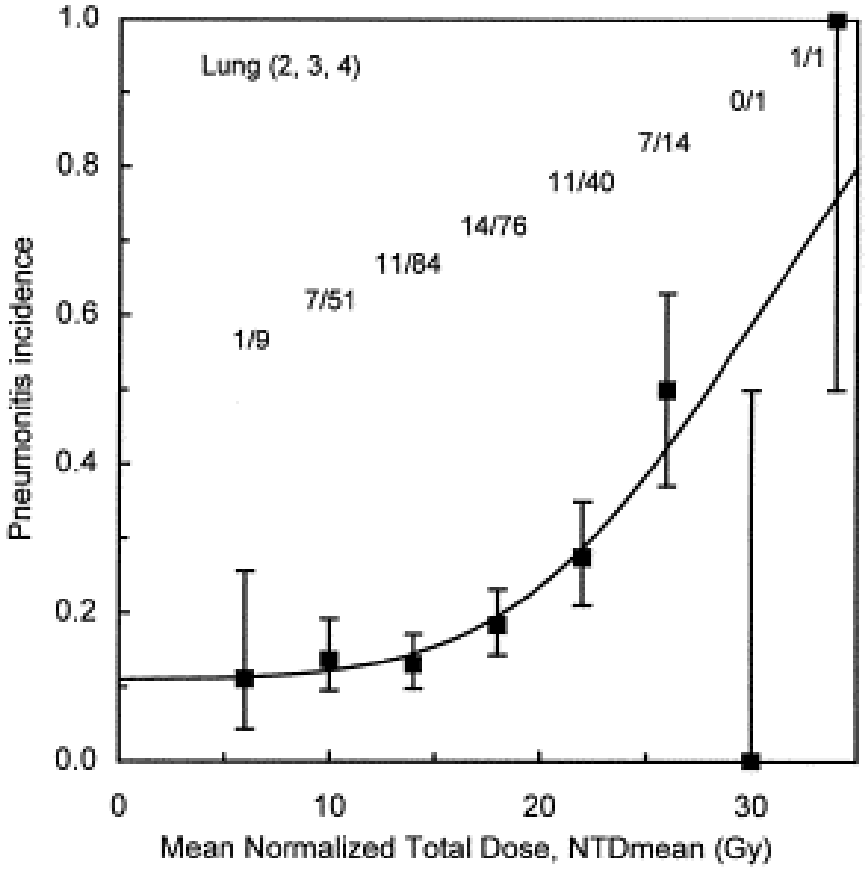
Possible ways to individualise

1. Physical (dose-volume) parameters
2. Characteristics of OAR on imaging
3. Genetics (“Radiogenomics”)

Possible ways to individualise

1. Physical (dose-volume) parameters
2. Characteristics of OAR on imaging
3. Genetics (“Radiogenomics”)

Dose-effect for RILD



Maximal

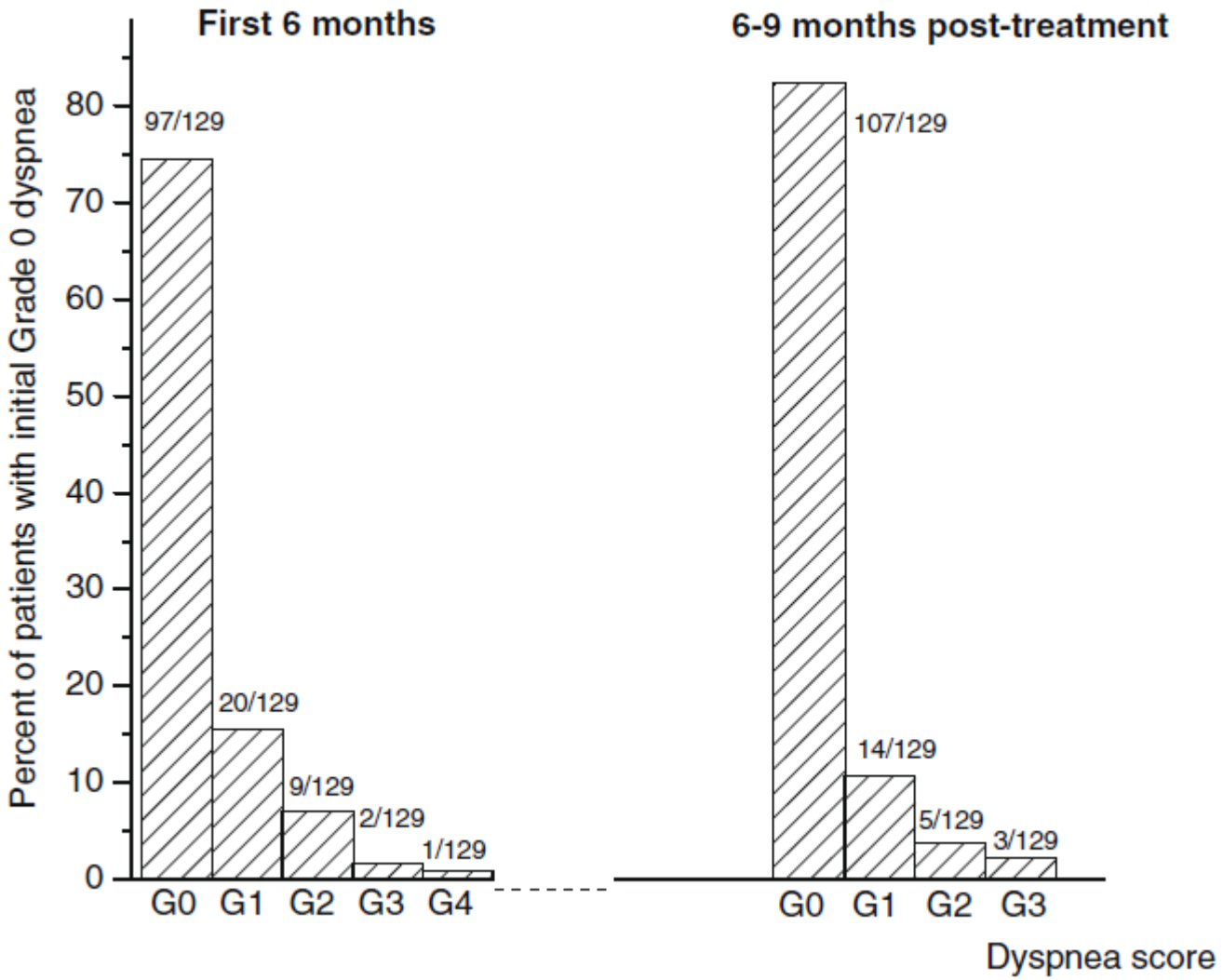
MLD = 20 Gy

V_{20} = 35 %

Below MLD = 20 Gy and V_{20} = 35 % no clear dose-response relation

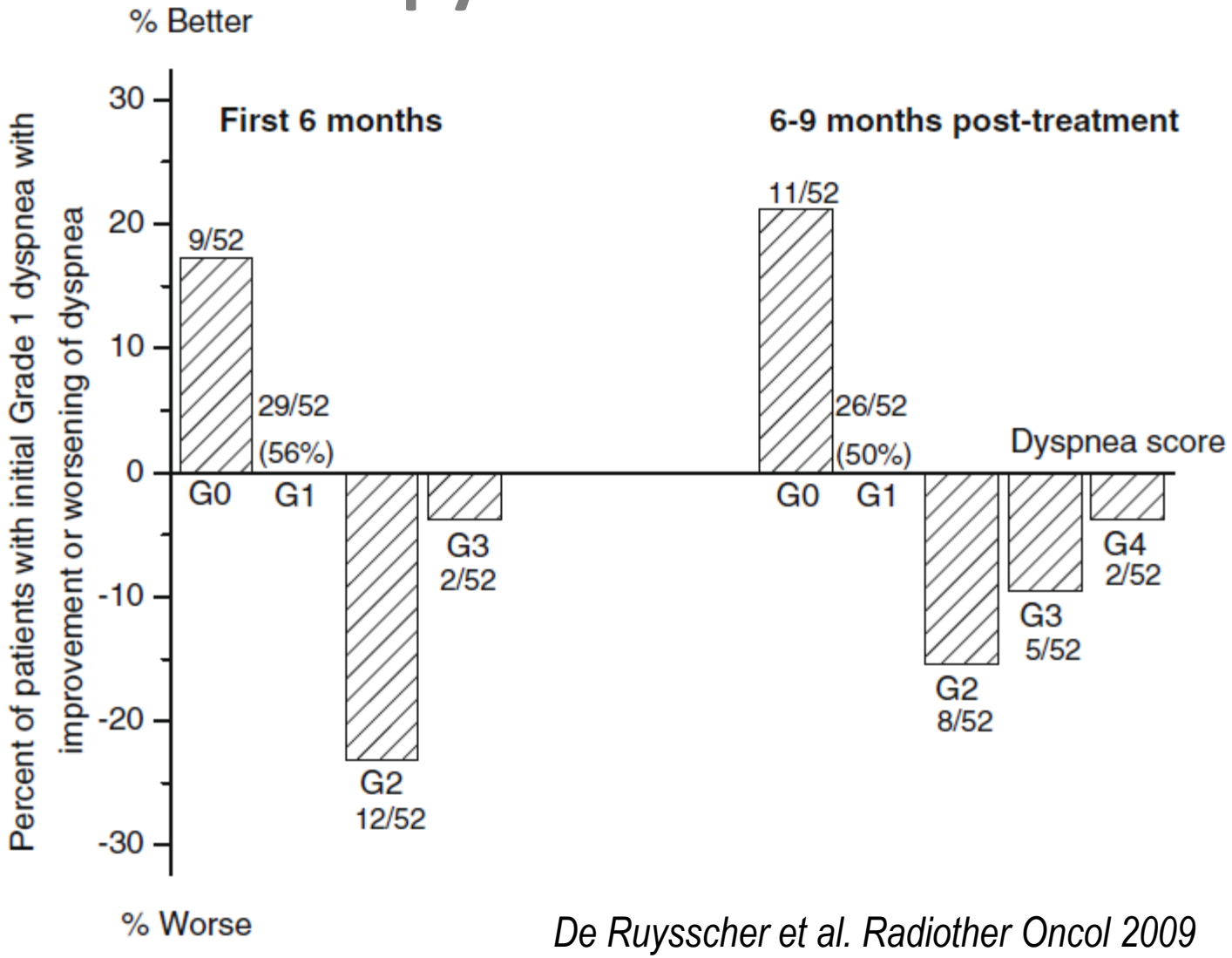
Kwa et al. Int J Radiat Oncol Biol Phys 1998; Dehing et al. Radiother Oncol 2009

Dyspnea evolution after radiotherapy: No baseline dyspnea



De Ruysscher et al. Radiother Oncol 2009

Dyspnea evolution after radiotherapy: Baseline dyspnea grade 1: 20 % no dyspnea after radiotherapy



De Ruysscher et al. Radiother Oncol 2009

Parameters related to RILD

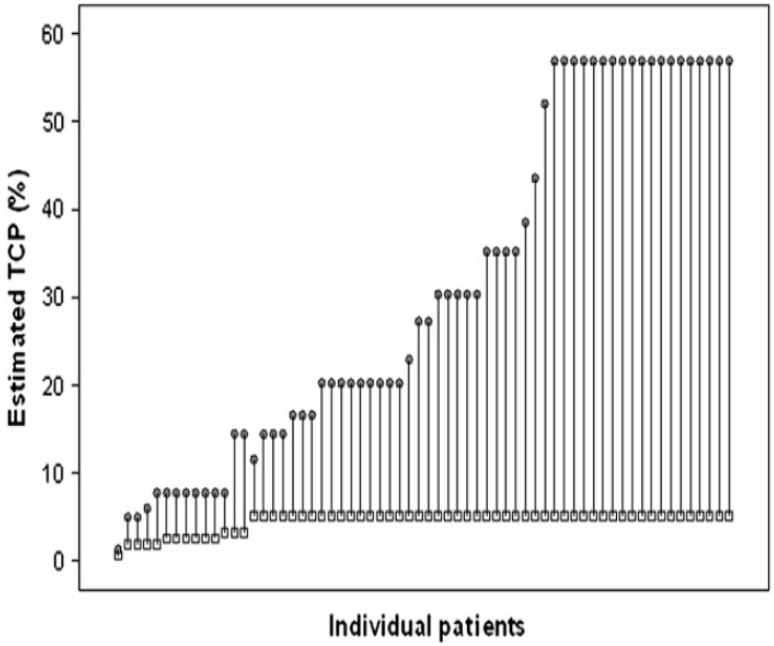
- **NOT**: concurrent administration of cisplatin, vinorelbine, etoposide; careful with docetaxel
- NTCP models
- DVH parameters (highly correlated with each other)
  - Mean dose
  - V_{20}
  - V_5
  - Smoking: *less* RILD

De Ruysscher et al. J Clin Oncol 2010

Palma DA et al. Int J Radiat Oncol Biol Phys 2013

INDividualised Accelerated Radiotherapy (INDAR)

- Escalate the dose to the maximum tolerance
- Delivered in a short overall treatment time
- Directed to areas that are 18F-deoxyglucose (FDG) positive



Van der Wel et al. Int J Radiat Oncol Biol Phys 2005

De Ruysscher et al. Radiother Oncol 2005

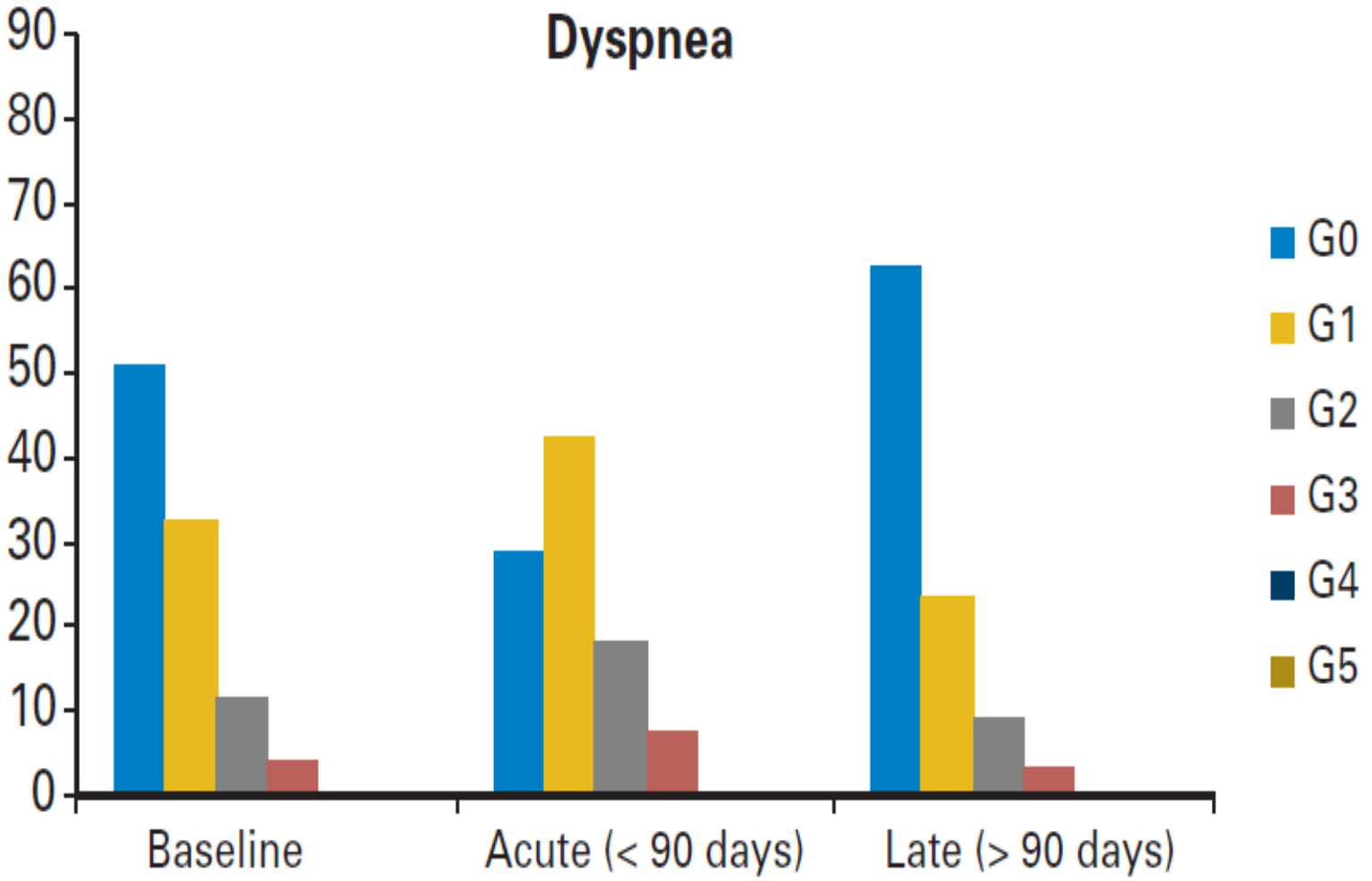
De Ruysscher et al. Int J Radiat Oncol Biol Phys 2005

De Ruysscher et al. Int J Radiat Oncol Biol Phys 2008

Van Baardwijk et al.
Int J Radiat Oncol Biol Phys 2008

Van Baardwijk et al.
Int J Radiat Oncol Biol Phys 2008

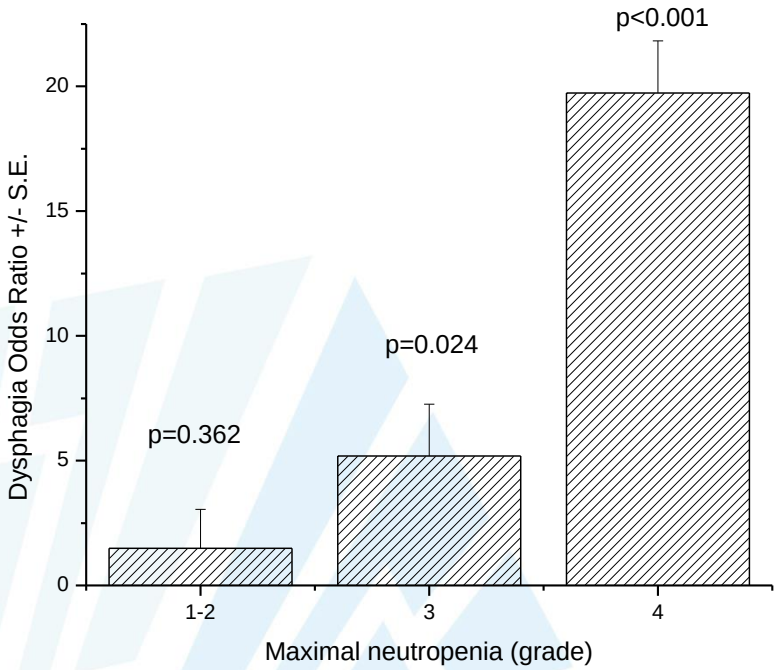
Dyspnea evolution after individualised radiotherapy: 10 % less patients with dyspnea

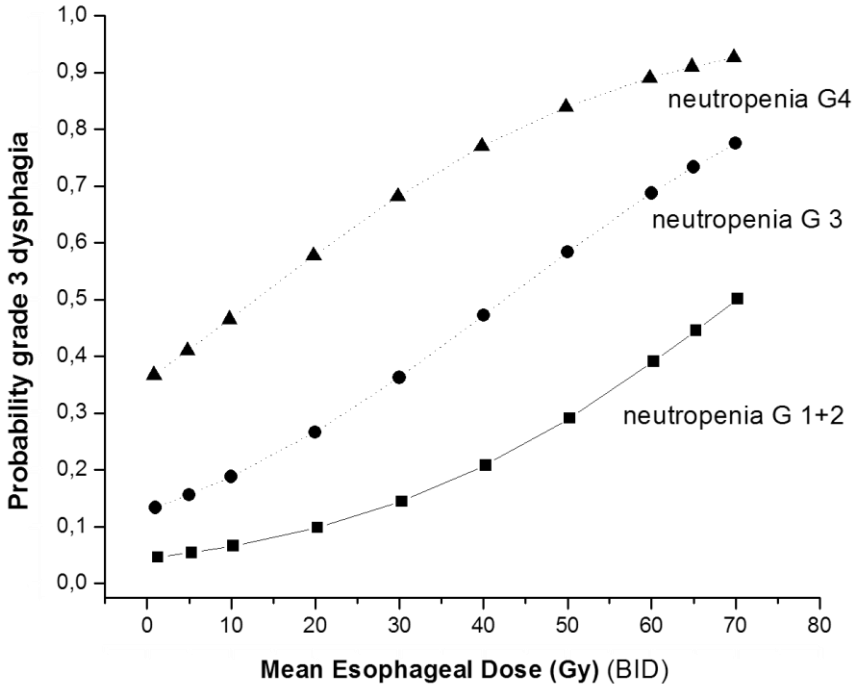


van Baardwijk et al. J Clin Oncol 2010

Correlation between acute esophagitis and neutropenia.

n=328

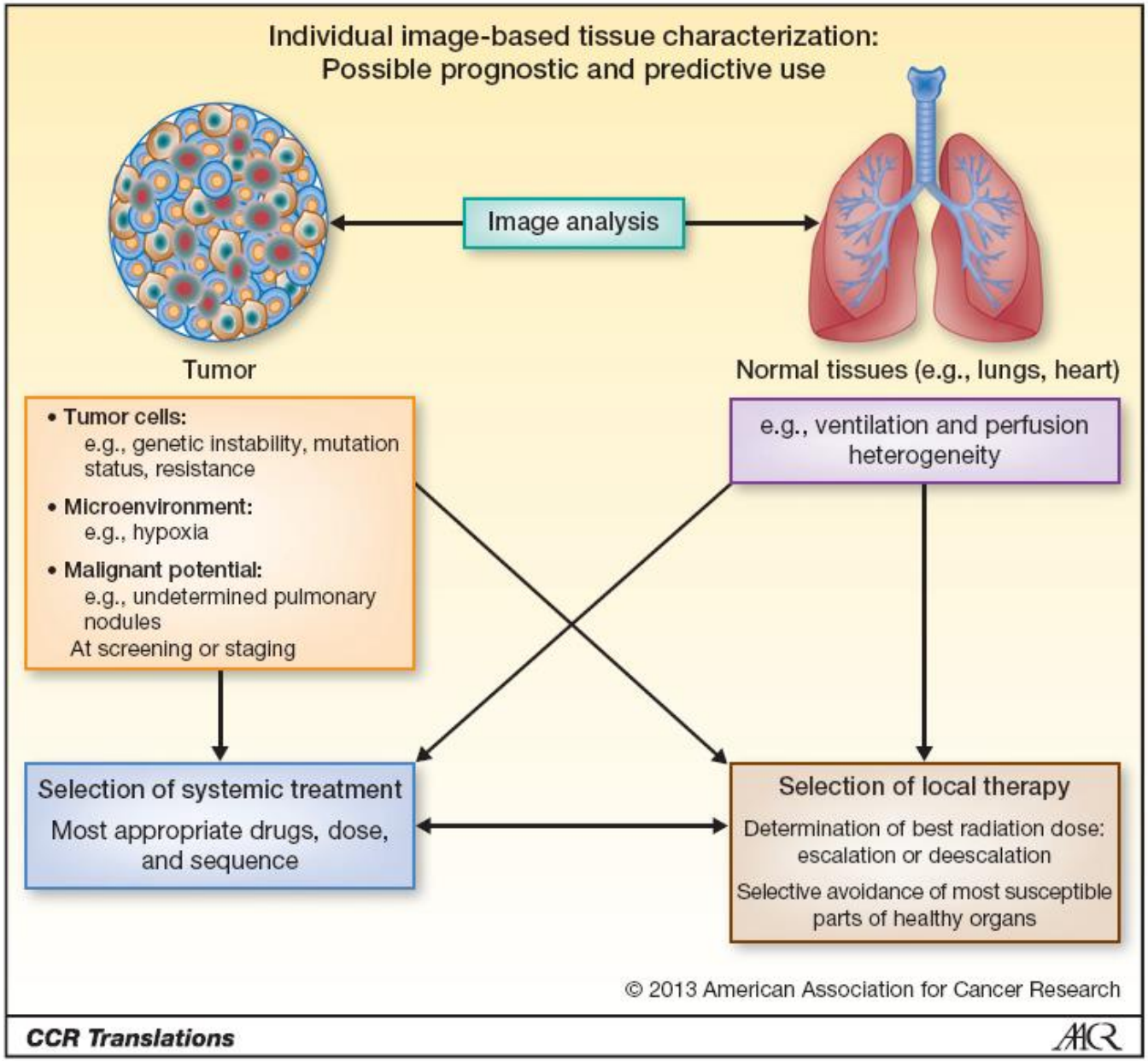




De Ruysscher et al. Ann Oncol 2007

Possible ways to individualise

1. Physical (dose-volume) parameters
2. Characteristics of OAR on imaging
3. Genetics (“Radiogenomics”)

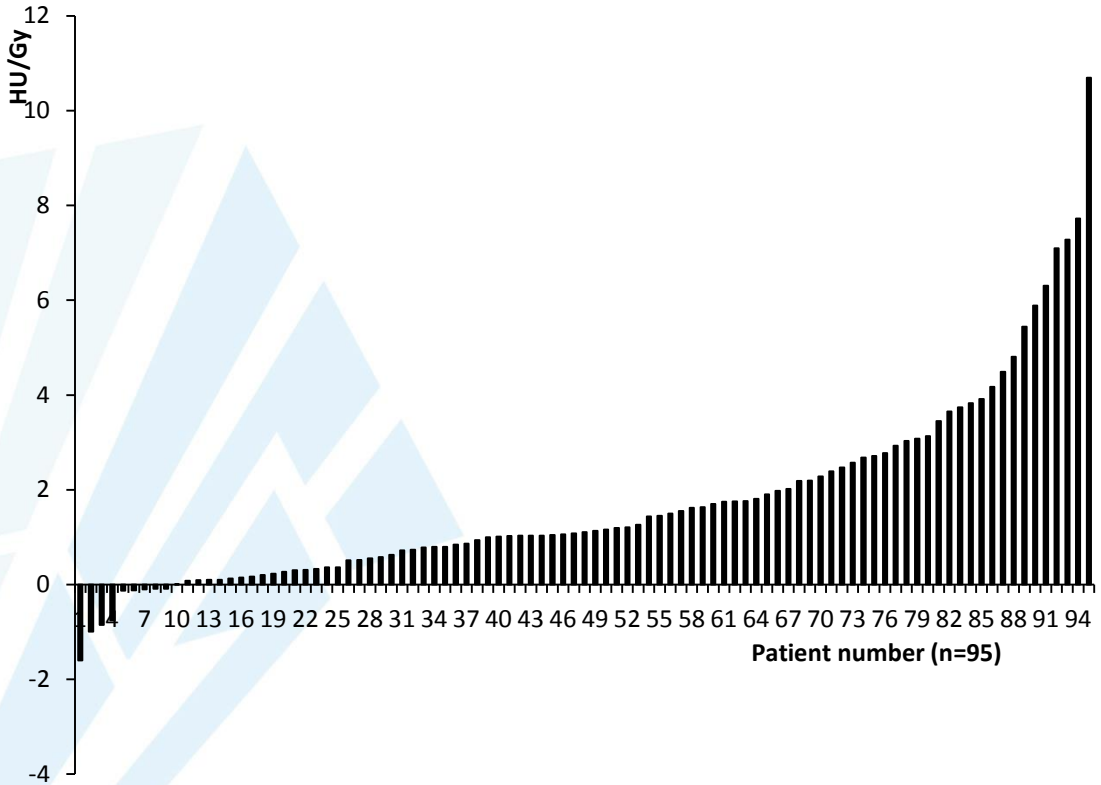


De Ruysscher D. Clin Cancer Res 2013

HU changes 3 months after radiotherapy

Change in Hounsfield Units (HU_{3M}-HU_0) per Gy for each individual patient:

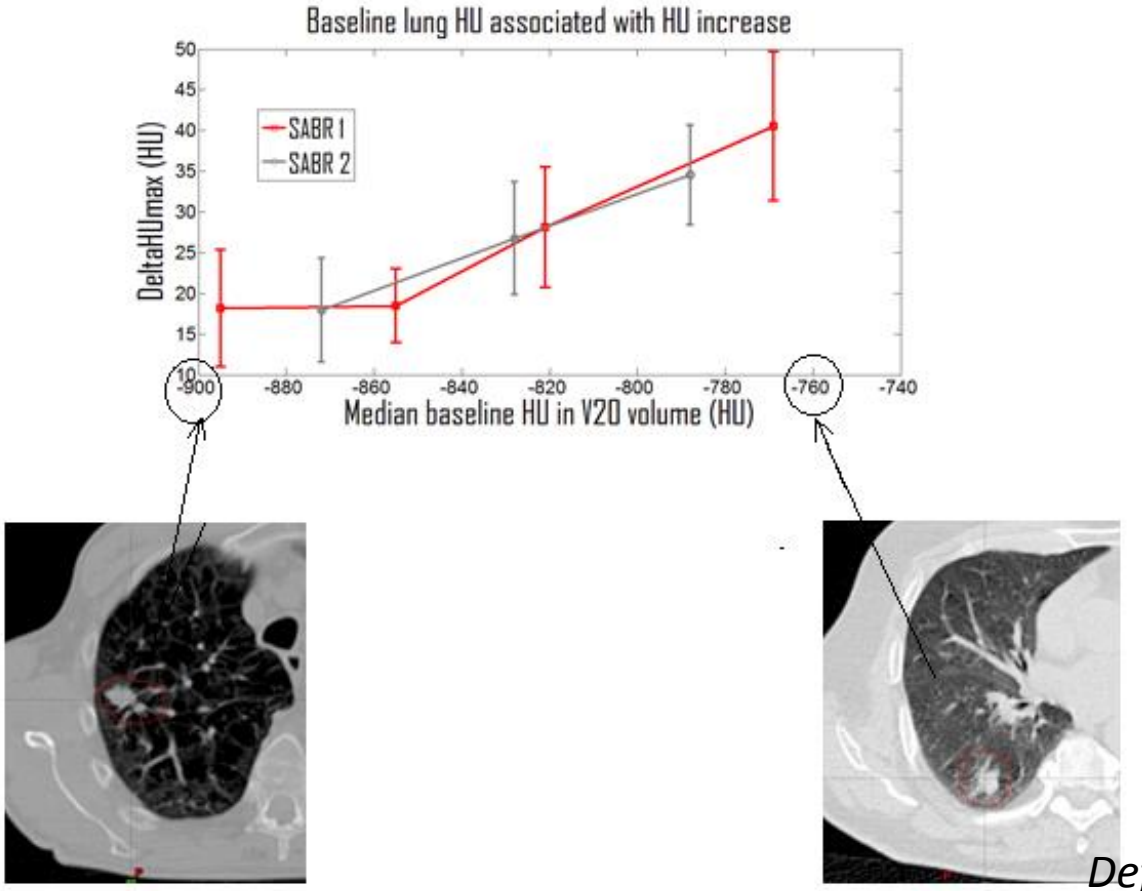
- continuous scale
- >10-fold difference in radiosensitivity



De Ruysscher et al. Acta Oncol 2013

Individual dose-response relation

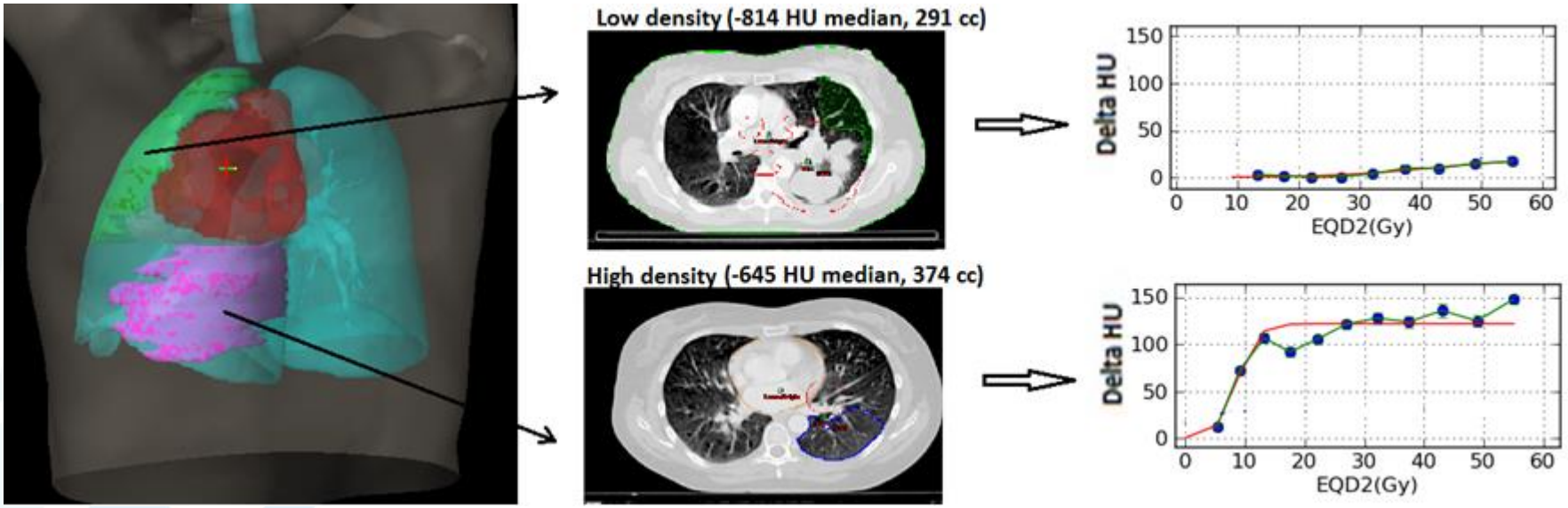
- SABR datasets
  - Saturation level ΔHU_{max} is a function of the baseline HU_0
  - Significant in SABR1 group (multivariate p<0.001)
  - AUC=0.77 for model predicting ΔHU_{max} >30HU



Defraene et al. submitted

Heterogeneity within one lung

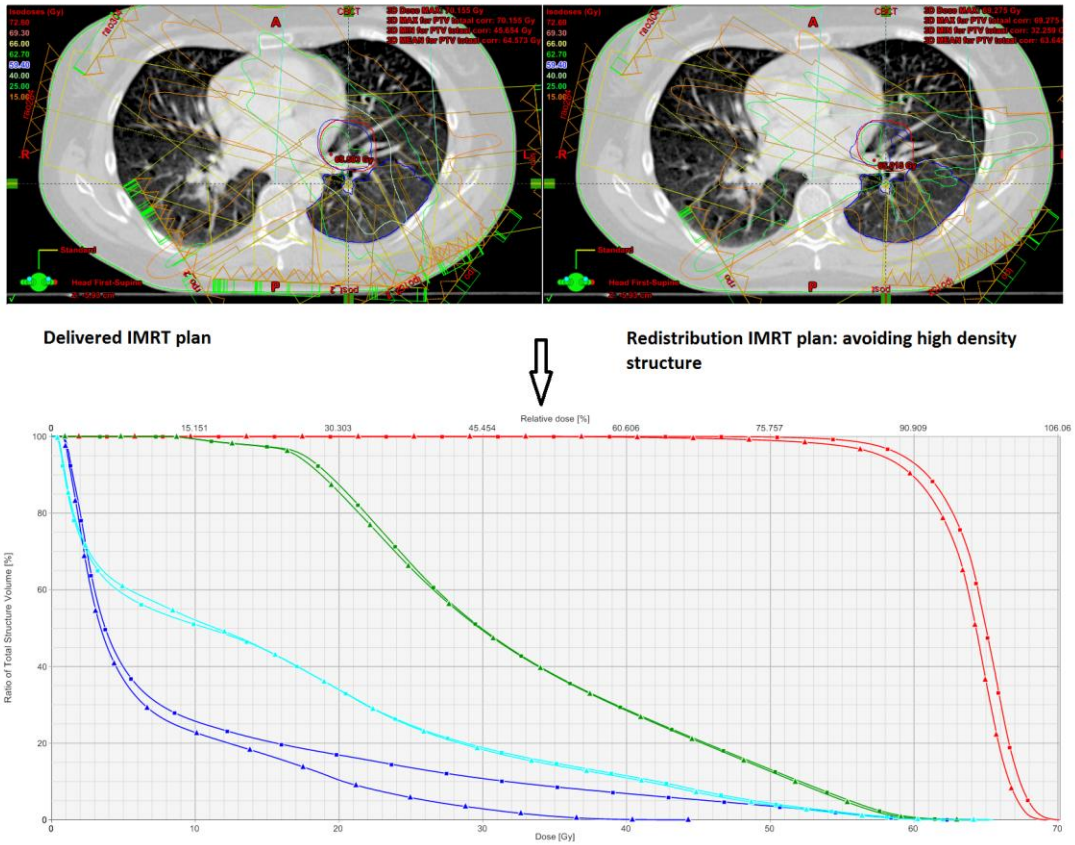
- Concept
  - Hypothesis: denser regions more prone to damage
  - Manually defined subregions maximally differing in density on planning CT
  - Lower lobe more radiosensitive



Defraene et al. submitted

Redistribution of radiation dose

- Maximally sparing high-risk subregion
- Same PTV and OAR constraints (identical MLD!)



- High-risk subregion: mean dose reduction of 6.6 Gy

Possible ways to individualise

1. Physical (dose-volume) parameters
2. Characteristics of OAR on imaging
3. Genetics (“Radiogenomics”)

Individual susceptibility on a genetic basis? Conflicting results in the past

VOLUME 27 · NUMBER 20 · JULY 10 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Single Nucleotide Polymorphism at rs1982073:T869C of the *TGFβ1* Gene Is Associated With the Risk of Radiation Pneumonitis in Patients With Non–Small-Cell Lung Cancer Treated With Definitive Radiotherapy

Xianglin Yuan, Zhongxing Liao, Zhensheng Liu, Li-E Wang, Susan L. Tucker, Li Mao, Xin Shelley Wang, Mary Martel, Ritsuko Komaki, James D. Cox, Luka Milas, and Qingyi Wei

Radiotherapy and Oncology 105 (2012) 296–298

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

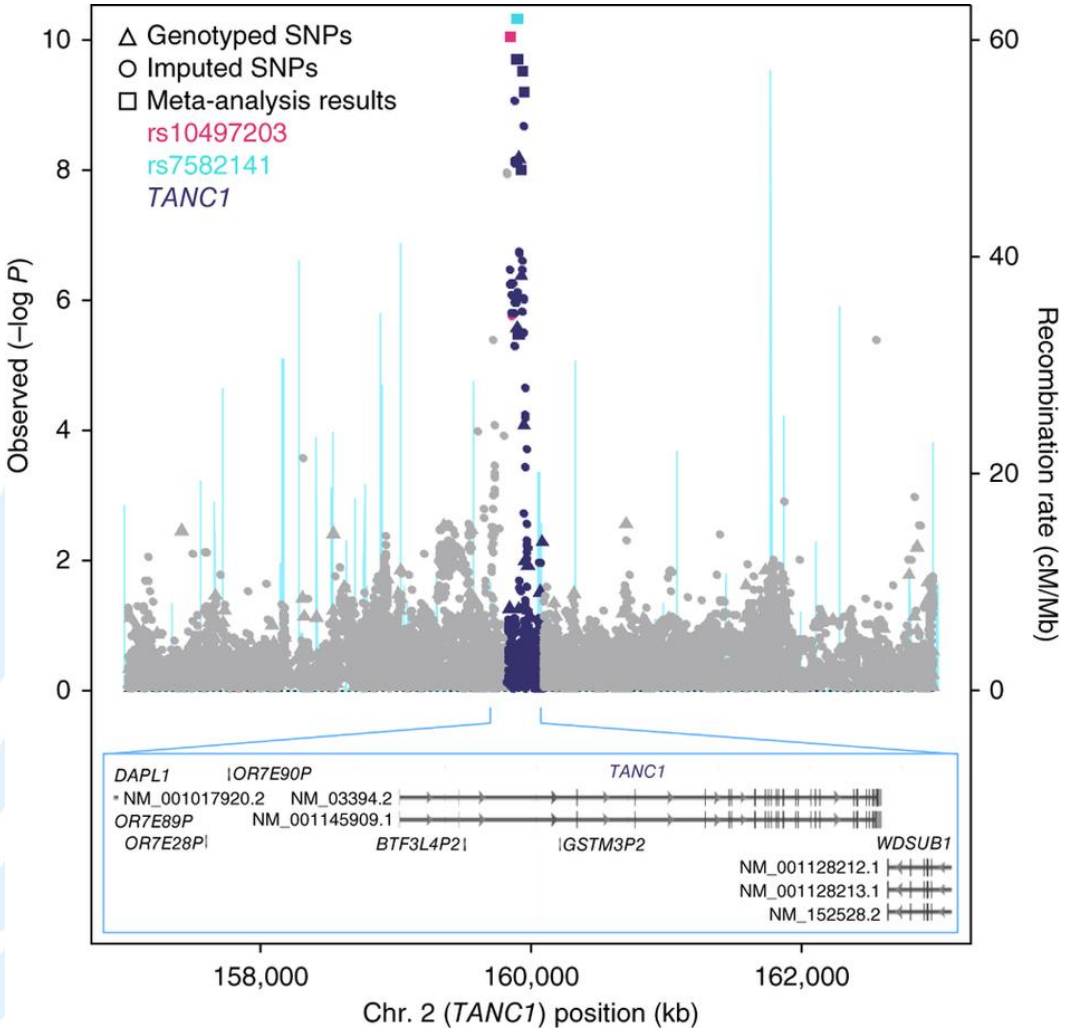
Clinical radiogenomics

No association between TGF-β1 polymorphisms and radiation-induced lung toxicity in a European cohort of lung cancer patients

An M. Voets [a], Cary Oberije [a], Robin B. Struijk [a], Bart Reymen [a], Kim De Ruyck [b], Hubert Thierens [b], Katrien Vandecasteele [c], Wilfried De Neve [c], Ruud Houben [a], Dirk De Ruysscher [a], Hubert J.M. Smeets [a], Philippe Lambin [a,*]

[a] *Maastricht University, The Netherlands;* [b] *Ghent University; and* [c] *Ghent University Hospital, Belgium*

At present: Robust results (not yet RILD)

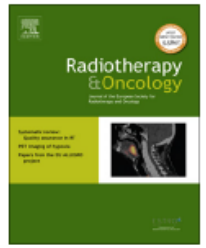


Fachal L et al. Nat Gen 2014

Contents lists available at ScienceDirect

Radiotherapy and Oncology

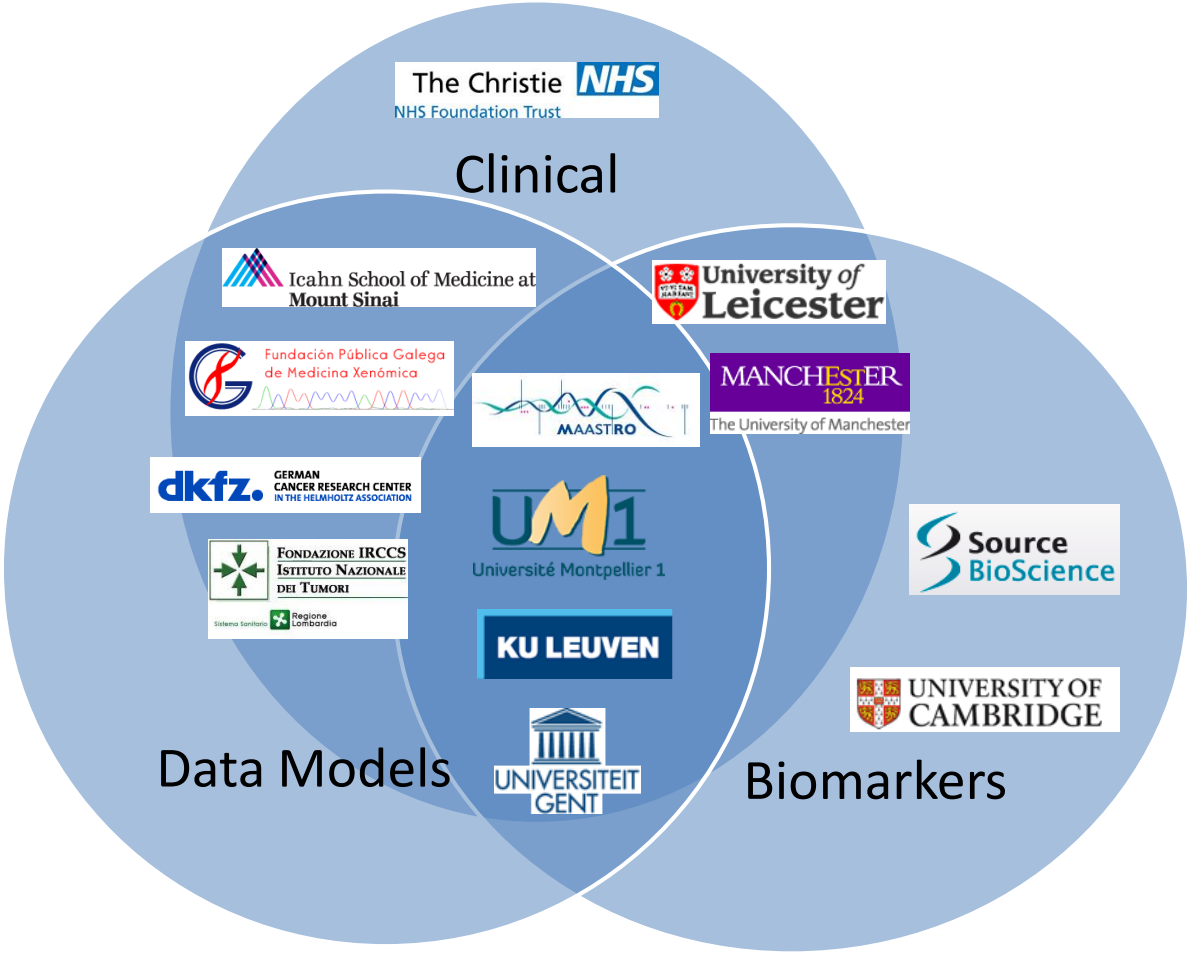
journal homepage: www.thegreenjournal.com



Review

STROGAR – STrengthening the Reporting Of Genetic Association studies in Radiogenomics

Sarah L. Kerns [a,b,c], Dirk de Ruysscher [d], Christian N. Andreassen [e], David Azria [f], Gillian C. Barnett [g], Jenny Chang-Claude [h], Susan Davidson [i], Joseph O. Deasy [j], Alison M. Dunning [k], Harry Ostrer [b,c], Barry S. Rosenstein [a], Catharine M.L. West [l], Søren M. Bentzen [m,*]


The Christie NHS
NHS Foundation Trust
Clinical
Icahn School of Medicine at Mount Sinai
University of Leicester
Fundación Pública Galega de Medicina Xenómica
MAASTRO
MANCHESTER 1824
The University of Manchester
dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION
UM1
Université Montpellier 1
Source BioScience
FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI
Regione Lombardia
KU LEUVEN
UNIVERSITY OF CAMBRIDGE
UNIVERSITEIT GENT
Data Models
Biomarkers

Great future …