

Stockholm University
Centre for Radiation Protection Research



SWEDISH NATIONAL COMMITTEE FOR
RADIATION PROTECTION RESEARCH
THE ROYAL SWEDISH ACADEMY OF SCIENCES

Individual Response to Ionizing Radiation



RADIUMHEMMETS
FORSKNINGSFONDER





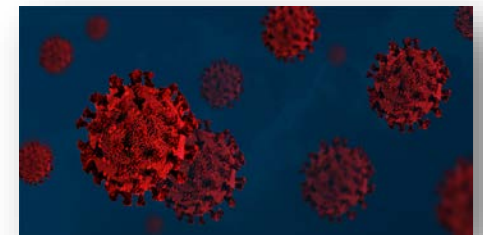
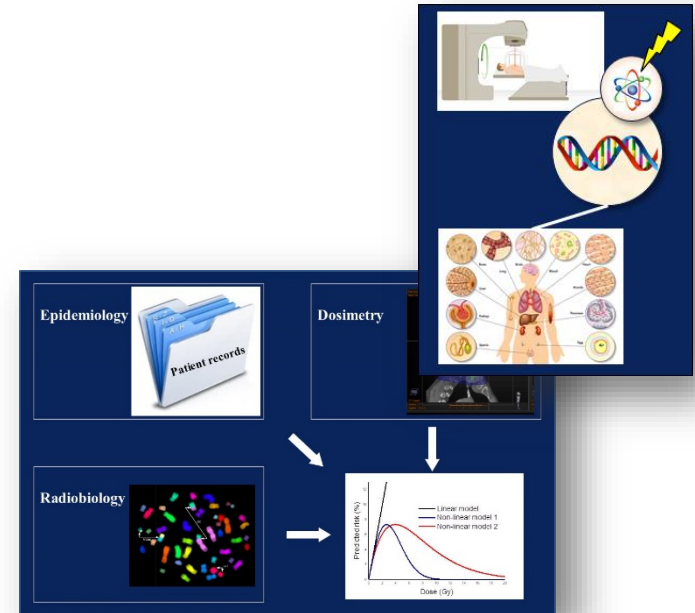
Stockholm workshops series

2014 *Biological basis of radiotherapy:
where do we stand?*

2016 *Risk of second cancer following
radiotherapy*

2018 *Current challenges of patient re-irradiation*

2020 *Individual response to ionizing radiation*





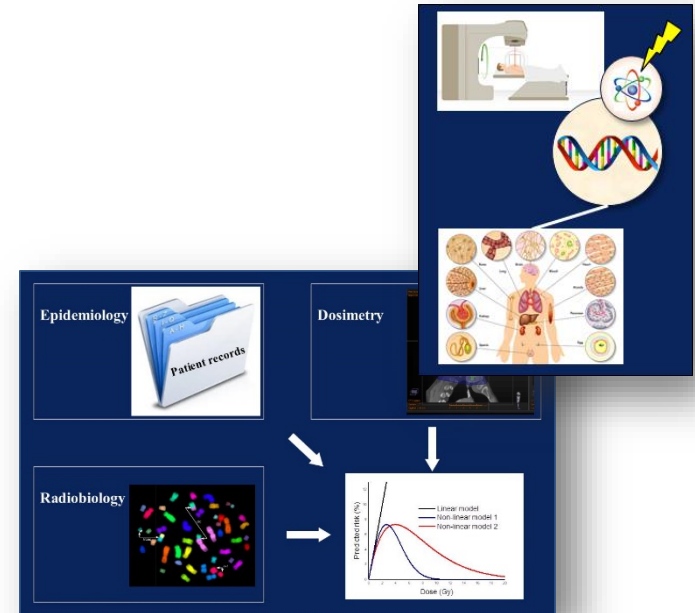
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2022 *Individual response to ionizing radiation*





Individual response to ionizing radiation

Thursday September 1 2022 – Normal tissue effect		
Introductory lecture		
09:00-09:30	Can and should radiological protection be individualised?	<i>Simon Bouffler</i>
Session 1 – Factors influencing the risk of tissue effects <i>Chairperson: Pamela Akuwudike</i>		
09:30-10:00	Incidence and mechanisms of normal tissue reactions to radiotherapy	<i>Claudia Rübe</i>
10:00 – 10:30 Coffee break		
10:30-11:00	Use of GWAS to predict individual patient response	<i>Catharine West</i>
11:00-11:30	Functional assays to predict individual patient response	<i>Michel Bourguignon</i>
11:30-12:00	How much can radiotherapy benefit from biomarkers of normal tissue response to radiotherapy?	<i>Navita Somaiah</i>
12:00-13:00 Lunch break		
Session 2 - Factors influencing the risk of late and stochastic effects <i>Chairperson: Milagrosa Lopez-Riego</i>		
13:00-13:30	Genetic factors influencing individual risk of radiogenic cancer	<i>Preetha Rajaraman</i>
13:30-14:00	Life-style factors influencing individual risk of radiogenic cancer and risk transfer between populations	<i>Andrzej Wojcik</i>
14:00-14:30	Age-related variation in radiogenic cancer risk (including childhood CT studies)	<i>Michael Hauptmann</i>
14:30-15:00 Coffee break		
15:00-15:30	Sex-related variation in radiogenic cancer risk	<i>Kyoji Furukawa</i>
15:30-16:00	Individual risk of radiogenic non-cancer effects	<i>Nobuyuki Hamada</i>
16:00-17:00	General discussion	<i>Moderator: Simon Bouffler</i>

Normal tissue



Individual response to ionizing radiation

Friday September 2 2022 - Cancer tissue effects		
Introductory lecture		
09:00-09:30	Individual tumour response – current challenges and opportunities	<i>Iuliana Toma-Dasu</i>
Session 3 – Intrinsic tumour response - molecular and genetic assays <i>Chairperson: Mattias Hedman</i>		
09:30-10:00	Radiobiological assays for individual tumour response	<i>Iuliana Toma-Dasu</i>
10:00 – 10:30 Coffee break		
10:30-11:00	Molecular and genetic biomarkers of tumour response	<i>Kristina Viktorsson</i>
11:00-11:30	From <i>in vitro</i> cell line radiosensitivity to the response of <i>in vivo</i> tumours	<i>Anthony Chalmers</i>
11:30-12:00	Individual tumour response and side effects – clinical experience on stereotactic body radiation therapy of thoracic tumours	<i>Karin Lindberg</i>
12:00-13:00 Lunch break		
Session 4 - Individual tumour radiosensitivity assays <i>Chairperson: Emely Kjellsson Lindblom</i>		
13:00-13:30	Role of functional imaging in assessing the individual tumour radiosensitivity	<i>Marta Lazzeroni</i>
13:30-14:00	Genome-based models for individualising the radiotherapy dose	<i>Gabriel O. Sawakuchi</i>
14:00-14:30	Role of radiogenomics in the individualisation of tumour response	<i>Issam El Naqa</i>
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15:00-15:30	Radiobiological modelling of individual radiosensitivity	<i>Alexandru Dasu</i>
15:30-16:00	Individual tumour response to therapy - photons <i>versus</i> particles	<i>Michael Story</i>
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Tumour



Individual response to ionizing radiation

Individual tumour response – current challenges and opportunities

What does it mean “Individual response to ionizing radiation” when we refer to tumours?

Individual tumour response = Tumour radiosensitivity?

Or do we have to look for a systemic response?



Individual tumour response = Tumour radiosensitivity

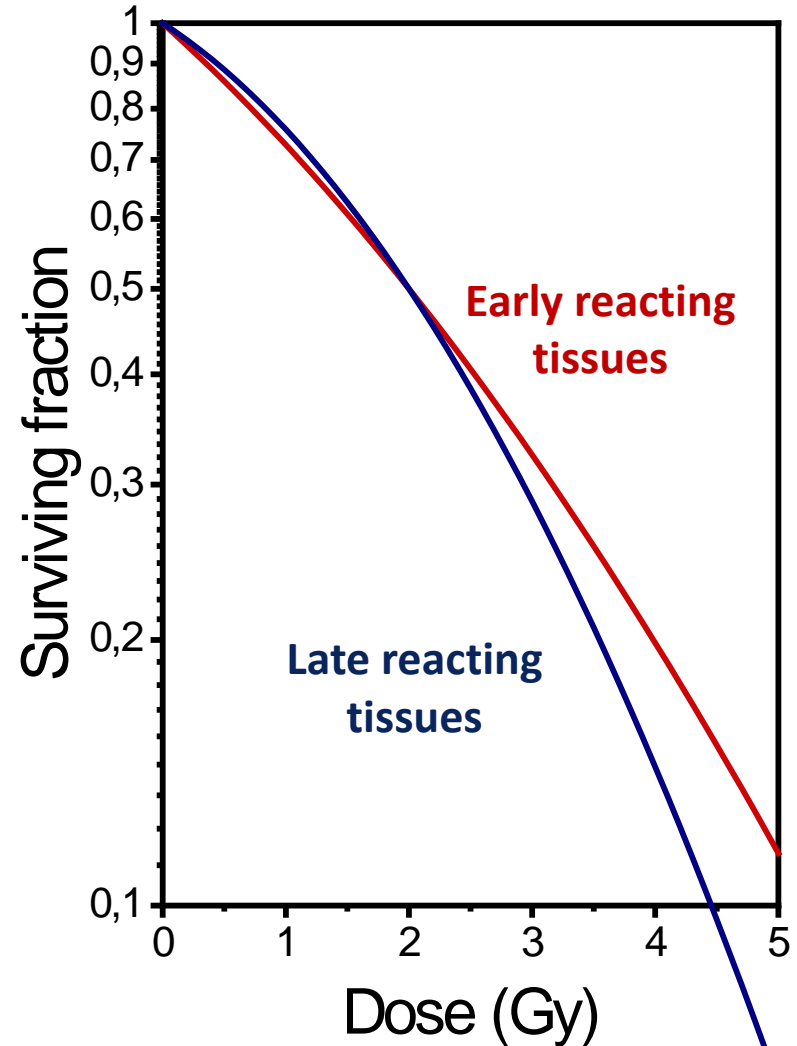
- How can it be determined/measured?
- Knowing it, does it have a *clinical value*?
- What would the future bring?



Tumour radiosensitivity

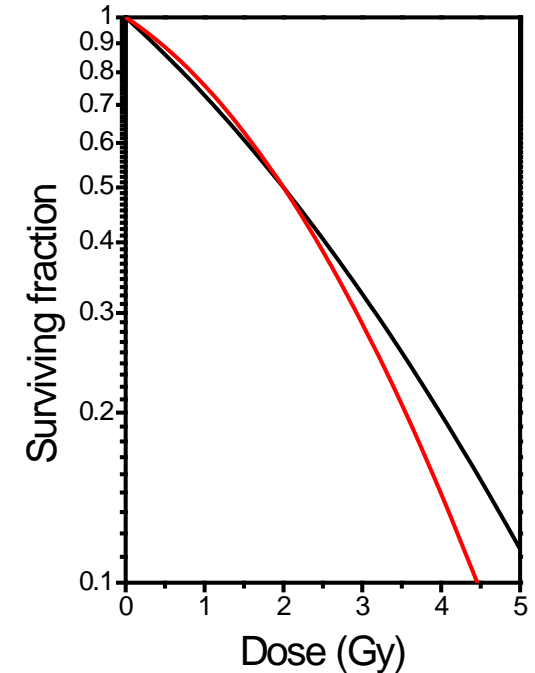
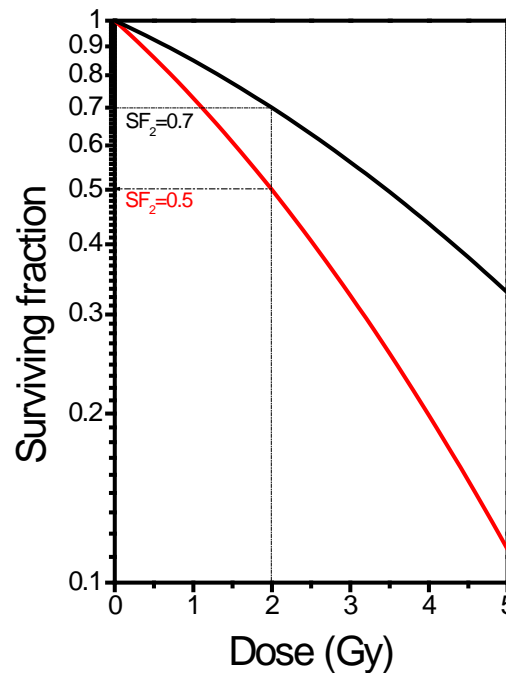
- **Late responding tissues:**
 - i.e. kidney, CNS
 - low α/β ratio
 - ***slowly proliferating tissues***
- **Early responding tissues:**
 - i.e. skin, mucosa
 - **tumours (with some exceptions)**
 - high α/β ratio
 - ***rapidly proliferating tissues***

But α/β is not a measure of the radiosensitivity *per se*, but a measure of the sensitivity to fractionation!





Tumour radiosensitivity



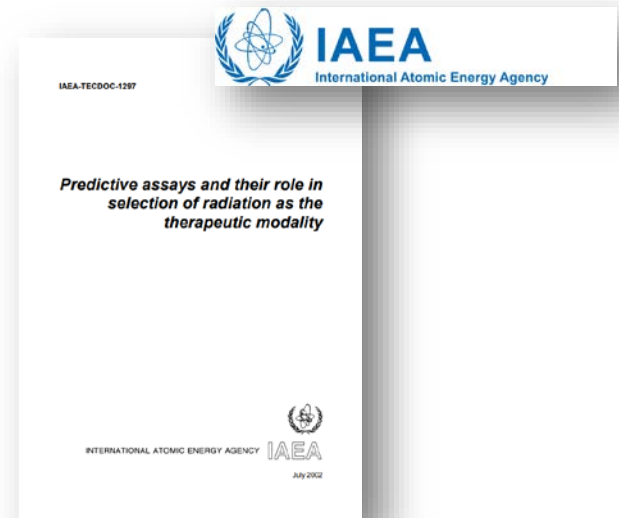
- Radiosensitivity is the radiation dose required to produce a defined level of cell inactivation.
- Radiosensitivity is usually indicated by the surviving fraction at 2 Gy (SF_2)



Individual tumour response – current challenges and opportunities

- ***Radiobiological assays for individual tumour response***

- Promising/Inconclusive \neq Reliable
- Time consuming \neq Efficient
- Expensive \neq Cost effective
- etc.



- ***Molecular and genetic biomarkers of tumour response***

- ***From in vitro cell line radiosensitivity to the response of in vivo tumours***



Individual tumour response – current challenges and opportunities

Individual response to ionizing radiation = Tumour radiosensitivity

- How can it be determined/
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- Knowing it, does it have a
clinical value?
- What would the future bring?

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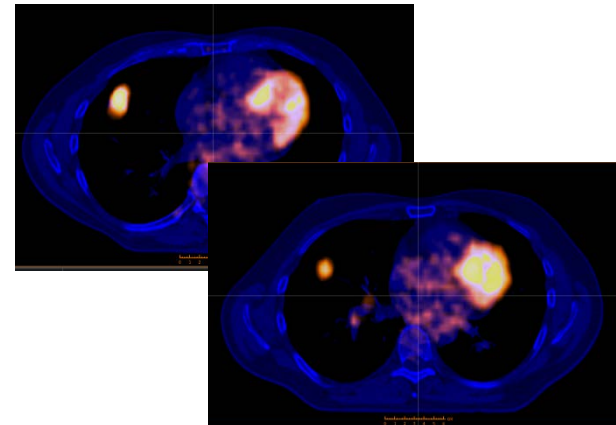
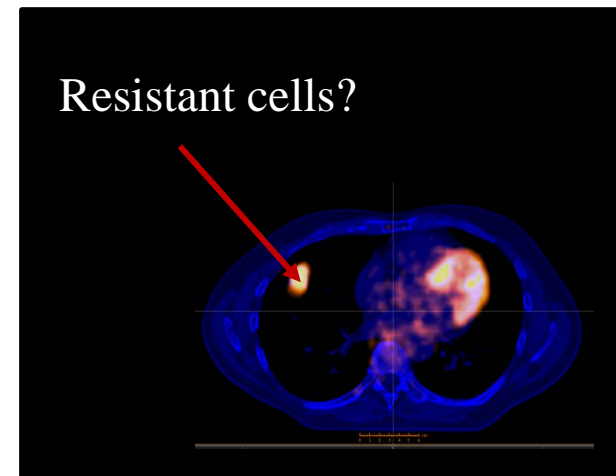


Individual response to ionizing radiation = Tumour radiosensitivity

- Local recurrence is related to resistant foci not eradicated by the currently prescribed and delivered doses.
- Functional imaging allows mapping the target in terms of *radioresistance*.

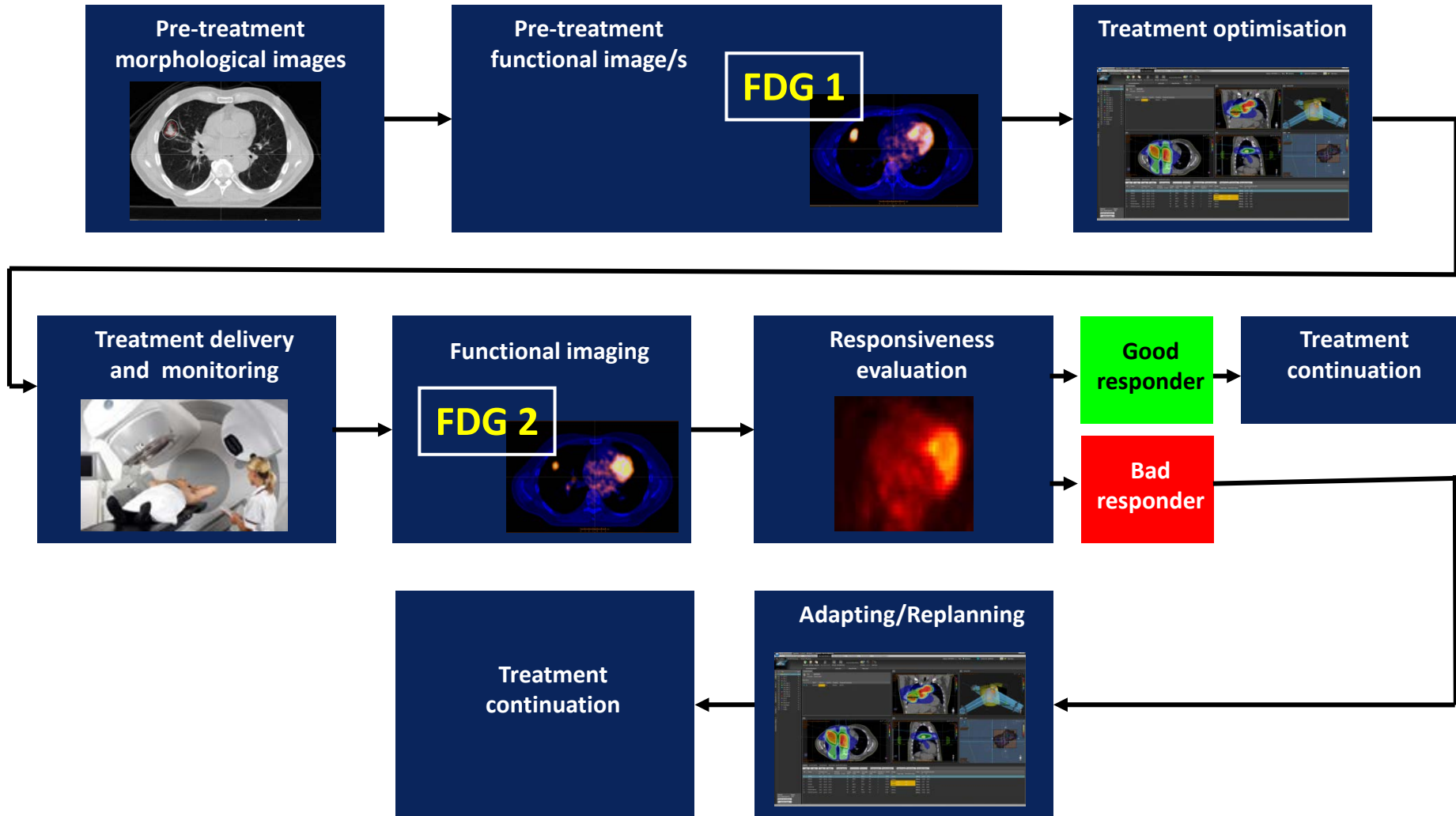
Hypothesis:

Repeated functional images allow mapping the tumour in terms of treatment *responsiveness*.



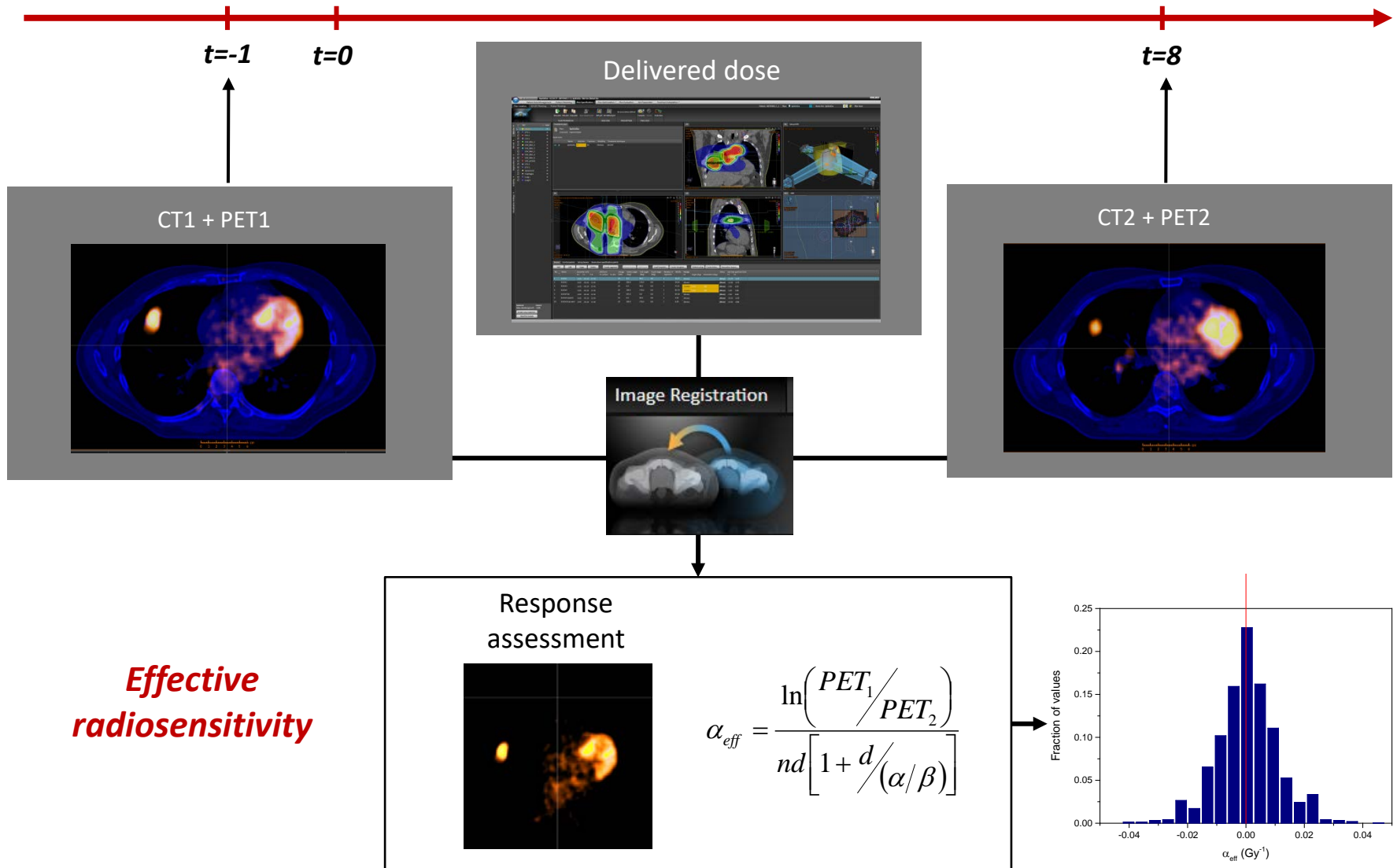


Individual tumour response – current challenges and opportunities





Individual tumour response – current challenges and opportunities

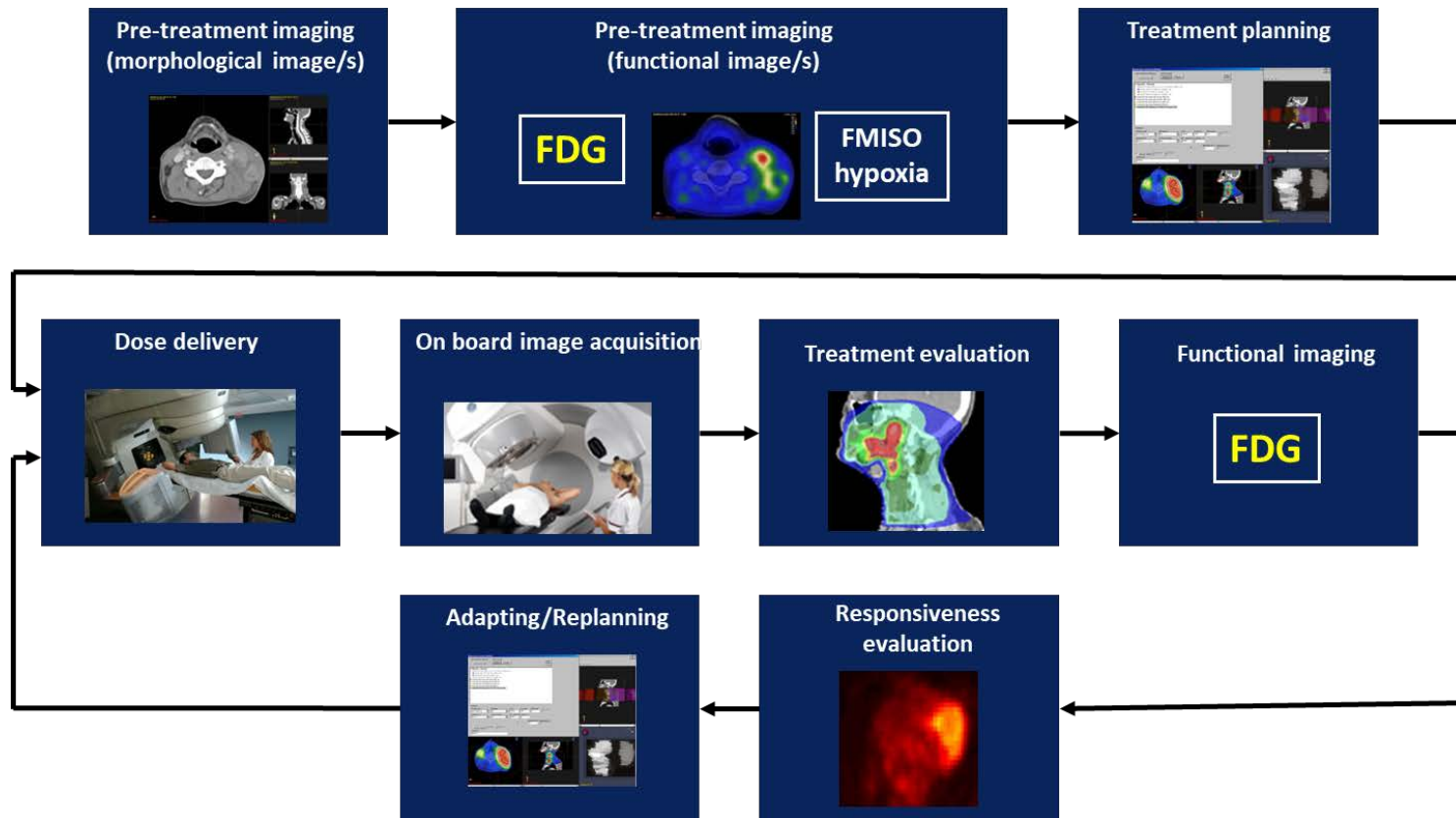


**Effective
radiosensitivity**



Individual tumour response – current challenges and opportunities

- Role of functional imaging in assessing the individual tumour radiosensitivity***





- ***Role of functional imaging in assessing the individual tumour radiosensitivity***

IMAGING

- Choice of the tracer
- Method for quantification of tracer uptake
- Optimal imaging time

- Spatial resolution
- Partial volume effects
- Image reproducibility

- Temporal artefacts
- Movement artefacts

- *etc.*

RADIOBIOLOGY

- Definition of the BTV

- Choice of the model for interpreting the tracer uptake

- Choice of dose prescription function or level

- Accounting for the dynamics of the system

- *etc.*

TREATMENT DELIVERY

- Need for delivering highly heterogeneous dose distributions
- High gradients in the dose
- Penumbra issues

- Need for re-planning or adaptive treatment

- *etc.*



Individual tumour response – current challenges and opportunities

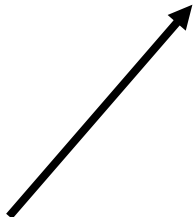
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- **Role of radiogenomics in the individualisation of tumour response**
- **Radiobiological modelling of individual radiosensitivity**
- **Individual tumour response to therapy - photons versus particles**

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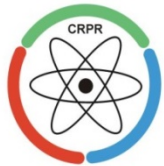


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