Challenges of Radiological Protection in Research and Society referring to Medical Field

October 3/2024

Milan, Italy

Sala Napoleonica/Via Sant'Antonio, 12
Università di Milano

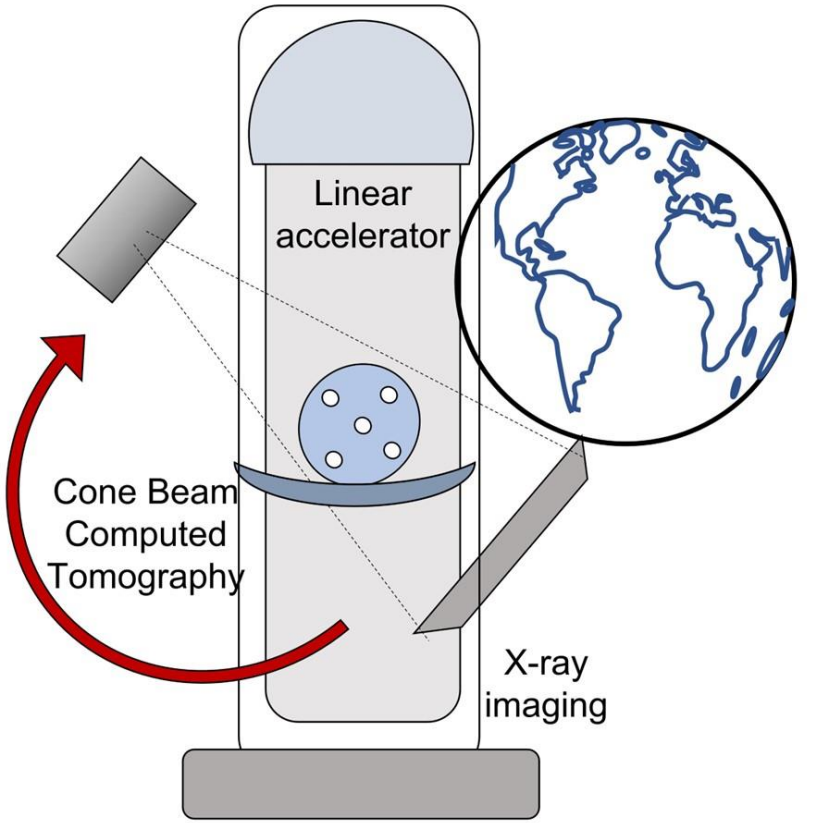
University of Glasgow

Radiation protection issues for imaging in radiotherapy

Dr Colin J Martin

University of Glasgow, Scotland, UK

ICRP Committee 3 on Protection in Medicine

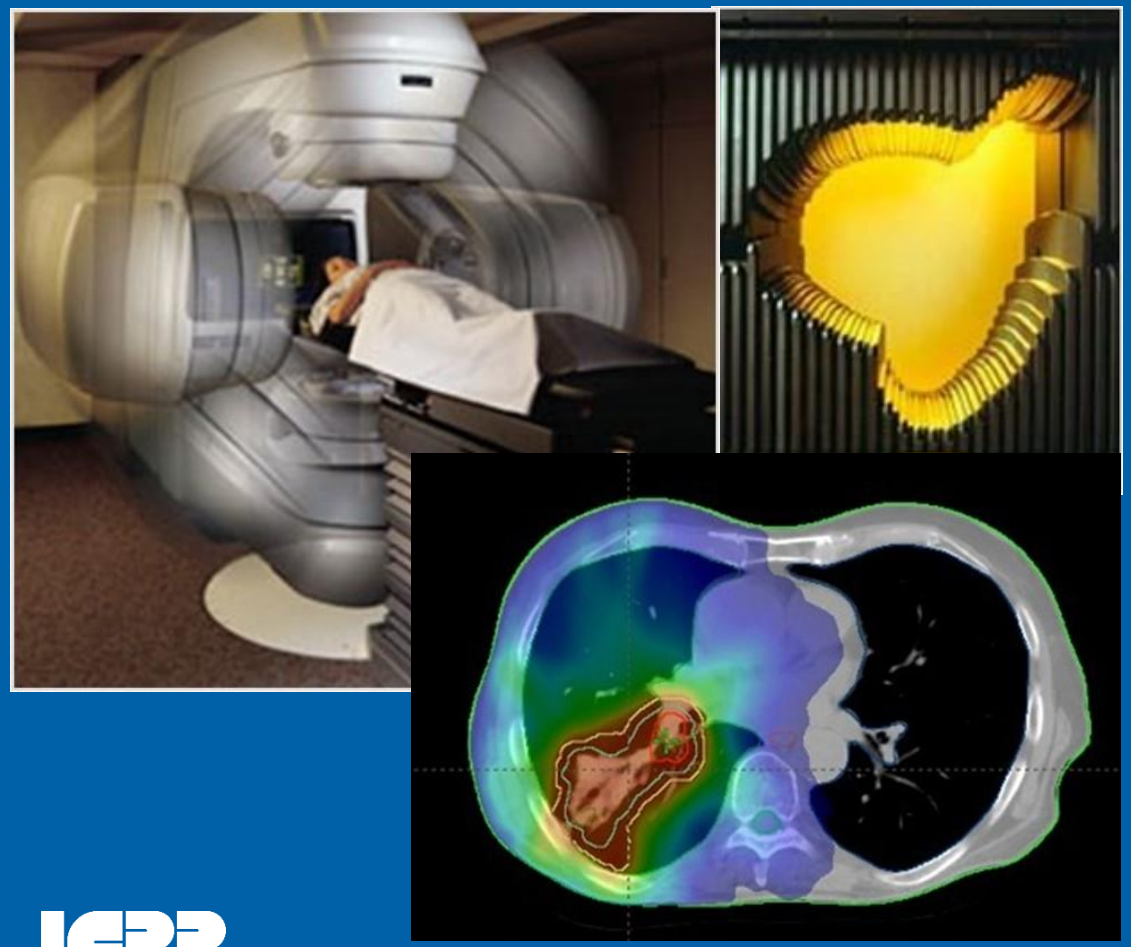


ICRP

Radiation protection issues for imaging in radiotherapy

- Conforming the radiation field to tumour target
- Use of images in radiation treatments
- Reduction of high dose margins with imaging
- TG116 survey of imaging practices in radiotherapy
- Imaging techniques and frequencies during treatment
- Optimisation of verification imaging
- Recording patient doses from cone beam CT imaging

Conformal Radiotherapy

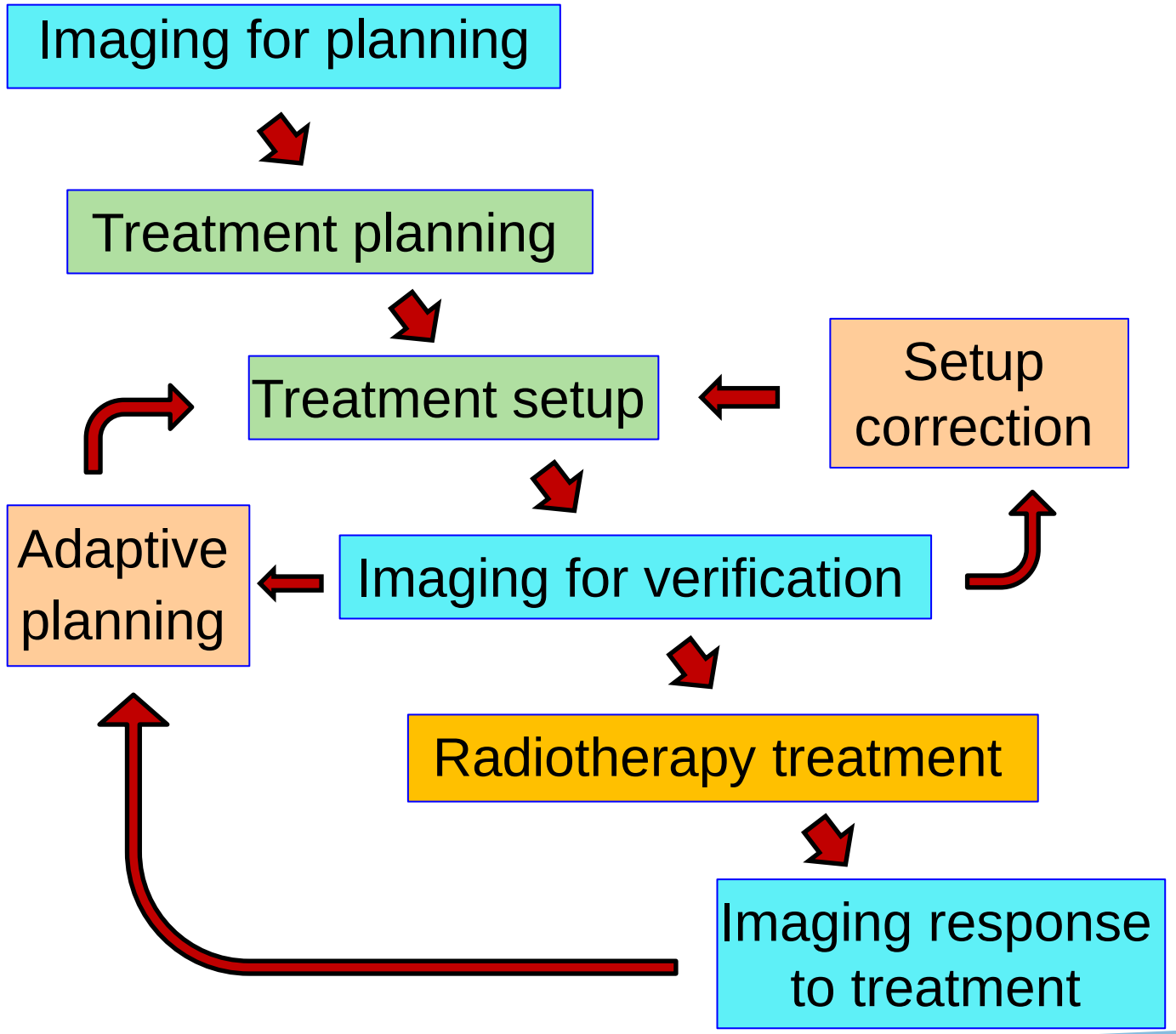


- Conformal treatment fields are delivered from multiple directions to focus the therapeutic dose on the tumour
- The machine continuously reshapes the beam and changes the intensity as the gantry moves around the patient
- This enables the radiation fields to be conformed more accurately to tumour shapes and allows doses to healthy tissues surrounding the tumour to be reduced
- Improvements in treatment can only be realised if patients are positioned precisely and radiation fields are delivered with mm accuracy. This requires imaging.

Image guided radiation therapy (IGRT)

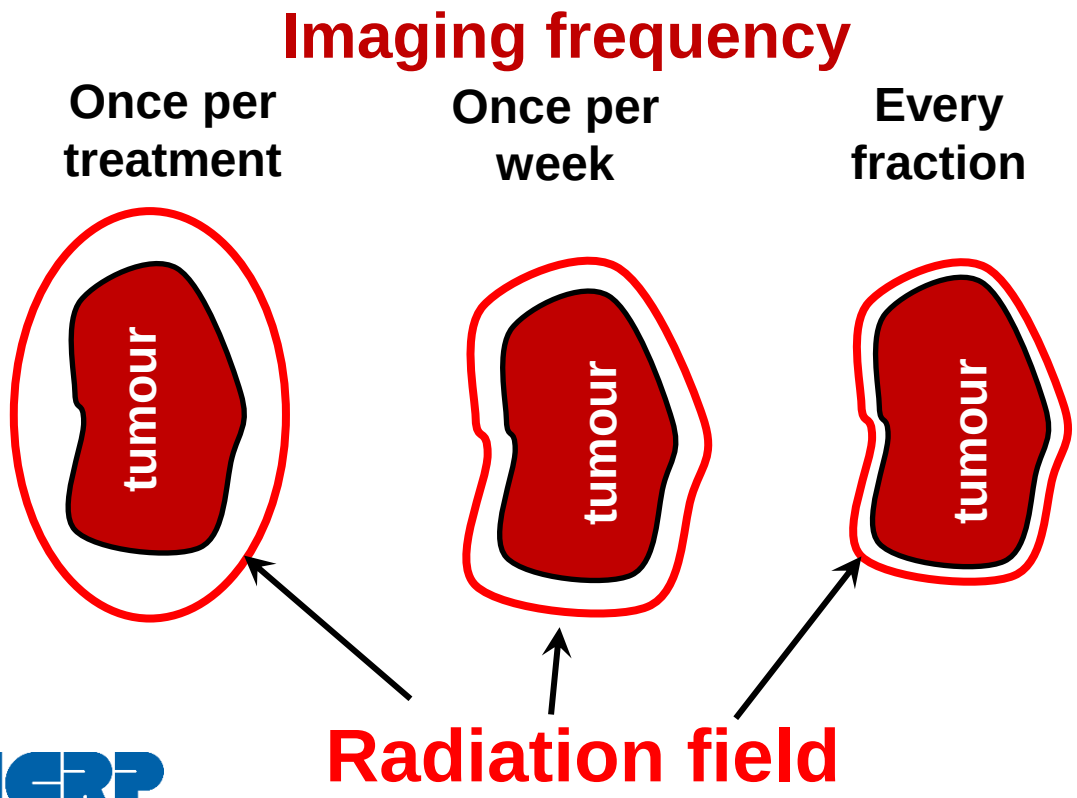
Images of patient recorded for:

- **Planning**
- **Verification** immediately before treatment delivery to adjust for positional uncertainty
- **Assess response** at a later stage



The balance between doses from imaging and reduction in treatment margins

- A high dose margin is left around the tumour target to account for uncertainty in delineation, anatomical changes and movement
- More frequent imaging allows margins to be reduced to protect normal tissue.



- Imaging fields cover a larger area of normal tissue surrounding the tumour
- Cumulative doses from imaging contribute to the risk of second primary cancers.
- There is a balance between reducing the high dose margin around the target and lowering the dose from imaging to surrounding normal tissues

Objectives of imaging during treatment delivery

- **Verification of the treatment field** outline in relation to anatomy and the treatment beam.
- **Verification of target or organ position** in relation to the isocentre.
- **Adaptive radiotherapy**: Assessment of organ shape or size prior to treatment to adjust for any changes.
- **Motion management**: Monitoring motion of target and critical structures during delivery to allow for breathing motion.
- Motion management requires an imaging frequency commensurate with the speed of motion.

Imaging in Radiotherapy

Imaging for Planning

- Static
  - Anatomy: *CT, MRI*
  - Function: *PET, MRI*
- Breathing Motion: *Fluoroscopy, 4DCT*

Imaging for Verification

- Prior to delivery
  - Anatomy: *kV imaging, EPI (MV), CBCT, MRI, Optical imaging*
  - Motion: *kV imaging, CINE EPI (MV), CBCT, US, MRI, Optical imaging*
- During delivery: *kV imaging, US, MRI, Optical imaging*

- **Imaging for verification:** requires fields covering the area surrounding the tumour
- **kV imaging systems:** x-ray tube and image detector plate can rotate around the patient and record planar or cone beam CT (CBCT) images
- **MV therapy sources:** can be used with electronic portal imaging devices to produce images, but contrast is poor and doses are higher

EPI – Electronic Portal Imaging, CBCT – Cone Beam CT, US - Ultrasound

Justification and Optimisation of Imaging exposures

Imaging may be performed at many fractions, all exposures should be justified and techniques optimised to minimise doses to adjacent organs and tissues

Justification should be given for:

i. The imaging modalities to be used

ii. The frequency at which imaging is required for the treatment

Optimisation of radiological protection can be for a population group or individual patient:

i. The volume of the region to be imaged

ii. Exposure factors and reconstruction parameters required to achieve the appropriate level of image quality for the clinical task









Mentee Project

	Country	HDI	No. of RTCs
A	Germany	0.947	10
B	Australasia	0.944	12
C	USA	0.926	30
D	Cyprus	0.887	2
E	Saudi Arabia	0.854	4
F	Malaysia	0.81	7
G	Colombia	0.767	14
H	Algeria	0.748	9
I	Egypt	0.707	9

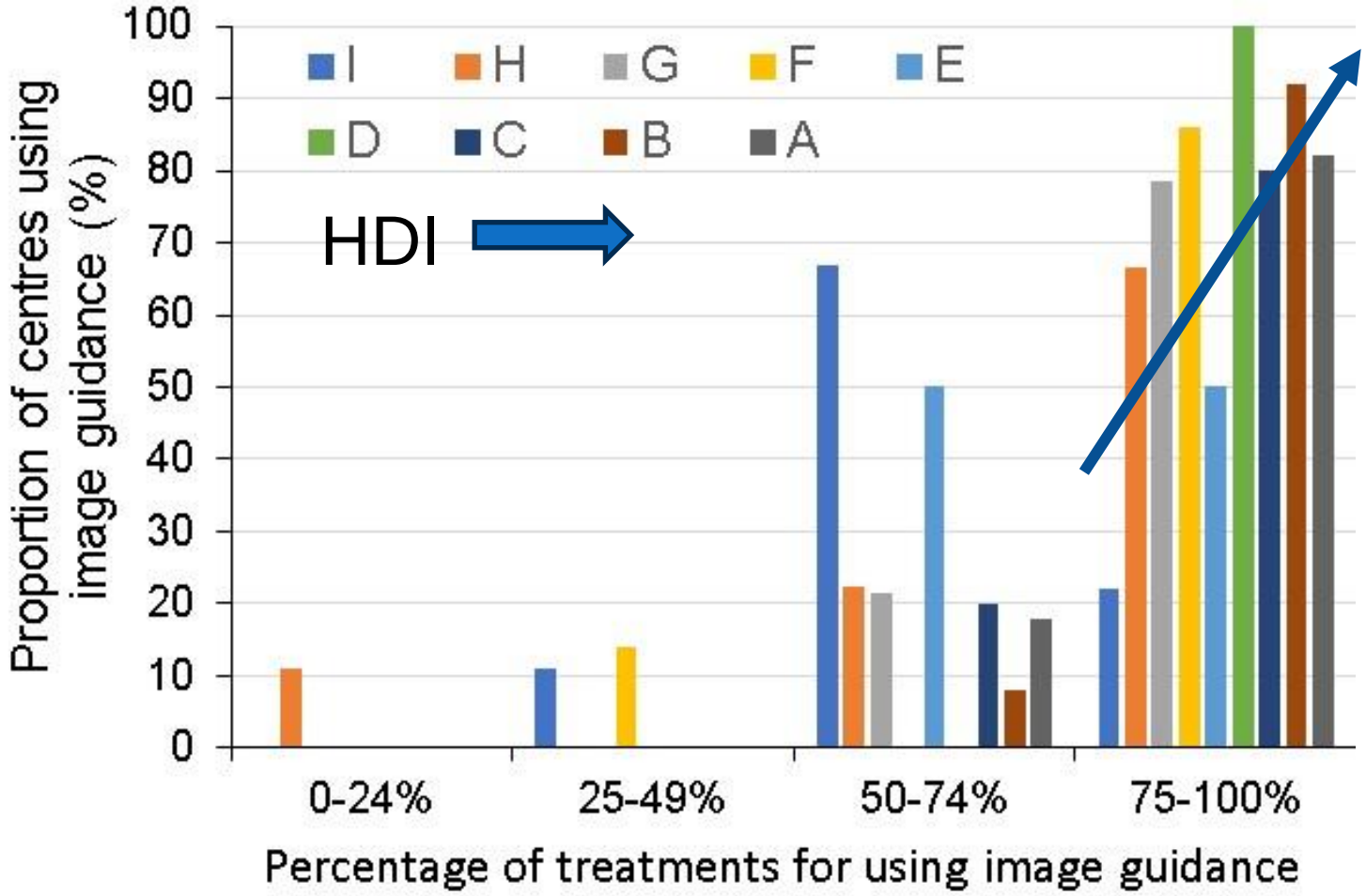
- Information on practices in the use of imaging in radiotherapy (RT) from many countries is limited
- ICRP set up a Mentorship programme in 2018 and TG116 used the opportunity to initiate a mini-survey of use of imaging in RT around the world
- This gave a snapshot of practices in countries at different stages of development
- Data ordered in terms of the Human Development Index (HDI) that measures life expectancy, education and income.
- HDI moves towards 1.0 as the level of development rises.

Verification images used to guide treatment

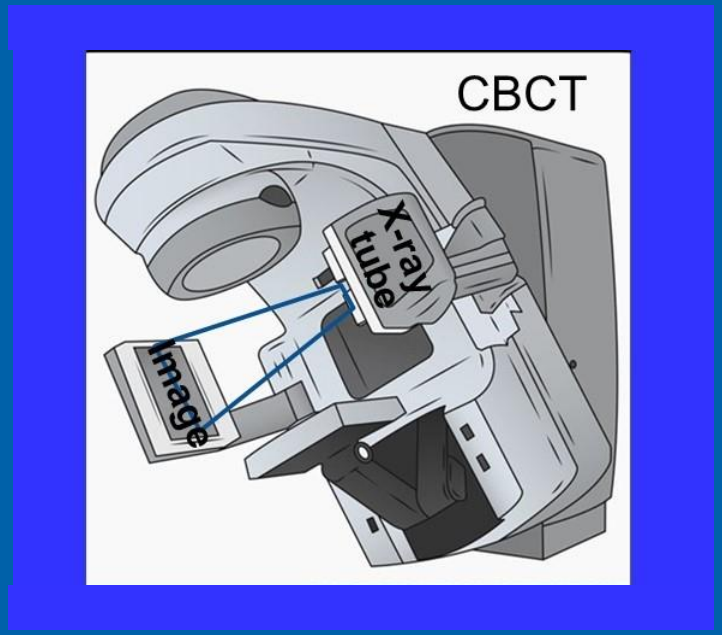
Image guidance is used in the radiotherapy centres in all countries

The proportion of centres using image guidance for verification for most treatments increased with the HDI value

Percentages of treatments for which centres use some image guidance



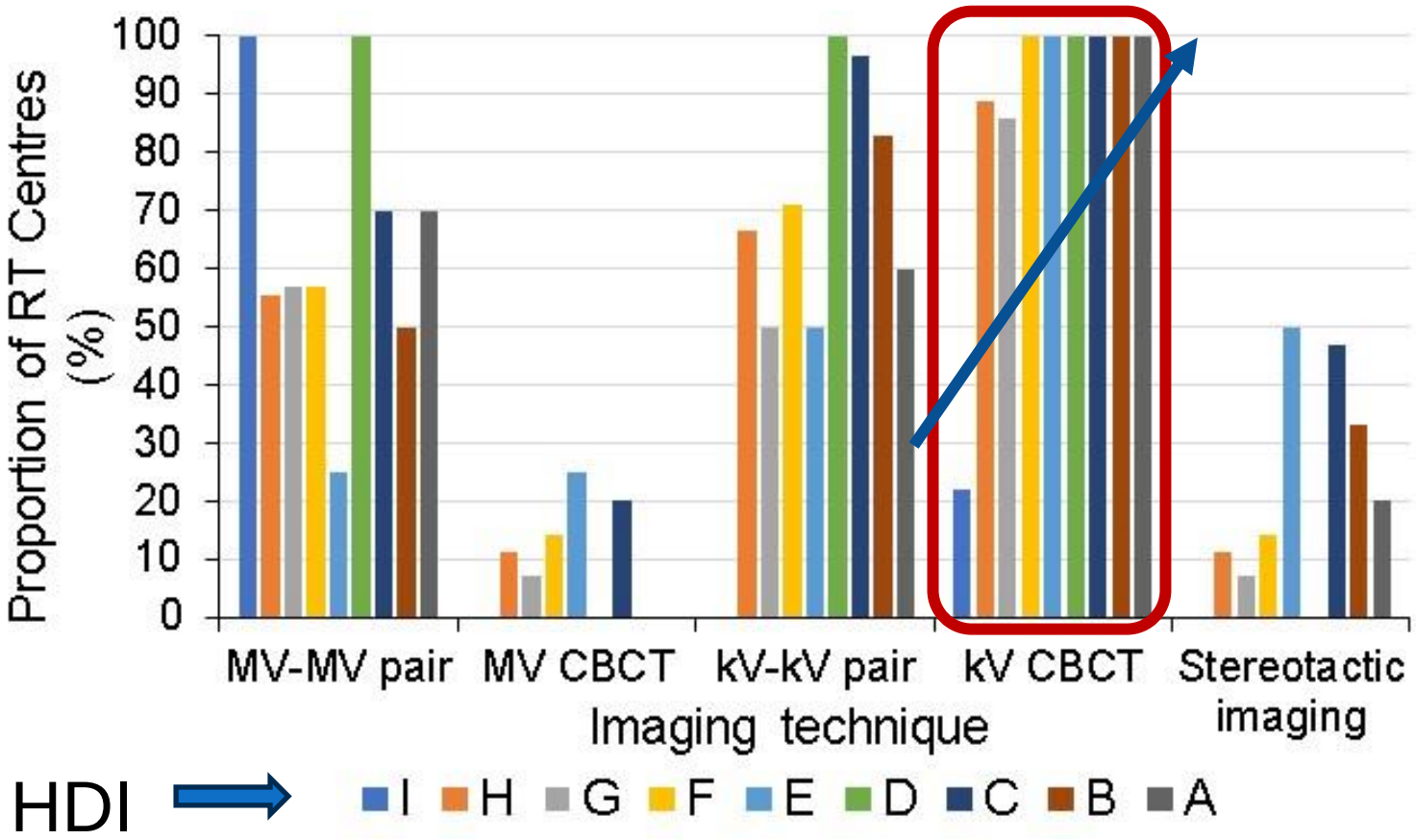
Techniques used for image guidance



kV cone beam CT (CBCT) is the main technique used for verification imaging

Countries with lower HDI values have fewer Linacs with kV imaging facilities

Cone beam CT



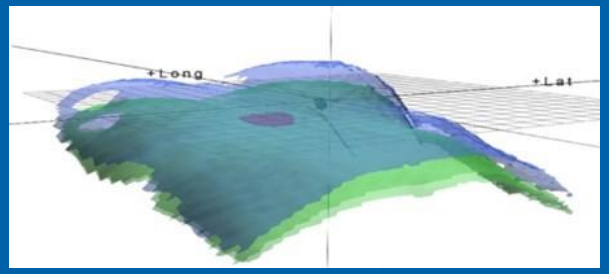
Typical doses to organs and tissues in the trunk from one image set

MV-MV pair	MV CBCT	kV-kV pair	kV CBCT
10–45 mGy	10–20 mGy	0.5–1.5 mGy	2-10 mGy

Non-ionising radiation imaging in verification

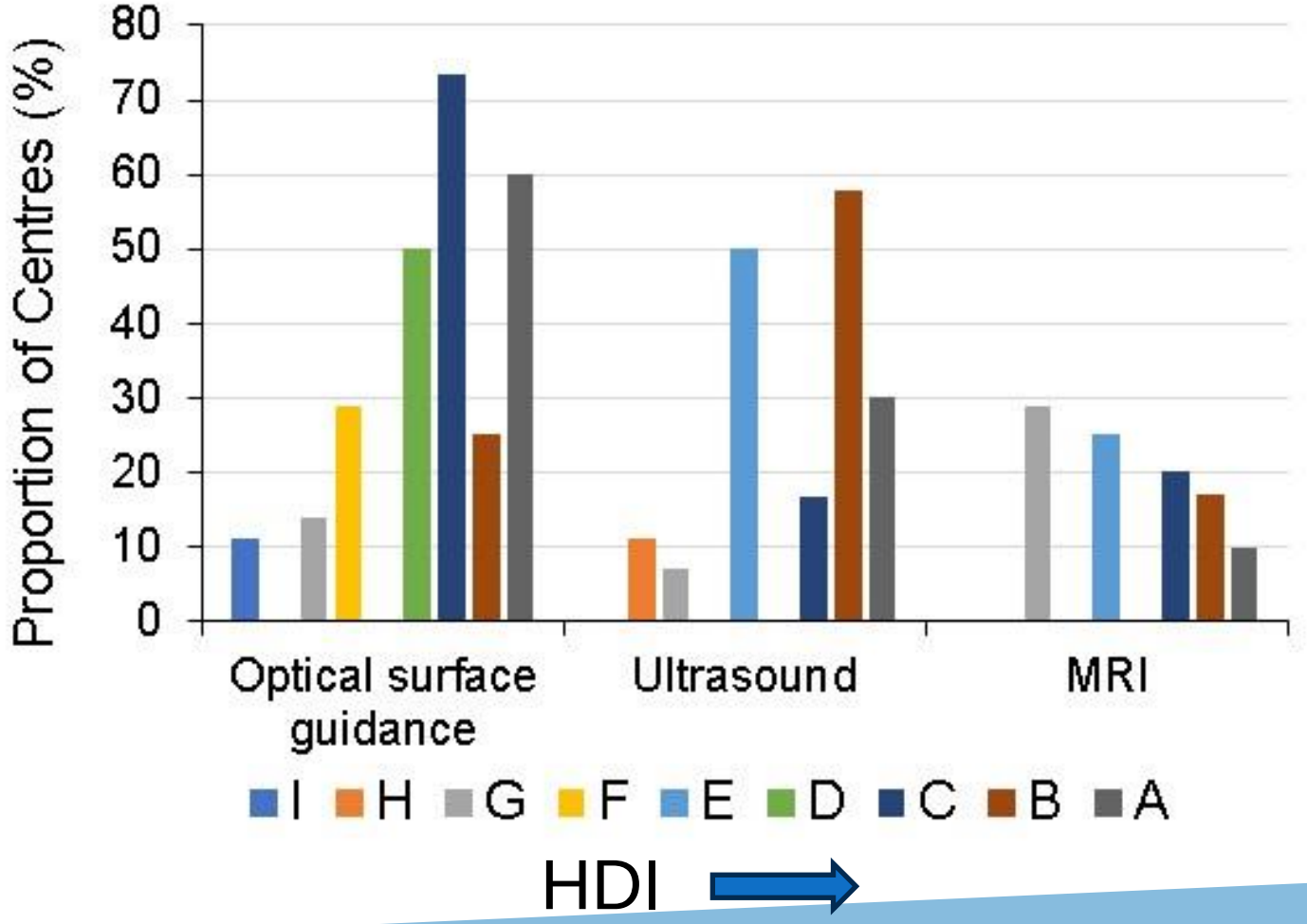
Magnetic resonance imaging (MRI): available on some linacs

Optical surface guidance: for monitoring skin surface



Ultrasound image guidance: provides real-time, volumetric imaging

- Optical surface guidance or ultrasound were used in about half of centres and MRI in 10%-25%
- Used more by countries with higher HDIs



Frequency of verification imaging
Breast and Prostate

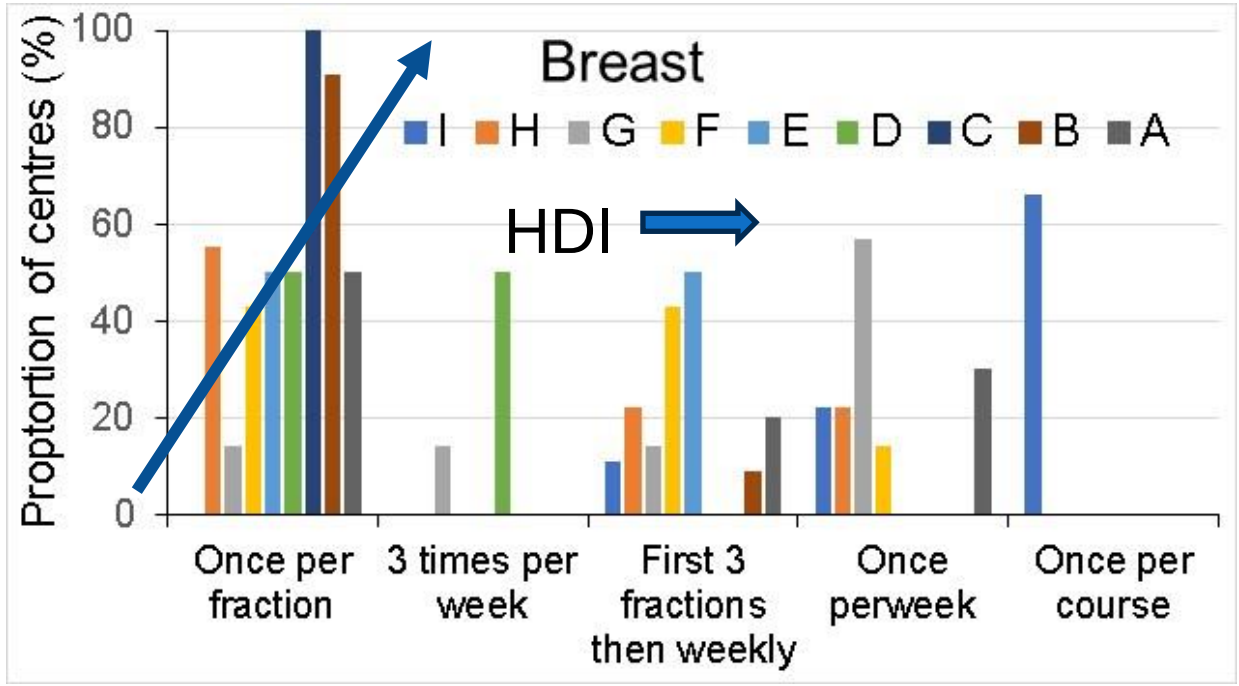
Main options used

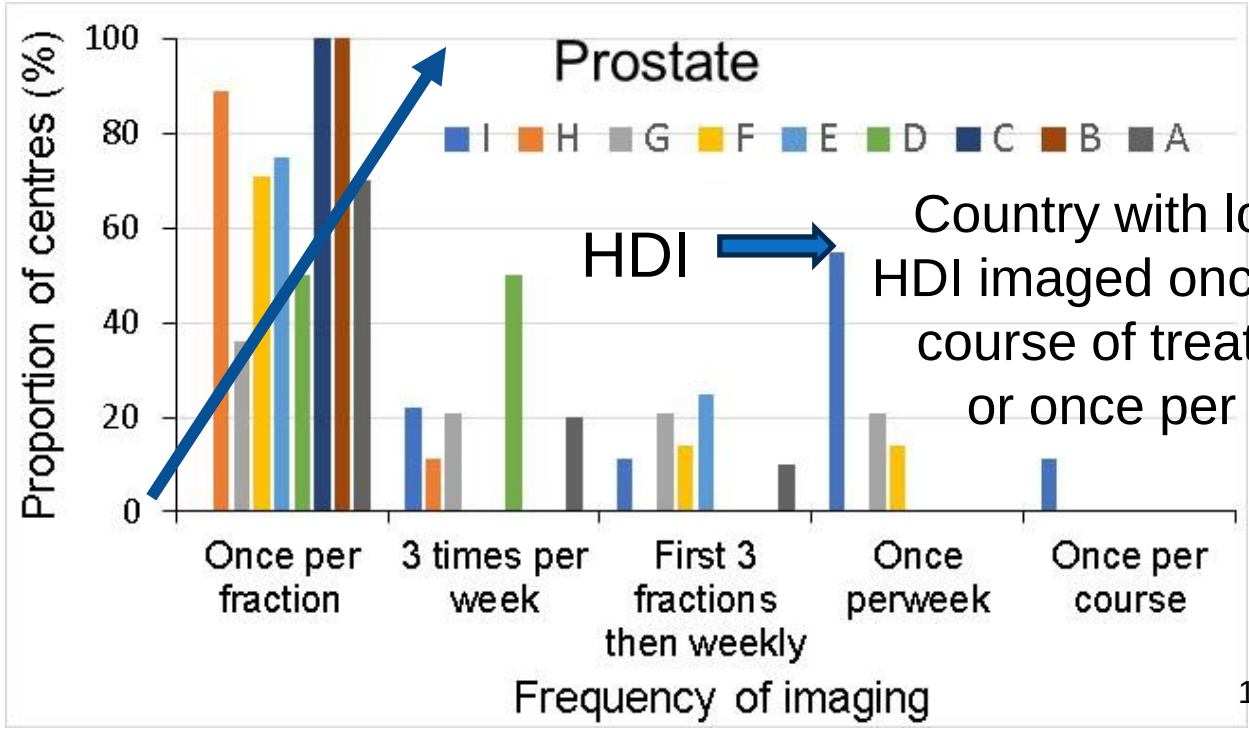
- *Every fraction*
- *3 times per week*
- *First 3 fractions then weekly*
- *Once per week*
- *Once per course of treatment*

Higher income countries frequently image at every fraction, but numbers are less for countries with a low HDI

Reasons are:

- Availability of kV imaging equipment
- More patients treated per linac





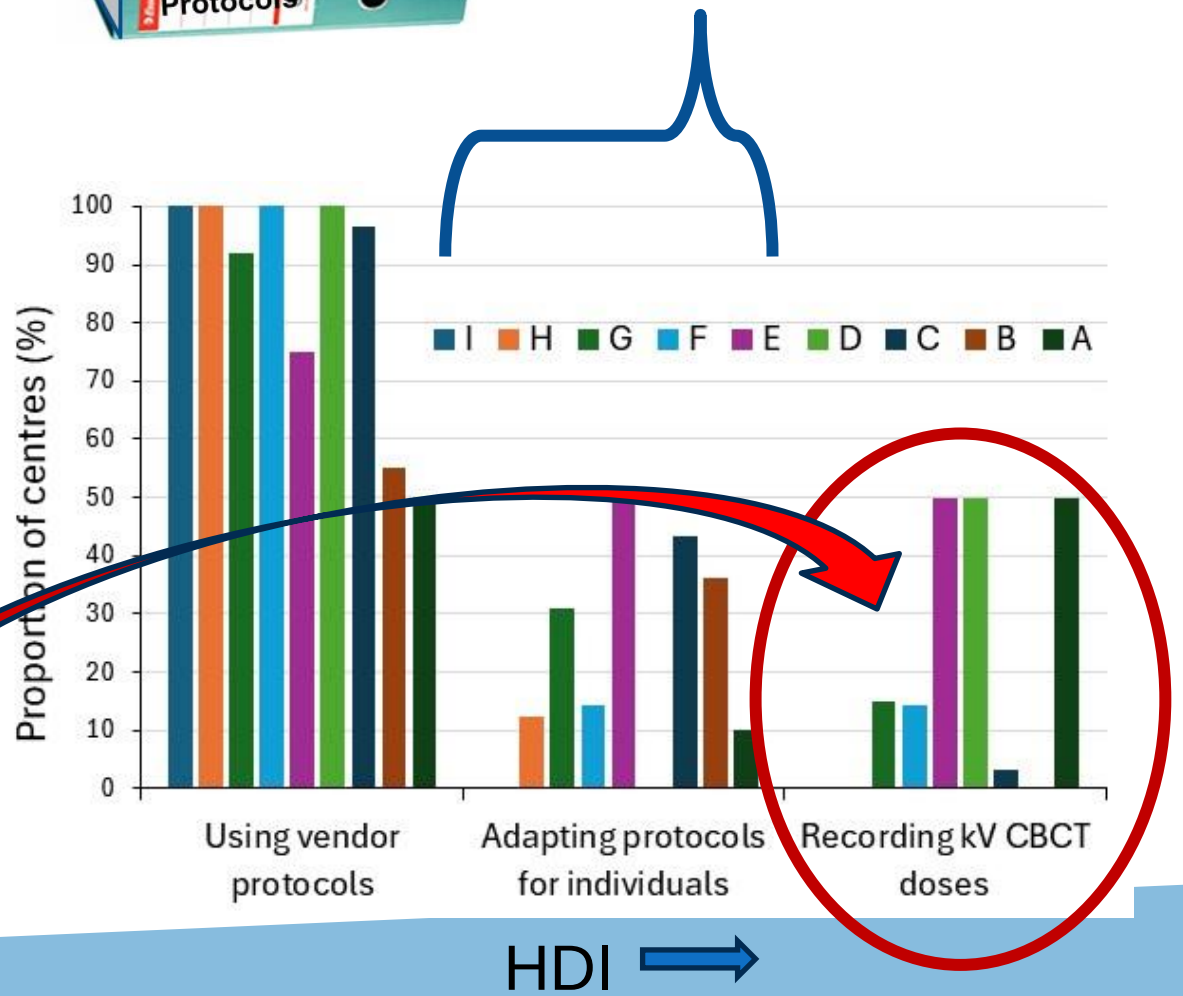
Country with lowest HDI imaged once per course of treatment or once per week

Adaption and optimisation of CBCT imaging protocols

Choices in optimisation of IGRT:

- Level of image quality required (dose)
- Volume of tissue to be imaged
- 90% of RT centres use imaging protocols supplied by the vendor
- Surveys have shown that vendor protocols are often not optimised for radiological protection
- The vendor protocols should provide a starting point from which optimised protocols are developed
- Optimisation of radiological protection requires a knowledge of patient doses
- Only between 10% - 50% of RT centres recorded patient doses

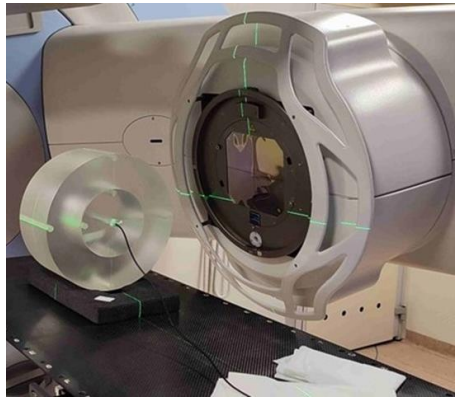
Fewer than 50% of RT centres make adjustments to optimise protocols for individual patients



Cone beam CT patient dose surveys

- Standard dosimetry quantity displayed on radiotherapy CBCT equipment is the **Wide Beam CT Dose Index** ($CTDI_{IEC}$) (IEC, 2016). This is a development of the CTDI defined for narrow CT beams.
- Display of the CTDI on therapy equipment is limited and this makes dose surveys difficult.
  - Measurement of the CTDI is not straight forward.
  - We proposed use of the Cone Beam Dose Index (CBDI) for patient dose surveys, until displays of $CTDI_{IEC}$ become available, as it is easier to measure.
  - The CBDI is measured with a 100 mm ionisation chamber in a standard CTDI phantom with the wide beam used for the procedure.
  - Many centres do not have 100 mm chambers or CT phantoms, so an alternative using solid water slab phantoms and Farmer chamber is proposed

CBDI Measurement



Alternative method with slab phantom

Selection of Recommendations in Task Group Report

Radiotherapy centres

- Resources should be allocated for image dose assessment and optimisation of radiological protection for imaging
- Radiotherapy centres should employ or have access to a suitably qualified medical physicist with diagnostic imaging specialisation
- Systems for periodic audit of patient imaging doses should be established through measurement of the Cone Beam Dose Index in the short term.
- Results from dose surveys should be considered, when optimising imaging protocols and lead to the establishment of dose reference levels (DRLs).

Radiotherapy equipment vendors

- Vendors should include displays of measurable dose quantities (e.g. $CTDI_{IEC}$) linked to the exposure factors for all imaging systems.
- Features to facilitate optimisation of radiological protection for imaging procedures should be included in therapy imaging equipment.

Summary – The need for imaging in radiotherapy

- Improvements in radiation treatment delivery require accurate patient positioning
- Radiation fields for imaging expose normal tissues surrounding the target
- A high dose margin is left around the target to allow for uncertainty in delineation
- Reducing the high dose margin must be balanced against the dose from imaging to surrounding normal tissues
- A survey of imaging practices in RT has been conducted through ICRP TG116
- Most RT centres use images for verification in 75%-100% of treatments

Summary – Imaging practices and doses in radiotherapy

- kV cone beam CT is the main technique used in high- and middle-income countries
- These countries frequently image at every fraction while countries with limited kV imaging facilities may only image once per week
- Most centres use protocols supplied by vendors with limited optimisation
- Fewer than 50% of RT centres record doses received by patients from imaging
- Display of $CTDI_{IEC}$ on therapy equipment is limited, which makes dose surveys difficult
- Vendors are recommended to include displays of $CTDI_{IEC}$ linked to exposure factors
- The CBDI measured with a 100 mm chamber in a standard CT phantom with the wide beam used for the procedure is recommended for patient dose surveys in the meantime

I acknowledge contributions from the members of ICRP Task Group 116

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Thank you for your attention

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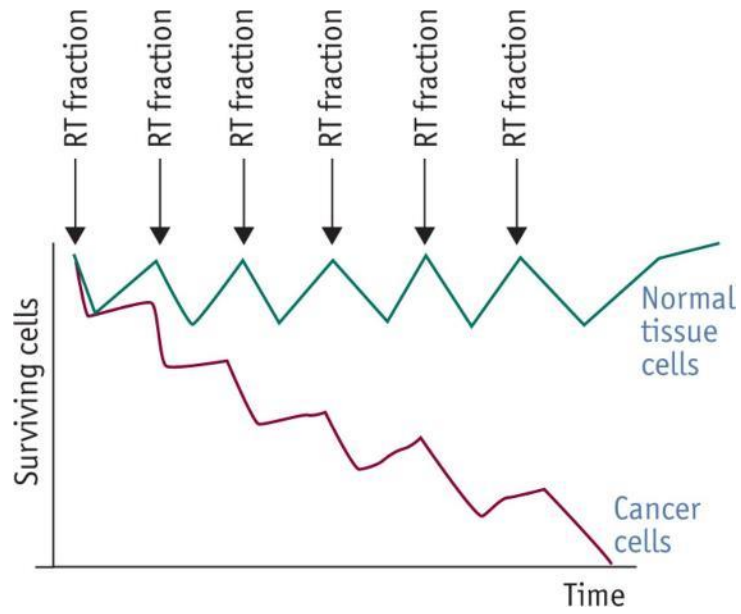
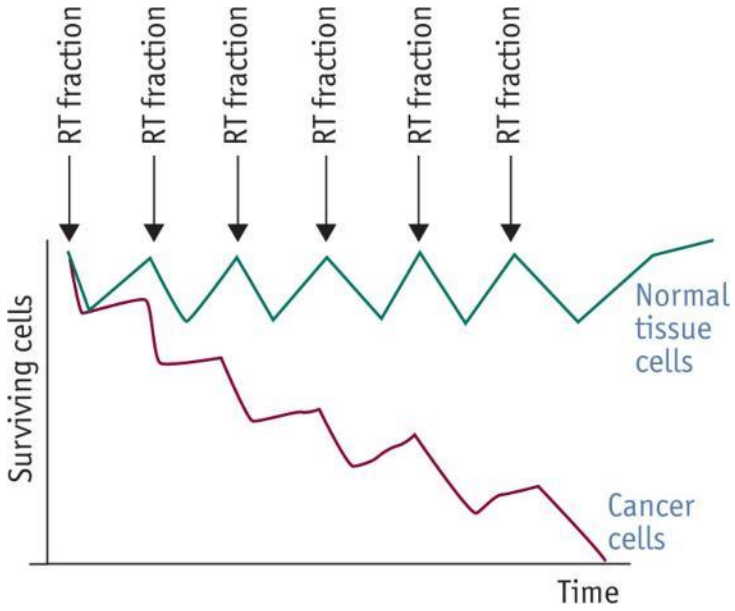
Radiobiological basis of hypofractionation (*SBRT/Radiosurgery*) and impact on patient Radiation Protection

Monica Mangoni
Universitv of Florence


RT fraction
RT fraction
RT fraction
RT fraction
RT fraction
RT fraction
Surviving cells
Normal tissue cells
Cancer cells
Time


RT fraction
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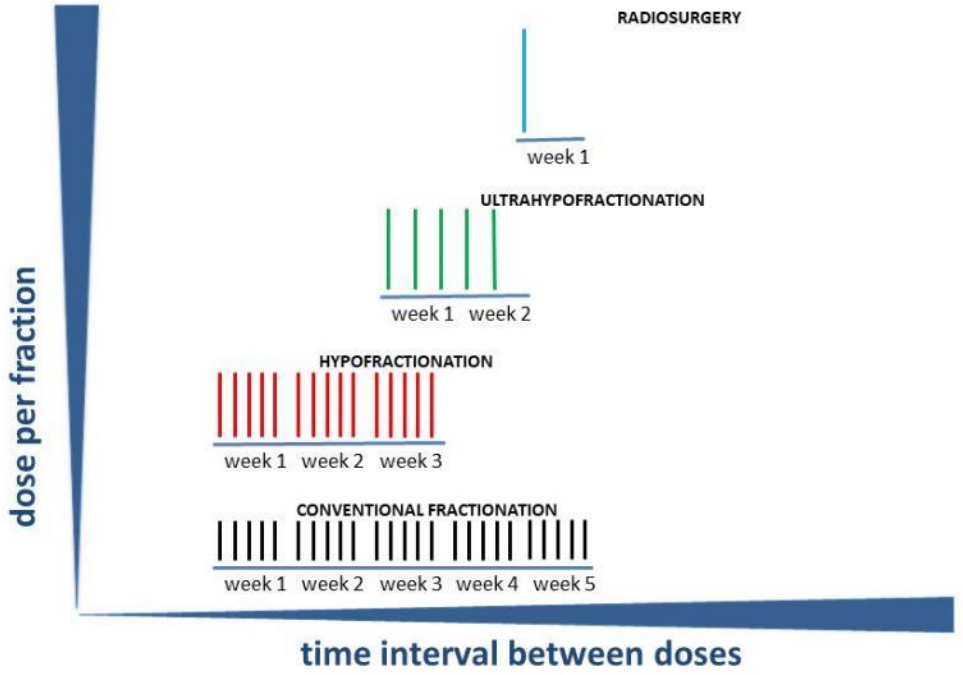
RT fraction
Surviving cells
Normal tissue cells
Cancer cells
Time


RADIOSURGERY
week 1
ULTRAHYPOFRACTIONATION
week 1 week 2
HYPOFRACTIONATION
week 1 week 2 week 3
CONVENTIONAL FRACTIONATION
week 1 week 2 week 3 week 4 week 5
dose per fraction
time interval between doses

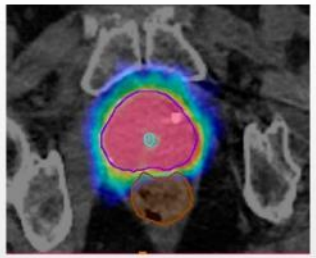
Stereotactic RT

- High dose per fraction
- Small volumes
- Single or very few fractions

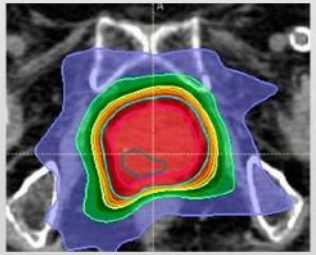
VS

Conventionnal RT

- Low dose per fraction
- Large volumes
- Multiple fractions

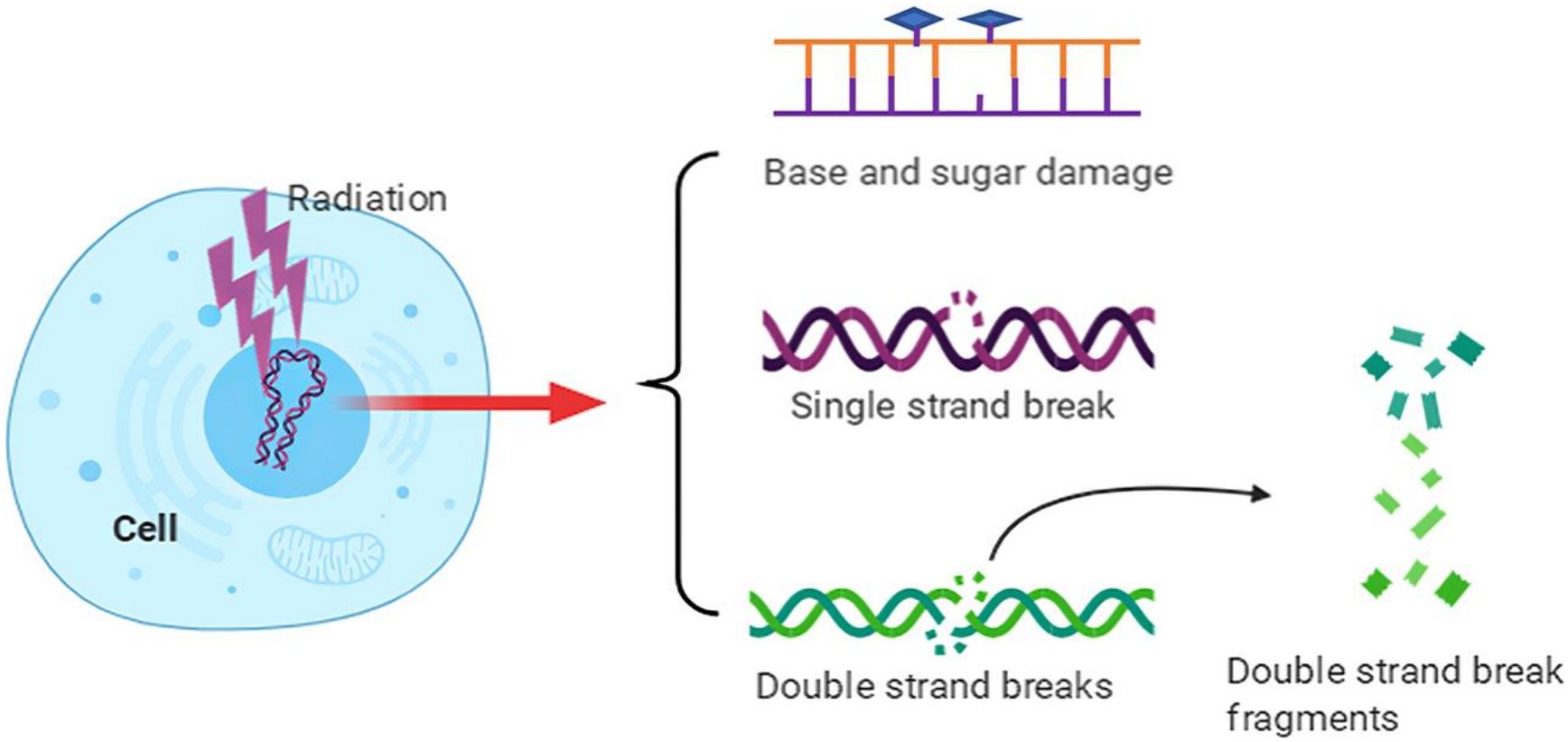


Prostate Cancer SBRT
36.25 Gy in 5 fractions
Tracking on fiducials : 3 mm margins

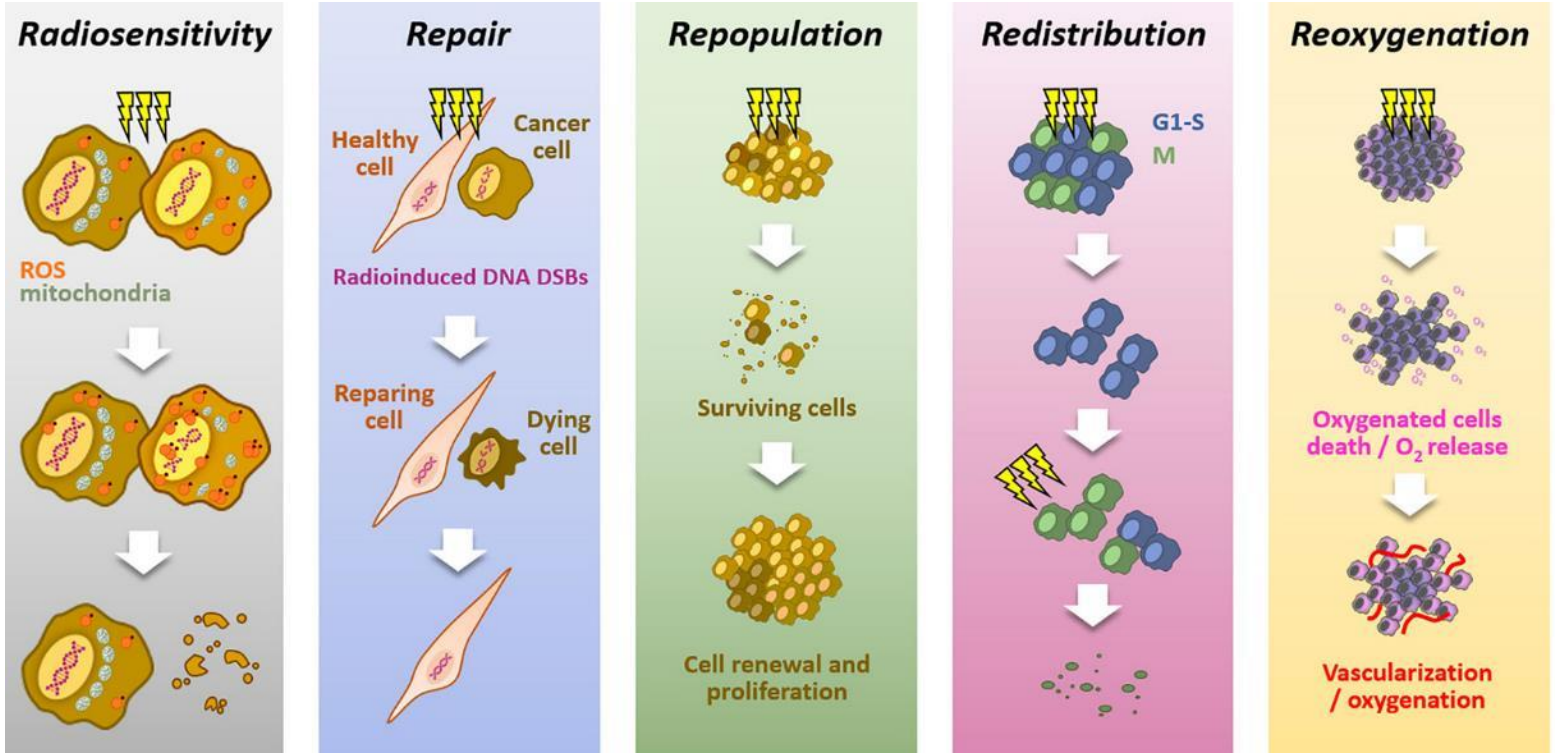


Prostate Cancer Conv-RT
78 Gy in 38 fractions
No tracking : 5 mm margins

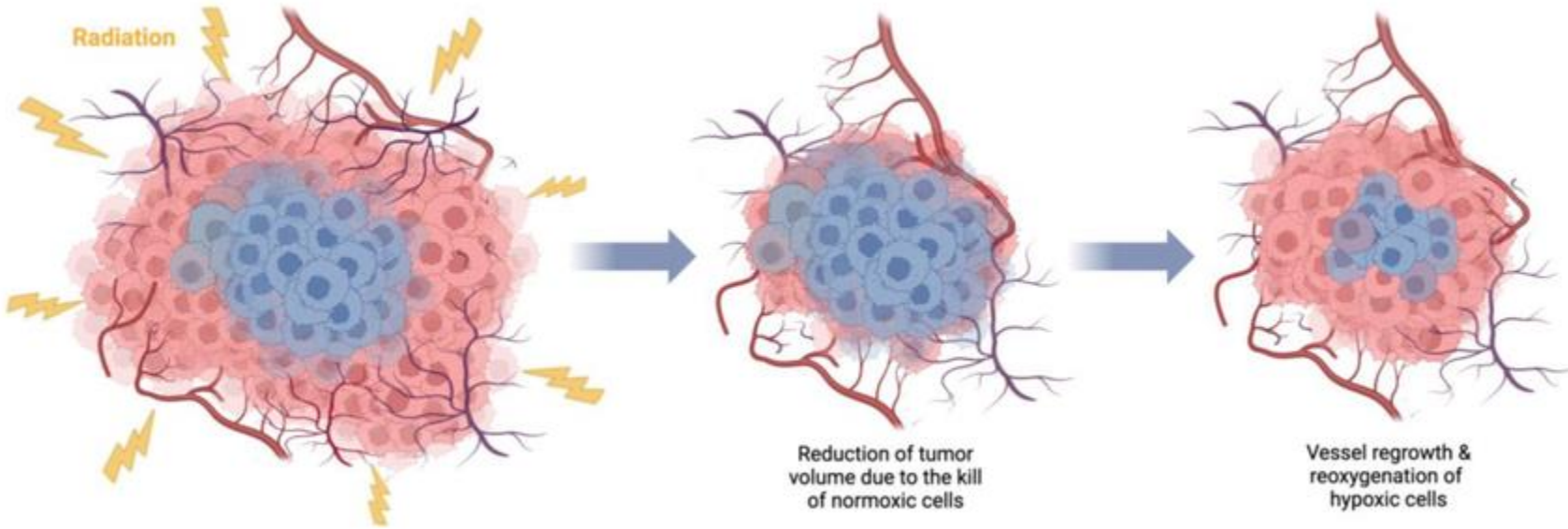
Kinj, R.; Bourhis, J. How Stereotactic Radiotherapy Changed the Landscape in Cancer Care. *Cancers* **2023**, *15*, 1734.


Radiation
Cell
Base and sugar damage
Single strand break
Double strand breaks
Double strand break fragments

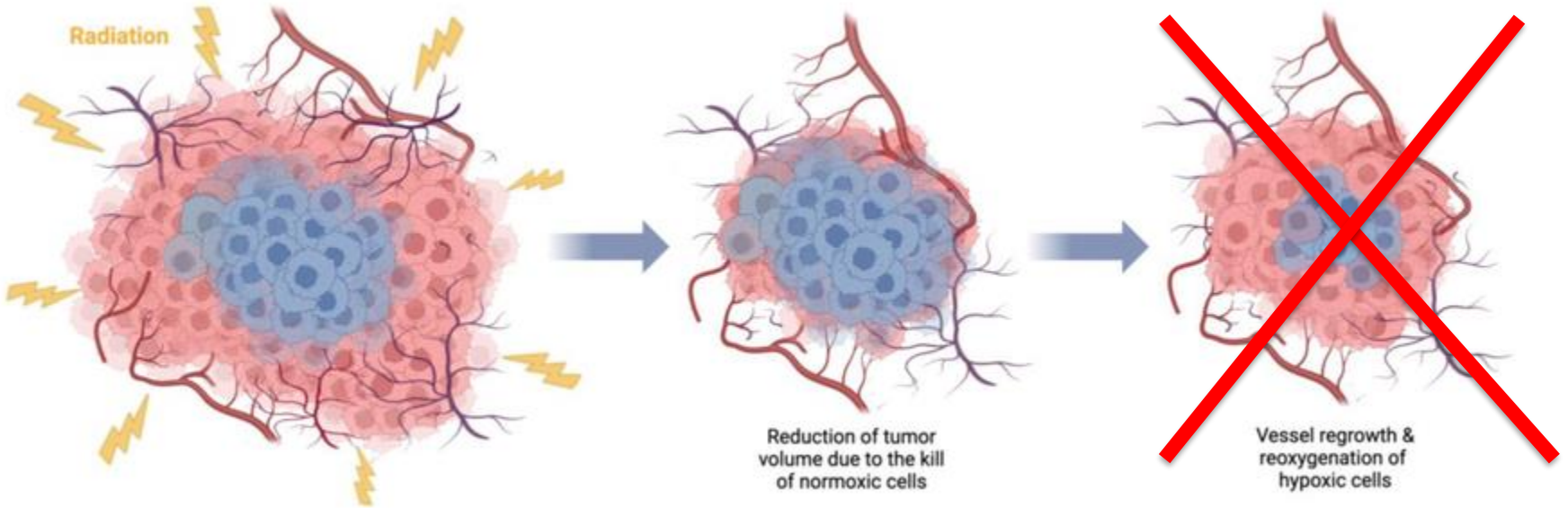
The «Rs»


Radiosensitivity
ROS
mitochondria
Repair
Healthy cell
Cancer cell
Radioinduced DNA DSBs
Reparing cell
Dying cell
Repopulation
Surviving cells
Cell renewal and proliferation
Redistribution
G1-S
M
Reoxygenation
Oxygenated cells death / O_2 release
Vascularization / oxygenation

Re-oxygenation

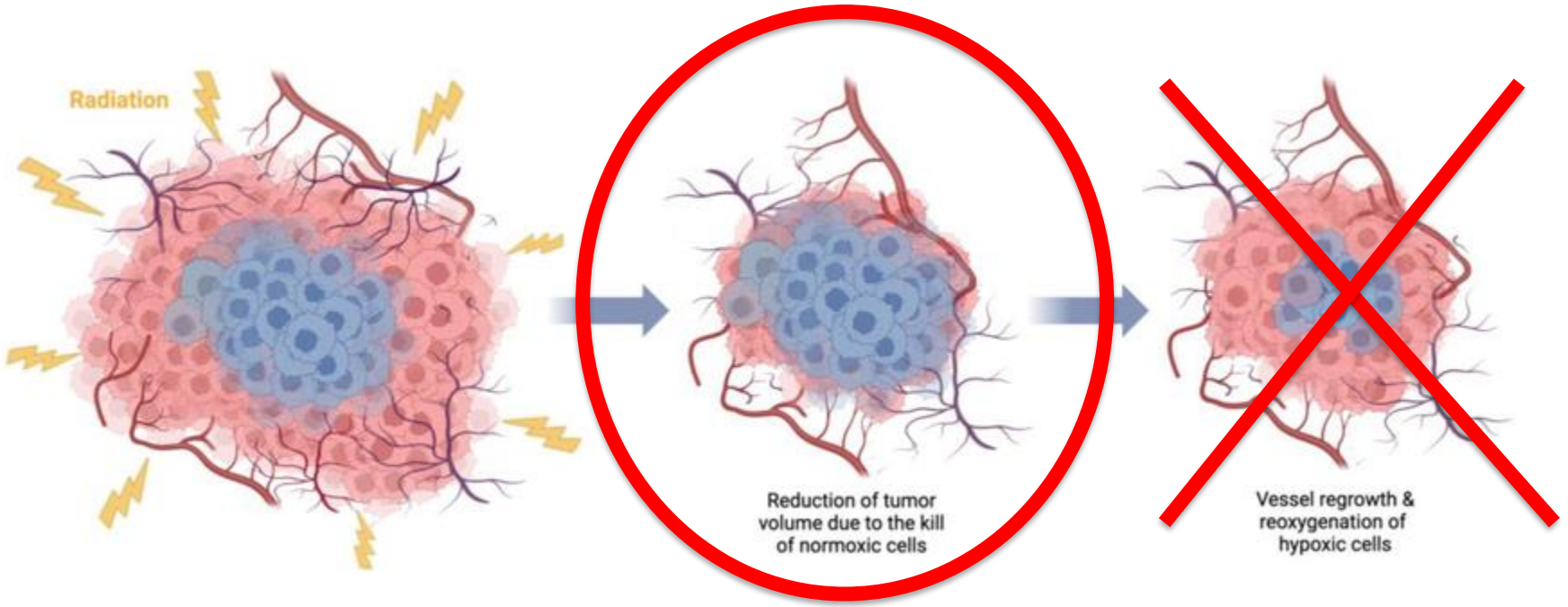


Re-oxygenation



radiosurgery

Re-oxygenation

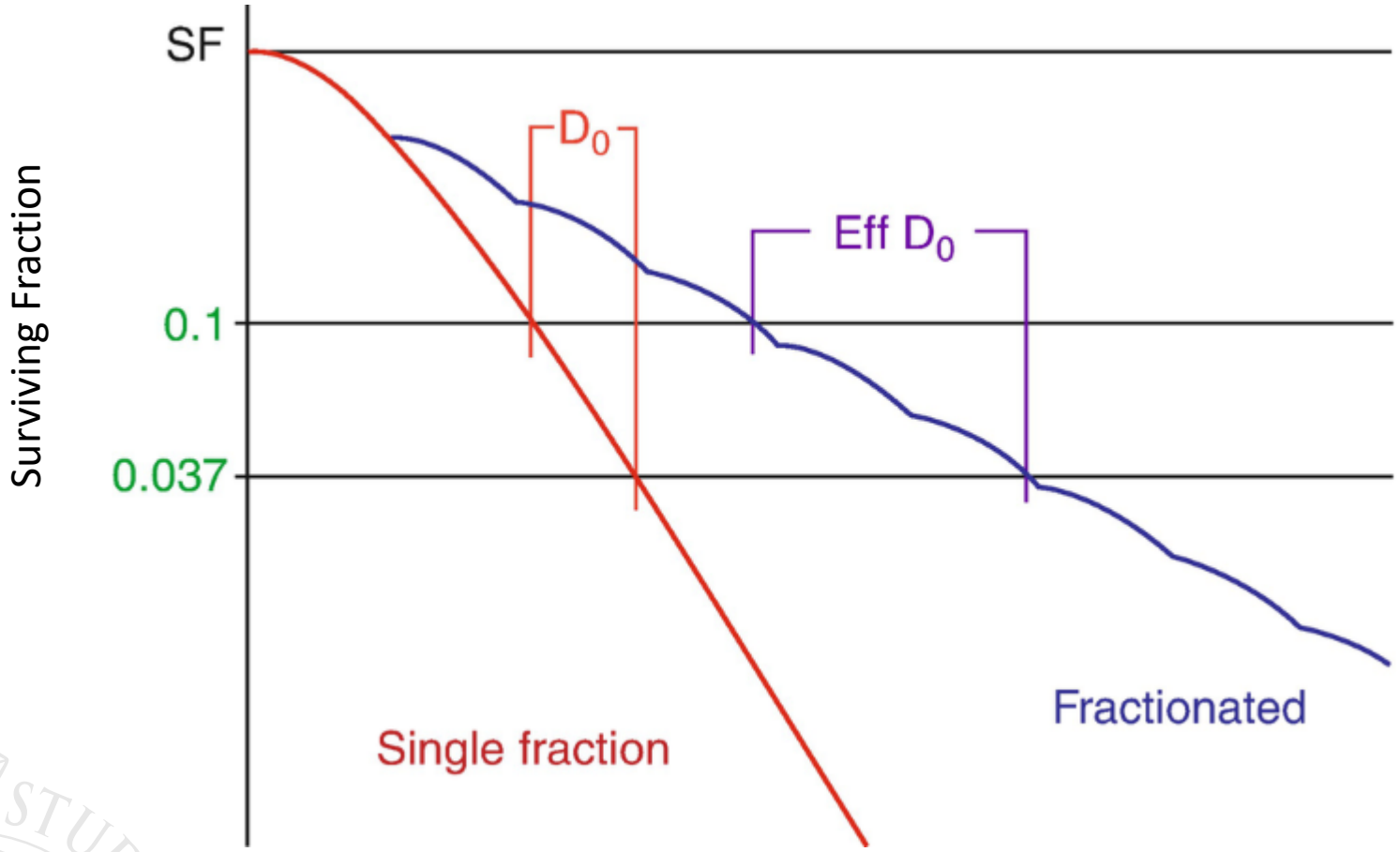


moderate hypofractionation

radiosurgery

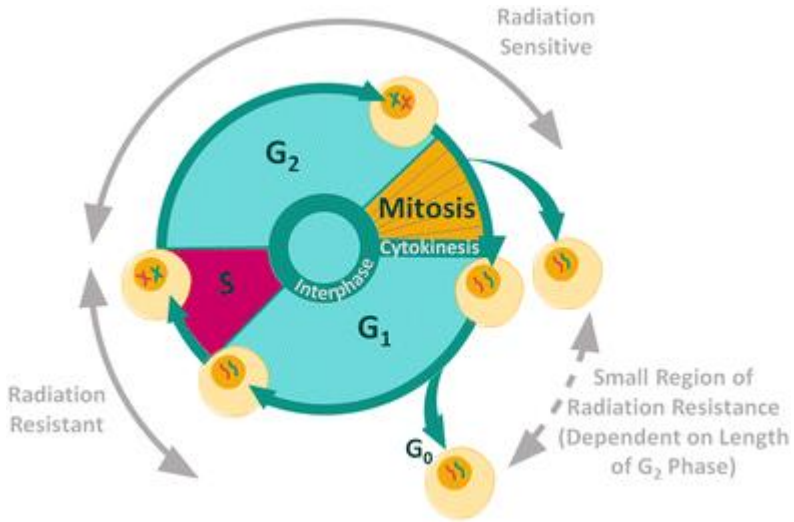
Repair

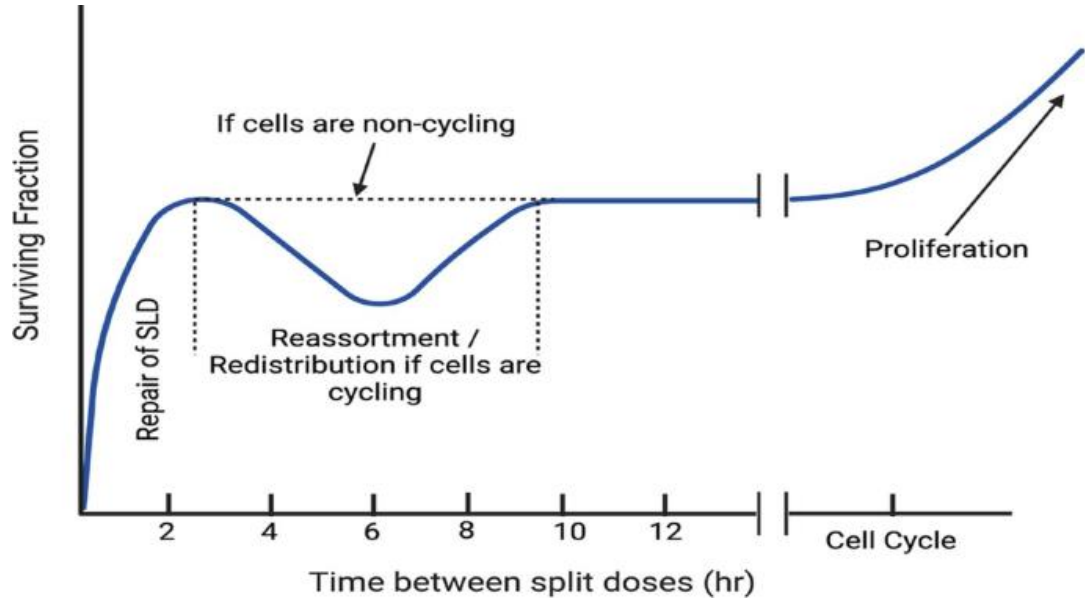
REPAIR OF SUBLETHAL DAMAGE



Prolonged delivery time

Redistribution





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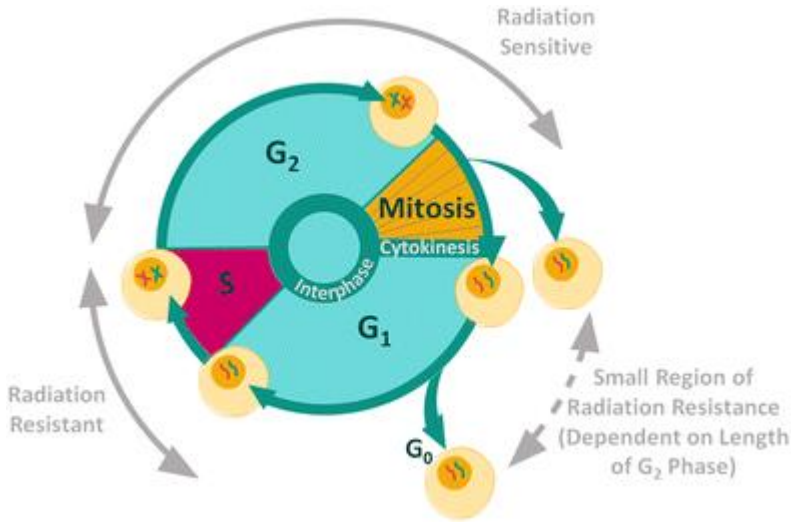
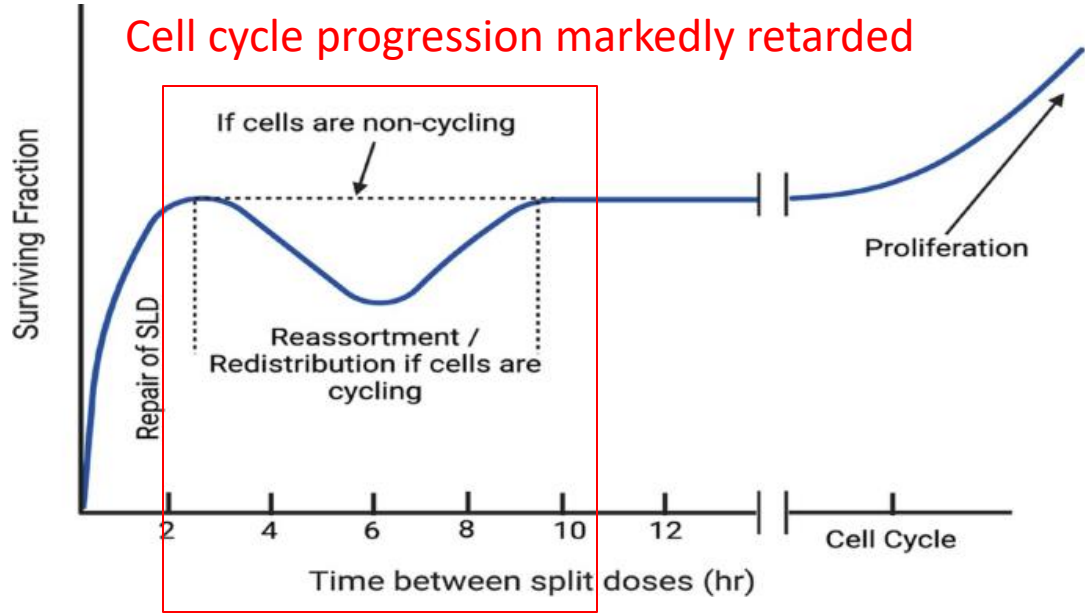
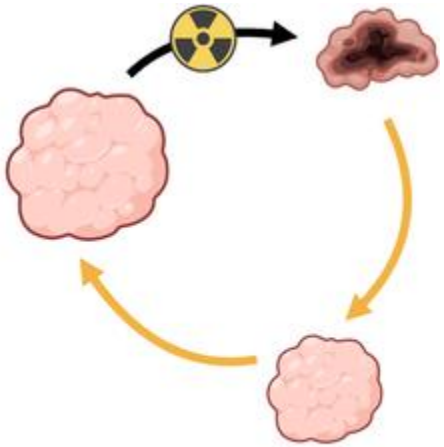
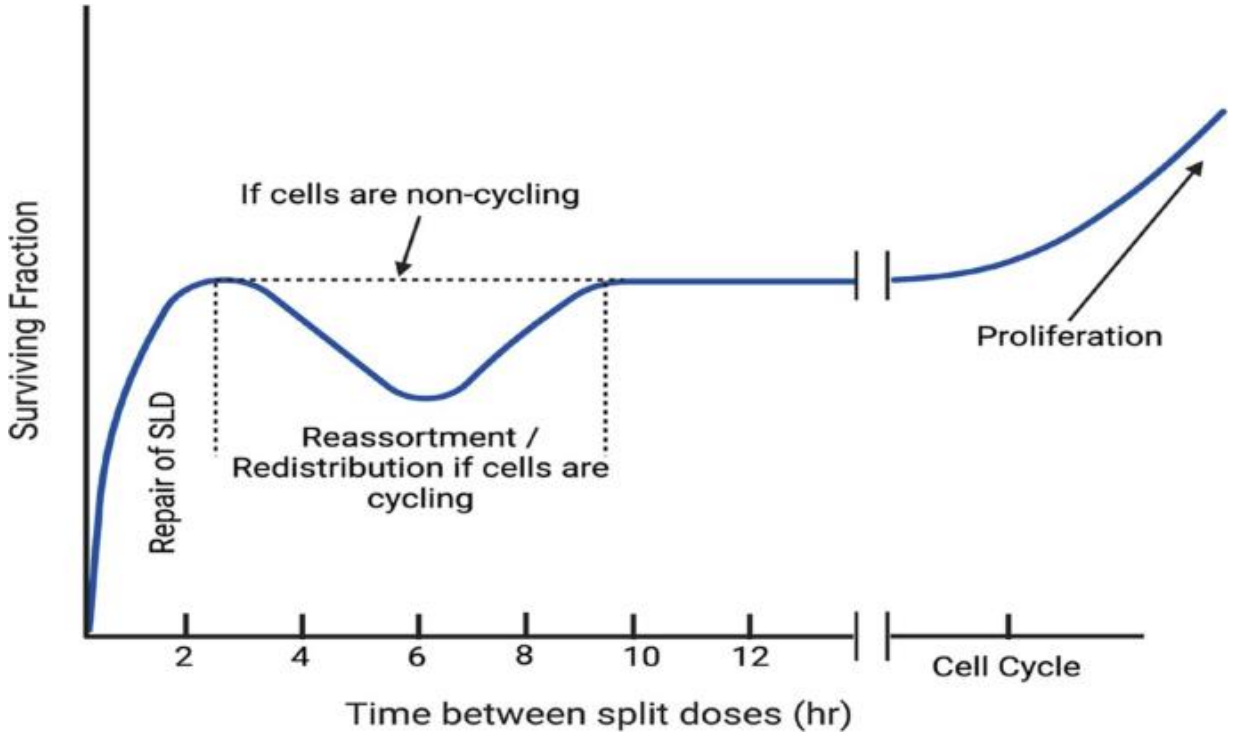


Cell cycle progression markedly retarded

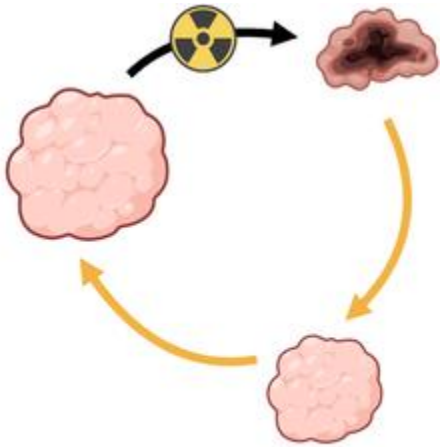


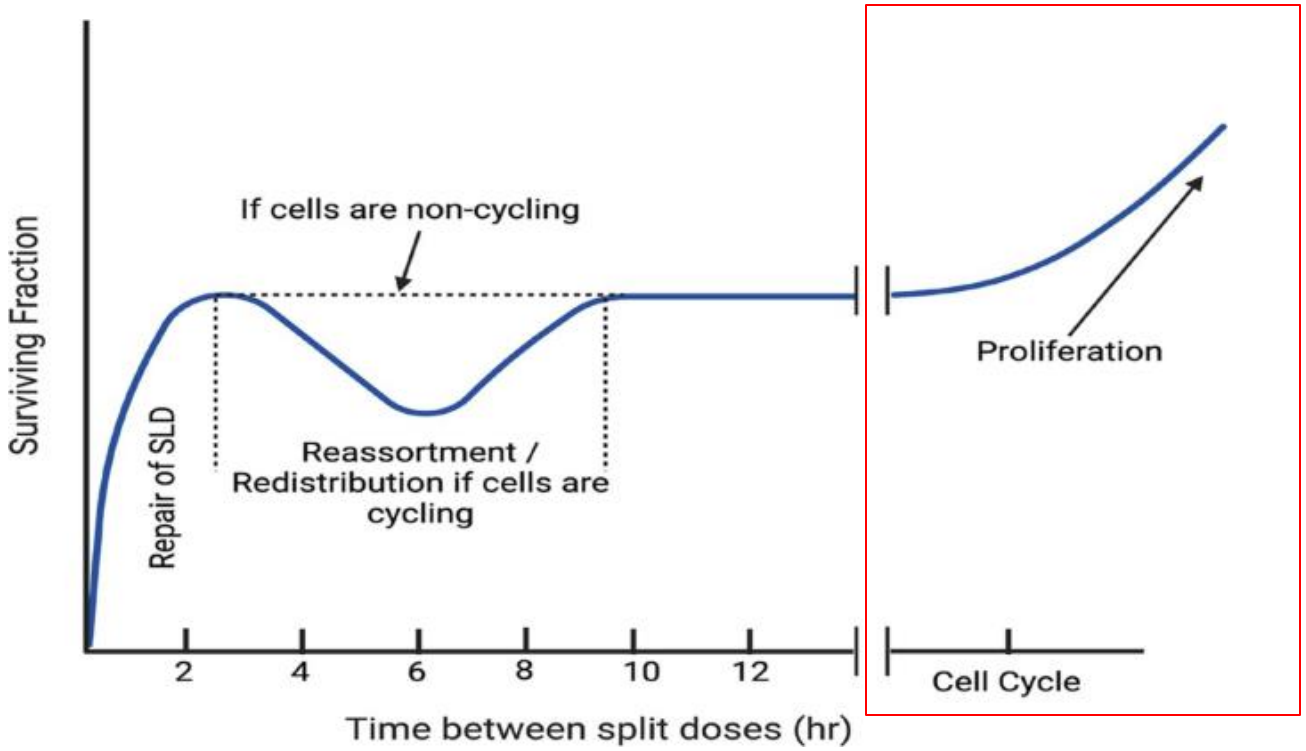
Repopulation



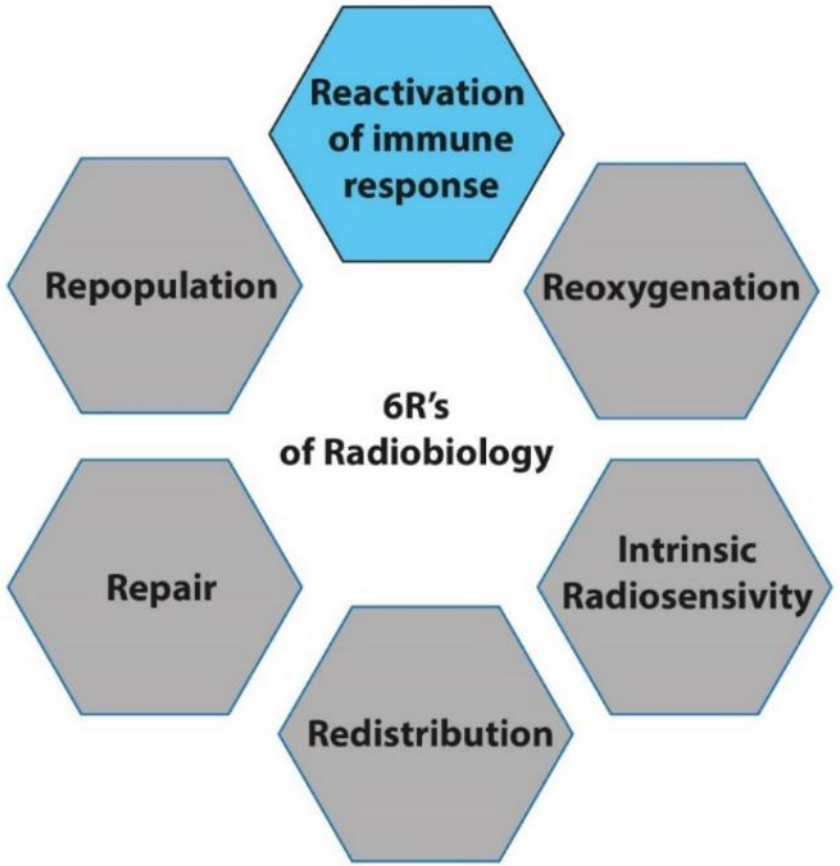


Repopulation



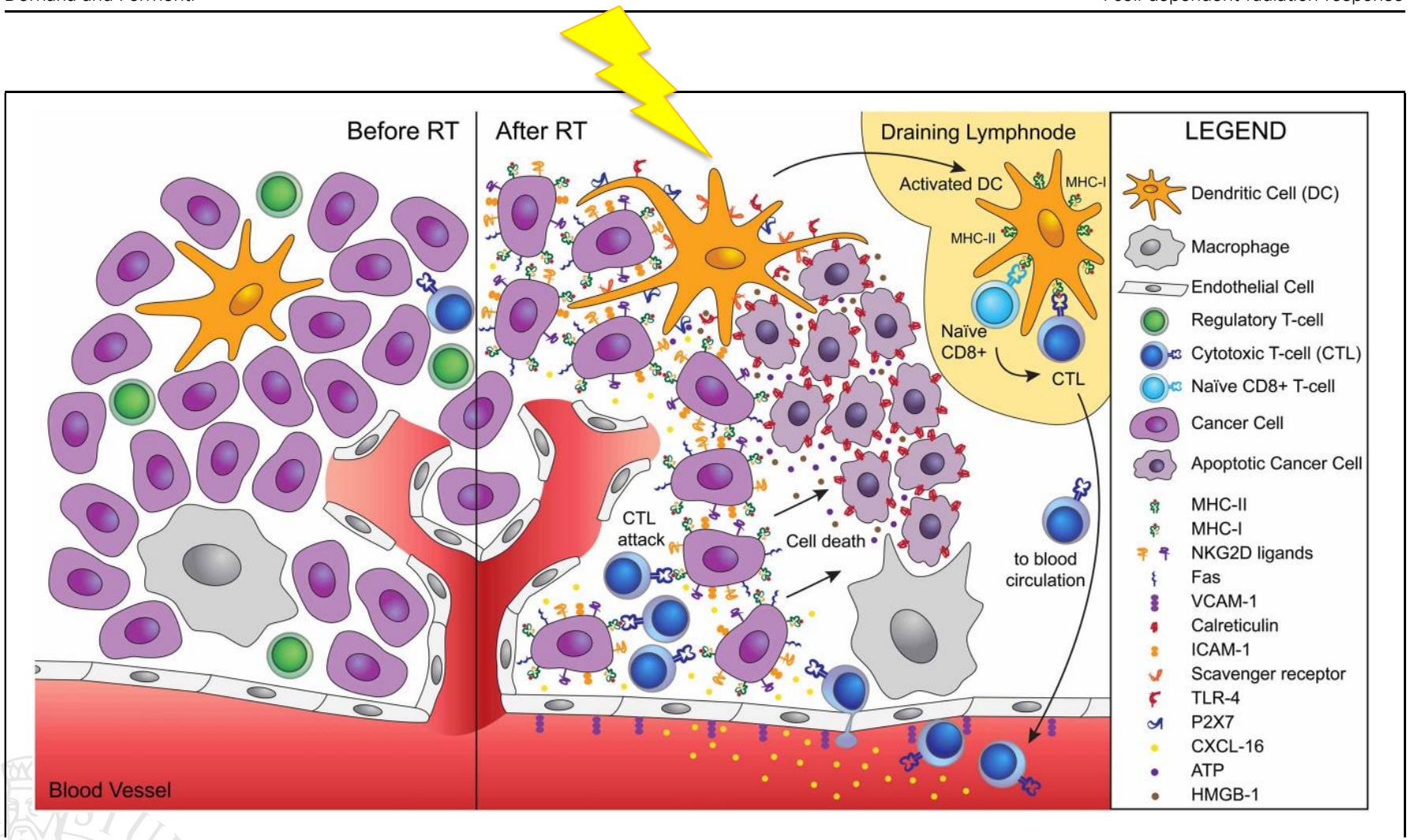


Antigen-induced damage and immune response



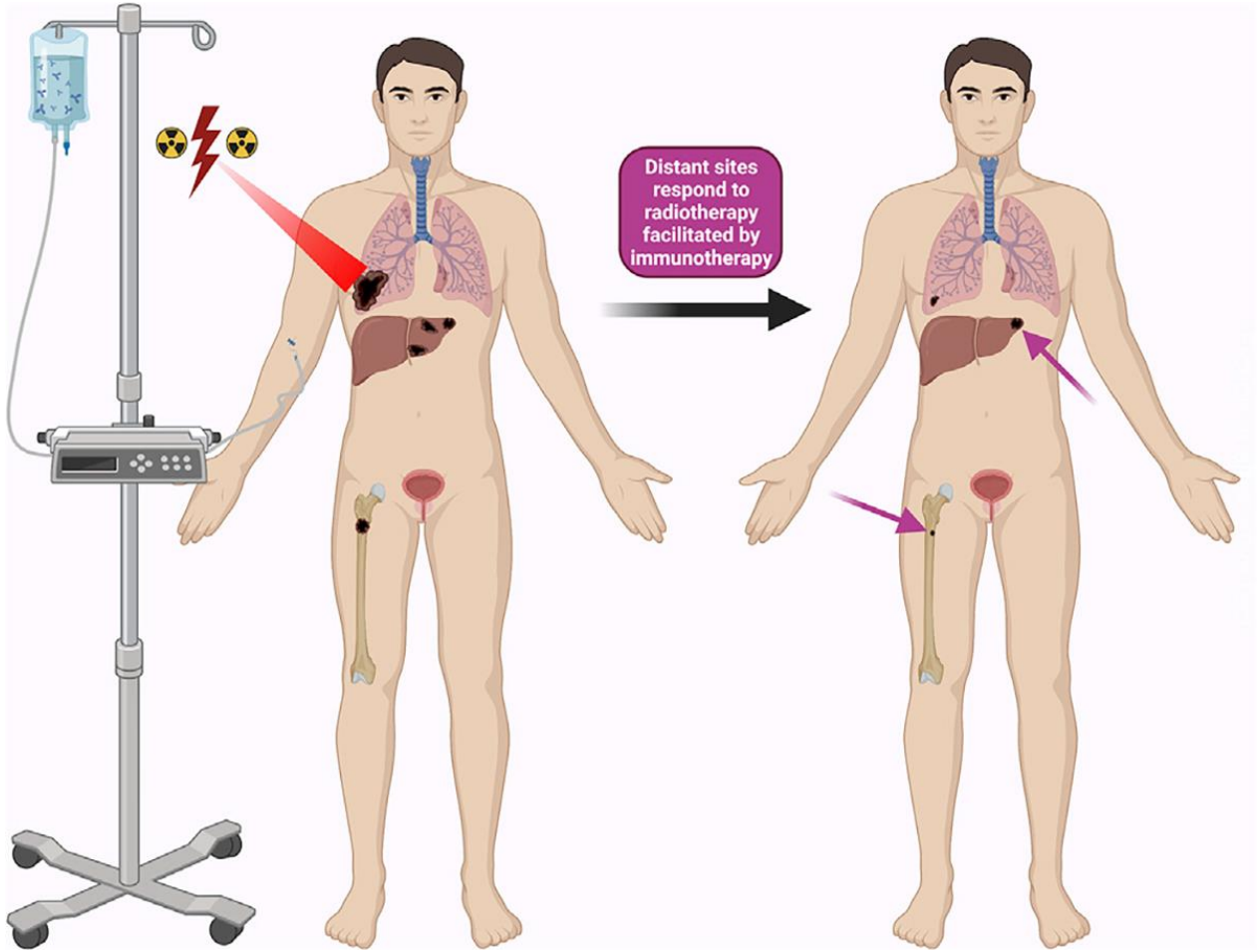
Boustani J, Grapin M, Laurent PA, Apetoh L, Mirjolet C.
The 6th R of Radiobiology: Reactivation of Anti-Tumor Immune Response. Cancers (Basel). 2019 Jun 20;11(6):860.

In situ vaccine

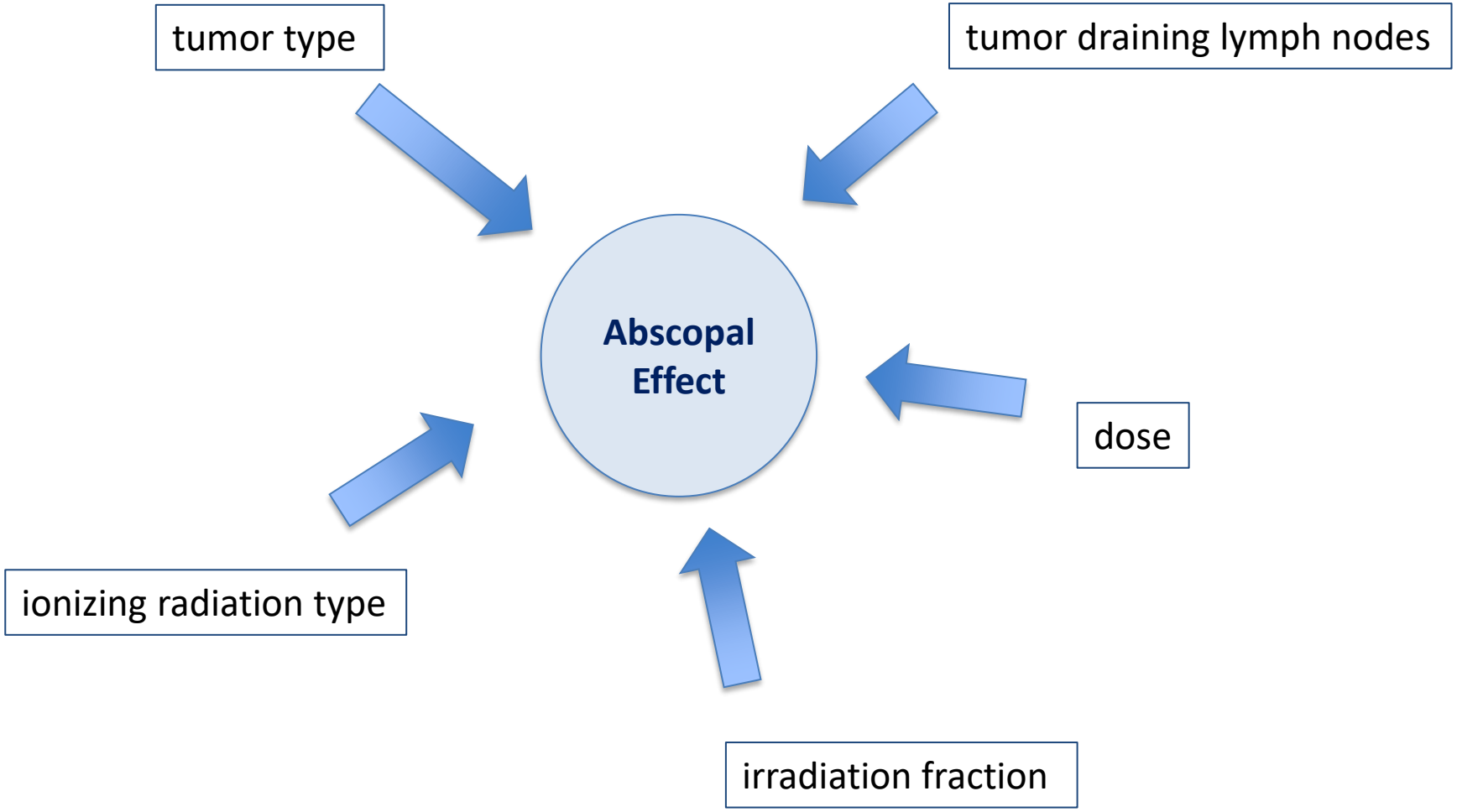


Demaria S, Frontiers in Oncology 2012

Abscopal effect



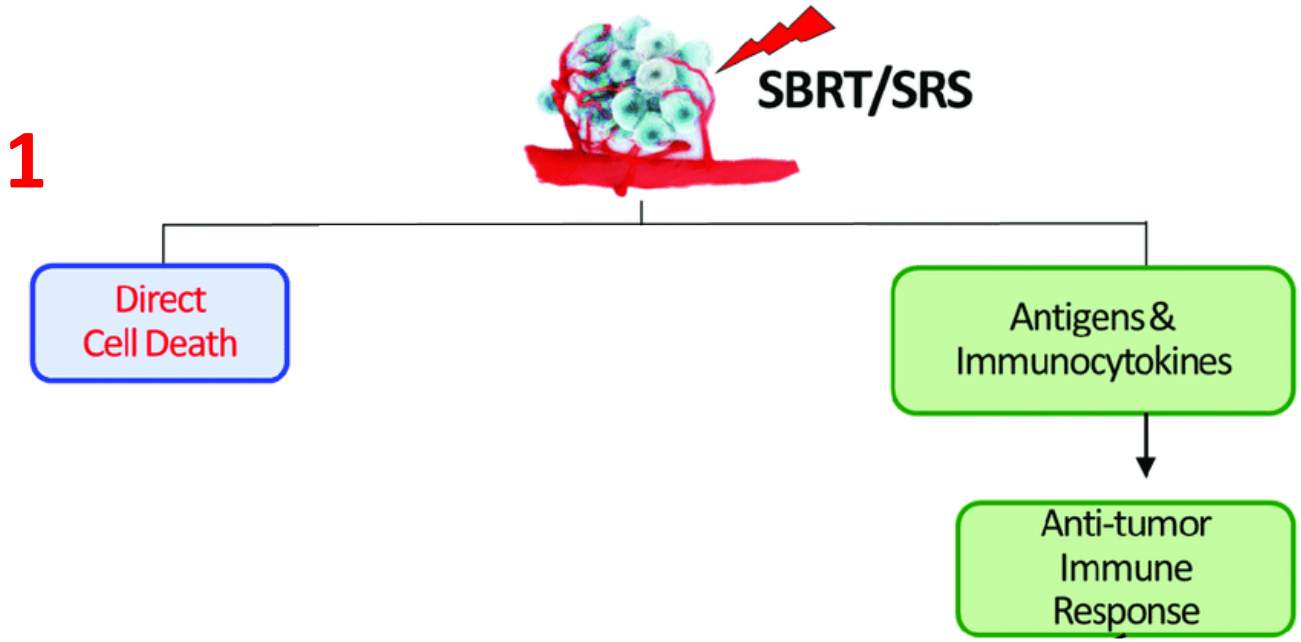
RT + immunotherapy



Rev in

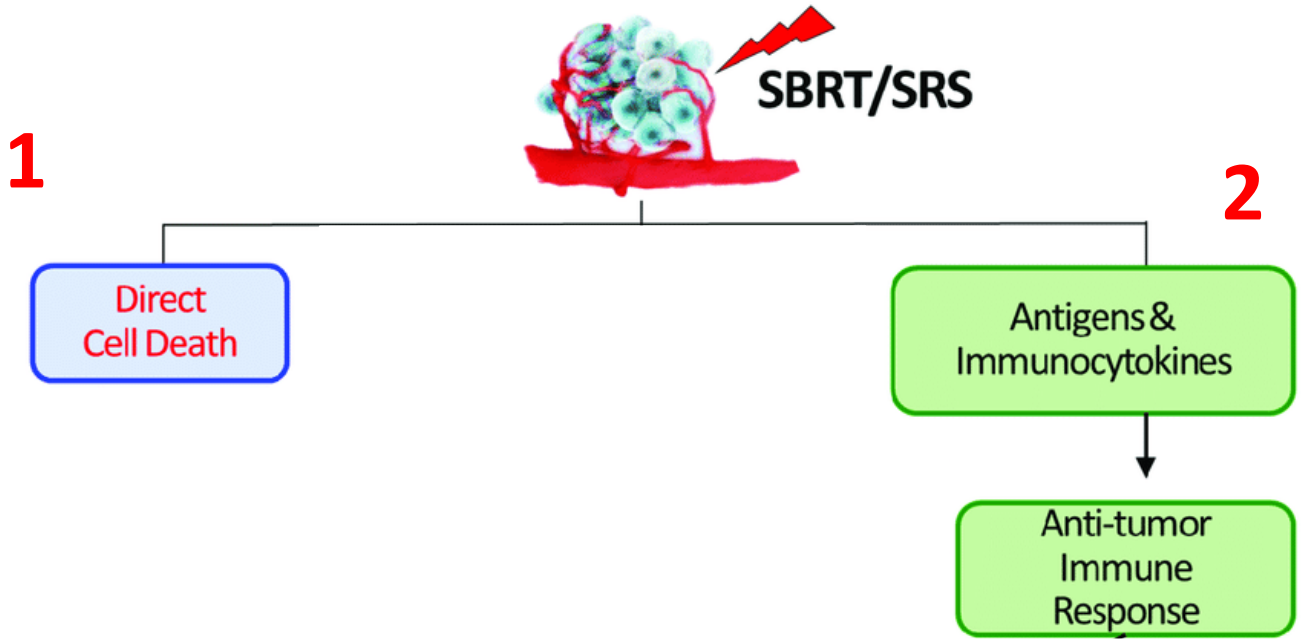
B. Yu et al. ”Killing two birds with one stone: Abscopal effect mechanism and its application prospect in radiotherapy” *Critical Reviews in Oncology / Hematology (2024)*

Tumor cells killing



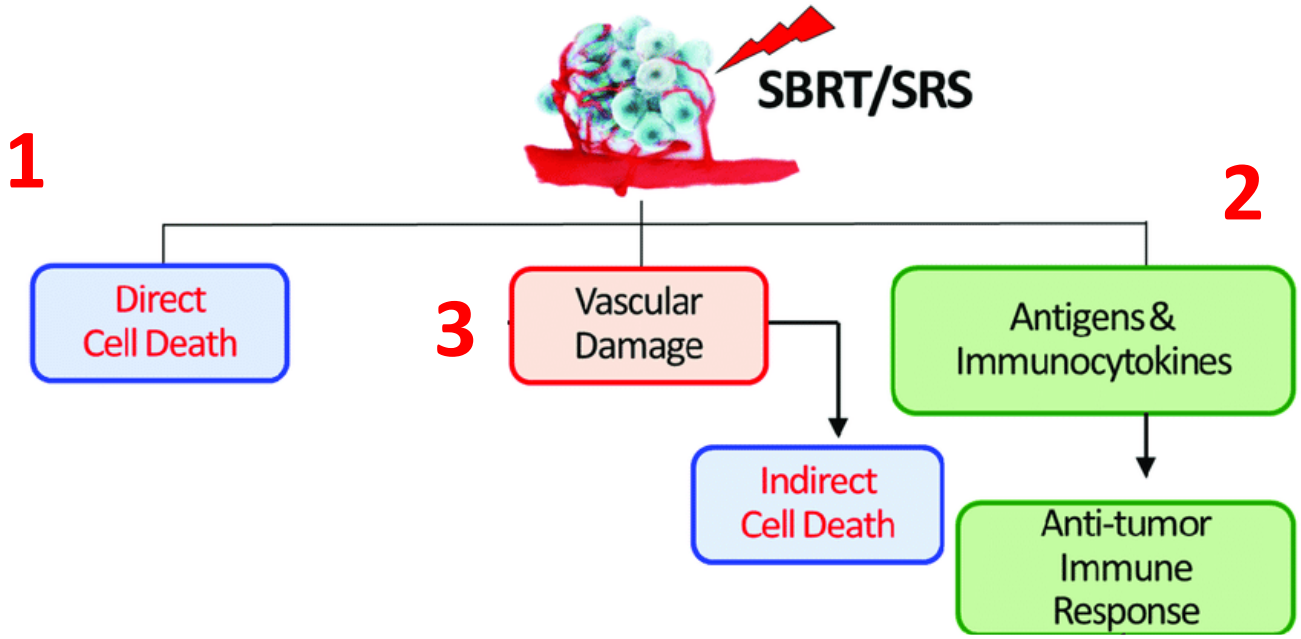
Song et al. Int J Radiation Oncol Biol Phys, Vol. 110, No. 1, pp. 21e34, 2021

Tumor cells killing

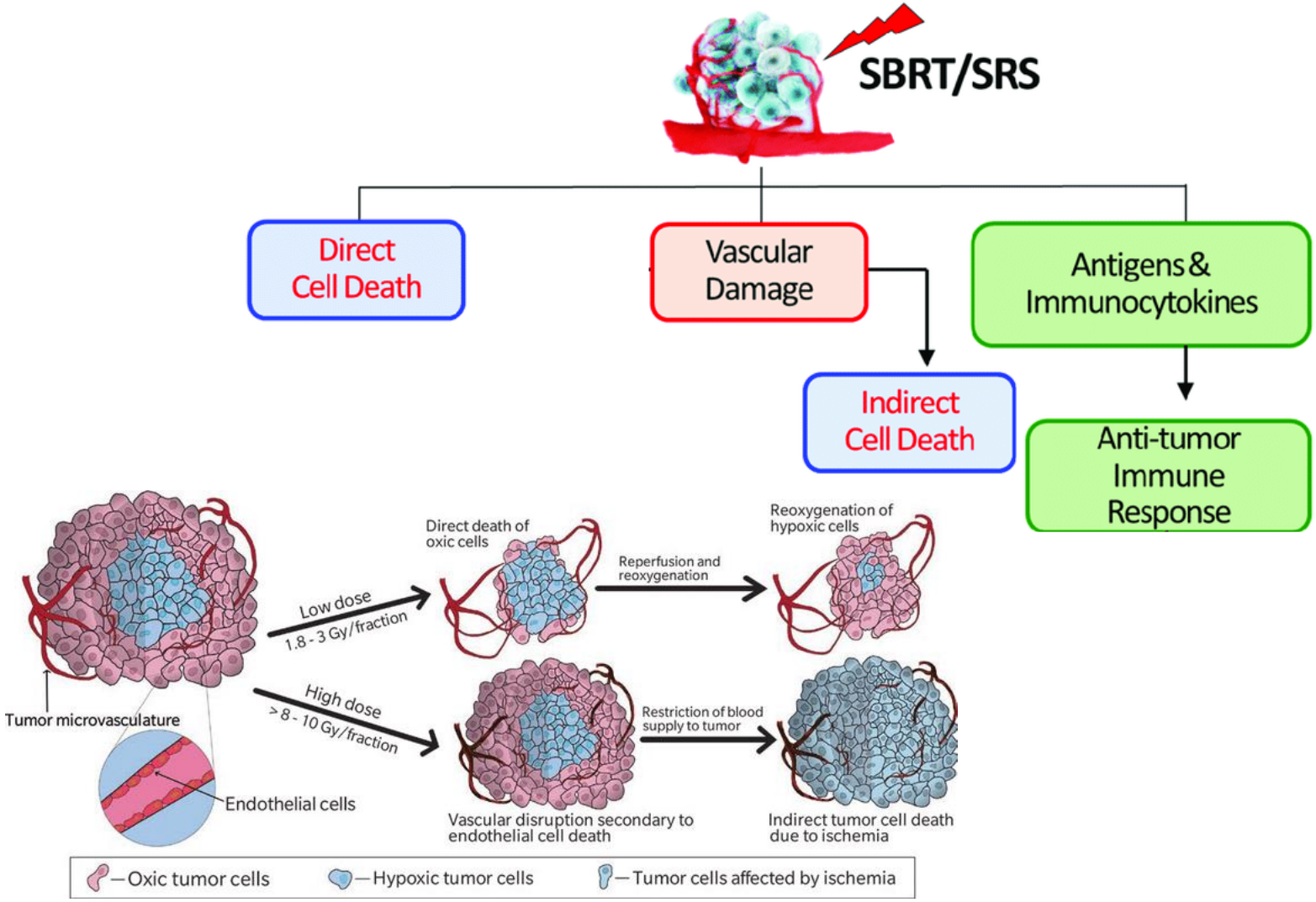


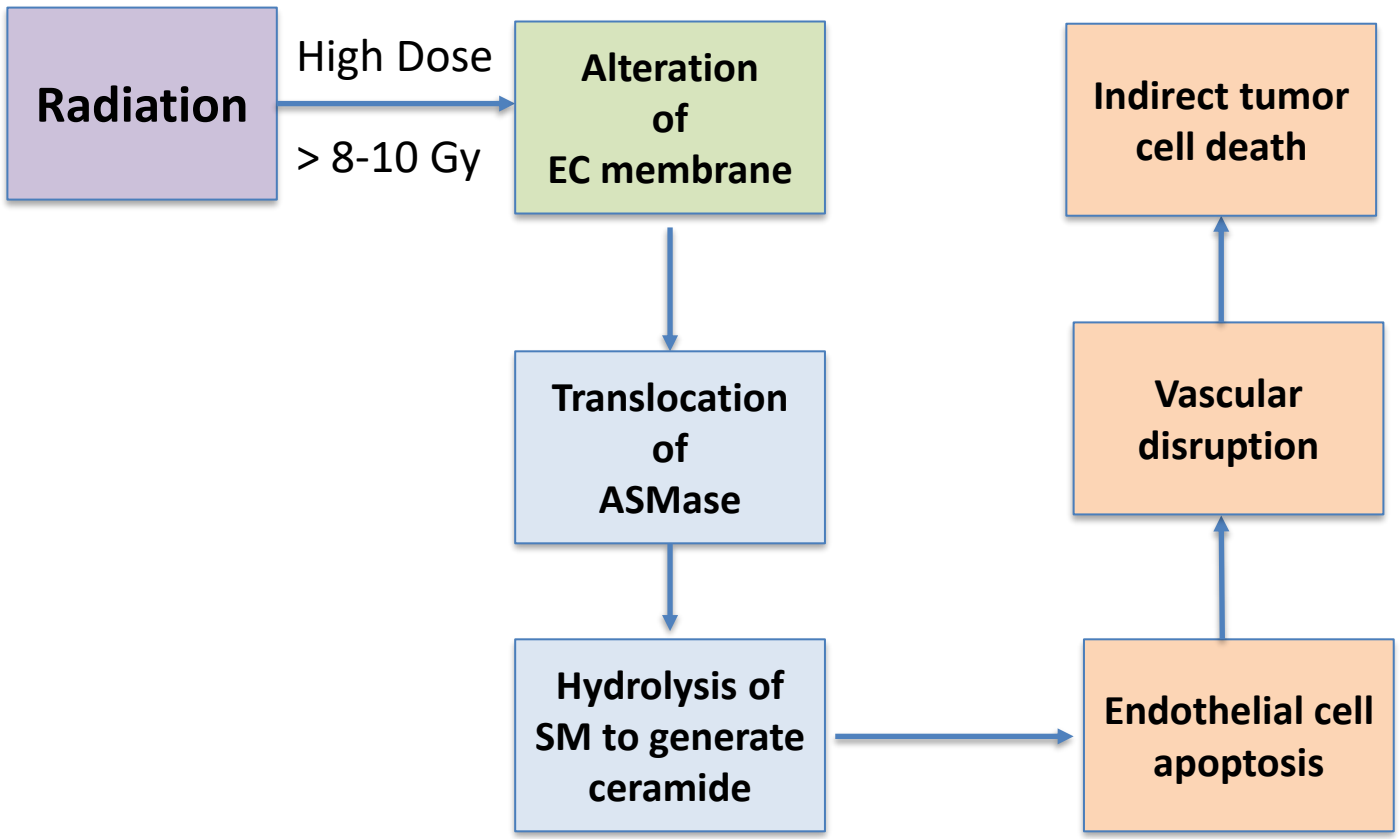
Song et al. Int J Radiation Oncol Biol Phys, Vol. 110, No. 1, pp. 21e34, 2021

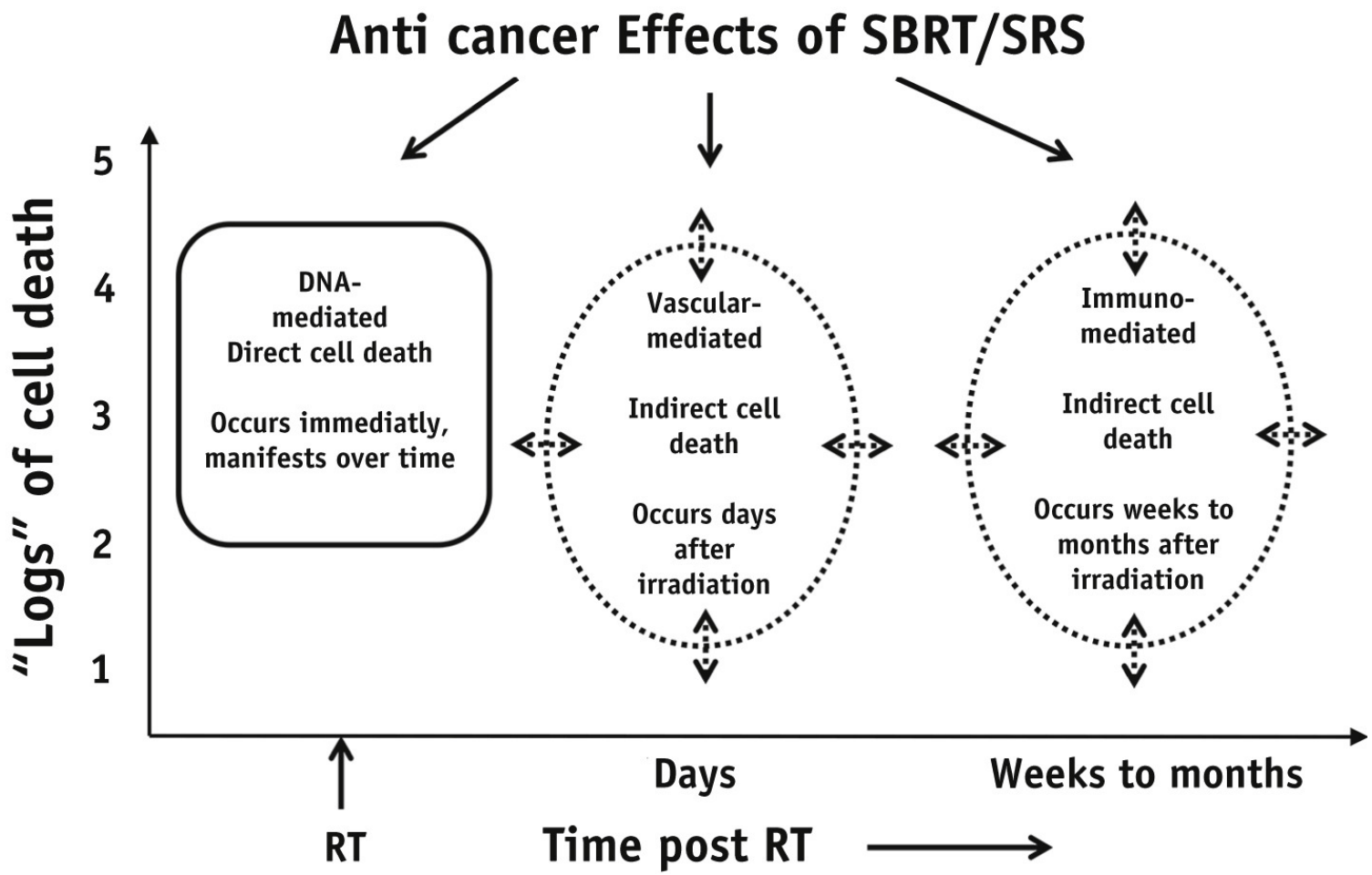
Indirect death



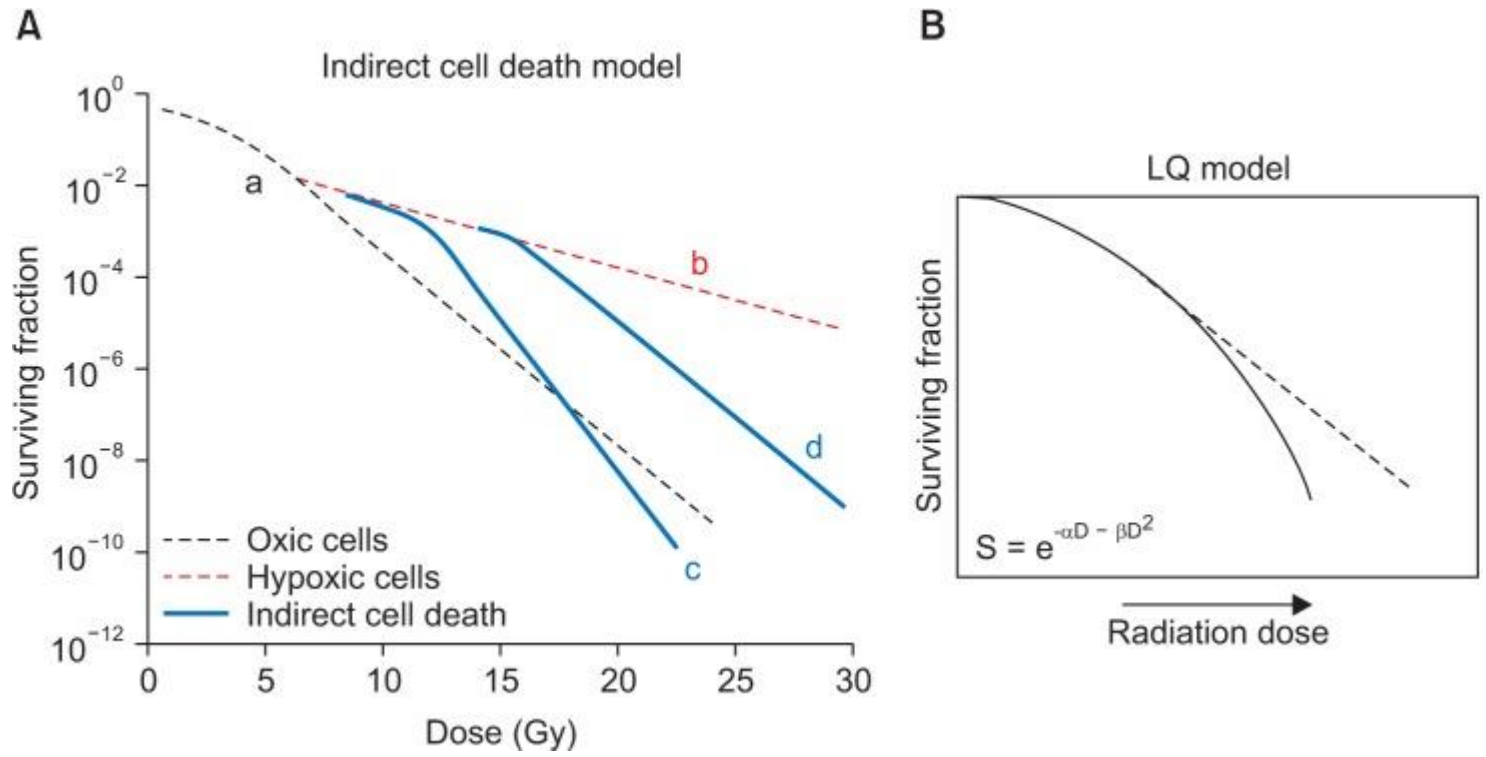
Indirect death




Radiation
High Dose
> 8-10 Gy
Alteration of EC membrane
Translocation of ASMase
Hydrolysis of SM to generate ceramide
Endothelial cell apoptosis
Vascular disruption
Indirect tumor cell death


Anti cancer Effects of SBRT/SRS
"Logs" of cell death
5
4
3
2
1
DNA-
mediated
Direct cell death
Occurs immediatly,
manifests over time
Vascular-
mediated
Indirect cell
death
Occurs days
after
irradiation
Immuno-
mediated
Indirect cell
death
Occurs weeks to
months after
irradiation
RT
Days
Weeks to months
Time post RT

The linear quadratic model

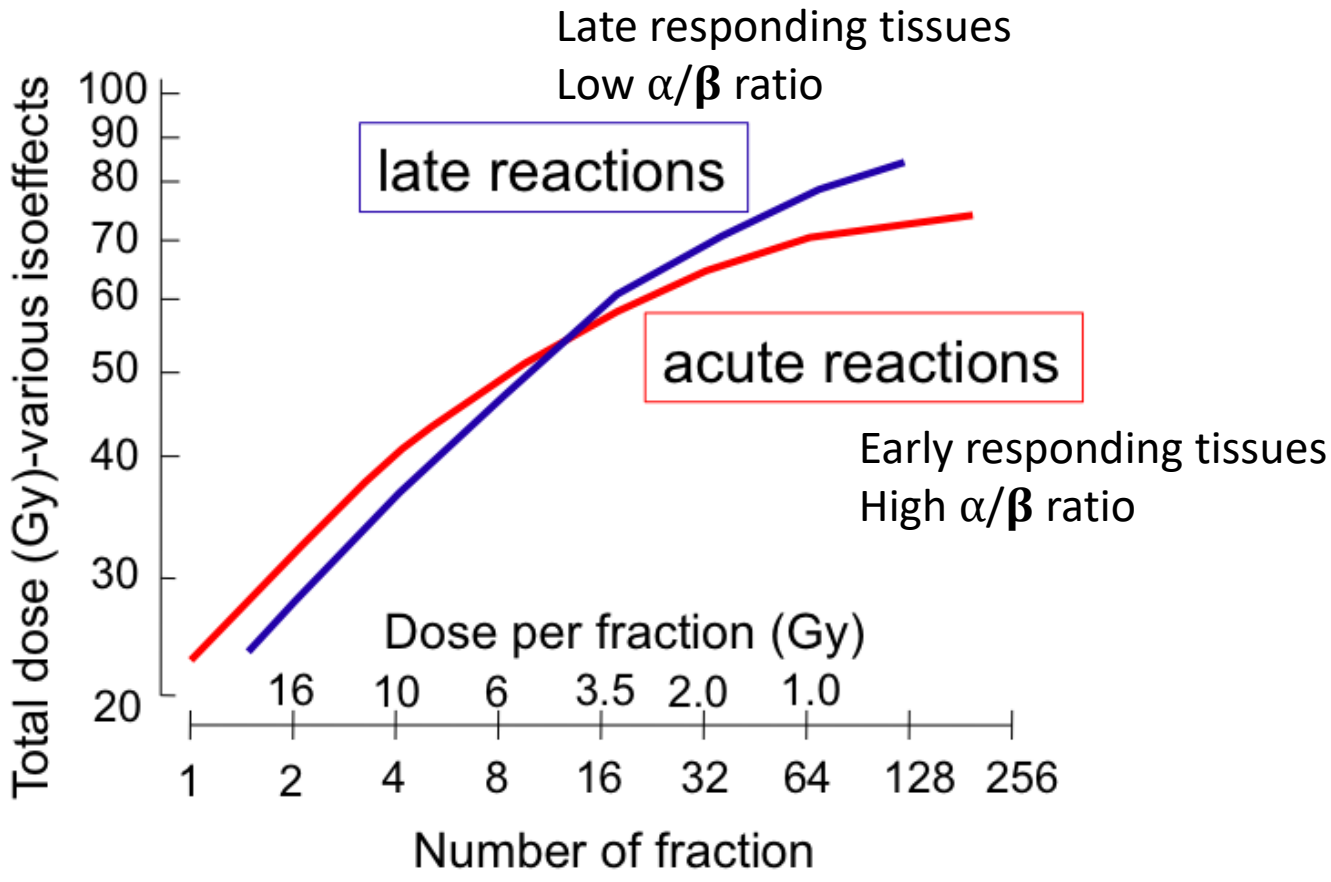


Kim MS, et al. Radiobiological mechanisms of stereotactic body radiation therapy and stereotactic radiation surgery. Radiat Oncol J. 2015

Implications of high dose per fraction on normal tissue

Relationship between isoeffective dose and dose per fraction

Implications of high dose per fraction on normal tissue



Relationship between isoeffective dose and dose per fraction

Implications of high dose per fraction on normal tissue

"vascular mediated" mechanisms have been suggested as the primary mode of

radiation-induced late normal-tissue effects

Implications of high dose per fraction on normal tissue

- radiation-induced vascular damage in normal tissue progresses slowly
- ischemic cell death and necrotic breakdown will gradually develop in normal tissues
- later cell death and tissue damage occur in a dose-dependent manner in normal tissues
- take measures to avoid normal-tissue damage: patient selection, target delineation, dose prescription, and treatment delivery accuracy during SBRT/SRS.
- imperative to limit the volume of normal tissues exposed to high doses per fraction

Challenges of Radiological Protection in Research and Society referring to Medical Field

October 3/2024

Milan, Italy

Sala Napoleonica/Via Sant'Antonio, 12
Università di Milano

Adaptive Radiotherapy in patient Radiation Protection

Michela Buglione di Monale e Bastia
Associazione Italiana Radioterapia e Oncologia Clinica (AIRO)
University and ASST Spedali Civili, Brescia

Line

- Adaptive RT
- What about its utility?
- Patient’s radioprotection during radiotherapy
- Doses during adaptive radiotherapy using ionizing radiations: are these clinically relevant?
- RM adaptive radiotherapy (not only for radioprotection reasons)
- Problems in ART: dose accumulation and deformable image registration
- Conclusions

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- Adaptive RT
- What about its utility?
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- ~~Problems in ART: dose accumulation and deformable image registration~~
- Conclusions

Adaptive radiotherapy

- Radiotherapy has evolved significantly over the years. Traditionally, treatment plans were based on initial scans used throughout the treatment course, accounting for changes in the patient's anatomy by additional margins to targets.
- However, the field has moved towards decreasing margins with the advancement of delivery and targeting accuracy in order to decrease toxicity, and the **increasing use of image guidance has illuminated patient anatomical changes such as organ deformation, weight loss, tumour shrinkage, and even biological changes** that are unaccounted for by the conventional approach.

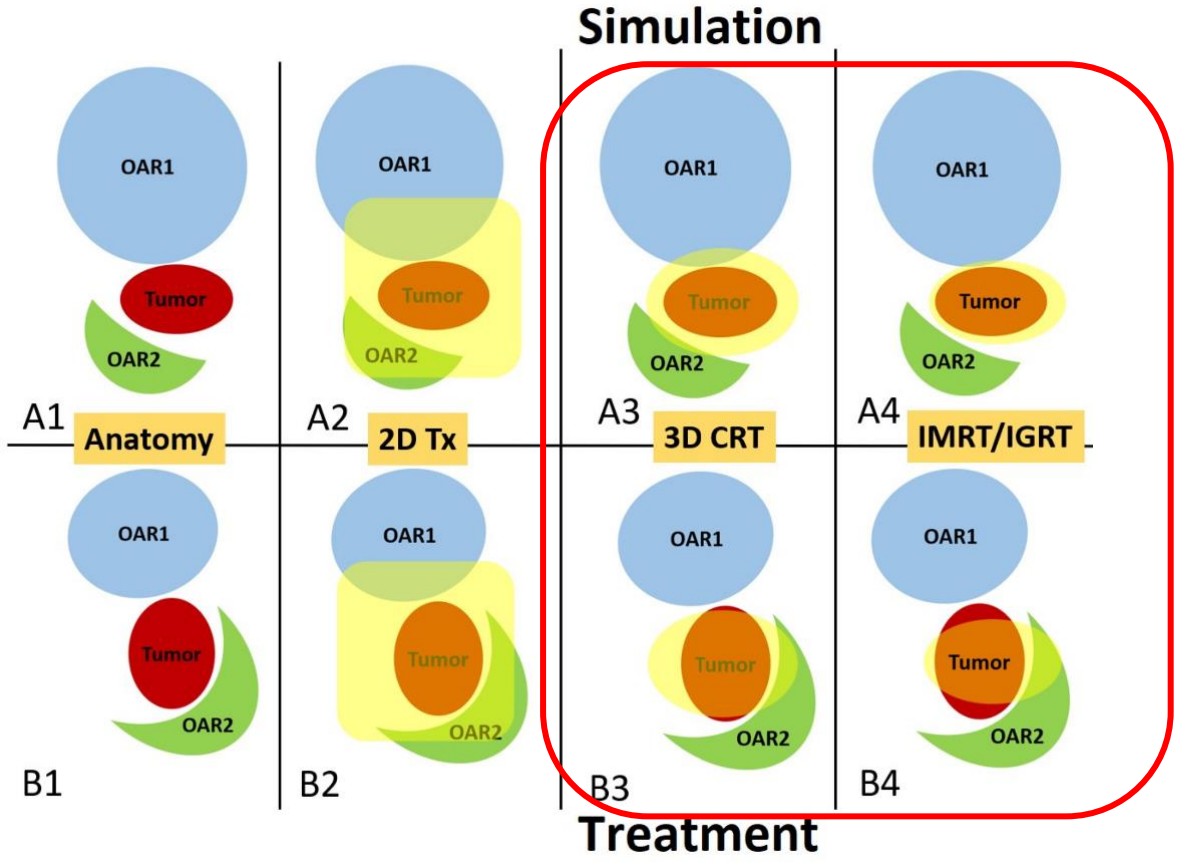
Adaptive radiotherapy (ART) addresses this by adjusting treatment plans according to these changes.

ART can be conducted in two ways:

- online (adjustments made during treatment sessions)
- offline (adjustments made between treatment sessions).

Dona Lemus, O.M.; Cao, M.; Cai, B.; Cummings, M.; Zheng, D. Adaptive Radiotherapy: Next- Generation Radiotherapy. *Cancers* **2024**,*16*,1206. https://doi.org/ 10.3390/cancers16061206

Nevertheless, as demonstrated in panels A3-4 and B3-4, when there is a **disparity between the anatomy on the treatment day and the anatomy during the simulation, as the treatment plan becomes increasingly sophisticated and tightly conformal to the original targets**, **the anatomical changes can lead to a greater deviation from the initial intention**. Consequently, the coverage of the tumour dose is compromised, and the OARs receive a higher dose than planning



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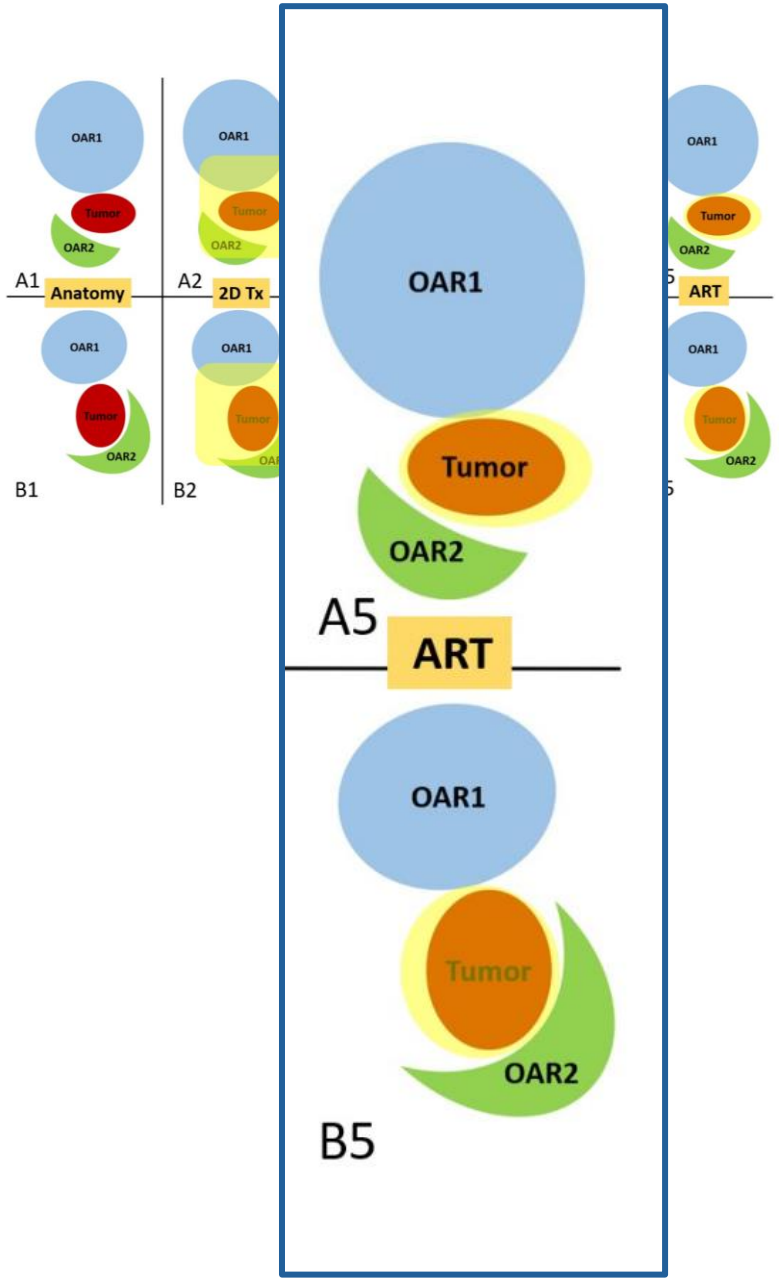

- - ART signifies a fundamental change from conventional radiotherapy, **as it involves dynamically reoptimizing the treatment plan to accommodate changes in the patient's anatomy**.

- - This guarantees the **preservation of accurate radiation dosage to the tumour while specifically protecting nearby OARs**, thus optimizing the therapeutic ratio that can be achieved with advanced radiotherapy technology.

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On-line vs off-line ART

Table 1. Summary of offline vs. online ART.

	Offline ART	Online ART
Frequency	Offline ART involves evaluation/adjustments to the treatment plan in between treatment sessions, with the patient off the table. Plan adjustments are based on anatomy imaged at a certain timepoint and applied for later sessions. It is often applied in lower frequency such as mid-treatment, biweekly, or weekly.	Online ART involves evaluations/adjustments based on the session anatomy, while the patient stays on the treatment table, and is applied for the treatment of the same session. It is currently more often applied in each treatment session.

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Complexity	When performed less frequently, it is generally less resource-intensive compared to online ART. At the same time, it could still be staff-time-demanding if offline ART has a less streamlined or automated workflow than available in online ART.	Online ART can be more complex and resource-intensive compared to offline ART because it requires specialized equipment and software and may be carried out more frequently.

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Treatment planning	Offline ART is not conducted on patient images obtained in the session the adaptive plan is intended to be applied. Instead, planning is conducted offline on previously obtained images to apply in future sessions.	It allows for a highly individualized and precise treatment plan for each session, taking into account the new anatomy in each treatment session. The adaptive plan is made based on the session image and applied to the same session.

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Clinical Applications	It is suitable for patients with tumors, OARs, and body habitus that are less likely to experience rapid anatomical changes and when the tumor is relatively distant from critical structures. It is commonly employed in situations such as head and neck cancers. Patient setup changes could also trigger the need for offline adaptation.	Used for cases where anatomical changes are expected on a daily basis. It is commonly employed in situations such as abdominal and pelvic malignancies. Based on the optimal trade-off between clinical benefits and required resources, the online ART platform may also be used for various disease sites to apply daily, weekly, or on-demand plan adaptation.

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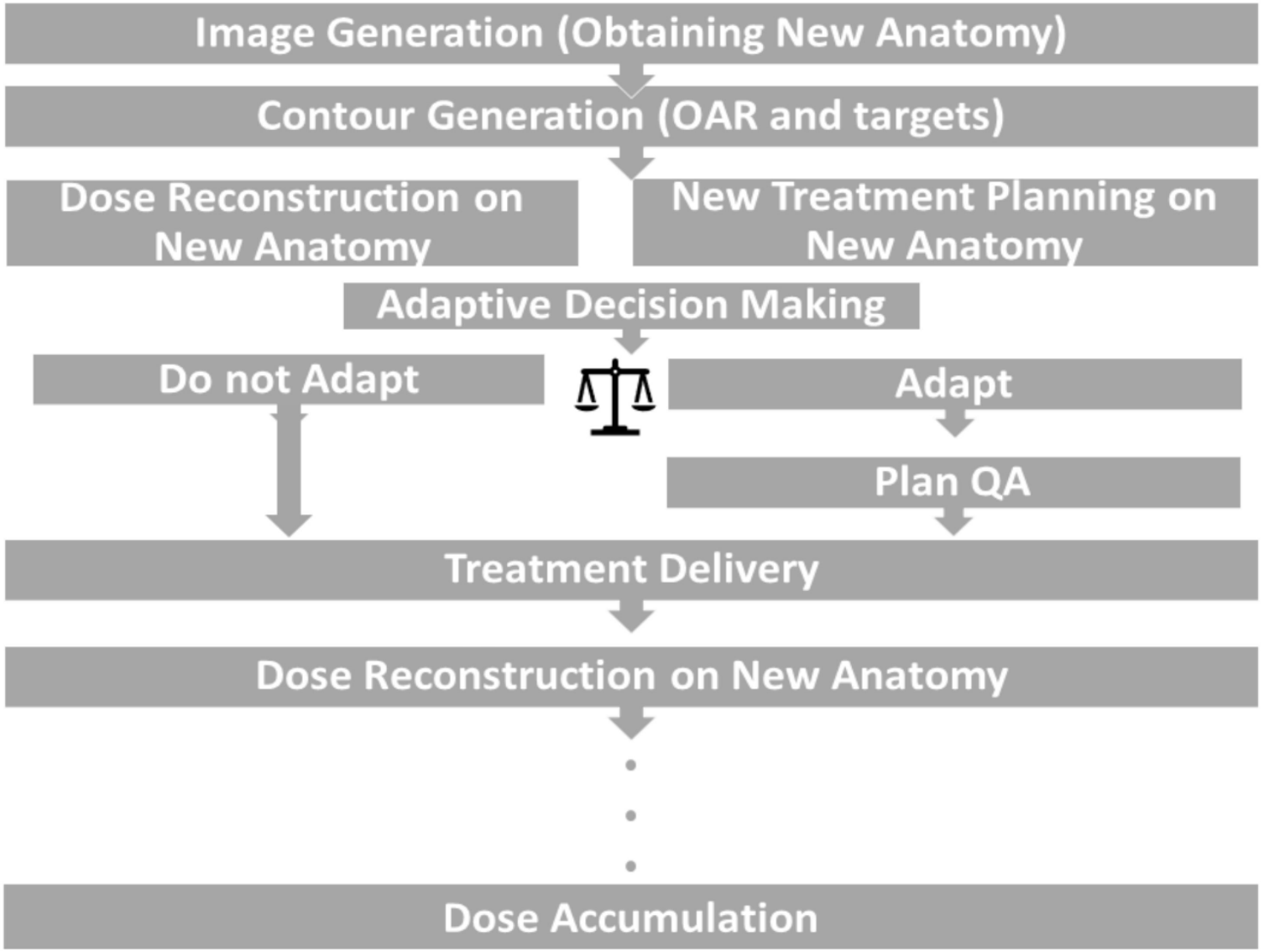
Basic workflow ART



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Basic principles of radioprotection

- Justification of the exposition
- Optimization of the dose
- Limitation of the maximal dose

Basic principles of radioprotection for patients treated with RT

- Justification of the exposition → radical/palliative **treatment of the tumor** → informed consent
- Optimization of the dose → **great attention to OAR, to dose distribution to G and CTV, to reduce unnecessary dose out of the target**
- Limitation of the maximal dose → **the maximal doses for general population are too low for patients treated with RT → but also for these patients the attention has to be posed to reduce the unnecessary dose and to deliver the minimum necessary dose**

Dose during ART workflow

Is it clinically relevant or not?

Radiation exposure during the acquisition of the CBCT scan, while minimal compared with the dose delivered during RT treatment, nevertheless prevents the use of CBCT for repeated images throughout the fraction; therefore, CBCT cannot be used for real-time ART or intrafraction motion assessment (46,56). The imaging dose for kilovoltage-CBCT typically ranges from 0.2 to 2 cGy per image (20,29). Skin dose has been measured to be a fraction of a centigray for low-dose head and neck imaging and 7 cGy for high-dose pelvic imaging (56).

In summary, the key advantages of CBCT-based ART include its ease of integration into the RT workflow and potential for rapid imaging and replanning, leading to feasible time frames for online adaptation. The major drawback is the inferior image quality due to poor resolution, scatter, and artifacts, which leads to reduced soft-tissue contrast and increased dosimetric uncertainty.

As online ART relies heavily on the quality of onboard imaging for treatment adaptation, there has been much enthusiasm about MRI platforms for online ART. Hybrid systems that combine linear accelerators with onboard MRI (MRI-linear accelerator systems) are commercially available and have been used in most clinical implementations of online ART to date (46), including in patients with lung tumors (38), liver and other abdominal malignancies (22), pancreas cancer (28), colorectal cancer (23), prostate cancer (21,37), and adrenal metastases (36).

While implementing MRI-guided ART can require a substantial investment of resources and pose many technical challenges, the increased soft-tissue resolution over CBCT and the potential for real-time and functional imaging offer important advantages to MRI-linear accelerator implementation for ART

Phys Eng Sci Med. 2022 Mar;45(1):231-237. doi: 10.1007/s13246-022-01105-7. Epub 2022 Jan 25.

Dose assessment for daily cone-beam CT in lung radiotherapy patients and its combination with treatment planning

Hassan Albarakati [1 2 3], Price Jackson [1 2], Okan Gulal [1], Prabhakar Ramachandran [2 4], Glen Osbourne [5], Michael Liu [5], Tomas Kron [6 7 8], Moshi Geso [9]

Affiliations + expand

PMID: 35076869 DOI: 10.1007/s13246-022-01105-7

Abstract

With the increased use of X-ray imaging for patient alignment in external beam radiation therapy, particularly with cone-beam computed tomography (CBCT), the additional dose received by patients has become of greater consideration. In this study, we analysed the radiation dose from CBCT for clinical lung radiotherapy and assessed its relative contribution when combined with radiation treatment planning for a variety of lung radiotherapy techniques. The Monte Carlo simulation program ImpactMC was used to calculate the 3D dose delivered by a Varian TrueBeam linear accelerator to patients undergoing thorax CBCT imaging. The concomitant dose was calculated by simulating the daily CBCT irradiation of ten lung cancer patients. Each case was planned with a total dose of 50-60 Gy to the target lesion in 25-30 fractions using the 3DCRT or IMRT plan and retrospectively planned using VMAT. For each clinical case, the calculated CBCT dose was summed with the planned dose, and the dose to lungs, heart, and spinal cord were analysed according to conventional dose conformity metrics. Our results indicate greater variations in dose to the heart, lungs, and spinal cord based on planning technique, (3DCRT, IMRT, VMAT) than from the inclusion of daily cone-beam imaging doses over 25-30 fractions. The average doses from CBCT imaging per fraction to the lungs, heart and spinal cord were 0.52 ± 0.10, 0.49 ± 0.15 and 0.39 ± 0.08 cGy, respectively. Lung dose variations were related to the patient's size and body composition. Over a treatment course, this may result in an additional mean absorbed dose of 0.15-0.2 Gy. For lung V5, the imaging dose resulted in an average increase of ~ 0.6% of the total volume receiving 5 Gy. The increase in V20 was more dependent on the planning technique, with 3DCRT increasing by 0.11 ± 0.09% with imaging and IMRT and VMAT increasing by 0.17 ± 0.05% and 0.2 ± 0.06%, respectively. In this study, we assessed the concomitant dose for daily CBCT lung cancer patients undergoing radiotherapy. The additional radiation dose to the normal lungs from daily CBCT was found to range, from 0.15 to 0.2 Gy when the patient was treated with 25-30 fractions. Consideration of potential variation in relative biological effectiveness between kilovoltage imaging and megavoltage treatment dose was outside the scope of this study. Regardless of this, our results show that the assessment of imaging dose can be incorporated into the treatment planning process and the relative effect on overall dose distribution was small compared to the difference among planning techniques.

Keywords: 3DCRT; CBCT Dose; Daily CBCT; IMRT; Lung cancer; Monte Carlo; VMAT.

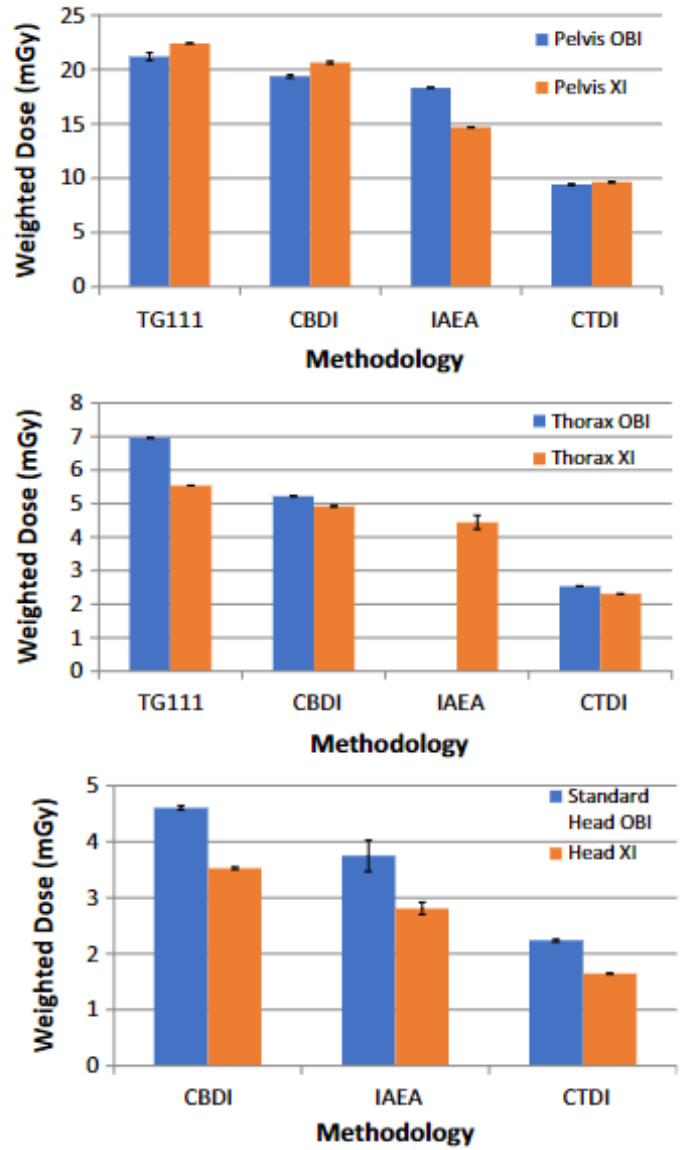

Fig. 4. Comparison of TG111, CBDI, IAEA, and CTDI methodologies on the OBI and XI imaging systems for pelvis (a) and thorax (b) protocols. The IAEA was not evaluated for OBI thorax. Comparison of CBDI, IAEA, and CTDI methodologies for OBI standard head and XI head protocols is shown in (c). Error bars represent one standard deviation from repeated measurements.

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DOI: 10.1002/acm2.12239
RADIATION ONCOLOGY PHYSICS
WILEY

Investigation of the radiation dose from cone-beam CT for image-guided radiotherapy: A comparison of methodologies

Jarryd G. Buckley[1] | Dean Wilkinson[2] | Alessandra Malaroda[1] | Peter Metcalfe[1]

Clinical dosimetric confirmation of adaptive procedures

lung

Abstract

Background Daily adaptive radiation therapy (ART) of patients with non-small cell lung cancer (NSCLC) lowers organs at risk exposure while maintaining the planning target volume (PTV) coverage. Thus, ART allows an isotoxic approach with increased doses to the PTV that could improve local tumor control. Herein we evaluate daily online ART strategies regarding their impact on relevant dose-volume metrics.

Methods Daily cone-beam CTs ($1 \times n = 28$, $1 \times n = 29$, $11 \times n = 30$) of 13 stage III NSCLC patients were converted into synthetic CTs (sCTs). Treatment plans (TPs) were created retrospectively on the first-fraction sCTs (sCT_1) and subsequently transferred unaltered to the sCTs of the remaining fractions of each patient (sCT_{2-n}) (IGRT scenario). Two additional TPs were generated on sCT_{2-n}: one minimizing the lung-dose while preserving the $D_{95\%}$(PTV) (isoeffective scenario), the other escalating the $D_{95\%}$(PTV) with a constant $V_{20Gy}(lung_{ipsilateral})$ (isotoxic scenario).

Results Compared to the original TPs predicted dose, the median $D_{95\%}$(PTV) in the IGRT scenario decreased by 1.6 Gy ± 4.2 Gy while the $V_{20Gy}(lung_{ipsilateral})$ increased in median by 1.1% ± 4.4%. The isoeffective scenario preserved the PTV coverage and reduced the median $V_{20Gy}(lung_{ipsilateral})$ by 3.1% ± 3.6%. Furthermore, the median $V_{5\%}$(heart) decreased by 2.9% ± 6.4%. With an isotoxic prescription, a median dose-escalation to the gross target volume of 10.0 Gy ± 8.1 Gy without increasing the $V_{20Gy}(lung_{ipsilateral})$ and $V_{5\%}$(heart) was feasible.

Conclusions We demonstrated that even without reducing safety margins, ART can reduce lung-doses, while still reaching adequate target coverage or escalate target doses without increasing ipsilateral lung exposure. Clinical benefits by means of toxicity and local control of both strategies should be evaluated in prospective clinical trials.

Keywords Adaptive radiation therapy, stage III NSCLC, Isotoxic dose-escalation, Isoeffective organ at risk sparing

Radiation Oncology (2023) 18:34

prostate

Inter-fraction organ variations cause deviations between planned and delivered doses in patients receiving radiotherapy for prostate cancer. This study compared planned (D_P) *vs* accumulated doses (D_A) obtained from daily cone-beam computed tomography (CBCT) scans in high-risk- prostate cancer with pelvic lymph nodes irradiation. An intensity-based deformable image registration algorithm used to estimate contours for D_A was validated using geometrical agreement between radiation oncologist's and deformable image registration algorithm propagated contours. Spearman rank correlations (r_s) between geometric measures and changes in organ volumes were evaluated for 20 cases. Dose-volume (DV) differences between D_A and D_P were compared (Wilcoxon rank test, $p < 0.05$). A novel region-of-interest (ROI) method was developed and mean doses were analyzed. Geometrical measures for the prostate and organ-at-risk contours were within clinically acceptable criteria. Inter-group mean (± SD) CBCT volumes for the rectum were larger compared to planning CT (pCT) (51.1 ± 11.3 cm^3 *vs* 46.6 ± 16.1 cm^3), and were moderately correlated with variations in pCT volumes, rs = 0.663, $p < 0.01$. Mean rectum DV for D_A was higher at V30-40 Gy and lower at V70-75 Gy, $p < 0.05$. Mean bladder CBCT volumes were smaller compared to pCT (198.8 ± 55 cm^3 *vs* 211.5 ± 89.1 cm^3), and was moderately correlated with pCT volumes, rs = 0.789, $p < 0.01$. Bladder D_A was higher at V30-65 Gy and lower at V70-75 Gy ($p < 0.05$). For the ROI method, rectum and bladder D_A were lower at 5 to 10 mm ($p < 0.01$) as compared to D_P, whilst bladder D_A was higher than D_P at 20 to 50 mm ($p < 0.01$). Generated D_A demonstrated significant differences in organ-at-risk doses as compared to D_P. A well-constructed workflow incorporating a ROI DV-extraction method has been validated in terms of efficiency and accuracy designed for seamless integration in the clinic to guide future plan adaptation.

Size-specific Effective Dose (SED)

- Results from the Monte Carlo simulations carried out in this study have compared values for SEDs between phantoms of different stature.
- This shows that patients who **are shorter or lighter will receive (significantly) higher doses if similar exposure factors and field sizes are used for CBCT scans on all patients**.

"A person who is 5 cm shorter will receive a SED that is 3%–7% greater for a chest scan and 4%–10% greater for a pelvis scan.
A person who is 10 kg lighter will receive a dose that is 11%–14% greater for a chest scan and 10%–13% greater for a pelvis scan.
The differences amount to 0.7 mSv to 1.6 mSv from one scan, but since radiotherapy treatments are often given in 20–30 fractions, the increase in cumulative dose can be significant if protocols are not optimised"

J. Radiol. Prot. **42** (2022) 031512

Size-specific Effective Dose (SED)

The culture of adapting imaging exposure parameters and field sizes to individual patients is less well established in IGRT than in diagnostic radiology

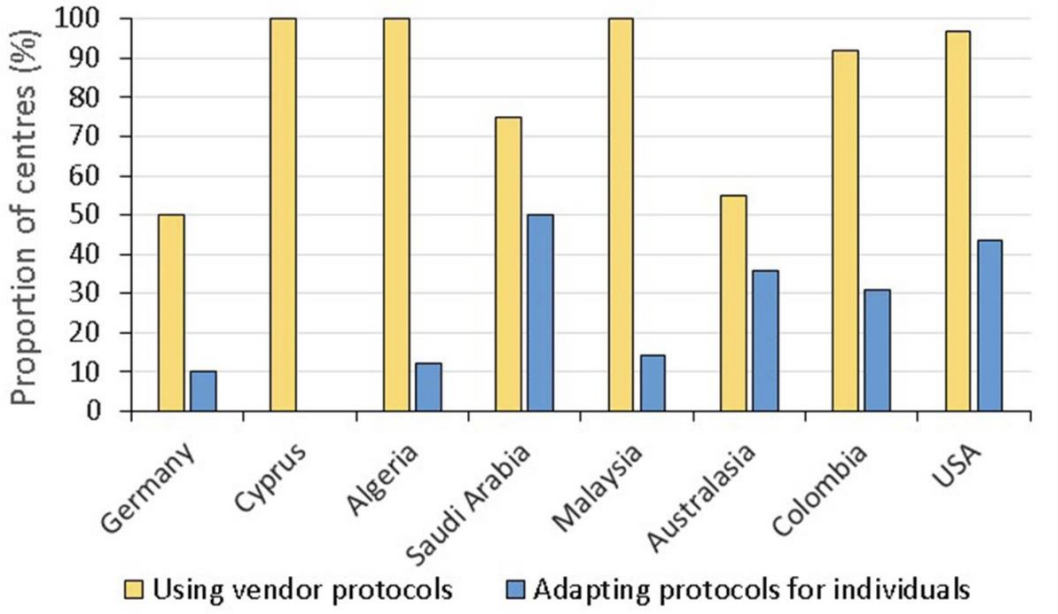


Figure 1. Bar charts showing the proportions of radiotherapy centres using vendor protocols for kV CBCT imaging and adapting CBCT protocols for individual patients in a recent survey of practices in a selection of countries [10].

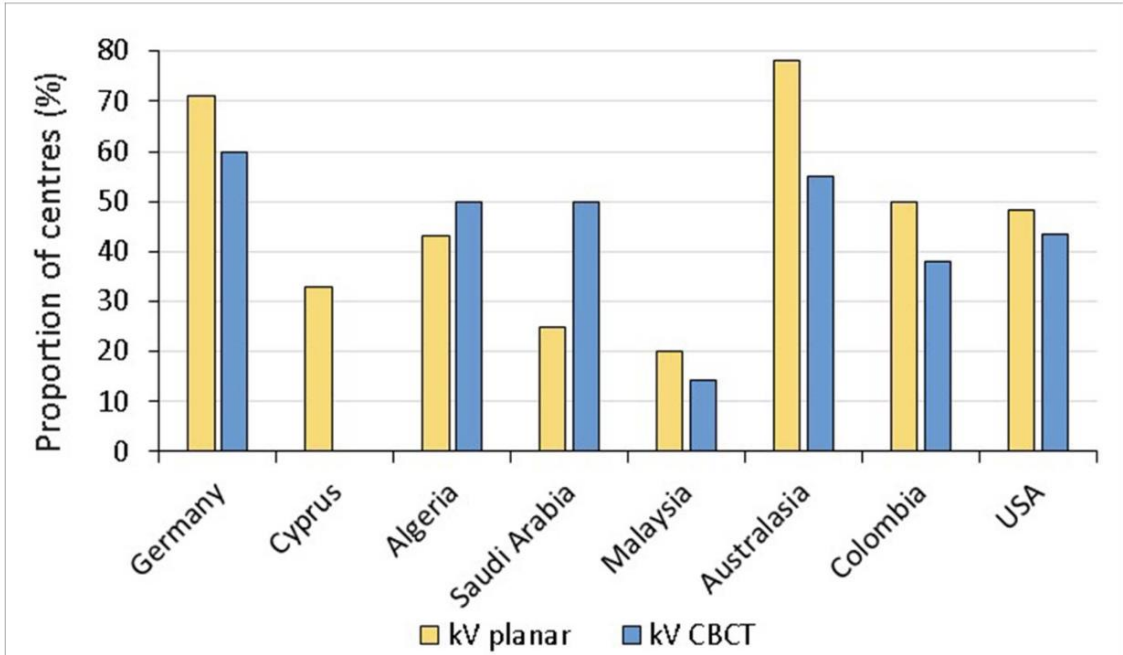


Figure 2. Bar charts showing the percentage of radiotherapy centres in different countries that adjust the field size for kV IGRT planar and kV CBCT imaging in a recent survey of imaging practices [10].

Elizaveta Lavrova, BA • Matthew D. Garrett, MD, MM • Yi-Fang Wang, PhD • Christine Chin, MD • Carl Elliston, MS • Michelle Savacool, MS • Michael Price, PhD • Lisa A. Kachnic, MD • David P. Horowitz, MD

Organ at Risk–sparing Achieved by Adaptive Radiation Therapy

Clinical Site	ART Type	No. of Patients	Clinical Implementation of ART?	Fractionation Scheme	OAR	OAR Dose Sparing
Oropharyngeal (14)	Offline	22	Yes	66–72 Gy, 30–33 fractions	Contralateral parotid	0.6 Gy or 2.8%
					Ipsilateral parotid	1.3 Gy or 3.9%
Head and neck (13)	Offline	13	No	70 Gy, 35 fractions	Parotids	3.1 Gy
Cervix (10)	Offline	9	Yes	45 Gy, 25 fractions	Rectum V95%	3.20%
					Bladder V95%	1.10%
Pancreas (35)	Online MRI-guided	36	No	40 Gy, 5 fractions	Duodenum V33 Gy	0.3 cm^3
Abdominopelvic (23)	Online MRI-guided	5	Yes		Small bowel V50 Gy (one patient)	67.8 cm^3
Adrenal (36)	Online MRI-guided	52	Some patients	24–60 Gy, 3–8 fractions	Stomach NTCP	8.70%
Bladder (26)	Online CBCT-guided	3	Yes		Bowel cavity V45 Gy	24%–30%
Prostate (15)	Online CBCT-guided	25	No	54 Gy, 27 fractions + prostate boost	Bladder D90%	13.10%
					Rectum D90%	6.50%
Abdominal oligometastatic (40)	Online CBCT-guided	8	No	50 Gy, 5 fractions	Stomach V36 Gy	0.36 cm^3
					Duodenum V36 Gy	0.96 cm^3
					Small bowel V36 Gy	1.09 cm^3
					Large bowel V36 Gy	0.8 cm^3

Note.—ART = adaptive radiation therapy, CBCT = cone-beam CT, D90% = minimum dose that 90% of the structure is receiving, NTCP = normal tissue complication probability, OAR = organ at risk, V33 Gy = volume receiving more than or equal to 33 Gy, V36 Gy = volume receiving more than or equal to 36 Gy, V45 Gy = volume receiving more than or equal to 45 Gy, V50 Gy = volume receiving more than or equal to 50 Gy, V95% = volume receiving at least 95% of the prescription dose.

: Coverage of Clinical Targets by Adaptive Radiation Therapy

Clinical Site	ART Type	No. of Patients	Clinical Implementation?	Fractionation Scheme	Target Coverage		Clinical Target Volume	
					Metric Evaluated	Change in Coverage	Metric Evaluated	Change in Volume
Oropharyngeal (14)	Offline	22	Yes	66–72 Gy, 30–33 fractions			CTV volume	−5%
Head and neck (13)	Offline	13	No	70 Gy, 35 fractions	CTV 70 D98%	+0.6%	PTV volume	No significant change
NSCLC (30)	Offline	50	Yes	45–75 Gy			CTV volume	−42%
Cervix (10)	Offline	9	Yes	45 Gy, 25 fractions	CTV coverage	Equivalent	PTV V95%	−87 cm^3
Pancreas (35)	Online MRI-guided	36	No	40 Gy, 5 fractions	GTV V95%	+1.1 Gy		
Abdominopelvic (23)	Online MRI-guided	5	Yes		PTV V95%	+14%		
Abdomen (22)	Online MRI-guided	20	Yes	50 Gy, 5 fractions	GTV V100%	+4%		
					PTV V95%	+3.2%		
Lung (38)	Online MRI-guided	50	Yes		PTV V100%	+4.4%		
Bladder (26)	Online CBCT-guided	3	Yes		PTV V95%	+11.4%	PTV volume	−42%
Prostate (15)	Online CBCT-guided	25	No	54 Gy, 27 fractions + prostate boost	CTV D98%	+2.9%		
Cervix (11)	Online CBCT-guided	13	No	45 Gy, 25 fractions + LN boost	CTV V95%	+7.9%		
Rectum (11)		15		50 Gy, 25 fractions	CTV V95%	+1.5%		
Prostate (25)	Online CBCT-guided	18	Yes	36.6 Gy, 6 fractions	PTV D99%	+6.7%		
Rectum (24)	Online CBCT-guided	12	Yes	25 Gy, 5 fractions	PTV V95%	Improved		
Abdominal oligometastatic (40)	Online CBCT-guided	8	No	50 Gy, 5 fractions	PTVopt V95%	+10.15%		

Note.—ART = adaptive radiation therapy, CBCT = cone-beam CT, CTV = clinical target volume, D98% = minimum dose that 98% of the target is receiving, D99% = minimum dose that 99% of the target is receiving, GTV = gross tumor volume, LN = lymph node, NSCLC = non–small cell lung cancer, PTV = planning target volume, PTVopt = PTV optimization structure, V95% = volume receiving at least 95% of the prescription dose, V100% = volume receiving at least 100% of the prescription dose.

Clinical Outcomes of Adaptive Radiation Therapy

Clinical Site	ART Type	No. of Patients	Fractionation Scheme	Clinical Outcome		Toxicity	
				Metric Evaluated	Outcome	Metric Evaluated	Outcome
Oropharyngeal (14)	Offline	22	66–72 Gy, 30–33 fractions	Local control Regional control	100% 95%	Comparison to IMRT	Comparable
NSCLC (30)	Offline	50	45–75 Gy	Local control Median PFS Median OS	70% 8.3 months 30.5 months	Comparison to RTOG 9410 clinical trial	Reduced
Adrenal (36)	Online MRI-guided	52	24–60 Gy, 3–8 fractions			≥ grade 3 toxicity	0%
Prostate (37)	Online MRI-guided	101	36.25 Gy, 5 fractions			≥ grade 2 early GI toxicity ≥ grade 2 early GU toxicity Comparison to HYPRO study	23.8% 5% Reduced
Lung (38)	Online MRI-guided	50		12 months, local control 12 months, OS 12 months, DFS	95.60% 88% 64%	≥ grade 2 toxicity ≥ grade 3 toxicity	30% 8%
Abdomen (22)	Online MRI-guided	20	50 Gy, 5 fractions	6 months, PFS 12 months, OS	89.10% 75%	≥ grade 3 acute toxicity	0%

Note.—ART = adaptive radiation therapy, DFS = disease-free survival, GI = gastrointestinal, GU = genitourinary, HYPRO = hypofractionated versus conventionally fractionated RT for patients with localized prostate cancer, IMRT = intensity-modulated RT, NSCLC = non–small cell lung cancer, OS = overall survival, PFS = progression-free survival, RTOG = Radiation Therapy Oncology Group.

To conclude (1):

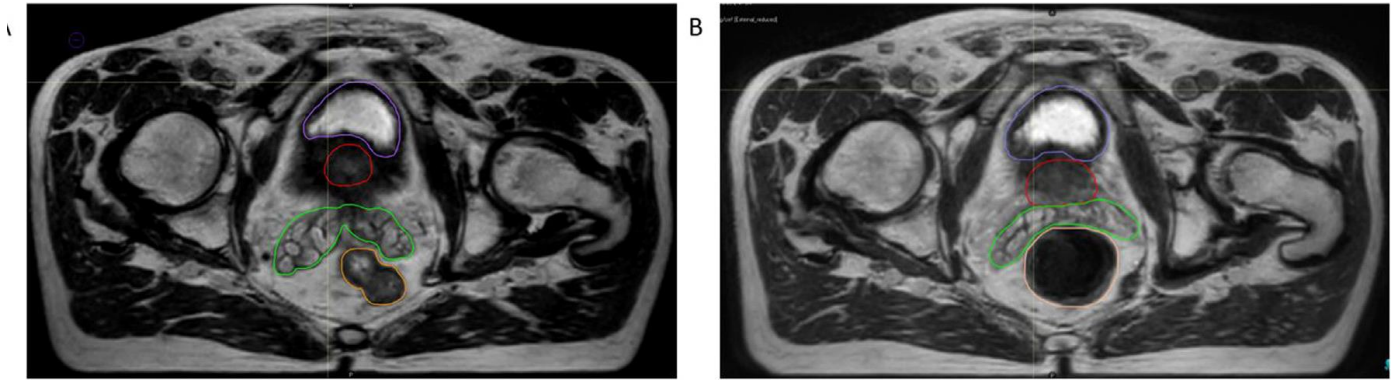
A few dosimetric evaluations are available in the literature regarding the contribution of CT scanning for ART to the dose received by the patient.

These doses are in general negligible when compared with the advantages of ART in terms of OAR sparing, better PTV coverage and reduction of the PTV volume.

The dose received because of ART by the patient varies with the target of the treatment and the PTV volume. Lighter and shorter people may receive higher doses by cone beam scanning and specific protocols may help to further reduce the dose received for them.

Is there a future?

Probably the MR-ART can be the future



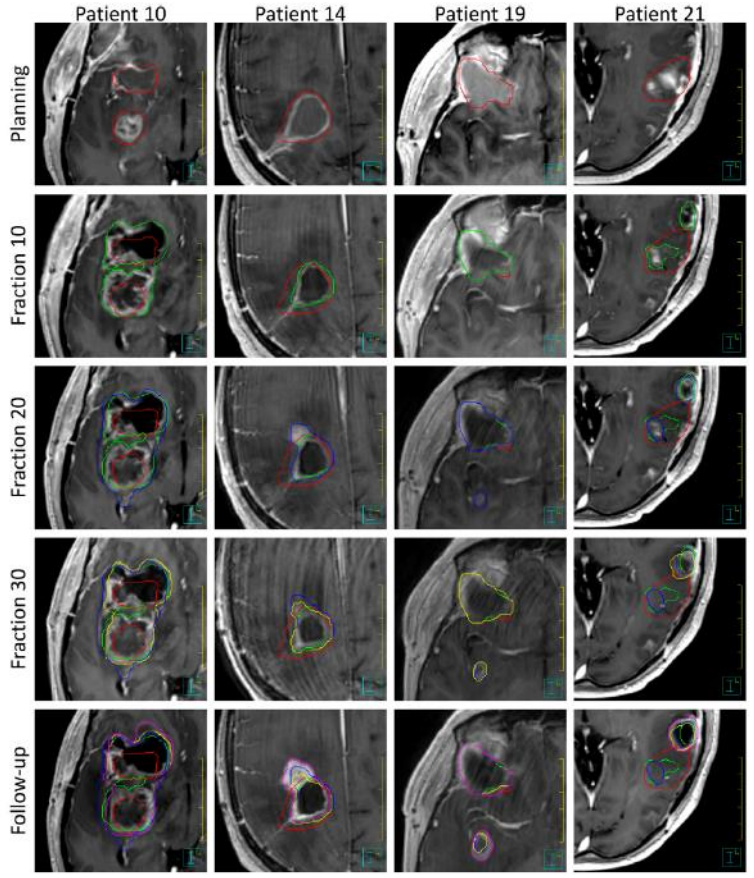
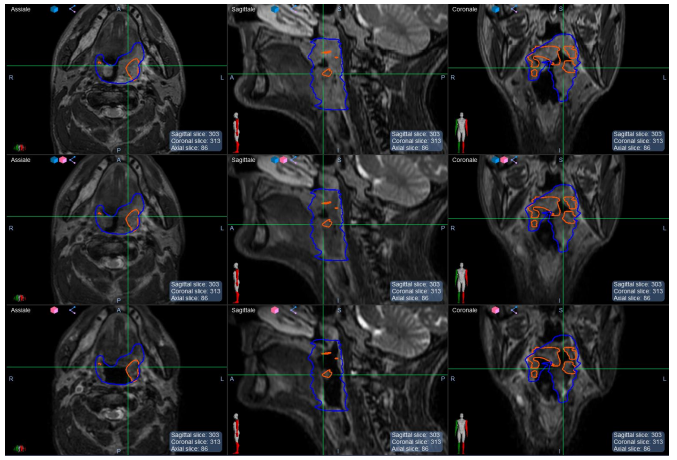


Table 4: Comparison between MRI-based and CBCT-based Online Adaptive Radiation Therapy Approaches

Feature	MR-linac Online ART	CBCT-based Online ART
Image quality	Superior (46)	Inferior image quality and soft-tissue definition (6,20,33,46,47)
Image artifacts	Susceptibility, motion, distortion (6)	Hardening, motion, scatter, ring, aliasing, misalignment (20,33,49)
Inaccuracies in determining size of target	NA	Cervix, prostate (57,58)
Information about physiologic characteristics of tissue (eg, diffusion, perfusion)	Superior	NA
Functional or quantitative imaging	Possible; not yet ready for clinical implementation (6,16)	NA
Limited field of view	Limited to 50 cm (6)	Limited to 16 cm in the longitudinal direction (6,55)
Image acquisition time	Longer (limited sequences within 2 min) (46)	Shorter (within 1–2 min) (46)
Conversion of image-of-the-day to electron density map	Synthetic CT; bulk density assignment to anatomic structures; multimodality DIR (6,16)	Conversion to Hounsfield units via DIR, CBCT calibration curves, dose deformation* (33,52)
Imaging-related radiation exposure	None	Up to 10 cGy per scan; typically, 0.2 cGy–2 cGy (6,20,29,46,56)
Continuous imaging (eg, motion gating, real-time tracking of dose accumulation)	Possible (6)	Limited by radiation exposure
Specialized training for MRI-based RT planning	Required (46)	NA
Radiation and MRI-compatible facilities	Required (46)	NA
Cost of linear accelerator, structural investment	Very high (46)	Reduced compared with MRI (46)
Limits on patient size	More restrictive (46)	Less restrictive (46)
Contraindications (claustrophobia, metallic implants)	Yes (46)	No (46)



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Treatment duration	Longer (21,22,46)	Potentially shorter (11,26,27)
Electron return effect†	Significant‡	NA
Significant geometric distortion	Due to magnetic-field gradient nonlinearities, field inhomogeneities§	NA
Patient-dependent geometric distortions‖	Possibly significant	NA

Note.—ART = adaptive radiation therapy, CBCT = cone-beam CT, DIR = deformable image registration, MR-linac = MRI-linear accelerator, NA = not applicable.

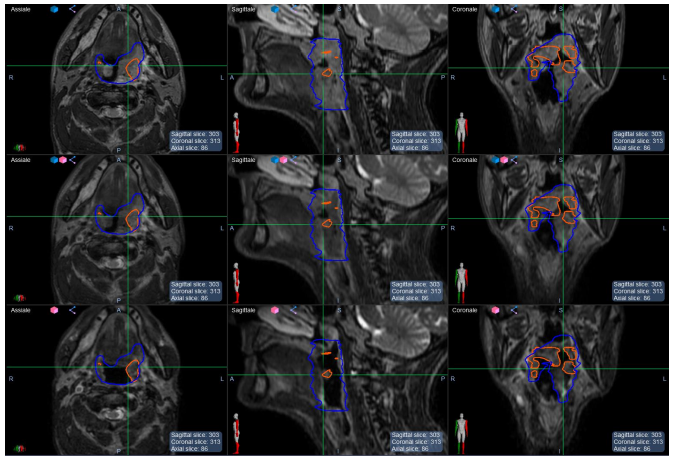
* Poorer image quality of CBCT images can lead to dose calculation inaccuracies.

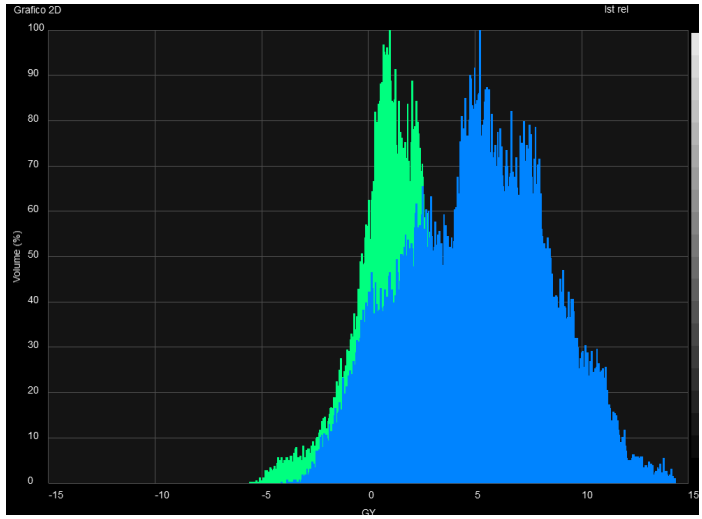
† The electron return effect refers to electron path distortion and increase in radiation dose delivery near air-tissue interfaces.

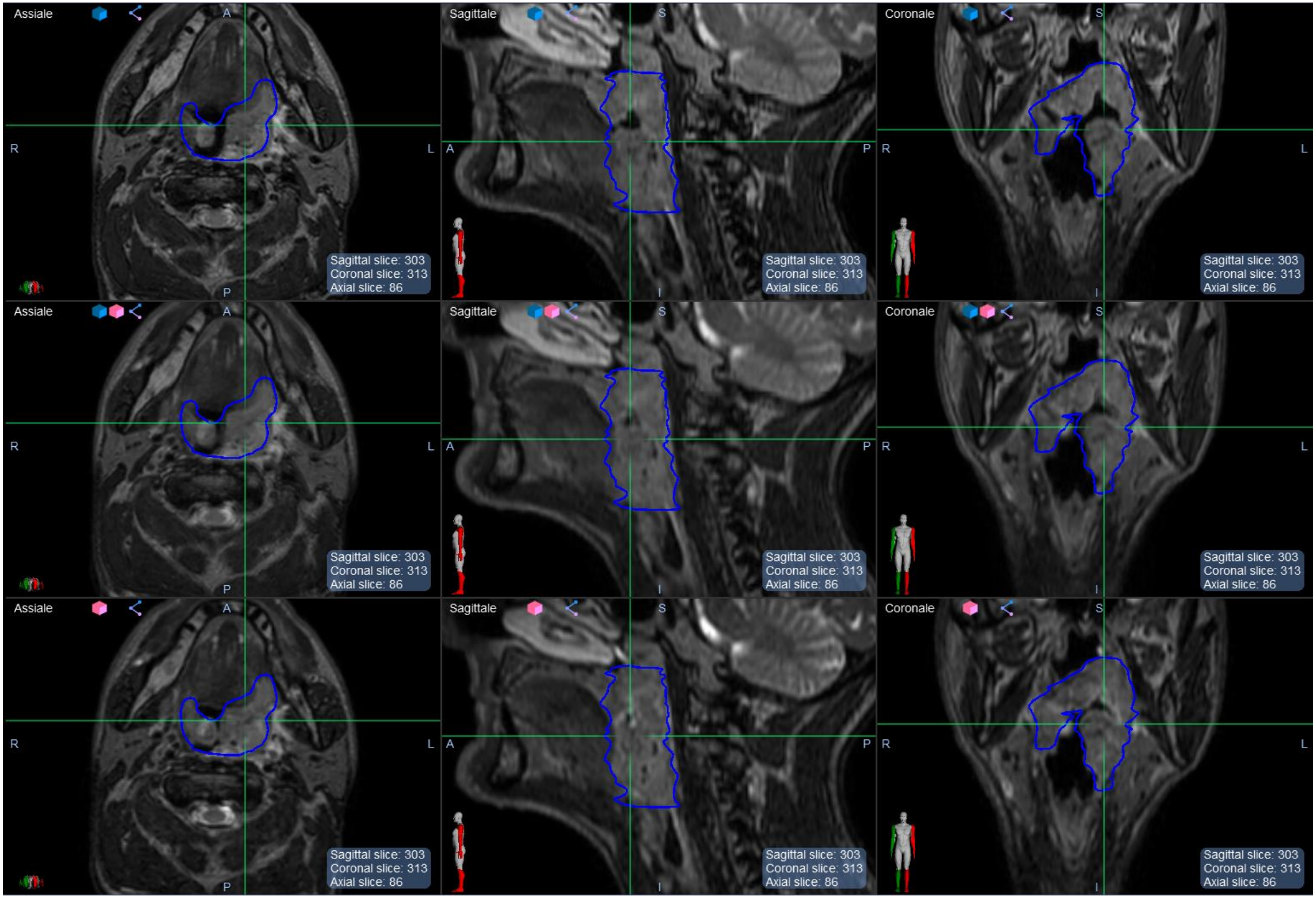
‡ The electron return effect with MRI can be addressed with Monte Carlo algorithms and multiple fields.

§ MRI geometric distortion can be accounted for by image processing algorithms.

‖ Patient-dependent geometric distortions result from local magnetic field inhomogeneities.

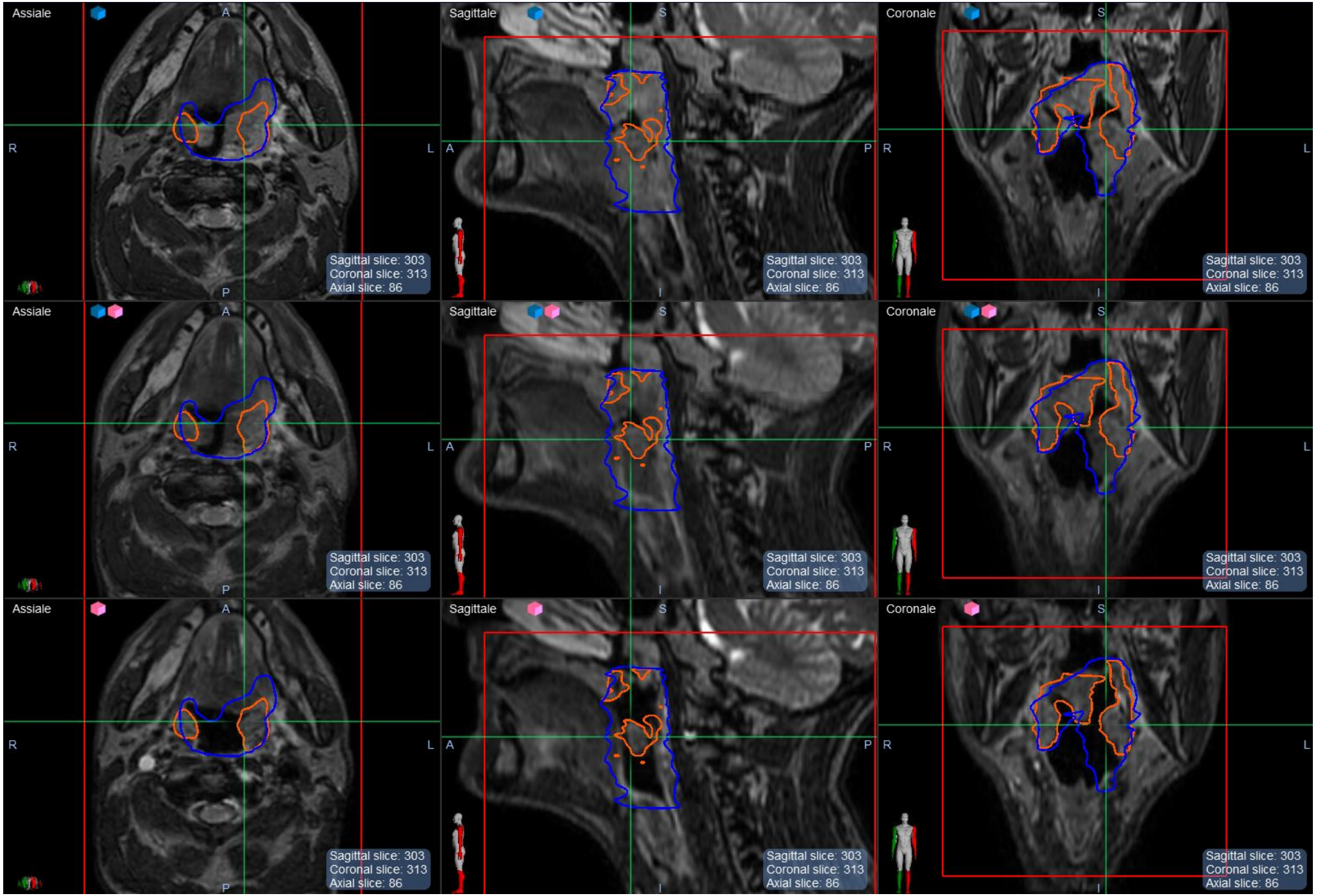





Assiale
Sagittale
Coronale
Sagittal slice: 303
Coronal slice: 313
Axial slice: 86

reference

1



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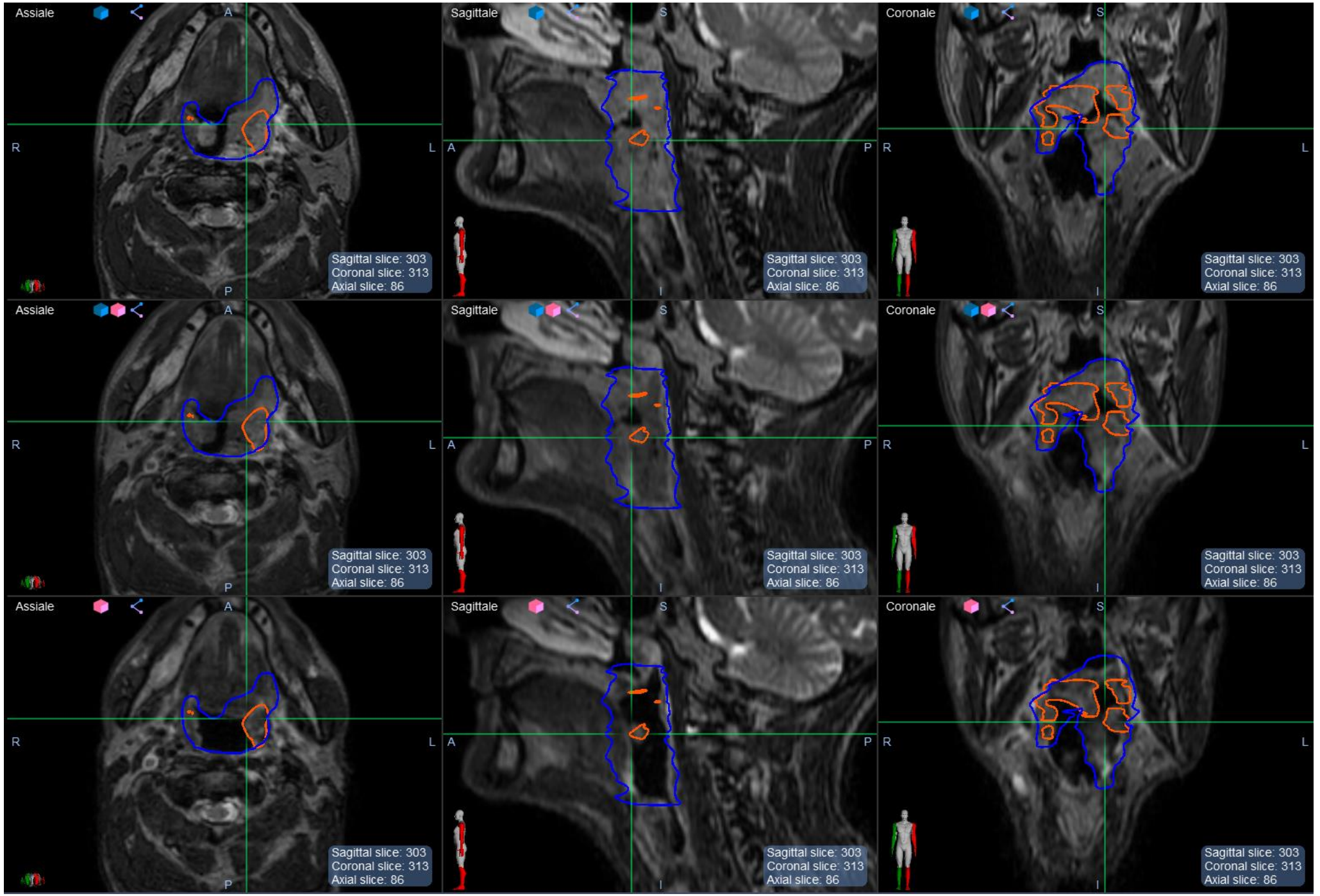
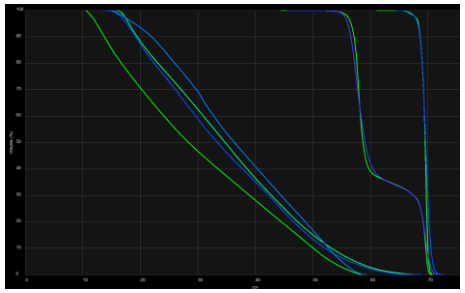
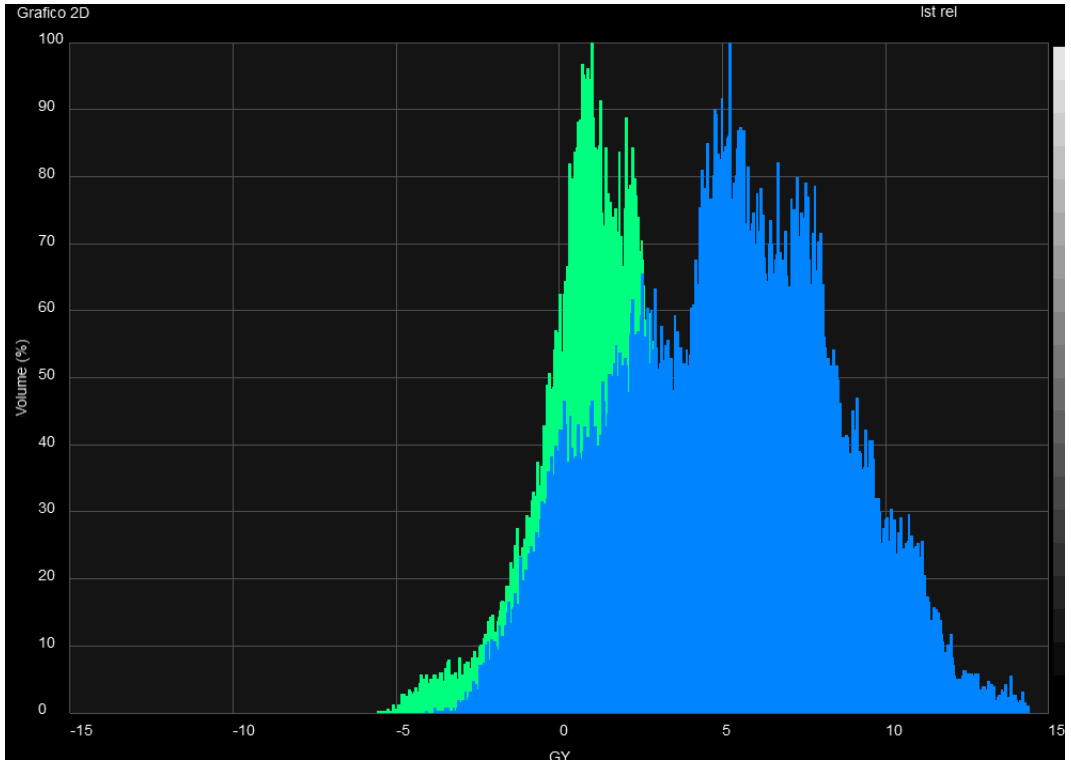


reference

24

H&N dose accumulation





Dose difference relative Volume Histogram
Parotids
Right (blue) - left (green)
If D>0 previsional dose > accumulated dose

Conclusions

- Adaptive RT: very useful, almost crucial, in a precise radiotherapy process

- On-line and off-line ART using cone-beam CT is much more common and can be easily used in all RT centres

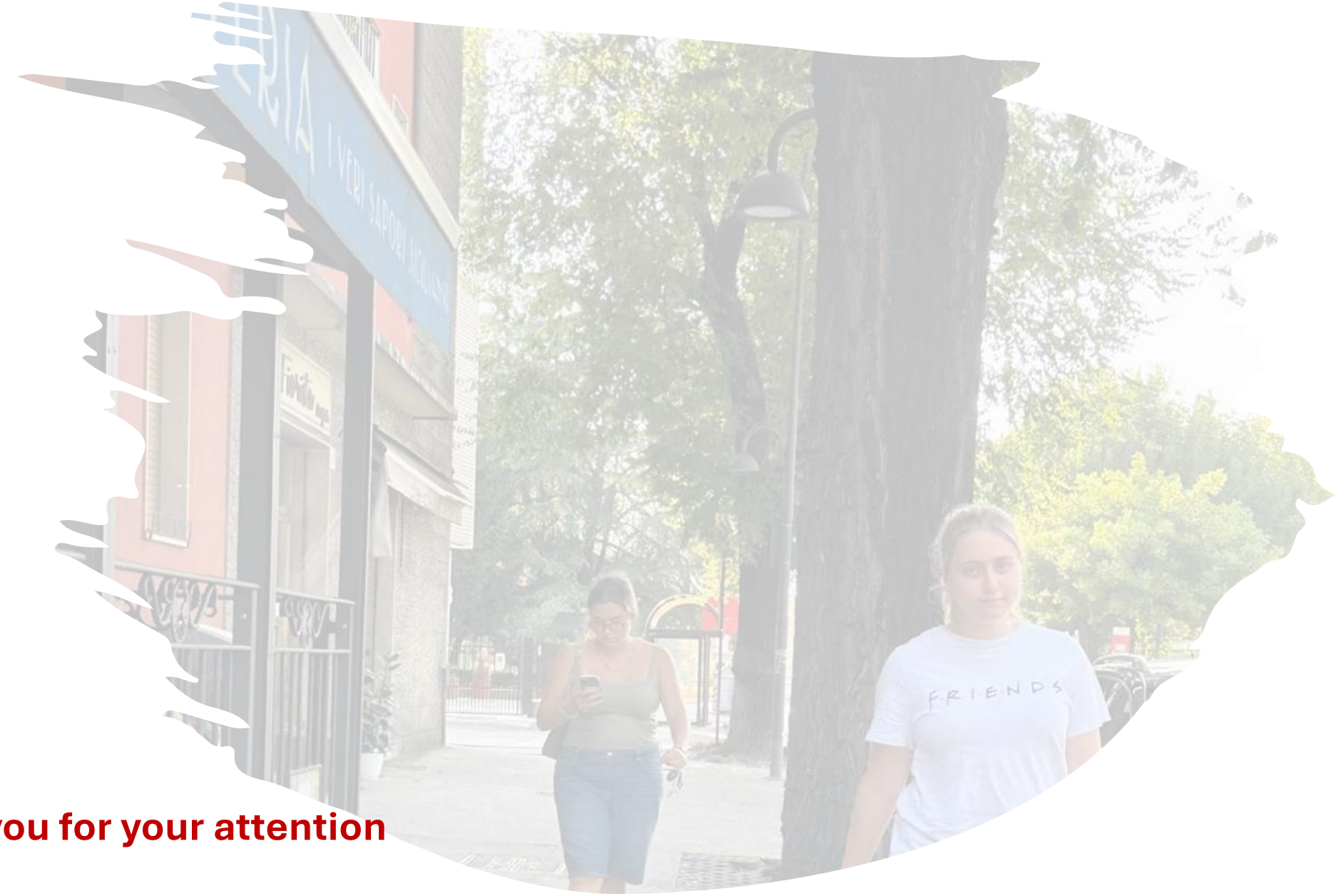
- Even if it is true that in patients treated with RT, the doses required for ART procedures are very low, it is also true that the ALARA principle has to be adopted for each patient and optimization procedures should be much more diffused than now

Conclusion 2. Attention for the future

- Procedures of deformable image registration and dose accumulation are the key passages to obtain best dosimetric results by ART;

- ART with MRI will consent better target and OAR identification, non-invasive knowledge of tumour biology and can be used better personalize the treatment and the delivered dose

- Prospective studies integrating all these aspect are necessary to confirm the still embryonal data



Thank you for your attention

Challenges of Radiological Protection in Research and Society referring to Medical Field

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Milan, Italy

Sala Napoleonica/Via Sant'Antonio, 12
Università di Milano