Microdosimetric study and RBE measurement at CATANA protontherapy facility for the treatment of ocular melanoma

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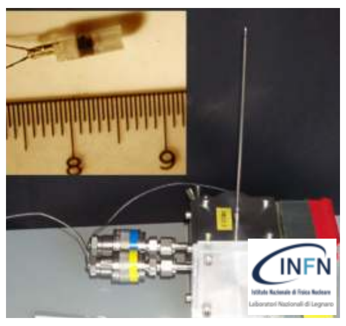
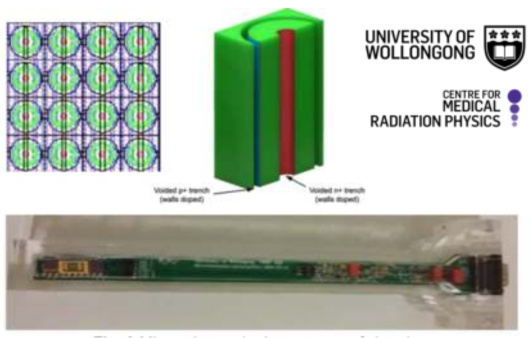
Scientific Motivation

CATANA (Centro di AdroTerapia ed Applicazioni Nucleari Avanzate) was the first Italian protontherapy facility. It has been in operation since 2002 at INFN-LNS Laboratories (Catania, Italy) and is dedicated to the treatment of ocular neoplastic pathologies [1]. Nowadays, a slightly increased biological effectiveness (with respect to reference low-LET radiation) is considered in clinical proton treatment planning by assuming a fixed RBE (Relative Biological Effectiveness) of 1.1 for the whole radiation field. However, data emerging from various studies suggest and highlight how variations in RBE, which are currently neglected, might actually result in deposition of biologically significant doses in healthy organs. Accurate knowledge of the RBE increase in eye protontherapy is of extreme importance as the distal part of the Spread-Out Bragg Peak (SOBP) often involves critical anatomical regions like the optic nerve and the macula, for which an excess of biologically effective dose could lead to patient's vision loss. In order to evaluate how the RBE value changes along a typical SOBP for eye protontherapy, a collaboration, between INFN-LNS, the University of Wollongong, the University of Naples, IBFM-CNR unit of Cefalù, the INFN-LNL, the INFN-TIFPA and INFN-MI, was established. The response of four different microdosimetric detectors was studied and uveal melanoma cells were irradiated; detectors and cells were placed at same positions. Monte Carlo (MC) simulations were performed to reproduce the experimental conditions and calculate the expected RBE and LET, evaluated using new algorithms developed for clinical applications.

Adopted detectors

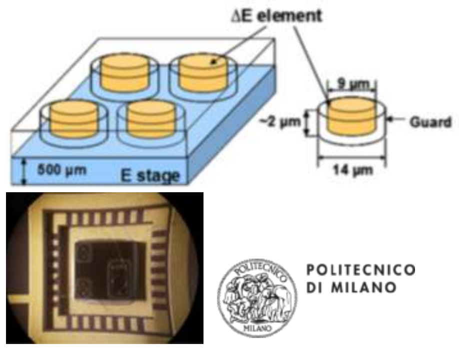


mini-TEPC realized by INFN-LNL group [2]



MicroPlus silicon probe realized by UoW group [3]

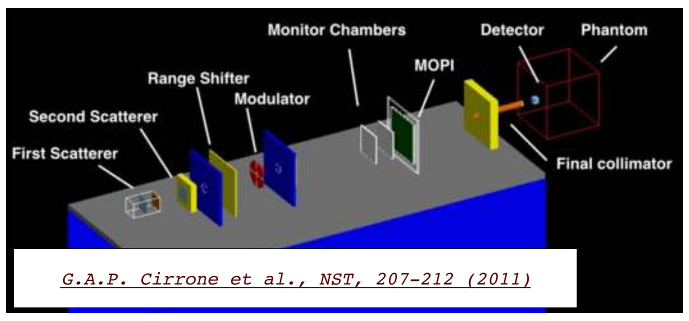
TEPC of Far West Technology TIFPA group [4]



Silicon telescope realized by Poli-MI group [5]

Experimental Set-Up and Monte Carlo simulations

The whole experimental set-up and the physical characteristics were simulated using Geant4 toolkit.



The novelty of this work lies in the implementation and testing of new algorithms for LET and RBE calculations based on the MC approach. The proposed methods for LET-dose and LET-track were designed in such a way to have a very low dependence from simulation transport parameters, like the production cut of secondaries. These parameters are intrinsic to any condensed-history MC simulation tool and have an impact in clinical practice.

LET-dose

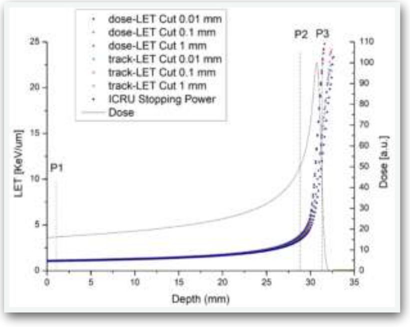
$$\bar{L}_D = \frac{\sum_{i=1}^{N} L_i \varepsilon_i}{\sum_{i=1}^{N} \varepsilon_i}$$

$$\bar{L}_D^{Total} = \frac{\sum_{j=1}^{n} [\sum_{i=1}^{N} L_i \varepsilon_i]_j}{\sum_{j=1}^{n} [\sum_{i=1}^{N} \varepsilon_i]_j}$$

LET-track

$$\bar{L}_T = \frac{\sum_{i=1}^{N} L_i l_i}{\sum_{i=1}^{N} l_i}$$

$$\bar{L}_T^{Total} = \frac{\sum_{j=1}^{n} [\sum_{i=1}^{N} L_i l_i]_j}{\sum_{j=1}^{n} [\sum_{i=1}^{N} l_i]_j}$$



The RBE was computed considering the mixed-field condition and by using a twofold approach: semi-empirical approach and coupled MC method to well-known radiobiological models (MKM and LEM) by using specific Look Up Tables. A more detailed description can be found in [6].

Lookup tables based on LEM model

fixed a specific cell line

→

Geant4 Simulation

Step-by-Step retrieved information: Z, A, Ekin, LET, Edep

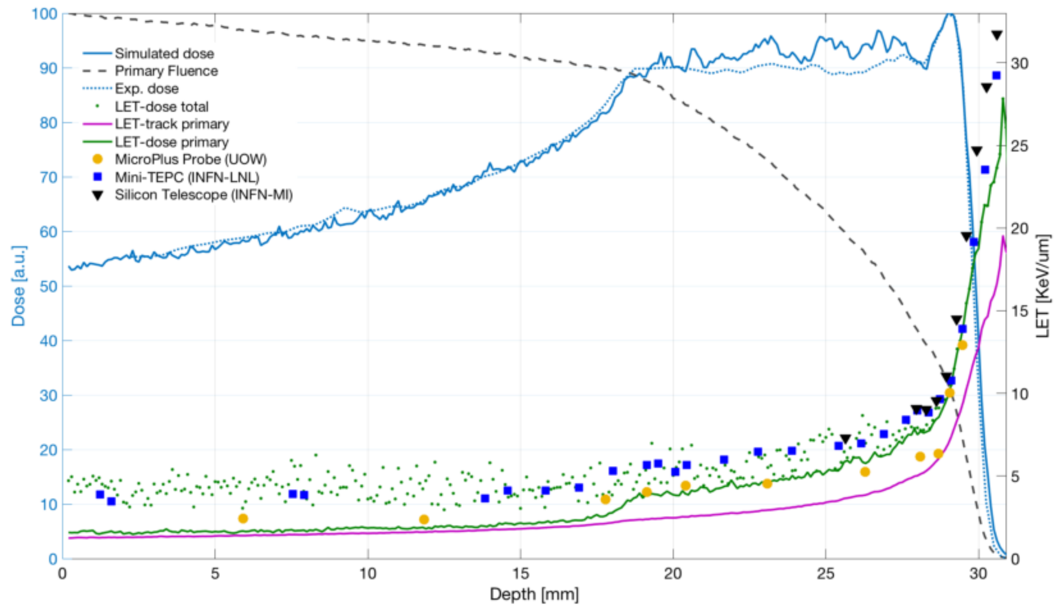
→

Fixed a voxel, for each step:

- LUT interpolation
- Computation of weighted Alpha and Beta parameteres

$$\bar{\alpha} = \frac{\sum_{i=1}^{n} \alpha_i E_i}{\sum_{i=1}^{n} E_i} \qquad \bar{\beta} = \left(\frac{\sum_{i=1}^{n} \sqrt{\beta_i} E_i}{\sum_{i=1}^{n} E_i}\right)^2$$

Preliminary results



Primary intercomparison between the three different microdosimetric detectors: mini-TEPC, Silicon Telescope and MicroPlus probe. Detector signal was compared with the simulated track-LET and dose-LET distributions calculated for 62 MeV of incident proton beam in water. This study was conducted in different positions along the Bragg peak.

[1] Cirrone GAP et al., Frontiers in Oncology, 10.3389/fonc.2017.00223, (2017); [2] L. De Nardo et al., Physica Medica XX, 71-77 (2004); [3] Linh T. Tran et al., Med. Phys. 44(11), 6085-6095, (2017); [4] http://www.farwestech.com; [5] S. Agosteo et al., Radiation Measurements, (2010); [6] G. Petringa et al., Physica Medica 58, 72-80, (2019)