MICROdosimetry-based assessment of Biological Effectiveness in Ion Therapy

Kick off meeting

3 February 2021

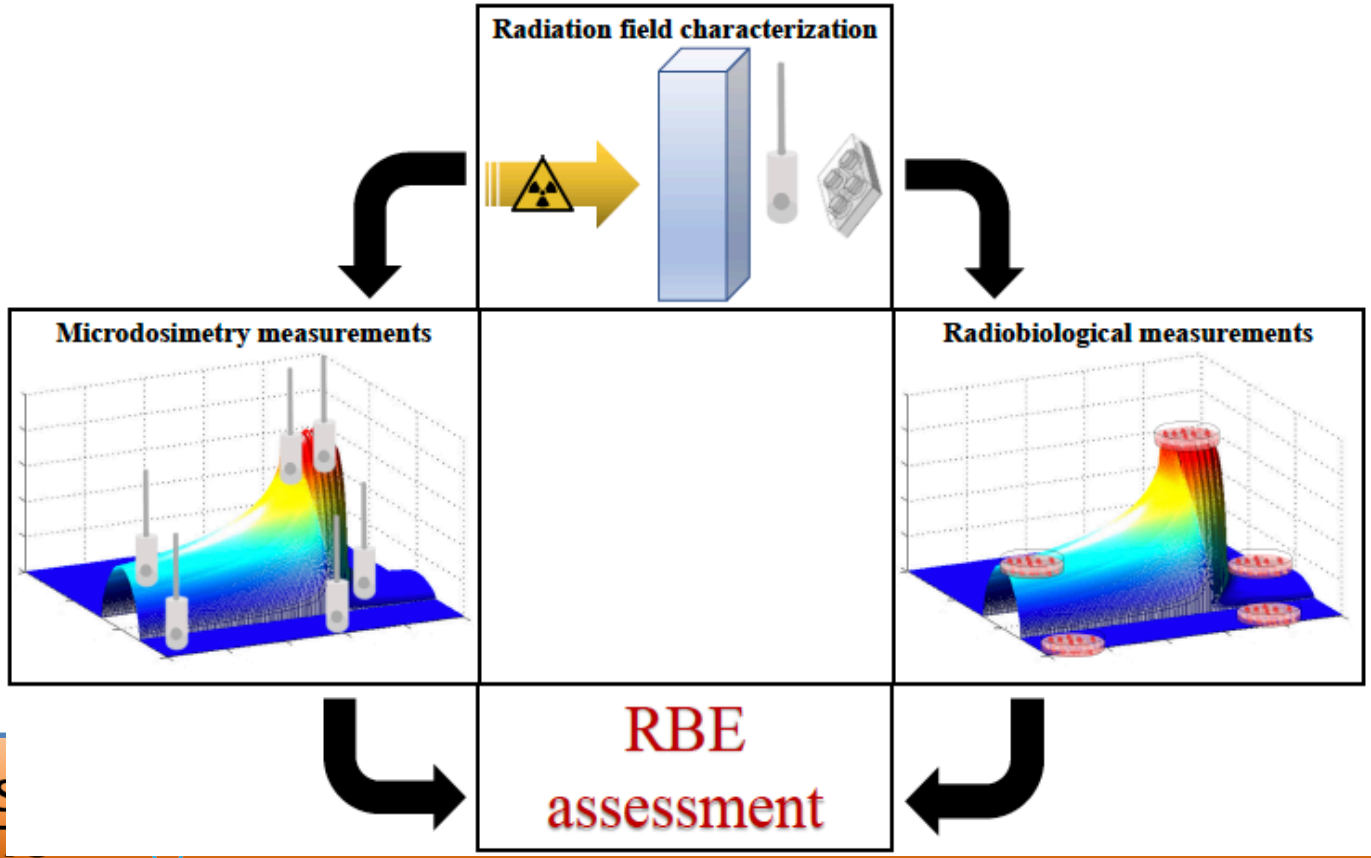
(Sadly online)

Goals of this meeting

- What is new compared to the project submission
- To program the activities of 2020 and in particular of the next 6 months (we should have another meeting before the summer)

MICROBE_IT goal

To develop a stochastic microdosimetry-based kinetic model (GSM² generalized stochastic microdosimetry model for radiobiological endpoints) for RBE to improve treatment planning accuracy and effectiveness, as well as to decrease toxicity in the normal tissue.



Novelties

i. Comprehensive comparison of all existing types of microdosimeters, including 2 new detectors (HDM and SiC) partially developed within this project. One nanodosimeter will be also used.

ii. Use of the full microdosimetry spectrum to calculate the dose deposited in each cell nucleus.

iii. Stochastic fluctuations of energy deposition (and thus damage induction) within the nucleus and from cell to cell are taken into account.

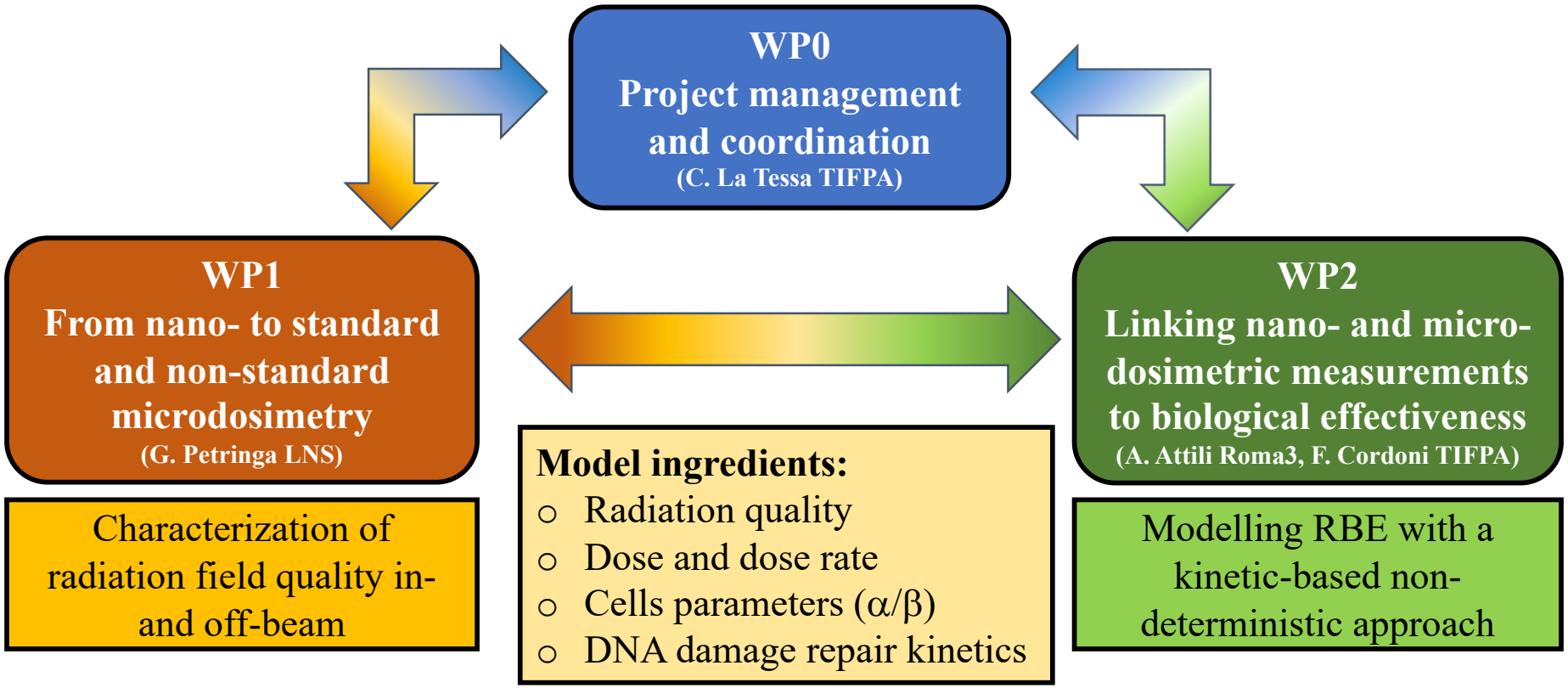
iv. Radiation field quality evaluated both in-beam and at the field edges (where toxicity is more likely to occur).

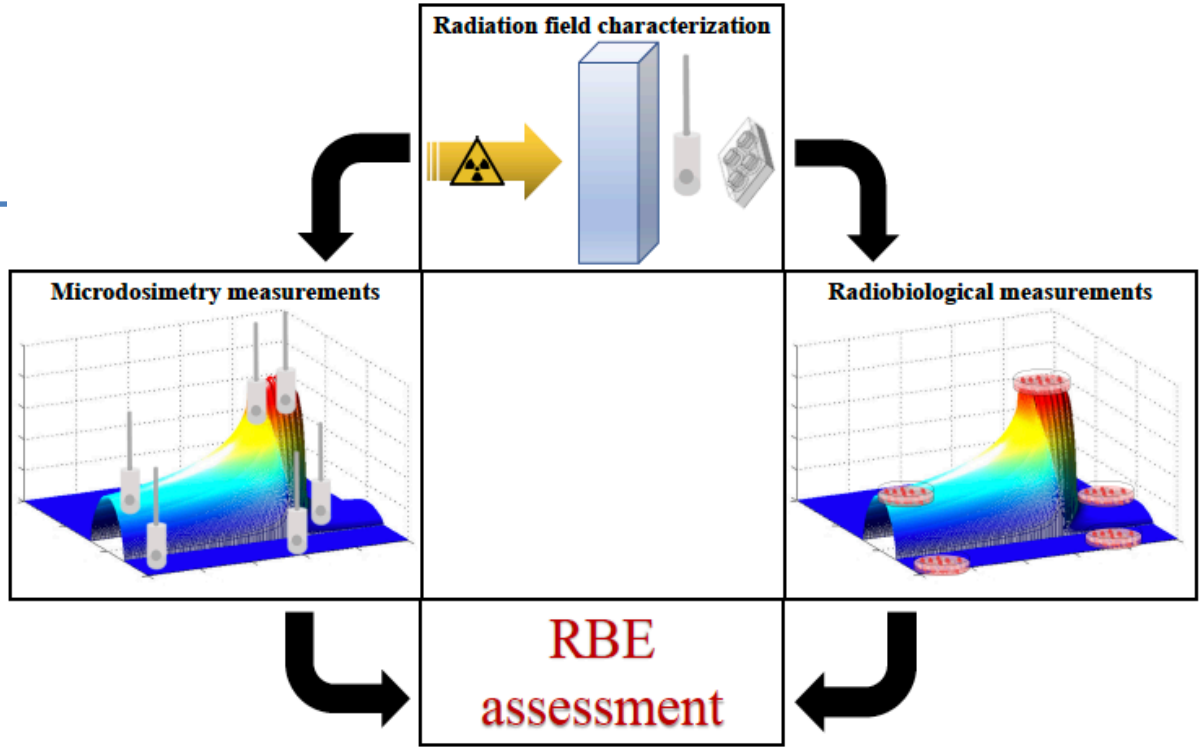
v. Explore the link between micro- (and nano-dosimetry) and radiobiological measurements.

vi. Radiobiology experiments performed both in acute and split dose

MICROBE_IT structure

Project duration: 2 years (2021-2022)
INFN Participant units: TIFPA, LNS, Roma3, Milano, LNL
External partners: APSS Trento and GSI Germany
INFN Referees: Libero Palladino and Sonia Tangaro





WP0: Project management and coordination (TIFPA)

- Coordination of all WPs
- Meeting organization
- Dissemination of the project results

WP1: From nano- to standard and non-standard microdosimetry (TIFPA, LNS, LNL, MI)

- HDM read-out and DAQ development (TIFPA)
- SiC read-out development (LNS)
- Test and measurement campaigns (TIFPA, LNS, LNL, MI)
- Geant4 Monte Carlo simulations of experimental data (TIFPA, LNS)

WP2: Linking nano- and micro-dosimetric measurements to biological effectiveness (TIFPA, LNS, RM3)

- Influence of radiation quality description on treatment plan outcomes (RM3, TIFPA)
- GSM^2 model development (RM3, TIFPA)
- Radiobiological measurements for GSM^2 development and validation (LNS, TIFPA)

WPs and FTEs

Microbe_IT

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WP2: Linking nano- and micro-dosimetric measurements to biological effectiveness (TIFPA, LNS, RM3)

- Influence of radiation quality description on treatment plan outcomes (RM3, TIFPA)
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- Radiobiological measurements for GSM^2 development and validation (LNS, TIFPA)

#	Unit	Unit coordinator	Total FTE	WP involvement
1	INFN-TIFPA	Chiara La Tessa	4.6	0, 1, 2
2	INFN-LNS	Pablo Cirrone	3.2	1, 2
3	INFN-LNL	Valeria Conte	0.2	1
4	INFN-MI	Stefano Agosteo	0.2	1
5	INFN-RO	Andrea Attili	0.4	0,1,2

TOTAL FTE: 8.6

Budget requested for year 1

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Cost Category	Item	I year	Unit	WP
Consumable	Beam time (Trento proton therapy center)	€ 9,400.00	TIFPA	0
	LGADs thinning	€ 1,000.00	TIFPA	1
	Resine Epoxy technology	€ 500.00	LNS	1
	Reagent and plastics for cellular biology	€ 5,000.00	LNS	2
	Antibody for western blot analysis	€ 3,000.00	LNS	2
	Preamplifier realization and assembling	€ 2,000.00	LNS	2
	TOTAL CONSUMABLES	€ 20,900.00		
Instrumentation	ABACUS chips for LGAD read-out	€ 26,000.00	TIFPA	1
	Red-Pitaya hardware kit for LGAD DAQ	€ 2,000.00	TIFPA	1
	PCB boards for ABACUS chips	€ 6,000.00	TIFPA	1
	FPGA Xilinx for LGADs read-out and DAQ	€ 5,000.00	TIFPA	1
	CAEN DT5485P Digital Controlled Power Supply for SiPM	€ 800.00	LNS	1
	Workstation for high-performace calculation	€ 4,000.00	Roma3	2
	TOTAL INSTRUMENTATION	€ 43,800.00		
Travels	Experimental activity at CNAO and collaboration meeting at LNS	€ 2,000.00	TIFPA	0, 1
	Experimental activities at PTC and CNAO and Collaboration meetings at LNS and TIFPA	€ 3,500.00	LNL	1
	Work meetings, collaboration meetings at LSN and TIFPA	€ 1,200.00	Roma3	2
	Experimental activities at PTC and collaboration meetings at LNS and TIFPA	€ 2,500.00	Milano	1
	Experimental activities at PTC and CNAO, collaboration meeting at TIFPA	€ 15,000.00	LNS	1, 2
	TOTAL TRAVELS	€ 24,200.00		

GRAND TOTAL	**€ 88,900.00**

Budget requested for year 1

Microbe_IT

Cost Category	Item	I year	Unit	VP
Consumable	Beam time (Trento proton therapy center)	€ 9,400.00	TIFPA	
	LGADs thinning	€ 1,000.00	TIFP	
	Resine Epoxy technology	€ 500.00		
	Reagent and plastics for cellular biology	€ 5,000.00		
	Antibody for western blot analysis	€ 3,000.0		2
	Preamplifier realization and assembling	€ 2,0		2
	TOTAL CONSUMABLES	€		
Instrumentation	ABACUS chips for LGAD read-out			1
	Red-Pitaya hardware kit for LGAD DAQ		PA	1
	PCB boards for ABACUS chips		TIFPA	1
	FPGA Xilinx for LGADs read-out and DA		TIFPA	1
	CAEN DT5485P Digital Controlled Power	800.00	LNS	1
	Workstation for high-perfo	€ 4,000.00	Roma3	2
	TOTAL INSTRU	€ 43,800.00		
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	perimental activities at PTC and CNAO, collaboration meeting at TIFPA	€ 15,000.00	LNS	1, 2
	TOTAL TRAVELS	€ 24,200.00		
	GRAND TOTAL	**€ 88,900.00**		

66,900 € have been assigned to the project this year (74% of the requested budget)

Budget TIFPA

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TYPE	REQUESTED	APPROVED	SUBJUDICE	DIFFERENCE
Consumable	10,500	-	5,000	-5,500
Instrumentation	39,000	12,000	26,000	-1,000
Travel	2,000	1,000	-	-1,000
Total	51,500	13,000	31,000	-7,500

85% of the requested budget has been assigned

Budget LNS

TYPE	REQUESTED	APPROVED	SUBJUDICE	DIFFERENCE
Consumable	10,500	9,000	-	-1,500
Instrumentation	1,000	-	-	-1,000
Travel	15,000	2,500	3,000	-6,500
Total	26,500	11,500	3,000	-9,000

55% of the requested budget has been assigned

Budget LNL, MILANO and ROMA3 (DTZ)

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LNL

TYPE	REQUESTED	APPROVED	SUBJUDICE	DIFFERENCE
Travel	3,500	1,000	1,000	-1,500

MILANO

TYPE	REQUESTED	APPROVED	SUBJUDICE	DIFFERENCE
Travel	2,500	1,000	-	-1,500

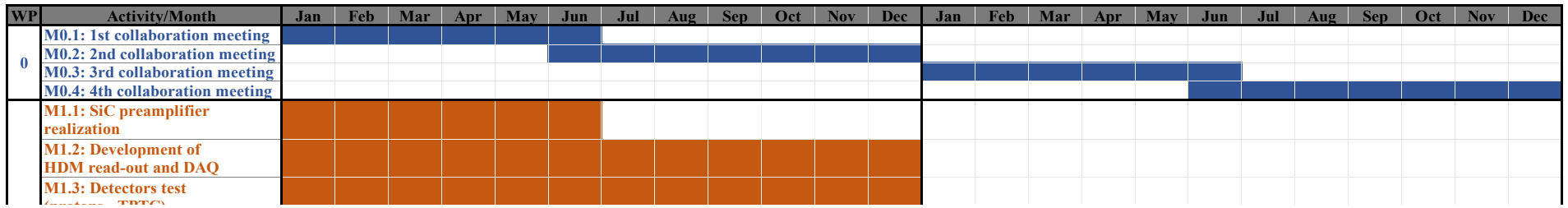
ROMA3

TYPE	REQUESTED	APPROVED	SUBJUDICE	DIFFERENCE
Instrumentation	4,000	4,000	-	-
Travel	1,500	500	-	-1,000
Total	5,500	4,500	-	-1,000

Conclusions on Budget

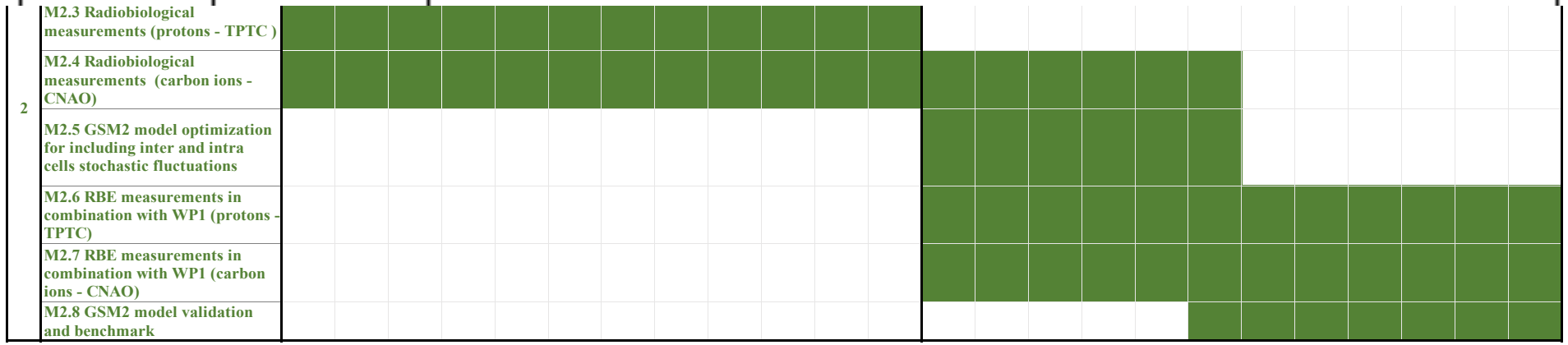
- We can start spending money.
- Beam time at TIFPA will be paid by WP1.
- Any request for freeing SJ?

WP	Activity/Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
0	M0.1: 1st collaboration meeting																								
	M0.2: 2nd collaboration meeting																								
	M0.3: 3rd collaboration meeting																								
	M0.4: 4th collaboration meeting																								
1	M1.1: SiC preamplifier realization																								
	M1.2: Development of HDM read-out and DAQ																								
	M1.3: Detectors test (protons - TPTC)																								
	M1.4: Detectors test (carbon ions- CNAO)																								
	M1.5: Optimization of SiC read-out																								
	M1.6: Characterization of radiation quality in- and off-beam at different depths (protons - TPTC)																								
	M1.7: Characterization of radiation quality in- and off-beam at different depths (carbon ions - CNAO)																								
	M1.8: Radiation quality measurements in combination with radiobology for GSM2 model validation (protons - TPTC)																								
	M1.9: Radiation quality measurements in combination with radiobology for GSM2 model validation (carbon ions - CNAO)																								
2	M2.1 Evaluation of the effect that a dose-average LET-based description of radiation quality has on a treatment planning																								
	M2.2 Preliminary development of GSM2 model																								
	M2.3 Radiobiological measurements (protons - TPTC)																								
	M2.4 Radiobiological measurements (carbon ions - CNAO)																								
	M2.5 GSM2 model optimization for including inter and intra cells stochastic fluctuations																								
	M2.6 RBE measurements in combination with WP1 (protons - TPTC)																								
	M2.7 RBE measurements in combination with WP1 (carbon ions - CNAO)																								
	M2.8 GSM2 model validation and benchmark																								



WP0 Milestones

Name	Month	Description
M0.1	1-6	1st collaboration meeting (remote)
M0.2	6-12	2nd collaboration meeting (in person at LNS)



WP1 Milestones

Name	Month	Description
M 1.1	1 - 6	SiC preamplifier realization.
M 1.2	1 - 12	Development of HDM read-out and DAQ system.
M 1.3	1 - 12	Test of all detectors with monoenergetic protons at TPTC. Intercomparison of energy deposition distribution as well standard microdosimetry, non-standard microdosimetry and nanodosimetry spectra.
M 1.4	1 - 12	Test of all detectors with monoenergetic carbon ions at CNAO. Intercomparison of energy deposition distribution as well as standard microdosimetry, non-standard microdosimetry and nanodosimetry spectra.
M 1.5	1 - 18	Optimization of SiC read-out system.
M 1.6	8-18	Characterization of the radiation field delivered with a 3D irradiation of protons TPTC. Beam quality measured in- and off-beam at several depths with all detectors.
M 1.7	8-18	Characterization of the radiation field delivered with a 3D irradiation of carbon ions at CNAO. Beam quality measured in- and off-beam at several depths with all detectors.

WP	Activity/Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
0	M0.1: 1st collaboration meeting																								
	M0.2: 2nd collaboration meeting																								
	M0.3: 3rd collaboration meeting																								
	combination with WP1 (carbon ions - CNAO)																								
	M2.8 GSM2 model validation and benchmark																								

WP2 Milestones

Name	Month	Description
M 2.1	1 - 6	Evaluation of the impact that an LET-based description of radiation quality has on treatment planning output.
M 2.2	1 - 12	Initial implementation of GSM^2 and preliminary case studies.
M 2.3	1 - 12	Radiobiological measurements (Table 4 and Table 5) with protons at TPTC.
M 2.4	1 - 12	Radiobiological measurements (Table 4 and Table 5) with carbon ions at CNAO.
M 2.5	12 - 18	Optimization of GSM^2 to include inter and intra cells stochastic fluctuations. Refinements on the basis of microdosimetry experimental data.

Activities and open questions for 2020

- Prepare a request for the TIFPA PAC (both WP1 and WP2).
- Issues about traveling (how will this affect the experimental campaign, especially for radiobiology).
- How to structure the beam schedule at TIFPA?
- Beam time at CNAO?
- …

Grazie a tutti e tutte per partecipazione!

Speriamo di fare il prossimo meeting dal vivo per:

a) fare una foto di gruppo

b) fare il tradizionale coffee break Catania-style