RECIST

http://www.eortc.org/recist/

# Imaging data and RECIST criteria for the evaluation of tumor response

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08/04/2016

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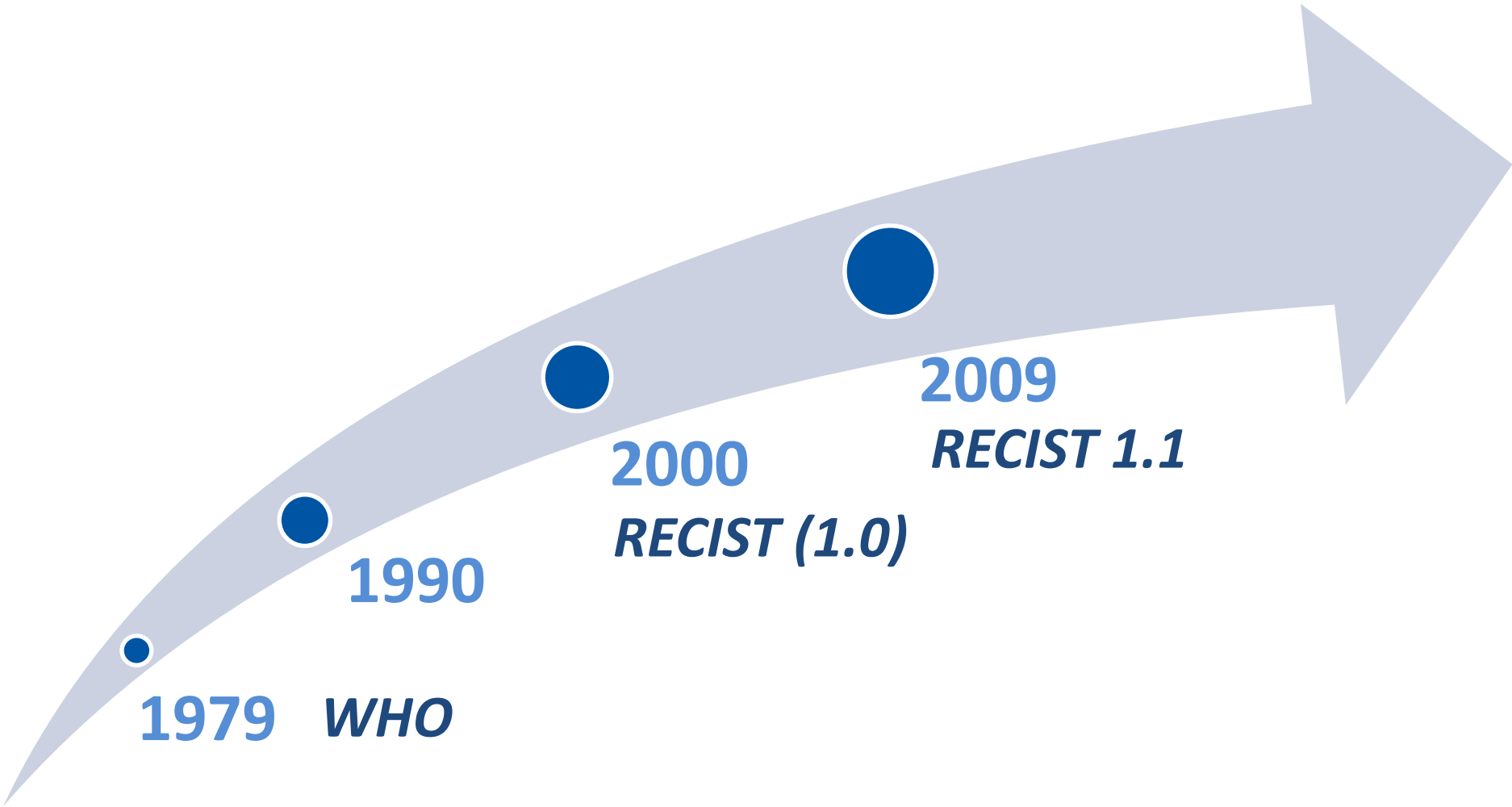
# A little bit of history



# Response Evaluation Criteria in Solid Tumors (RECIST)

*Therasse et al JNCI 2000*

- Intended for use in clinical trials with primary endpoint of objective response
- Measurable lesion >= 20 mm (10 if spiral CT)
- Unidimensional assessment: Tumor burden assessed by summing longest diameters of all measurable lesions up to 10 (5 per organ)
- Four categories of response: CR*, PR*, SD, PD
- RECIST widely adopted by cooperative groups, industry, academia

* Required confirmation

# Summary:
# What HAS changed in RECIST 1.1

| | RECIST 1.0 | RECIST 1.1 |
|---|---|---|
| Measuring tumor burden | 10 targets<br>5 per organ | For response: 5 targets<br>(2 per organ) |
| Lymph node | Measure long axis as for other lesions.<br>Silent on normal size | Measure short axis.<br>Define normal size. |
| Progression definition | 20% increase in sum | 20% increase and at least 5 mm absolute increase |
| Non-measurable disease PD | "must be unequivocal" | Expanded definition to convey impact on overall burden of disease. Examples. |
| Confirmation | required | Required when response primary endpoint—but not PFS |
| New lesions | -- | New section which includes comment on FDG PET interpretation |

# RECIST : a standardized tool

Simple, objective and uniform

- Across tumour types
- Across sites participating in a clinical trial
- Across clinical trials

While some diversifications can be implemented, RECIST cannot accommodate for all possible protocol specificities
*(Verweij et al EJC 2009)*

Criticisms of RECIST 1.1 include

- not adapted to specific tumor type
- purely based on anatomical burden (“size”)
- there are more refined imaging techniques
- not validated for targeted agents

# The road ahead

## Targeted agents:

- Different mode of action not necessarily leading to obvious tumor shrinkage
- We compiled a database of **50 clinical trials** (academia and industry) on approx **23.000 patients**

## Advanced imaging techniques – FDG-PET:

- Playing an important role in clinical practice, but results from clinical trials are difficult to compare. Lack of harmonization is an important obstacle
- We pooled data from **9 studies** (academia and industry) on approx **200 patients** to study the sources of heterogeneity of FDG-PET by looking at repeatability data
- We compiled a database of **18 clinical trials** (academia and industry) on approx **1.000 patients** to study its added value to the current RECIST

## Immunotherapy

- Immune-related response patterns may challenge the classical concepts of progression
- RECIST Working Group is trying to initiate a high-level collaboration with partners from academia, industry and regulatory to address this

# What do we need for a new version of RECIST?

*Sargent EJC 2009*

- Some biological rationale

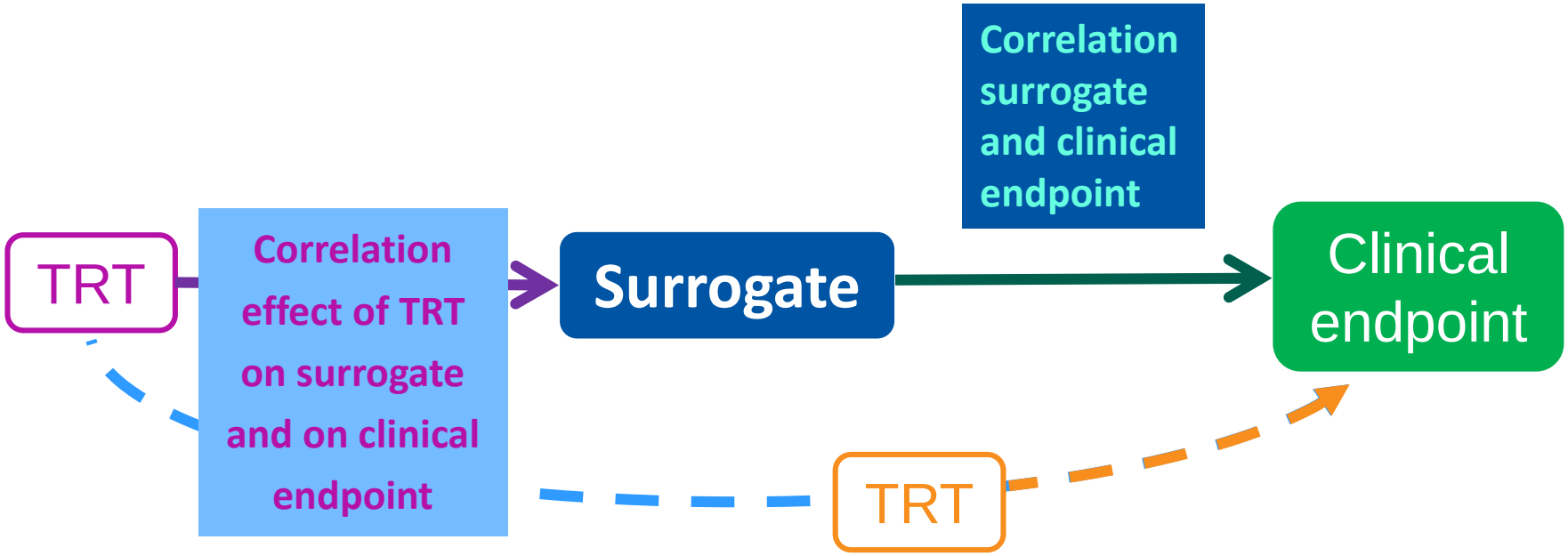
- Standardized protocol for interpreting measurements
  - Understanding sources of variability: imaging methodology, reader variability, patient heterogeneity, role of missing data

- Understanding of its limitation(s)

- Evidence of correlation with a true endpoint
  - Patient benefit (PRO?, OS?)

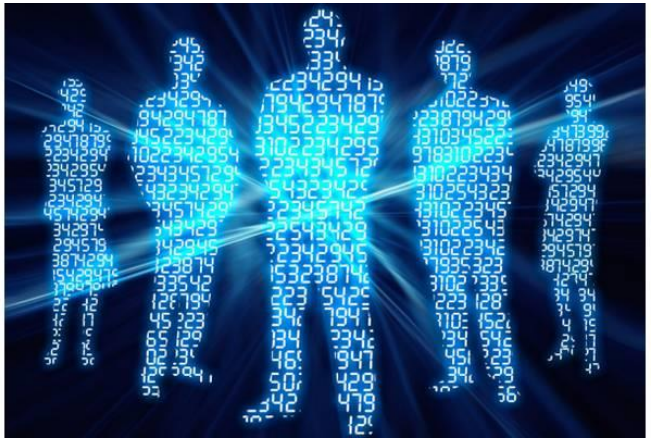
  There is no real 'consistent' gold standard

# Evidence of correlation: surrogacy?




When an event on the “surrogate” leads to a change in treatment decision, the relationship will be obscured

# What else is needed?



Collecting data for validation requires time, persistence and a lot (!) of data sharing negotiation

- Patient privacy
- Patient data anonymization
  - Digital images vs reported data
  - Resources
- Agreements not to report/repeat study level analyses

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*The future of cancer therapy*

# The clinical trial data as limiting factor

- **Elephant number 1: the chicken and egg issue of progression**
  - Sharing of scanned results starts with the study and stops at RECIST PD
  - Typically in advanced disease setting, this leaves us with few observations
  - … so we cannot assess less stringent definitions of "PD" because of lack of data

- **Elephant number 2: incomplete data.** In the RECIST 1.1 data warehouse
  - for 14% of patients no tumor lesion measurements provided at time of non-target progressive disease or new lesions
  - for 10% of patients measurements incomplete for target lesions at time of progression (i.e. only progressive lesion reported) resulting in a non-evaluable result

# The clinical trial data as limiting factor

- **Elephant number 3: the role of non-target and new lesions?**

Table 1
Reason to stop follow-up of target lesion measurements (note that categories are not mutually exclusive).

| Reason | Breast cancer ($n = 1141$) | Lung cancer ($n = 1853$) | Colorectal cancer ($n = 734$) |
|---|---|---|---|
| Occurrence of a new lesion | 507 (44%) | 530 (29%) | 309 (42%) |
| Non-target progressive disease | 280 (25%) | 505 (27%) | 247 (34%) |
| Death | 4 (0.4%) | 1 (0.1%) | 0 |
| Lost to follow-up[‡] | 28 (2.5%) | 8 (0.4%) | 3 (0.4%) |
| Progression of target lesions[§] | 437 (38%) | 961 (52%) | 417 (57%) |
| End of follow-up[†] | 320 (28%) | 552 (30%) | 197 (27%) |

[‡] Last measurement reported is also last known date to be alive.
[†] Defined as none of the above.
[§] Progression = increase from smallest sum of target lesions.

*Litière et al. EJC 2014*

# Final remark

- New technologies should be incorporated rapidly but this should be based on evaluation of fairly massive data (i.e. validated)
- Therefore, in order to validate new biomarkers and/or response criteria we need the community to pull together to
  - ensure standardization and harmonization of the data collection across different sites, and
  - pool the data in the context of large international collaborative efforts such as RECIST

# Acknowledgements

RECIST

http://www.eortc.org/recist/


- Jan Bogaerts
- Elizabeth de Vries
- Lesley Seymour

- Lalitha Shankar
- Larry Schwartz
- and the other members of the RECIST Working Group
- with special thanks also to
  - Sandra Collette
  - Gaëlle Isaac
  - Zeina Tayah

# Thank you

http://www.eortc.org/recist/