Exploration of distinct spatiotemporal dose distributions at LhARA

Yolanda Prezado

Radiotherapy: a paradigm shift in the 21th century

Fractionation

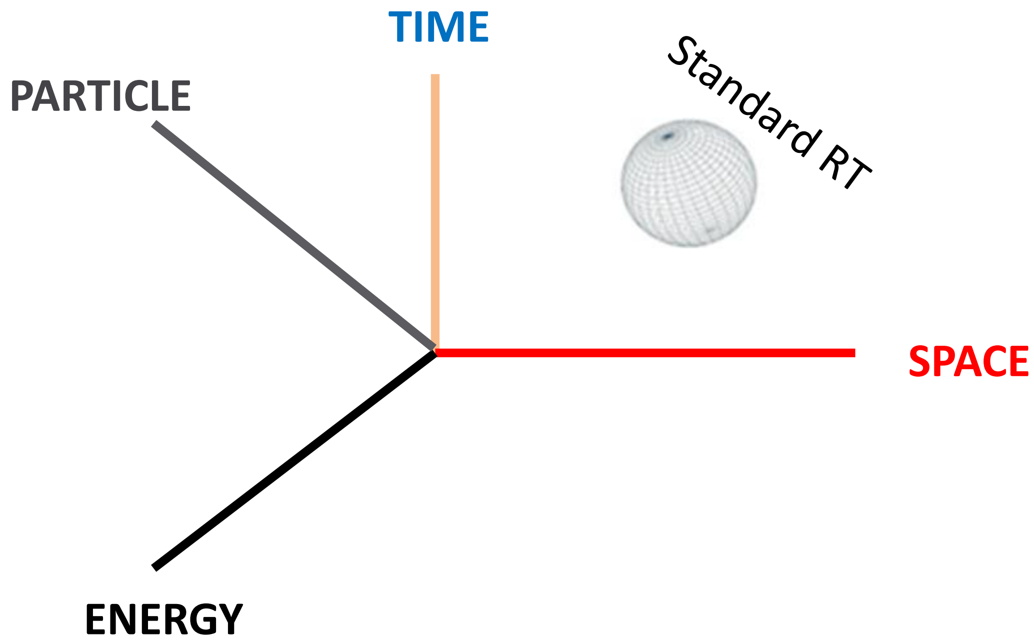
Dose rate

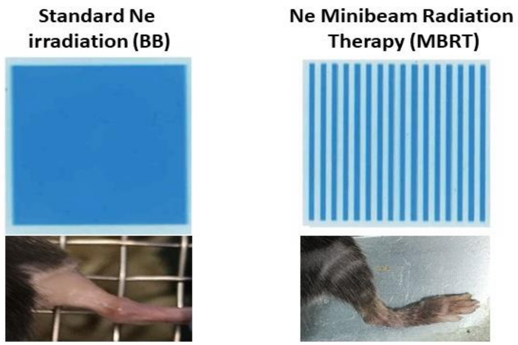
Pulse structure

Photons

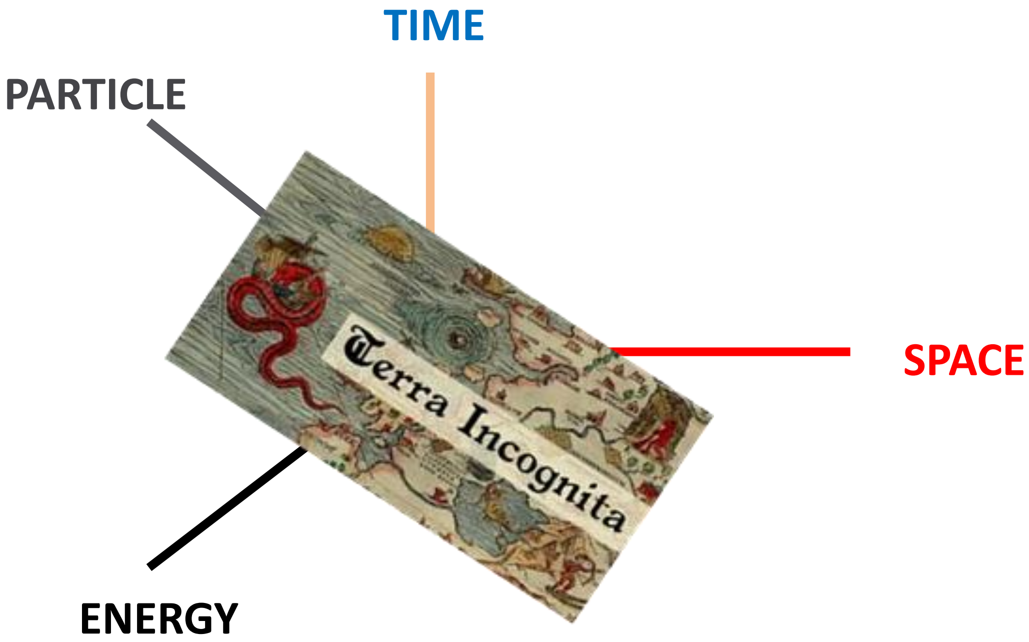
Protons

Heavy ions



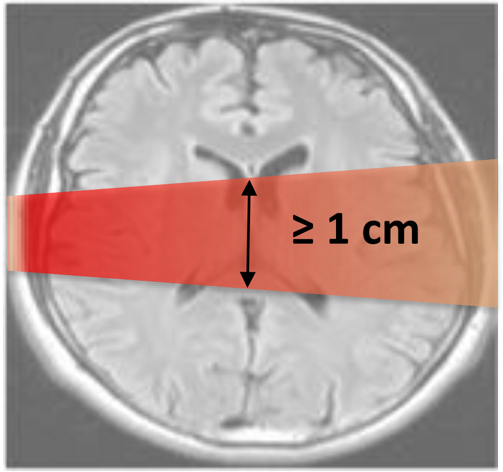


Exploration of the influence of the different parameters on the biological response



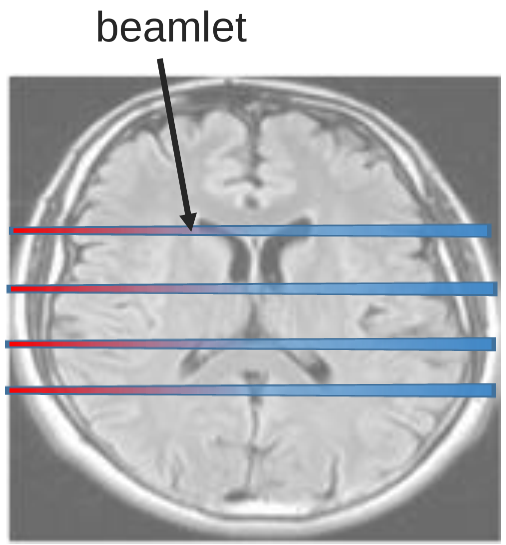
Spatially Fractionated Radiation Therapy (SFRT)

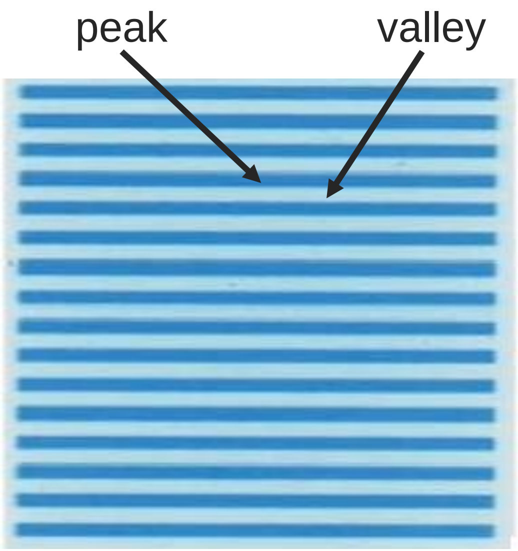
Standard RT



- large fields (≥ 1 cm)
- laterally homogeneous dose distributions

SFRT

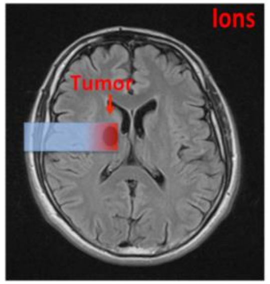




- field composed of smaller **beamlets**
- laterally **heterogeneous** dose distributions (*peaks* and *valleys*)

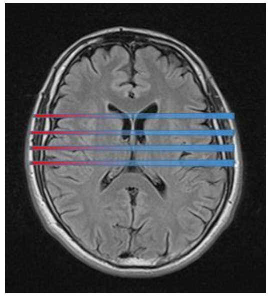
→ **increase** of **normal tissue tolerance**

*PROTON*MBRT: an innovative therapeutic approach



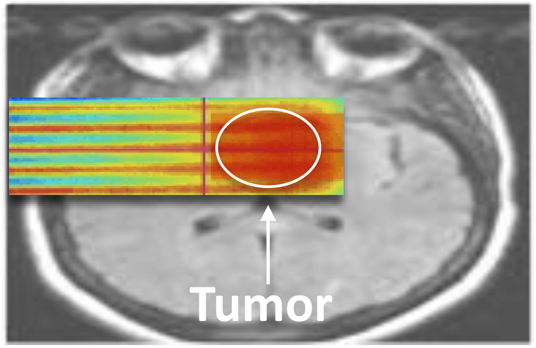
Charged particles

+



Minibeam radiation therapy (MBRT)

Proton MBRT



Prezado et al. 2013

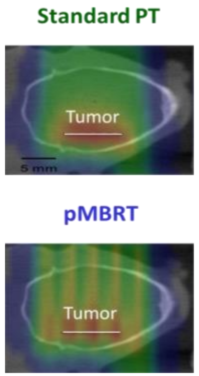
Beam width < 1 mm

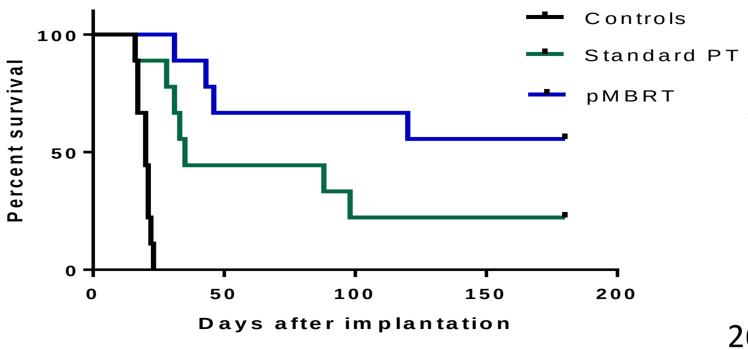
ERC consolidator grant

pMBRT increases the therapeutic index for high-grade gliomas

Equivalent or superior tumor (rat glioma) control than standard proton therapy

25 Gy/one fraction





5 days after IR

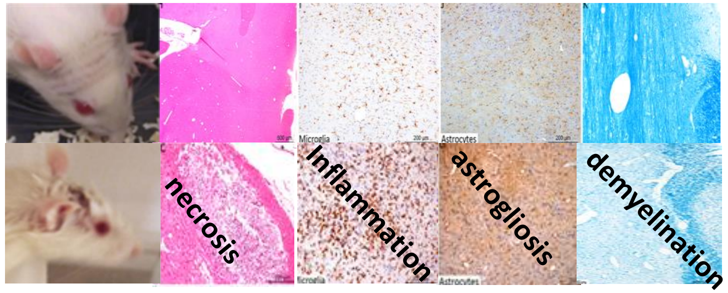
26 days after IR

Prezado et al. IJROP 2019

Net reduction of neurotoxicity

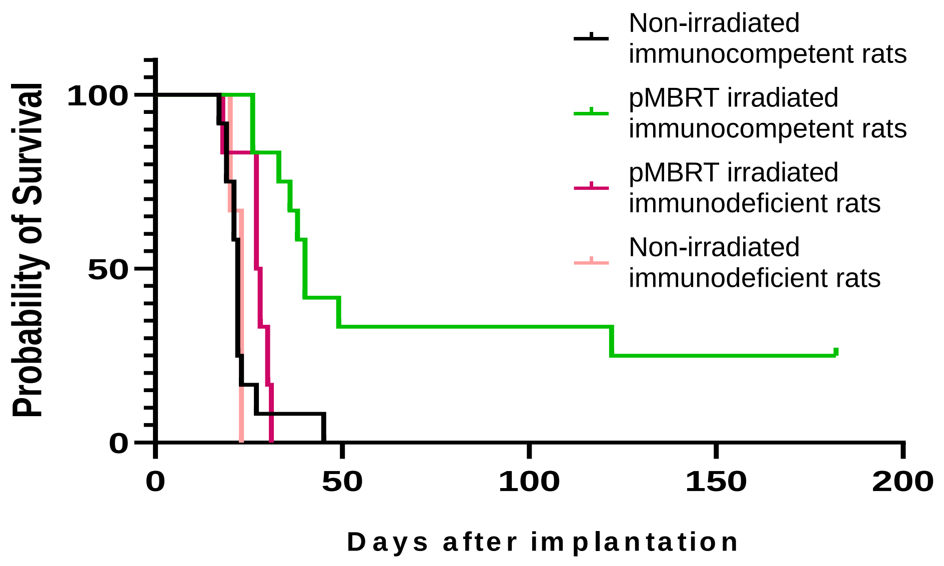
pMBRT

Standard PT

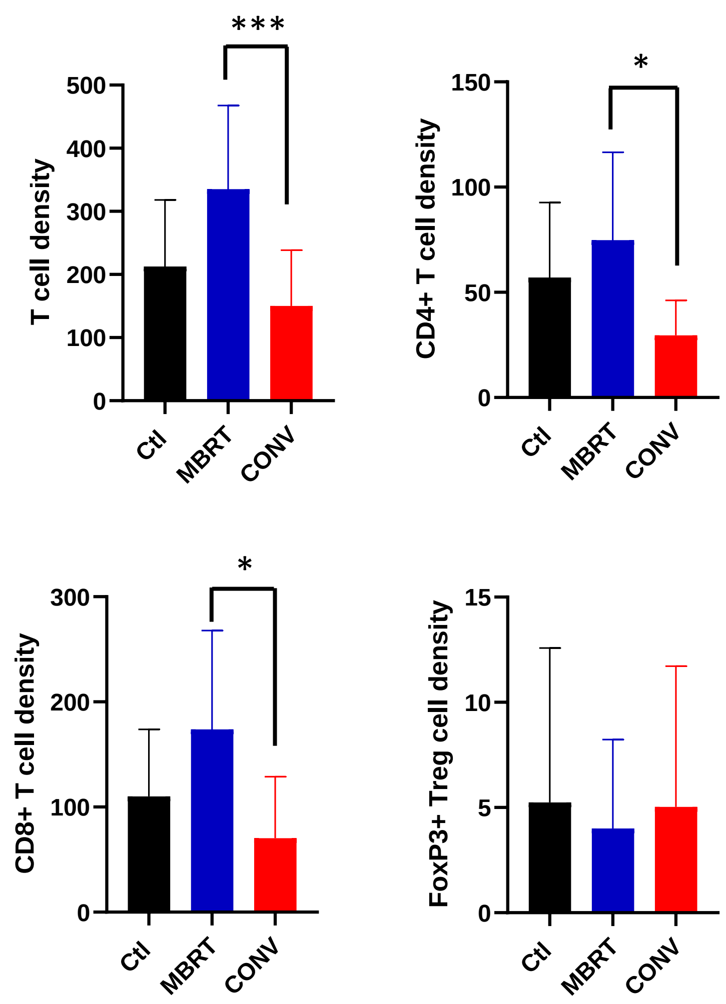


Prezado et al. Scie Reports 2017; Lamirault et al. Scie Reports 2020

Determinant role of immune system in the anti-tumor response of MBRT



48 h post-irradiation



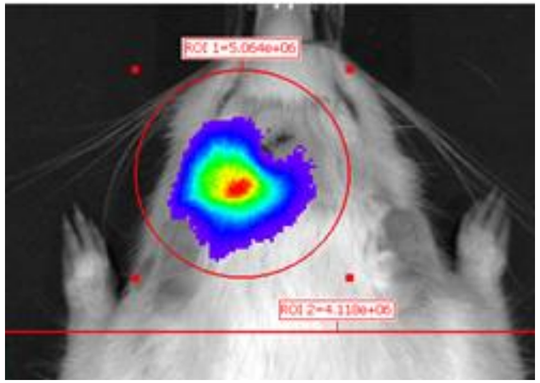
MBRT and Conventional irradiations leads to different temporal and spatial distributions

A. Bertho et al. Redjournal 2022

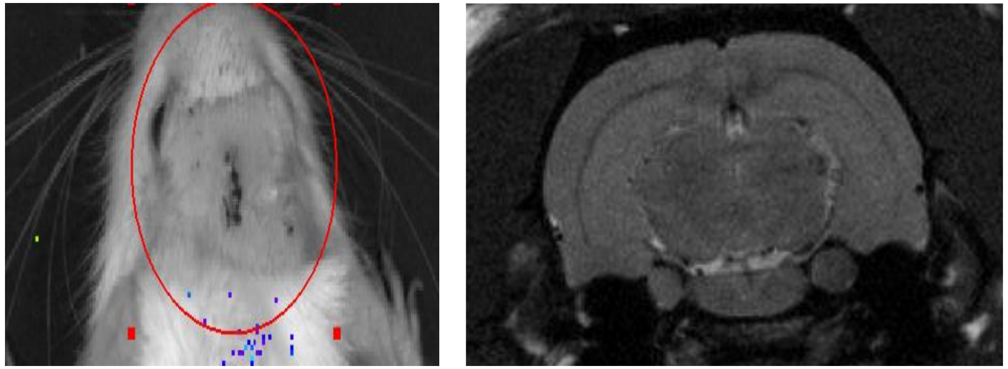
Minibeam radiation therapy could provide long-term anti-tumor immunity

Irradiated and cured immunocompetent RG2-bearing rats were rechallenged with RG2 tumor cells (3 to 6 months after irradiation). While naïve controls developed tumor normally, this was not the case for any of the previously irradiated animals.

CTRL



MBRT



A. Bertho et al. Redjournal 2022

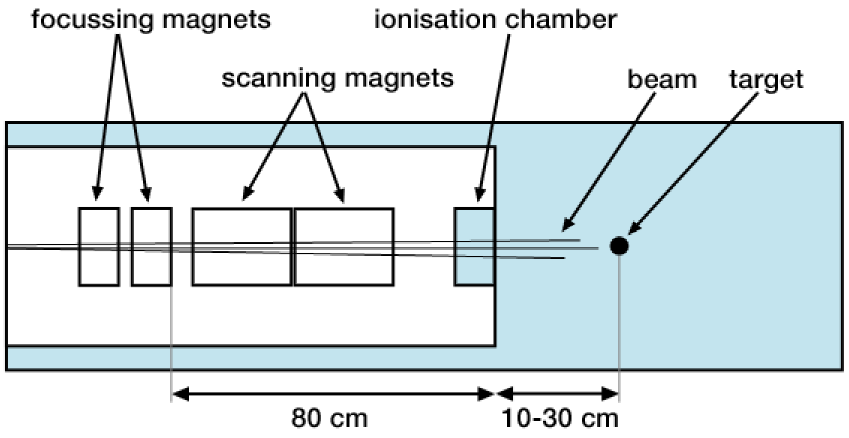
Beam characteristics LhARA

Ideal beam features

- Low divergence
- Small emittance

→ **Magnetically focussed minibeams**

LhARA → FWHM < 0.5 mm



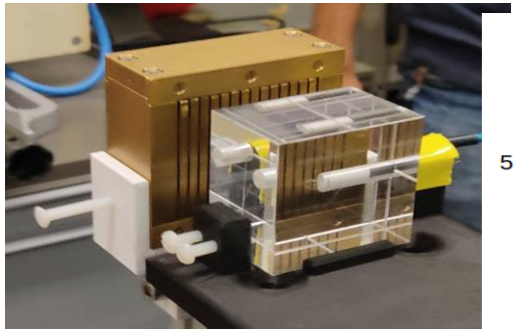
T. Schneider et al. Scientific Reports 2020

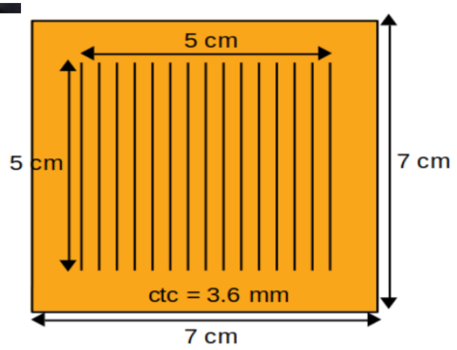
can pave the way towards combination of pMBRT + FLASH

Carbon minibeam radiation therapy @ GSI

180 MeV/A C ions

550 µm width

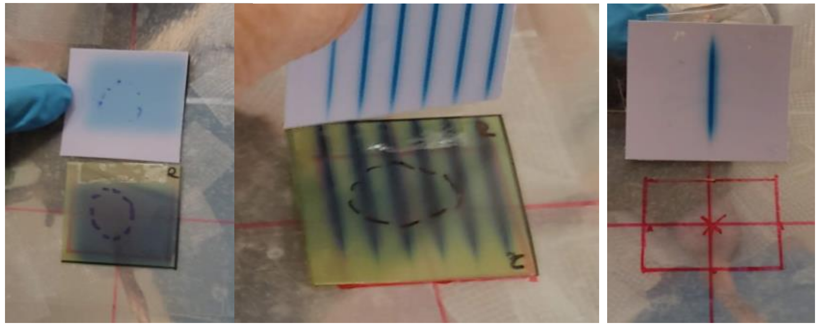




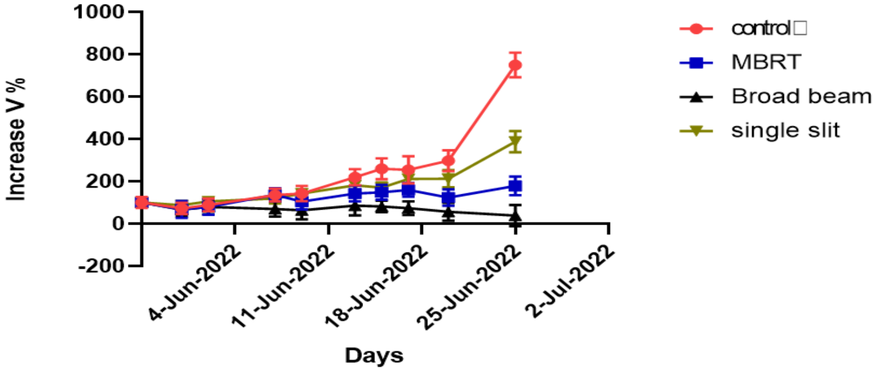
Dose prescription: 20 Gy average

LM8 mice osteosarcoma

Conv. IR MBRT Single slit



Dose peak = 121 ± 6 Gy,
D valley = 1.5 ± 0.1 Gy

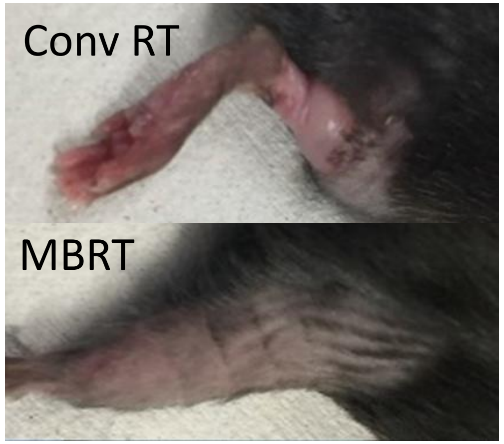


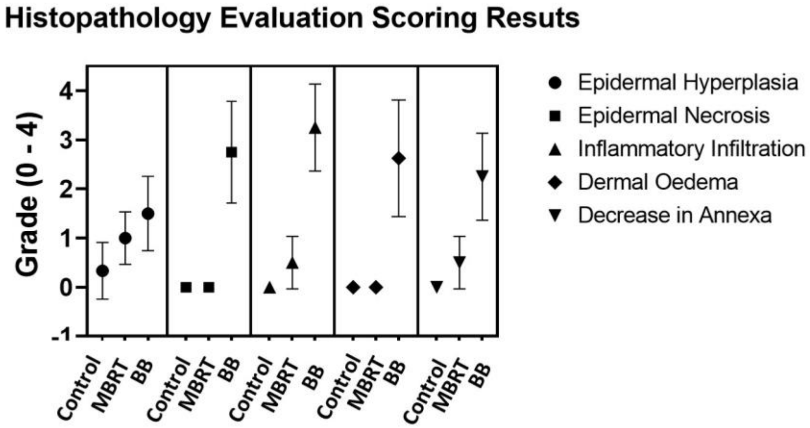
Less lung metastasis with Conv.RT and MBRT

Very heavy ions MBRT

Ne, Si and Ar ions used in the past, extremely efficient for the treatment of hypoxic tumors *(Castro 1994).*
HOWEVER, abandoned due to important side effects in normal tissues

Ne MBRT @ HIMAC, mice's legs irradiation

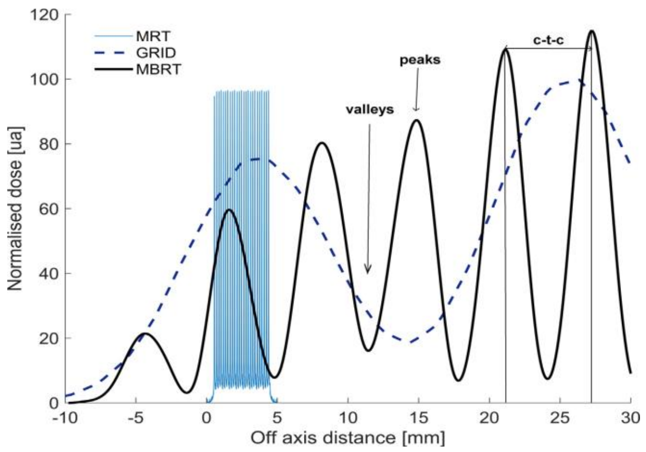




MBRT leads to a net reduction of toxicity as compared to BB
Potential renewed use of very heavy ions for therapy!

Prezado et al Cancers 2021

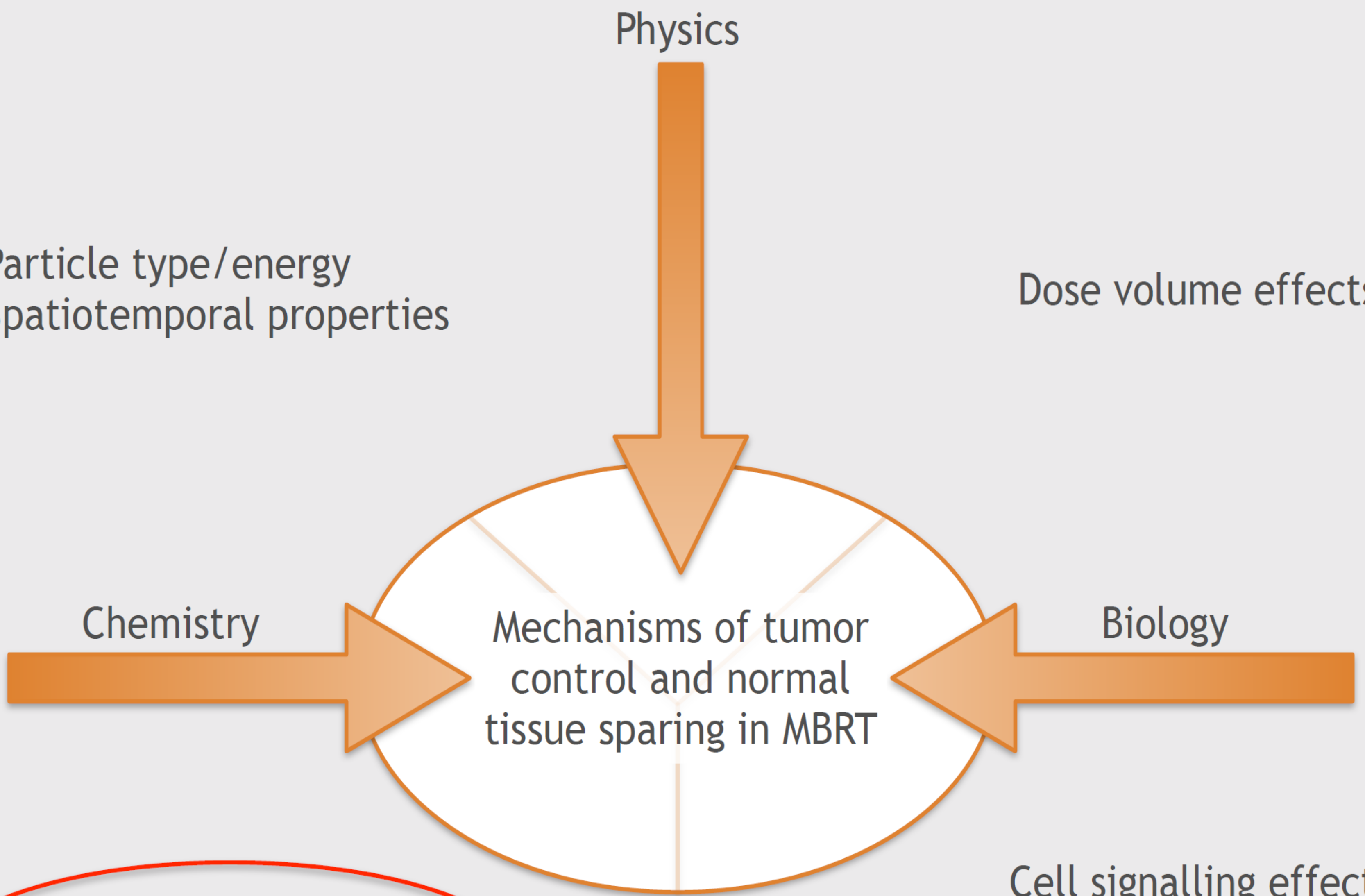
Missing the full picture



Normal tissues	Tumor
Vascular effects	
Prompt repair	Damage
Cell signalling	
Positive "bystander"-like effects	Cytotoxic "bystander"-like effects
Immune system	
Reduced inflammation	Immune infltration/activation
Cell migration, hyperplasia and proliferation	ROS production and difussion?

Particle type/energy
Spatiotemporal properties

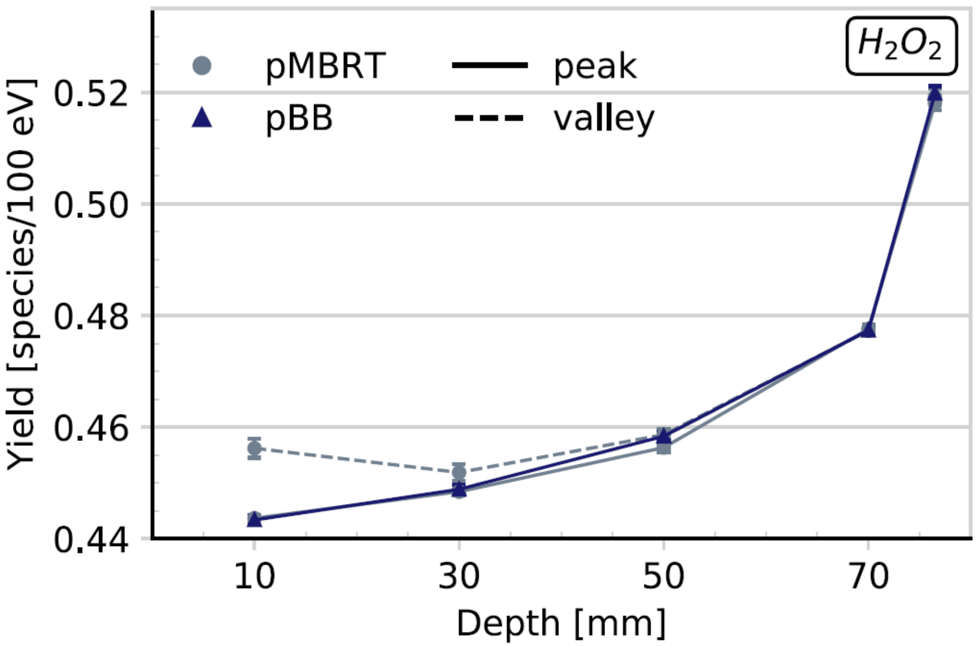
Dose volume effects

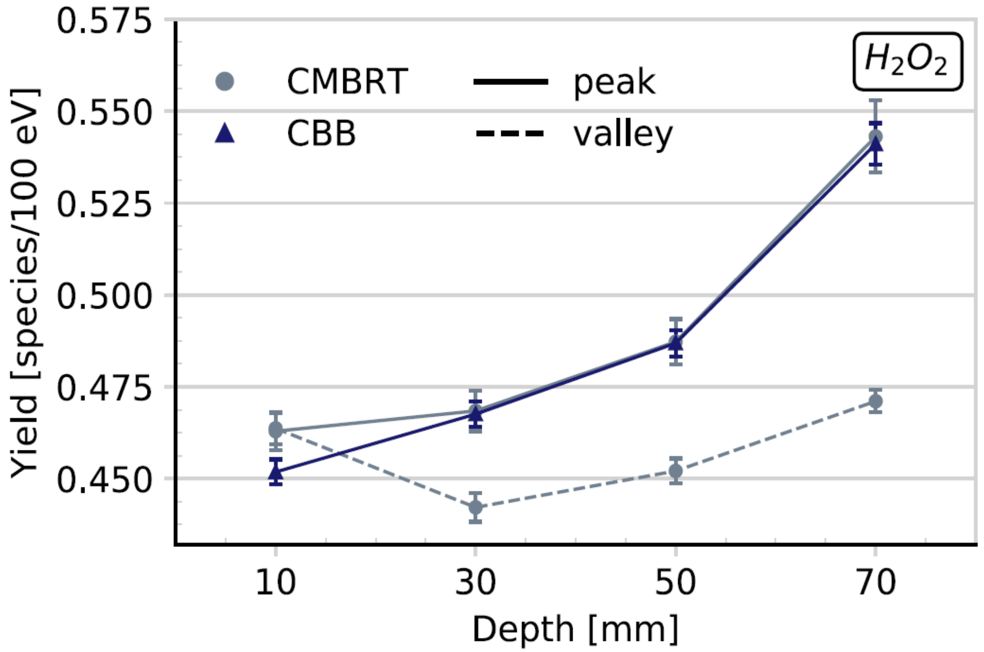


Reactive oxygen species (ROS)

Cell signalling effects (bystander/abscopal)
Anti-tumor immune response
Cell migration

ROS in pMBRT vs CMBRT





LhARA will open new a wide range of possibilities for exploration

- Evaluation of the influence of different fractionation schemes in SFRT

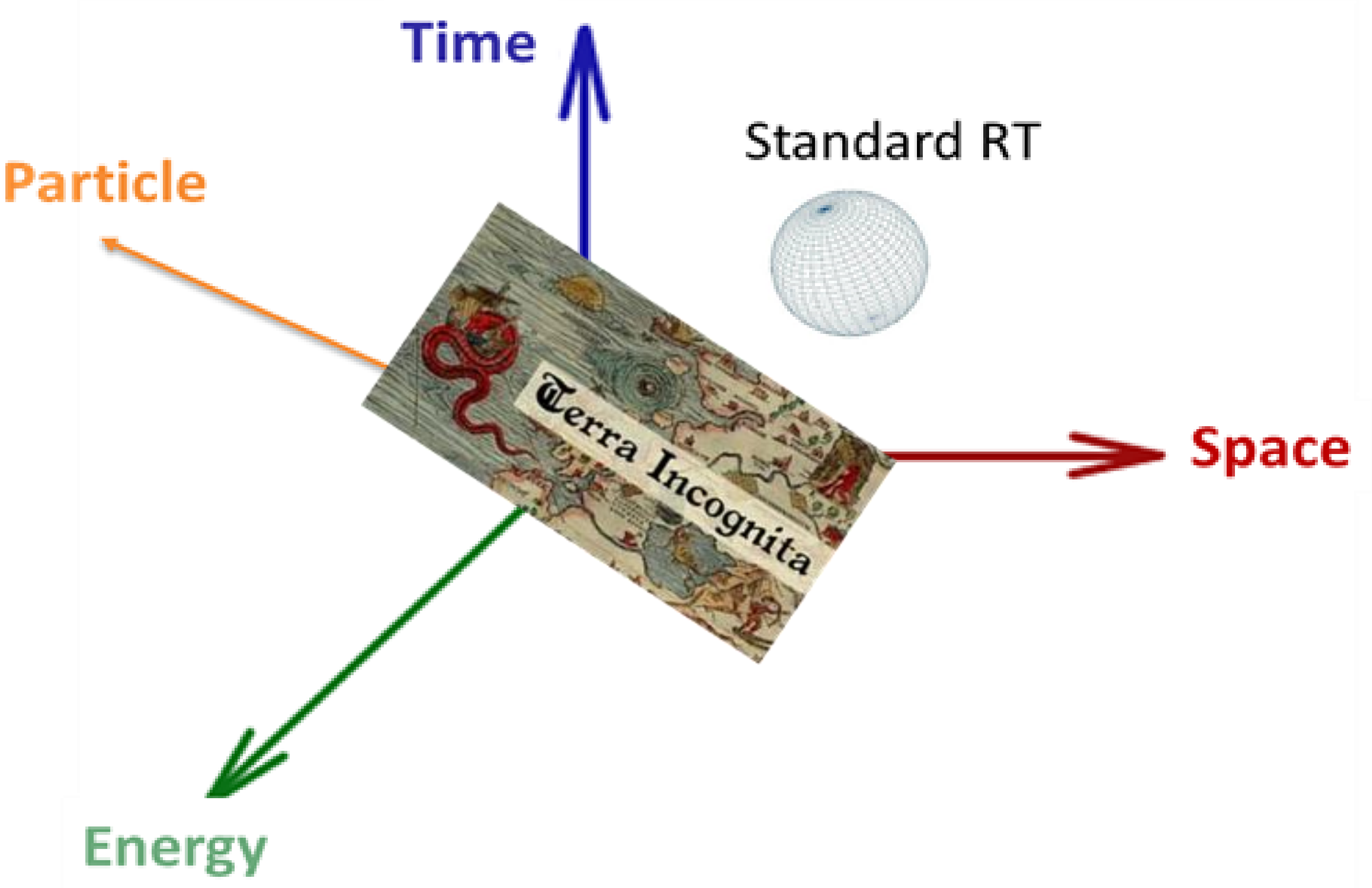
  Optimised spatiotemporal dose distributions

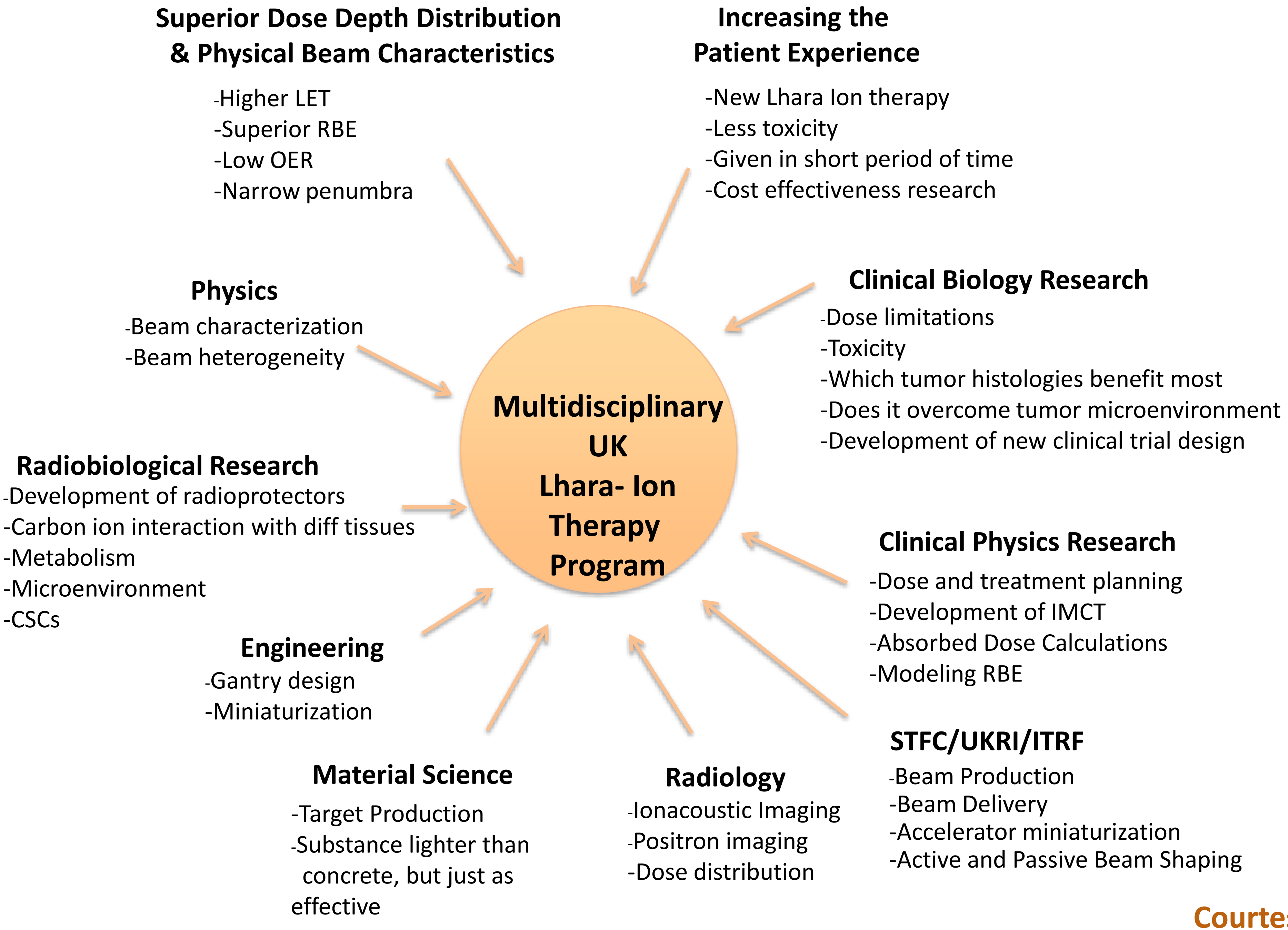
- Influence of the particle type

- Assessment on the (ultra high) dose-rate dependance in SFRT

- Influence of the particle type

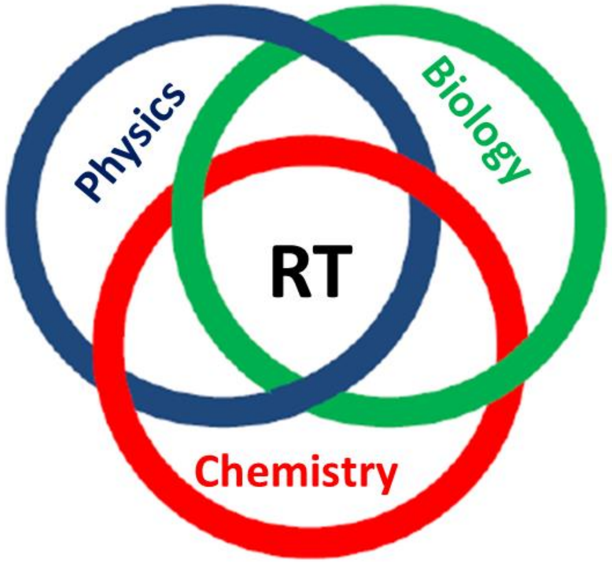
LhARA





Courtesy A. Giaccia

Thank you very much for your attention!



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