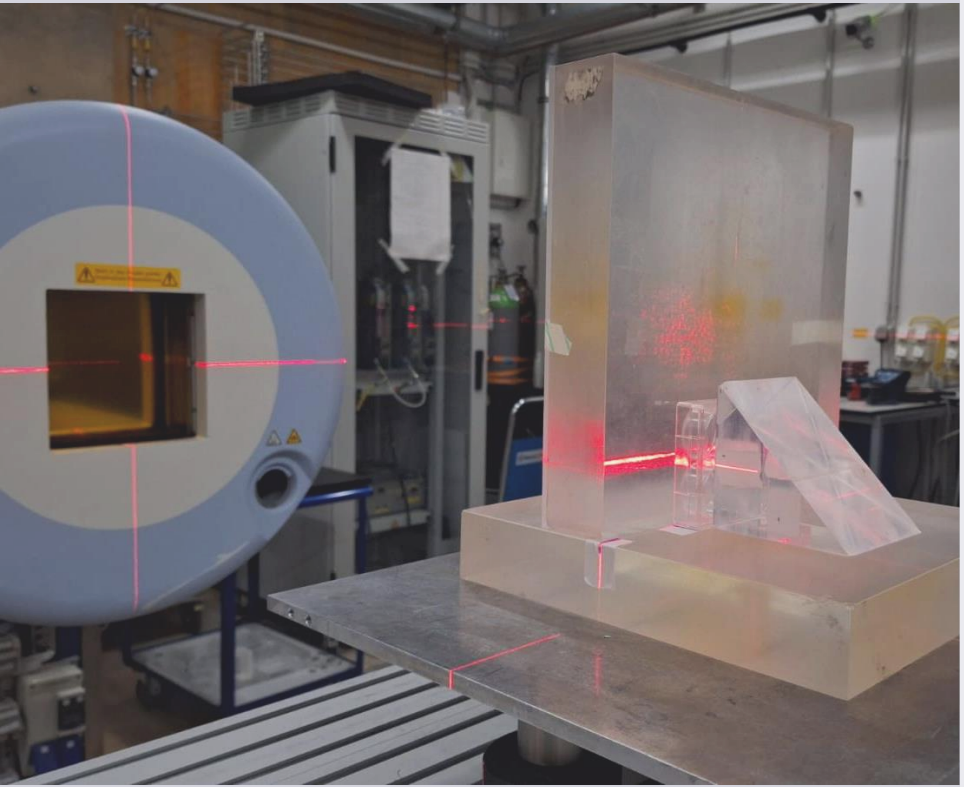

BIOphysical characterization of Helium and Oxygen ion beams for hadronTherapy

BIOHOT

Incontro Gr.V
Napoli, 20 marzo 2024

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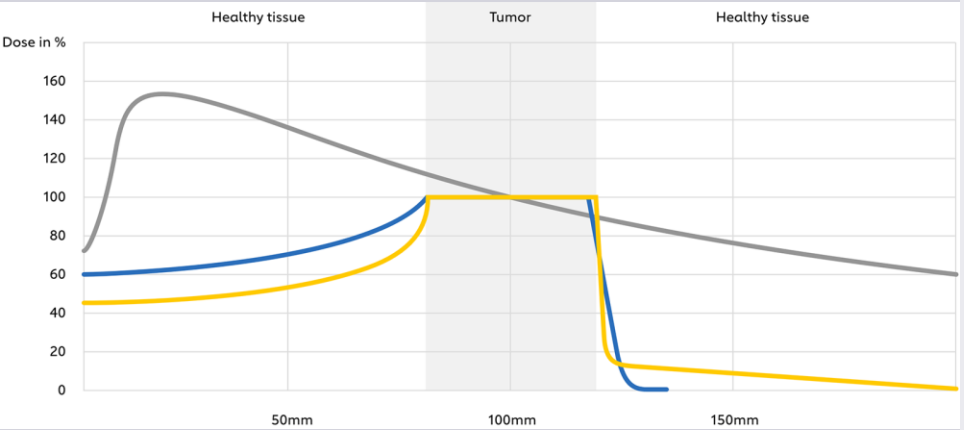


6-MV photons

Protons (up to 240 MeV)

^{12}C ions (up to 400 MeV/n)

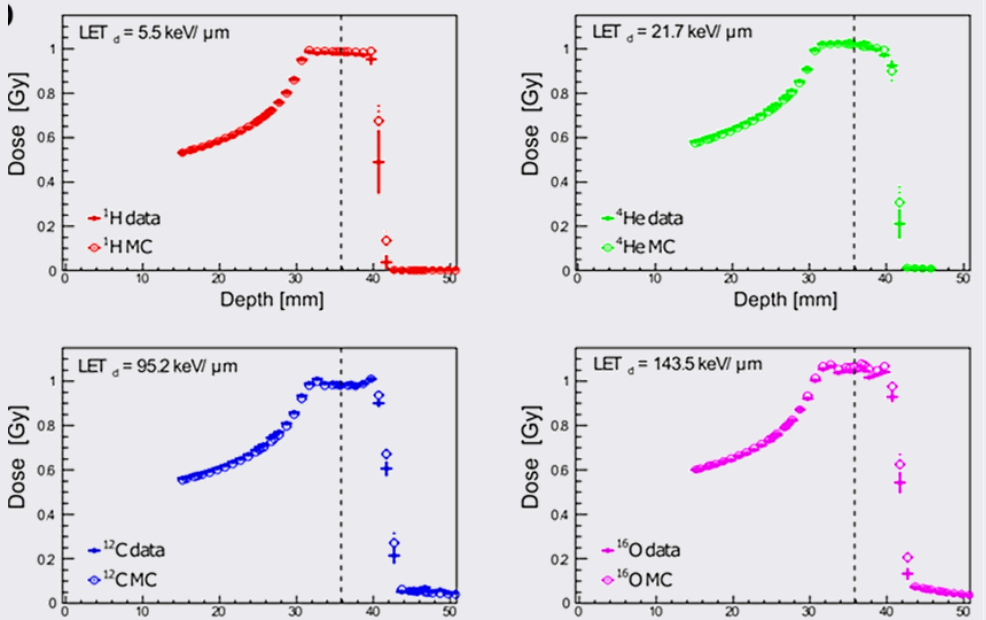
Source: MedAustron

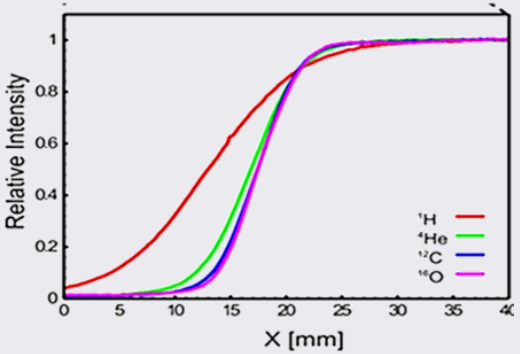
01

SCIENTIFIC MOTIVATION & AIM

Scientific Motivation

- ^{4}He ions present physical and radiobiological properties intermediate between those of protons and ^{12}C ions, with ^{16}O ions expected to be superior to ^{12}C in (hypoxic) tumour control.

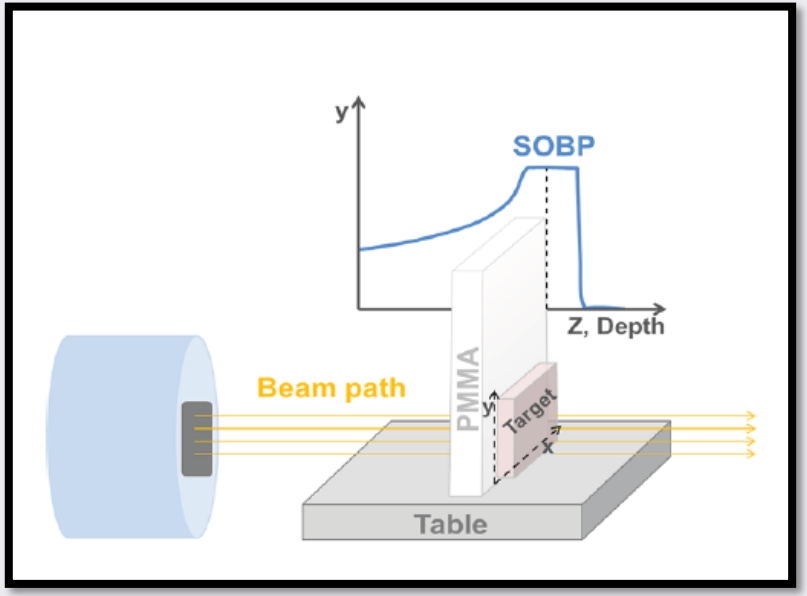




Dokic et al 2016 Oncotarget

Aim

- BIOHOT aims at biophysically characterizing clinical ^{4}He and ^{16}O beams through:
  - Experimental Radiobiology
  - Modelling
  - Microdosimetry



02

PARTICIPATING UNITS & COLLABORATIONS

Partecipating units & collaborations

INFN-NA

UNINA, Fondazione Pascale

INFN-PV

Centro Nazionale di Adroterapia Oncologica (CNAO), Fondazione Maugeri, UNIPV

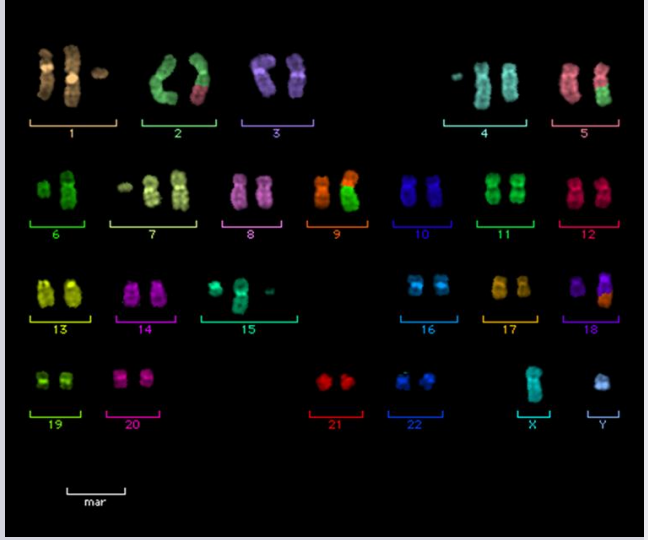
INFN-RM3

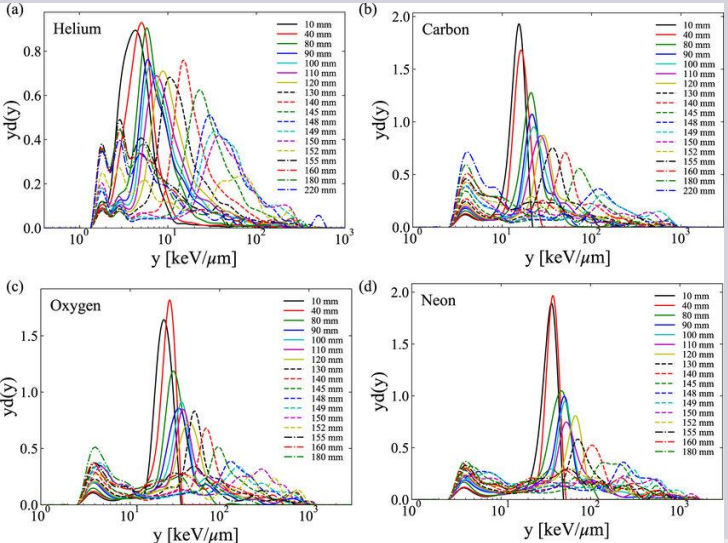
Università degli studi di Roma 3

INFN-LNS

Heidelberg

Heidelberg Ion-Beam Therapy Center (HIT)

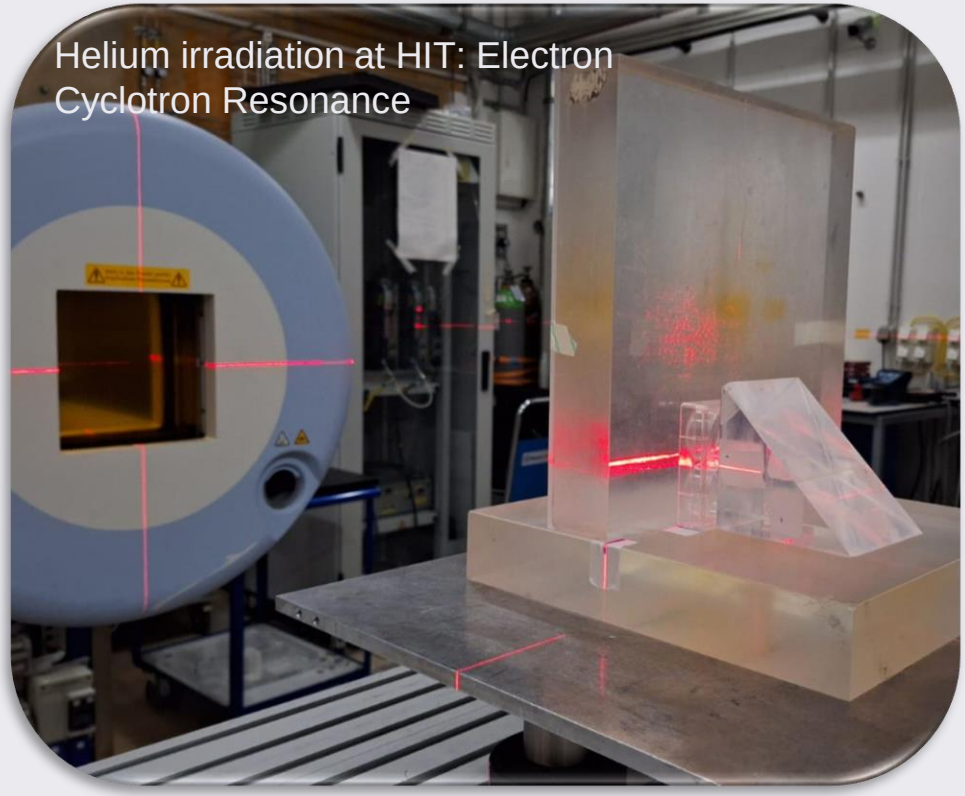




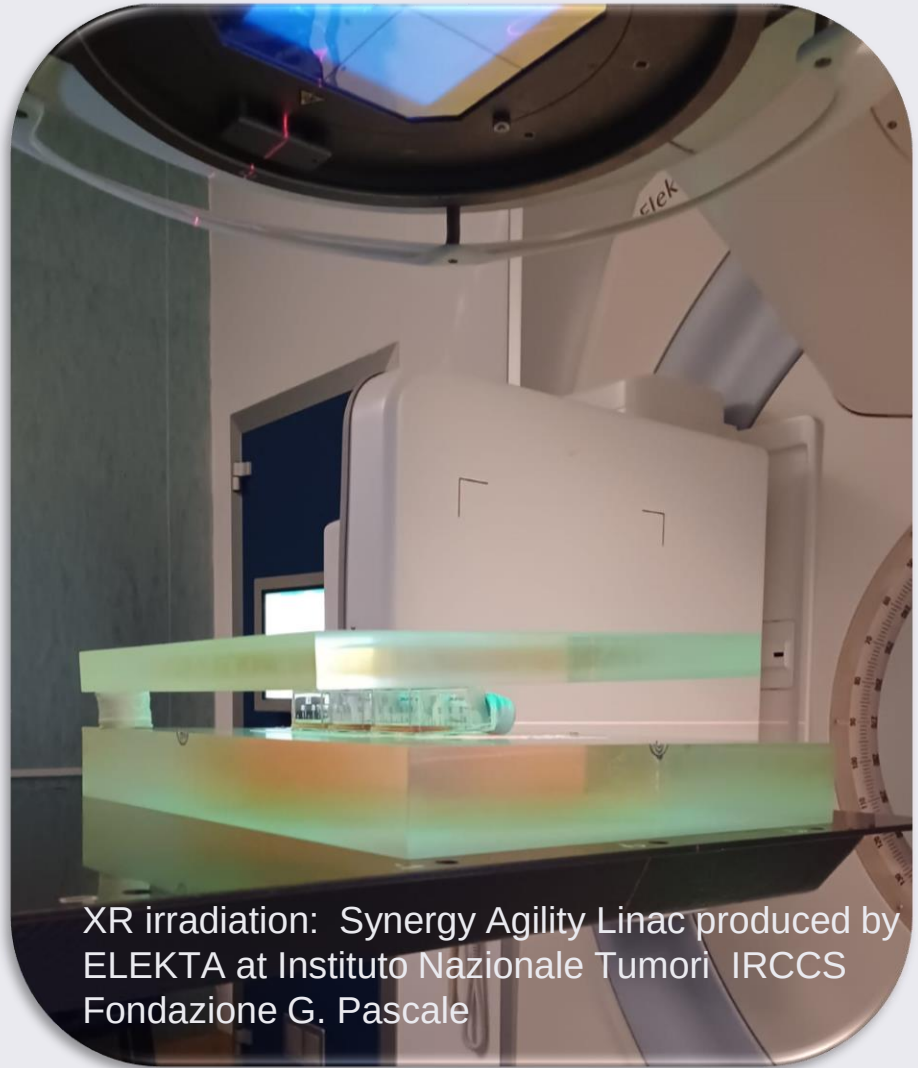
03

METHODOLOGY

IRRADIATION SETUP



Helium irradiation at HIT: Electron Cyclotron Resonance

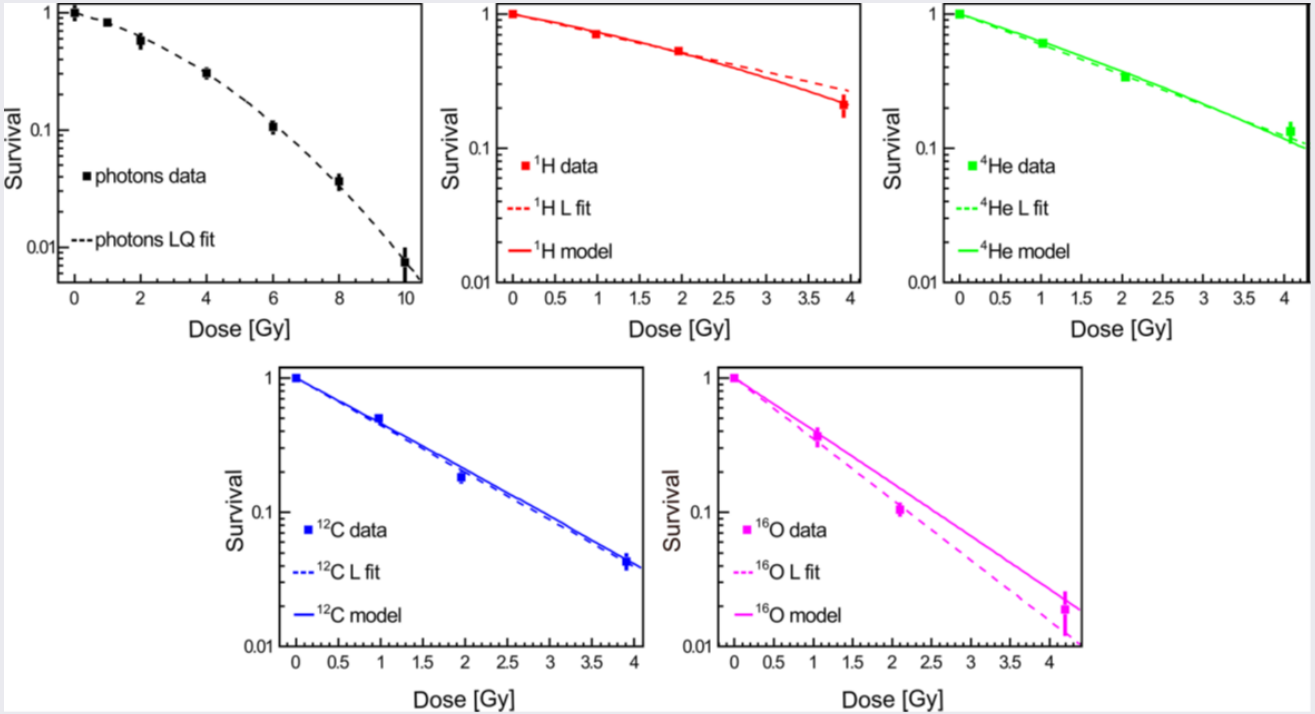


XR irradiation: Synergy Agility Linac produced by ELEKTA at Instituto Nazionale Tumori IRCCS Fondazione G. Pascale

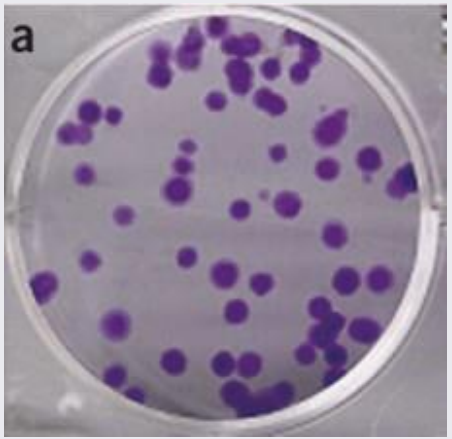
Methodology-Cancer cells

- Radiobiology
  - Techniques to be used for cancer cells (osteosarcoma and pancreas)
    - Clonogenic assay (RBE determination)
    - Apoptosis (cancer cell death)
    - Foci assay (quantification of radiation-induced repair efficiency)
    - Migration assay (evaluation of metastatic ability)

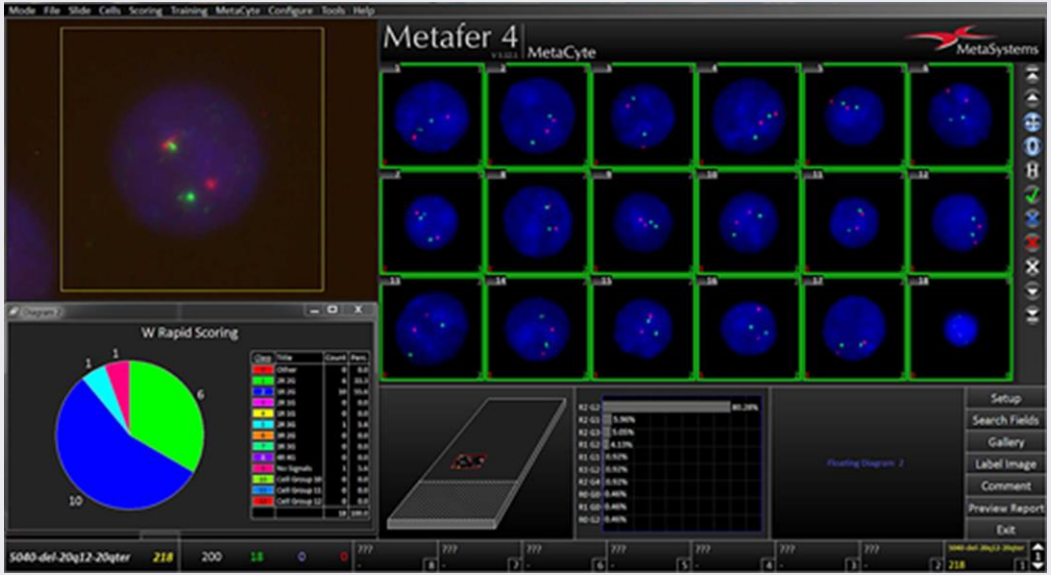
CLONOGENIC ASSAY

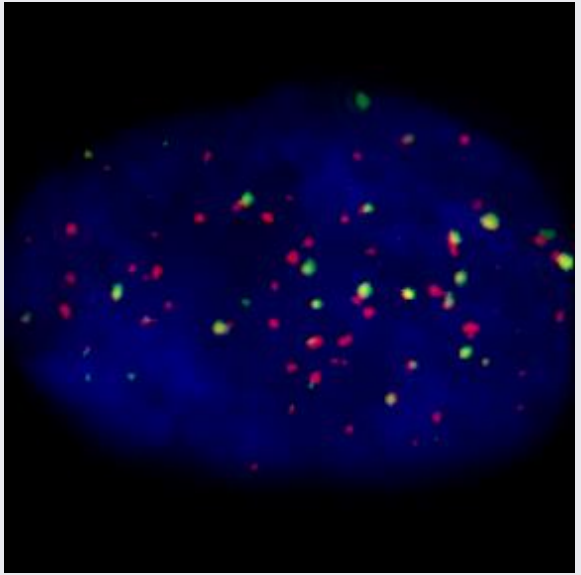


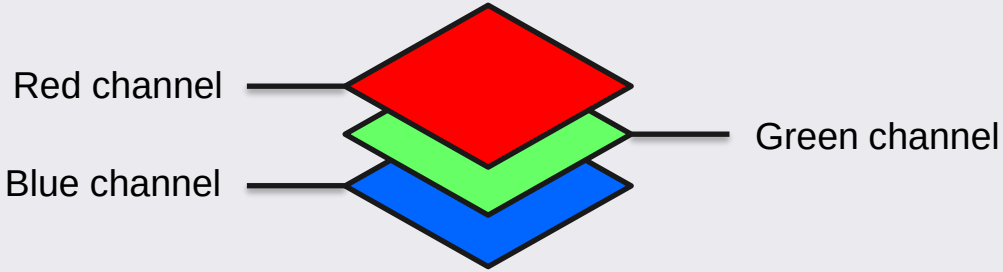
Dokic et al 2016 Oncotarget



FOCI ASSAY



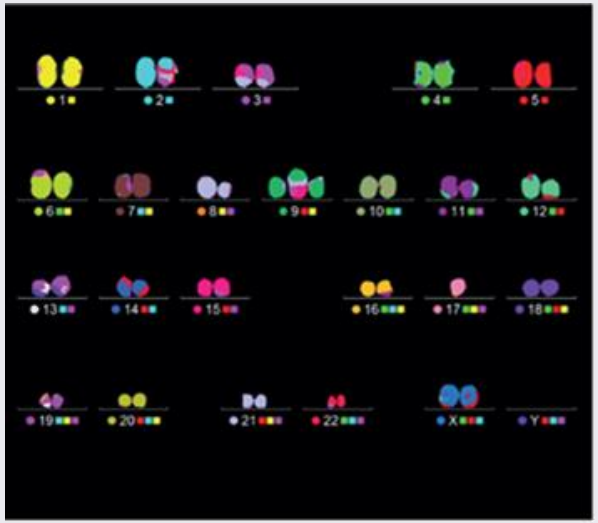


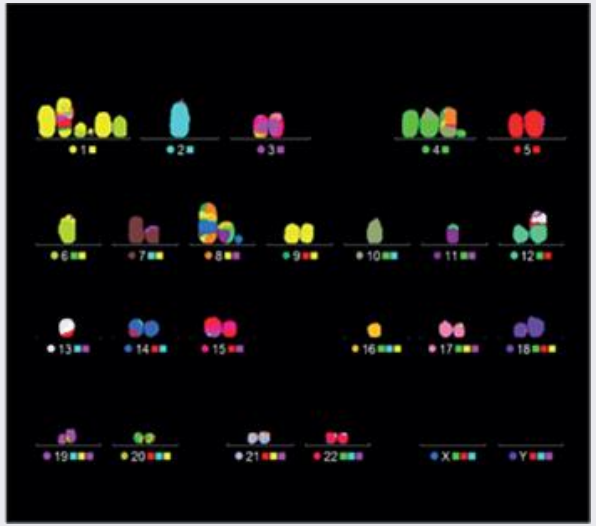


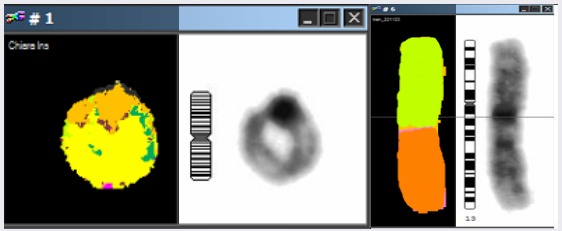
BIOHOT

Methodology-Non cancer cells

- Radiobiology
  - Techniques to be used for normal cells (fibroblasts and endothelial)
    - Premature senescence, oxidative stress, inflammation markers (late adverse reactions)
    - Chromosome aberrations (risk of secondary cancer) via m-FISH

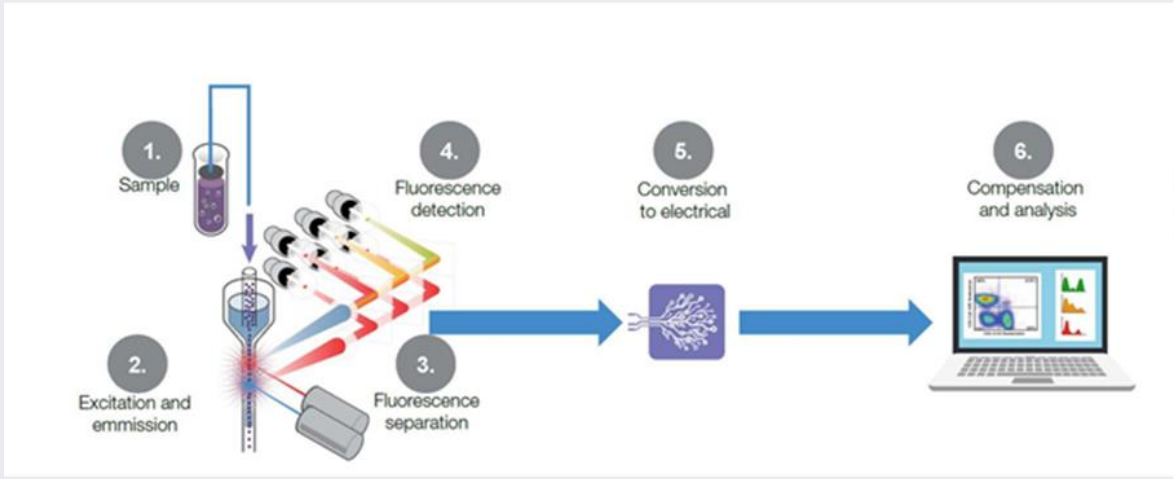




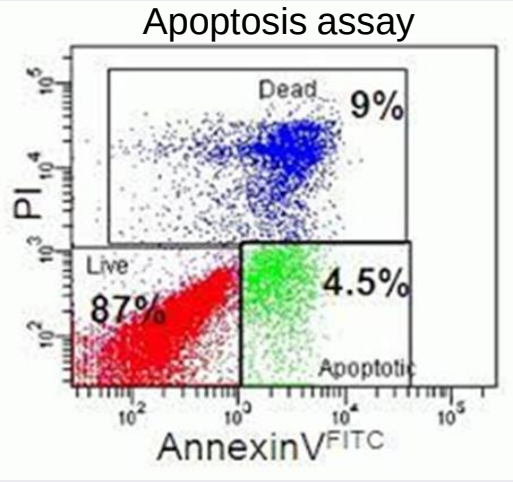


m-FISH technique

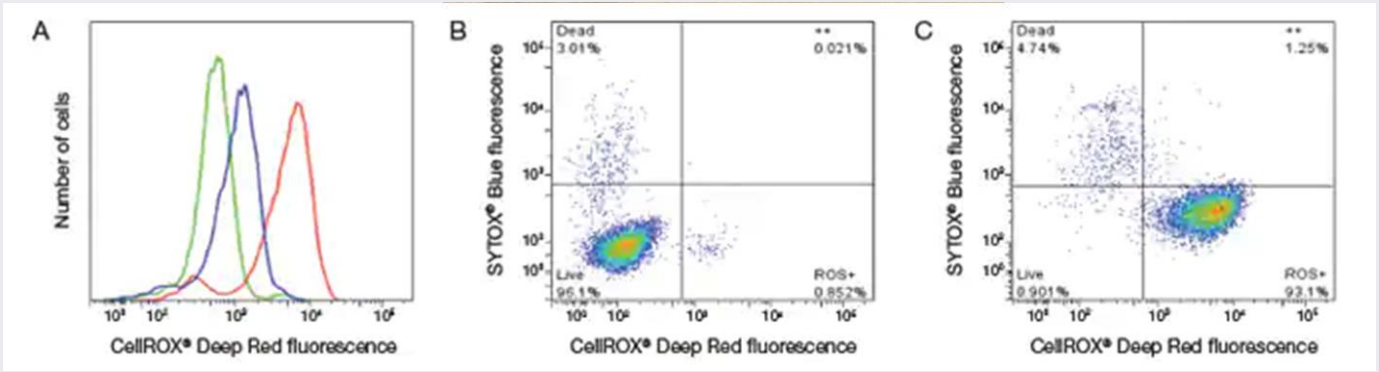
FLOW CITOMETRY-BASED ASSAYS



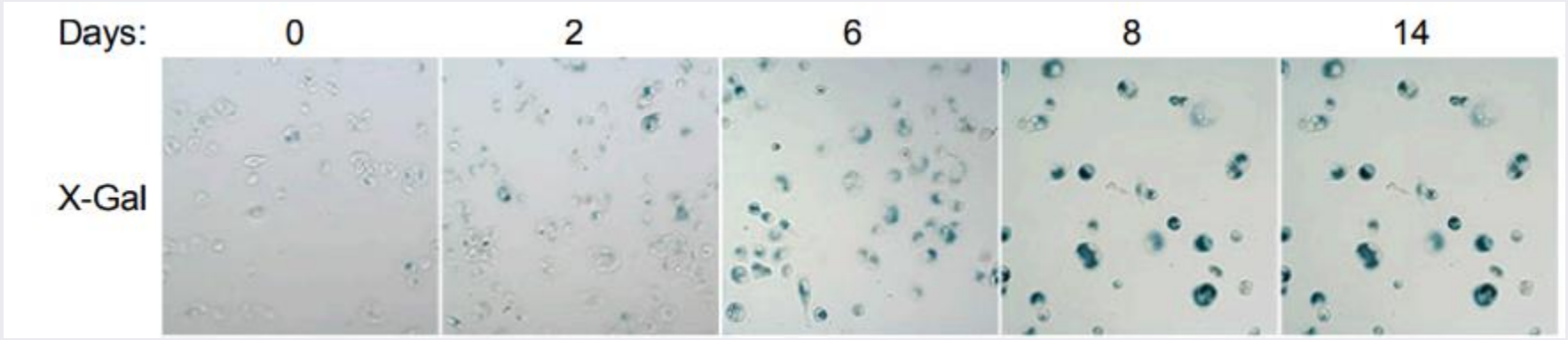
Apoptosis assay

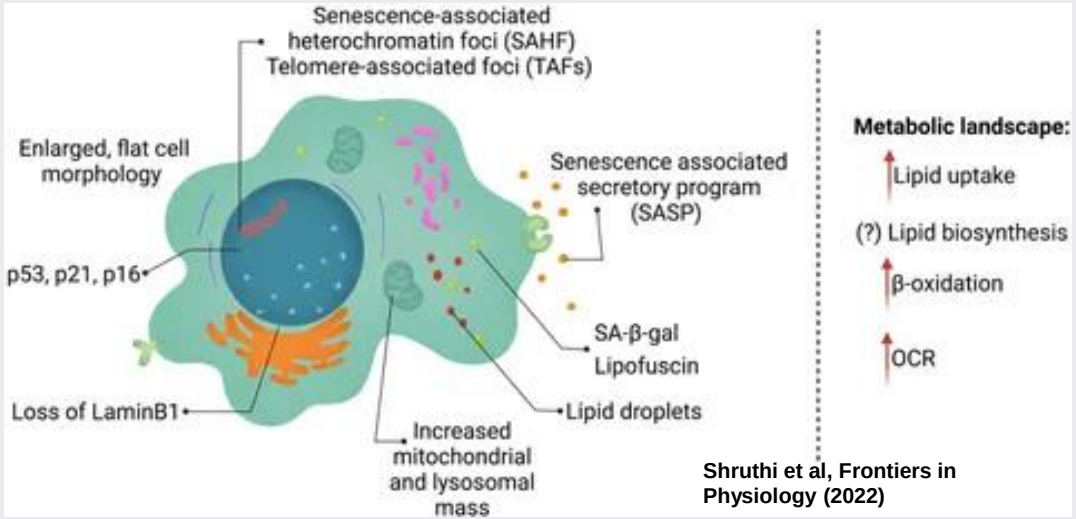


ROS assay



SENESCENCE ASSAY

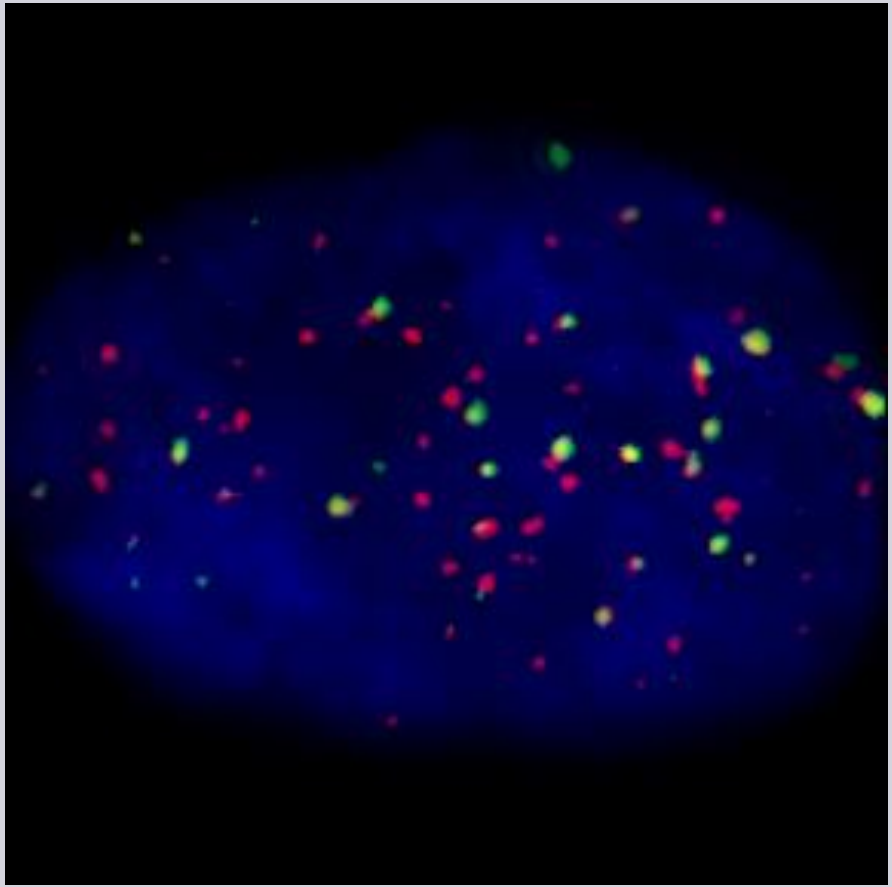




Shruthi et al, Frontiers in Physiology (2022)

Methodology-3

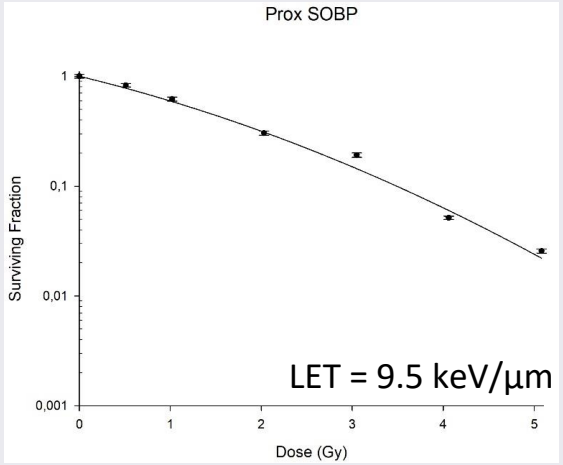
- Modelling and Microdosimetry
  - BIophysical ANalysis of Cell death and chromosome Aberrations (BIANCA): using inputs from photon survival curves and chromosome aberration data to predict ion-induced cell death and sublethal damage
    - LET distributions provided by GEANT4 will be used by BIANCA, for which the LET is one of the main inputs to run a simulation
  - Geant 4: simulations of track- and dose-averaged LET
  - Microdosimetric Kinetic Model (MKM): the microdosimetric spectra obtained from simulations and experimental data will be used as inputs for the MKM to directly link the microdosimetric characterization of ^{4}He and ^{16}O beams to cell survival probability and related RBE
    - Survival curves predicted by MKM will be compared with those predicted by BIANCA model for model intercomparison
  - Microdosimetry measurements to reconstruct LET distributions along ^{4}He and ^{16}O SOBP and benchmark Geant4 simulations

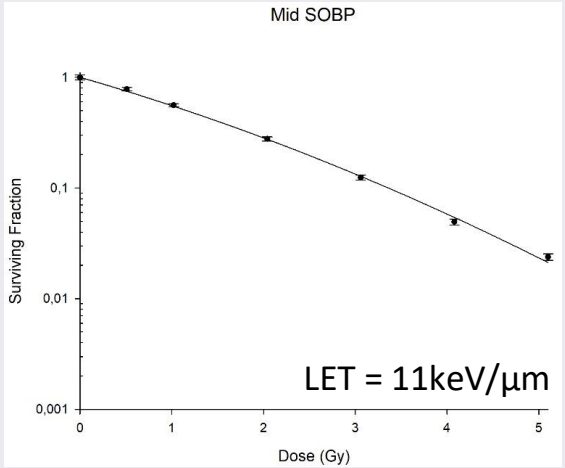


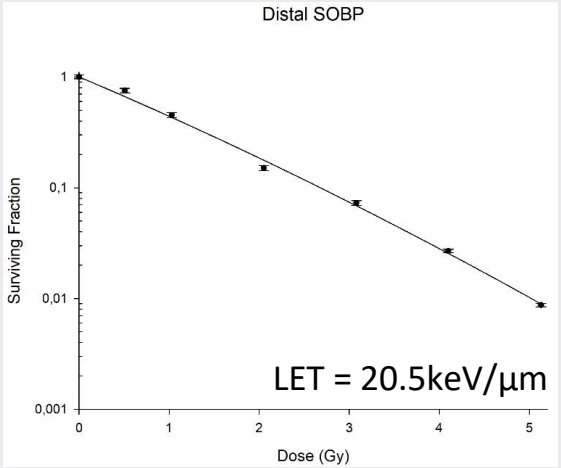
04

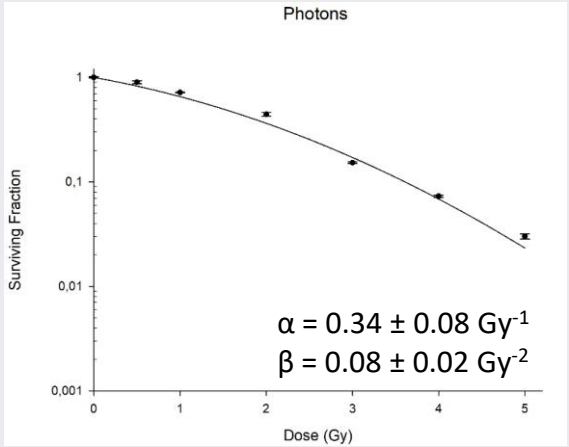
PRELIMINARY RESULTS

RBE for SAOS-2



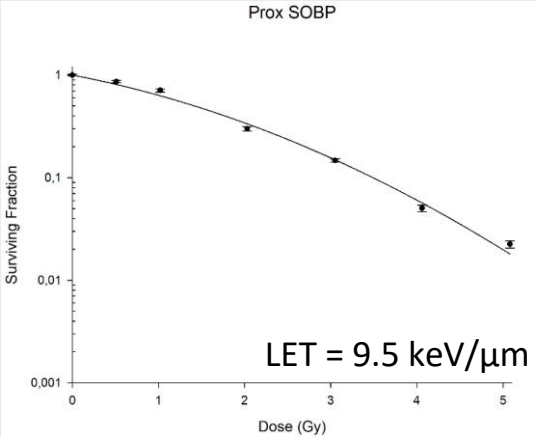


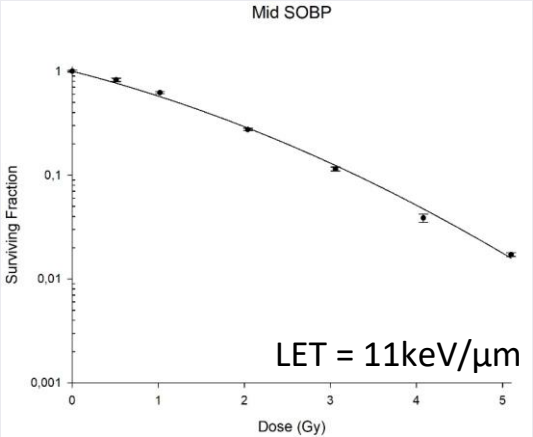


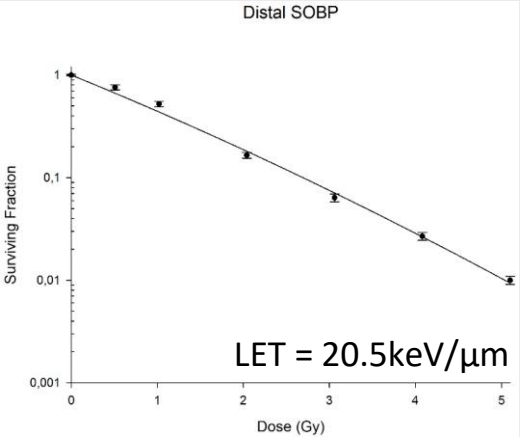


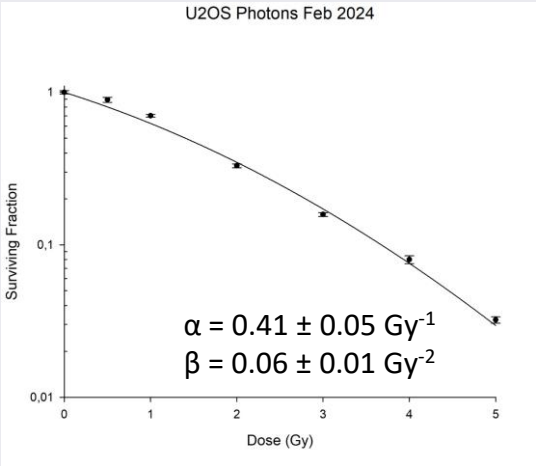
	α (Gy^{-1})	β (Gy^{-2})	RBE_{10}
Prox	0.47 ± 0.09	0.059 ± 0.024	1.05 ± 0.21
Mid	0.56 ± 0.03	0.042 ± 0.008	1.10 ± 0.15
Distal	0.81 ± 0.05	0.026 ± 0.013	1.38 ± 0.20

RBE for U2OS

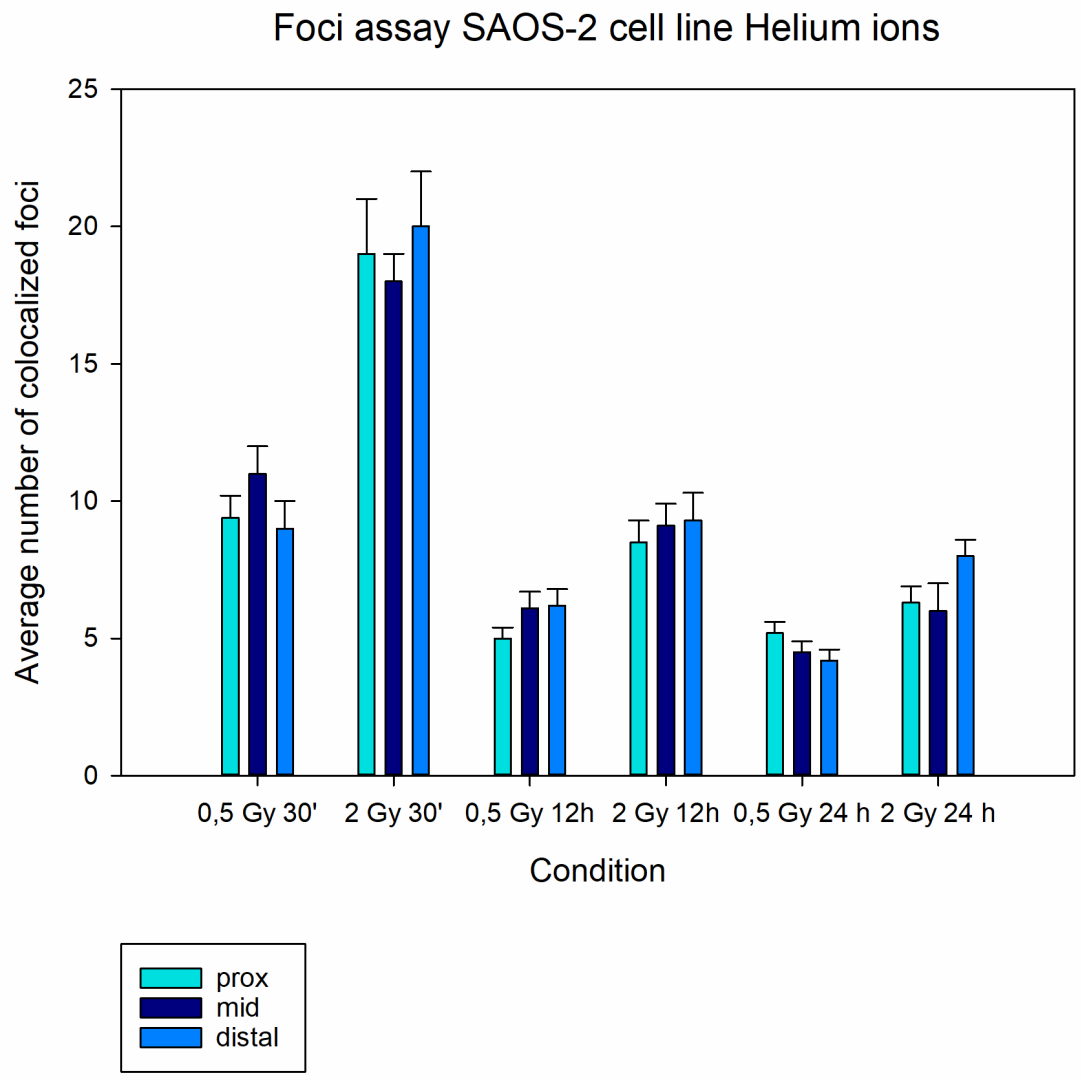




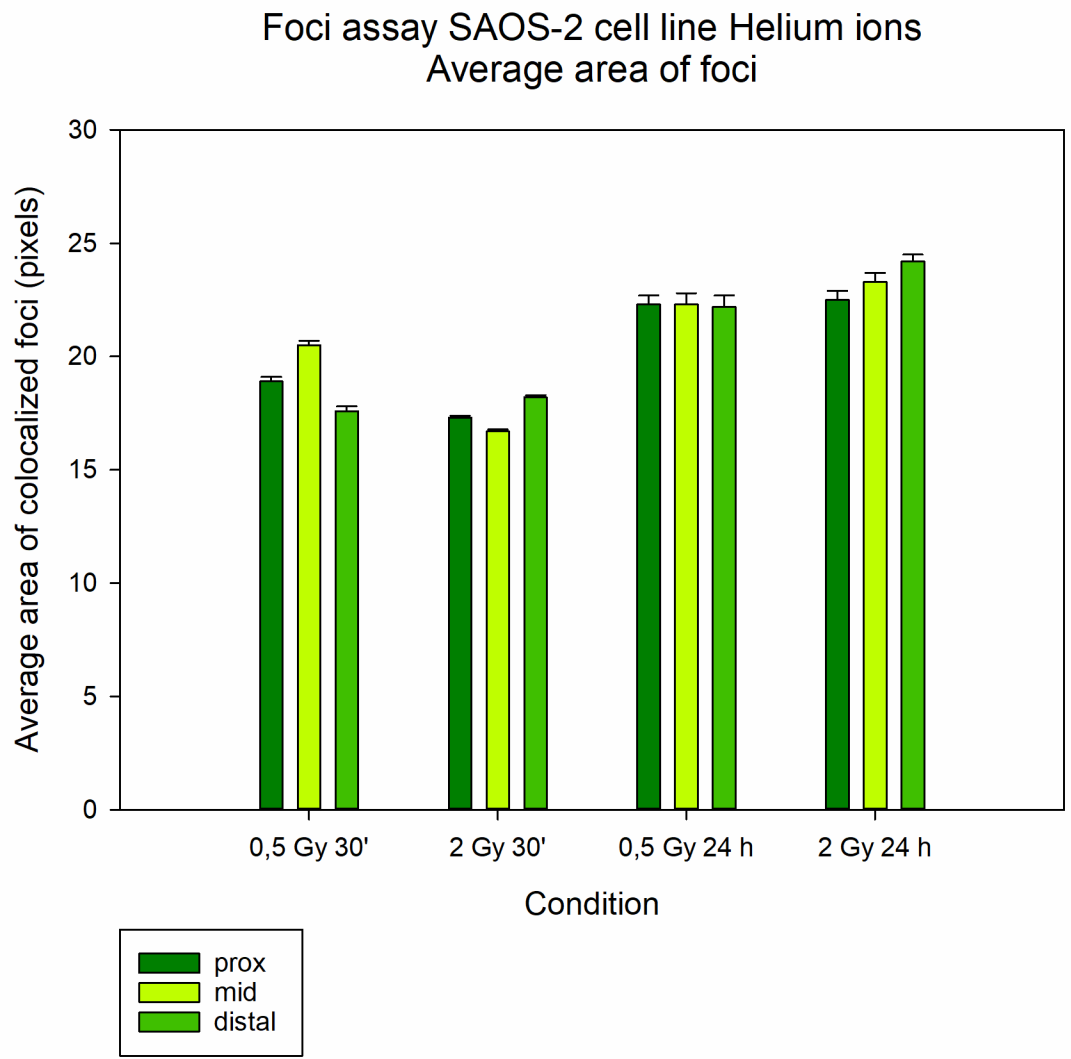




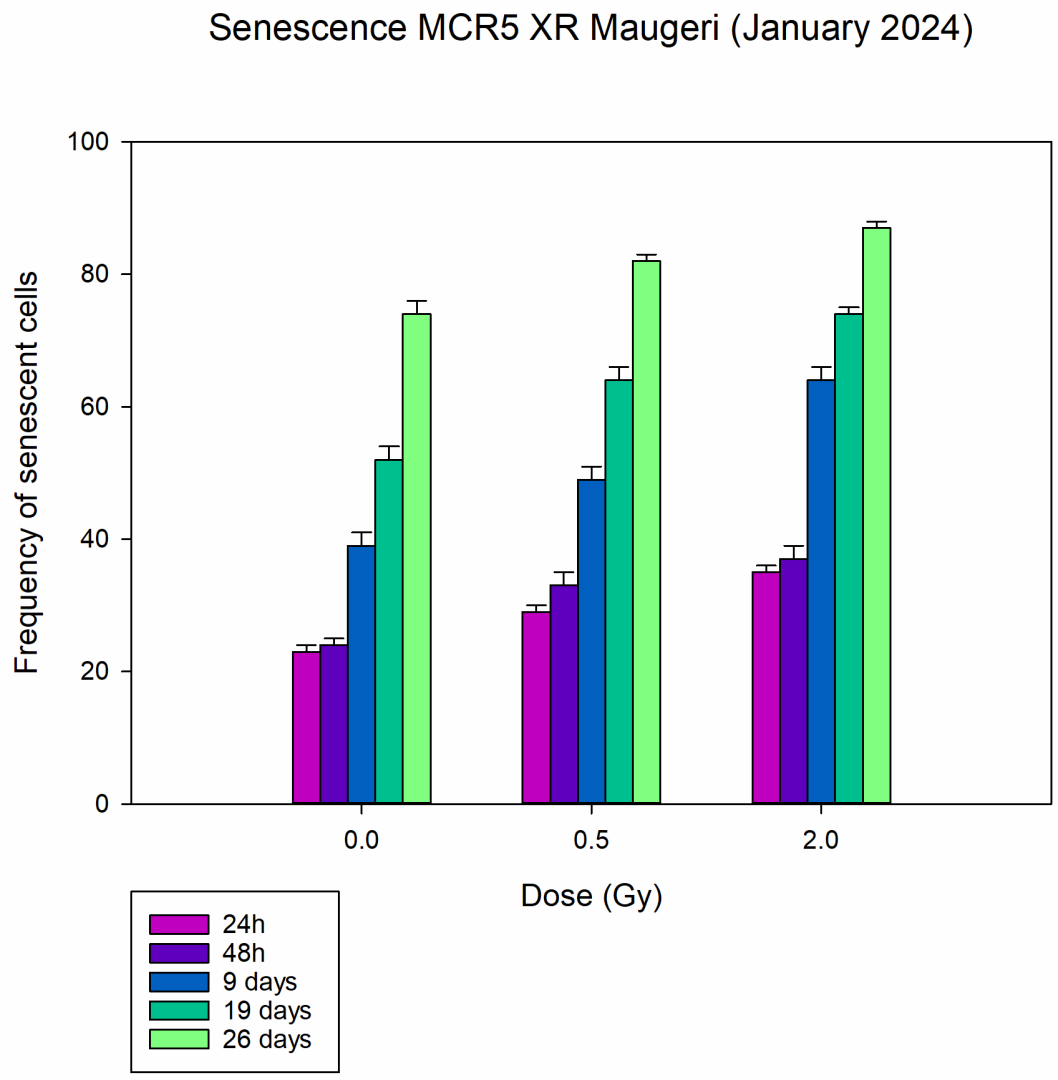
	α (Gy^{-1})	β (Gy^{-2})	RBE_{10}
Prox	0.38 ± 0.06	0.085 ± 0.020	1.07 ± 0.14
Mid	0.50 ± 0.04	0.066 ± 0.012	1.14 ± 0.12
Distal	0.80 ± 0.07	0.026 ± 0.020	1.39 ± 0.18



Foci Assay Results: SAOS-2 He



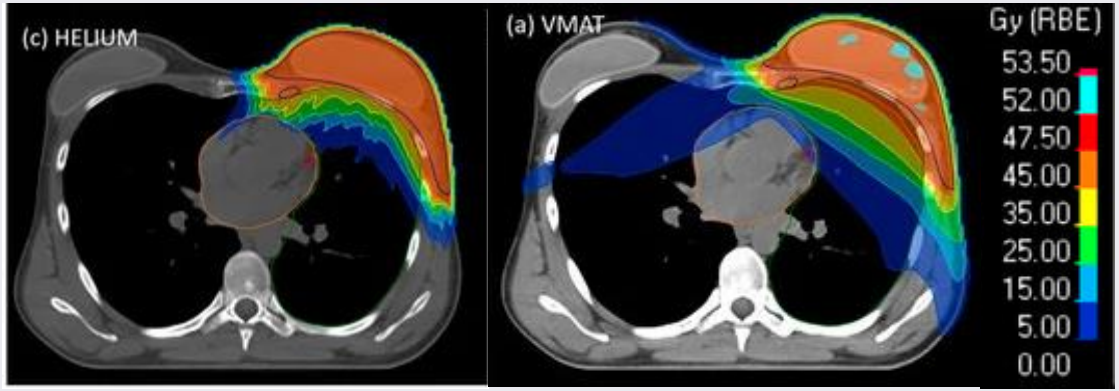
Foci Assay: Mean focus size



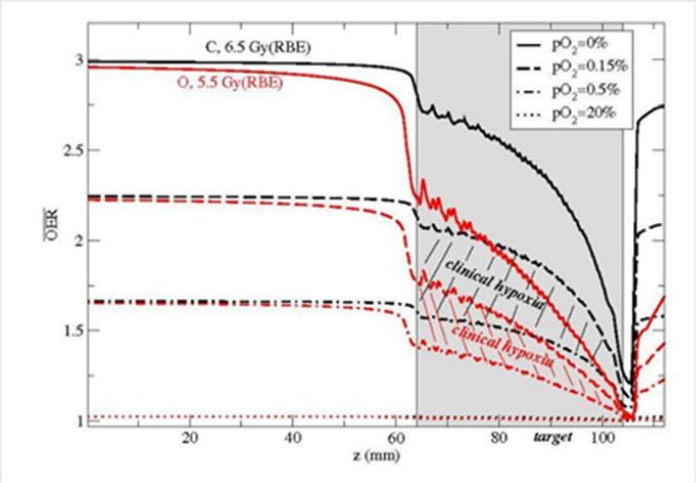
Senescence Assay

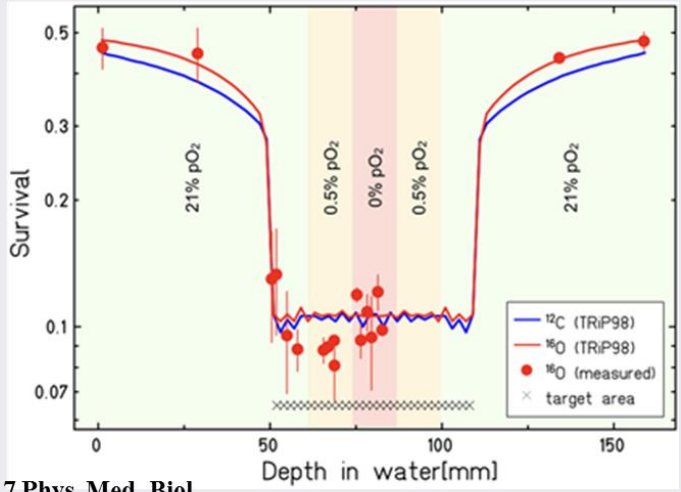
05

FUTURE PERSPECTIVES



Bonaccorsi et. al 2024, Cancers.





Sokol et al 2017 Phys. Med. Biol.

BIOHOT

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