Ministero degli Affari Esteri
e della Cooperazione Internazionale

Grande Rilevanza

GERMANIA
Large research infrastructures or centers located in Germany, which provide enabling and unique technologic or scientific facilities unavailable in Italy.

Identificativo	**PGR12400**

Elementi generali

Area di ricerca	**Large research infrastructures or centers located in Germany, which provide enabling and unique technologic or scientific facilities unavailable in Italy.**
Titolo (in Italiano)	**Misure di frammentazione dell'ossigeno per il miglioramento delle terapie ioniche**
Titolo (in altra lingua)	**Measuring Oxygen Fragmentation For Improved Ion Therapy Strategies (MOFFIITS)**
Parola chiave #1	**Hadrontherapy**
Parola chiave #2	**Fragmentation**
Parola chiave #3	**Cancer**

Ente proponente italiano

Denominazione	**Istituto Nazionale di Fisica Nucleare (INFN)**
Dp./Ist.	**INFN - Sezione di Bologna**
Indirizzo	**Via Berti-Pichat 6/2**
C.A.P.	**40127**
Città	**Bologna**
Telefono	**+39 051 2095209**
PEC	**bologna@pec.infn.it**
Ente pubblico	**Sì**
Codice fiscale	**84001850589**
Partita IVA	**84001850589**
IBAN/Conto Tesoreria	**IT66B0100003245348300165771**
Banca/Filiale	**BANCA D'ITALIA - ROMA TESORERIA PROV.LE STATO VIA MILANO, 60G 00100 ROMA(RM)**

Responsabile scientifico italiano

Titolo	**Prof.**
Cognome	**VILLA**
Nome	**MAURO**
Data Nascita	**18/08/1967**
Nazionalità	**Italiana**
Residenza	**Italiana**
Qualifica	**Professore Ordinario (Università)**
Indirizzo Istituzionale	**Dipartimento di Fisica e Astronomia, via Irnerio, 46**
C.A.P.	**40126**
Città	**Bologna**
Telefono	**+39051 209 1064**
PEC	**mauro.villa.bo@pec.it**

Cellulare	
Email principale	**mauro.villa@unibo.it**
Email secondaria	**villa@bo.infn.it**

C.V.

Full professor in Experimental Physics at the Bologna University since Sep. 2014.
Dean of the School of Science since Nov. 2018.
Coordinator of the “Open Physics Hub” (https://site.unibo.it/openphysicshub/en/) a 5 year project funded by the University of Bologna (2019-2023),
Spokesperson of the FOOT collaboration and National responsible of the FOOT experiment (INFN-CSN3)
Referee of JINST; reviewer of ERC projects; reviewer for the Italian research quality evaluation (VQR).
Member of the "National Scientific Abilitation" Commission (ASN 2016-2018) for the 02/A1 SC.

Relevant scientific roles covered in the past (selection):
Local PI for the INFN research projects Slim5, SuperB, Diapix, SHiP (2005-2017).
Local responsible for two funded PRIN projects (2007, 2009).
Coordinator of several work packages related to electronics, Trigger and Data Acquisition in different experiments or initiatives (2005-2021).

Chair of the Publication Committee of the FOOT Collaboration (2019-2021).
Member of the Editorial board of the Hera-B experiment.
Coordinator for the Research and Third Mission activities in the Quality Assurance of the Bologna University (mar. 2013-apr 2018).
Selected member for the CUN area 02 for research evaluation in the Bologna University (2010-2016).

Teaching
He teaches electromagnetism and waves at the electronic and telecommunication engineering degree, wave phenomena at the bachelor’s degree in physics and “Advanced Detectors” at the master degree in physics. He is an author of two basic physics textbooks and two exercise books, which are all widely adopted.

Bibliometric data on Aug 2023
Scopus: h_index: 122   Citable papers: 1322   Total citations: 80830
ORCID: 0000-0002-9181-8048

More information can be found at https://www.unibo.it/sitoweb/mauro.villa/

Pubblicazioni

1. G. Battistoni, M. Villa et al, Measuring the Impact of Nuclear Interaction in Particle Therapy and in Radio Protection in Space: the FOOT Experiment, Frontiers in Physics, 8 (2021), 568242.

2. S. Bettarini, M. Villa et al, The SLIM5 low mass silicon tracker demonstrator, Nucl. Instr.& Meth. A 623(2010), pp. 942–953

3. S. Frabboni, M.Villa et al, The Young-Feynman two-slits experiment with single electrons: Build-up of the interference pattern and arrival-time distribution using a fast-readout pixel detector, Ultramicroscopy, 116 (2012) pp. 73–76

4. ATLAS collaboration,
Improved luminosity determination in pp collisions at vs =7 TeV using the ATLAS detector at the LHC, European Physical Journal C, 73 (2013), pp. 2–39, 2518

5. ATLAS collaboration, Observation of a new particle in the search for the Standard Model Higgs boson with the ATLAS detector at the LHC, Phys. Lett. B 716(2012), pp. 1–29,

Membri gruppo di ricerca italiano

Cognome	Nome	Data Nascita	Qualifica
Cerello	**Piergiorgio**	**01/09/1965**	**Dirigente di Ricerca (Enti Pubblici Ricerca)**
Traini	**Giacomo**	**30/03/1989**	**Ricercatore III livello (Ric EPR)**
Cavanna	**Francesca**	**24/05/1987**	**Ricercatore III livello (Ric EPR)**
Barbanera	**Mattia**	**08/10/1989**	**Tecnologo III livello (Tec EPR)**
Toppi	**Marco**	**10/10/1983**	**Ricercatore Universitario TD (RTDA-RTDB)**
Muraro	**Silvia**	**20/02/1972**	**Ricercatore III livello (Ric EPR)**
Kraan	**Aafke-Christine**	**18/05/1976**	**Ricercatore III livello (Ric EPR)**
Galati	**Giuliana**	**08/03/1990**	**Professore Associato (Università)**

Ente proponente straniero

Denominazione	**GSI Helmholtzzentrum fuer Schwerionenforschung GmbH**
Indirizzo	**Planckstrasse 1, 64291 Darmstadt, Germany**
Telefono	
PEC	
Ente pubblico	**Sì**

Responsabile scientifico straniero

Cognome	**Durante**
Nome	**Marco**
Data Nascita	**09/07/1965**
Qualifica	**full professor**
Email	**M.Durante@gsi.de**

C.V.

EDUCATION
1992 PhD in Physics, University Federico II, Naples, Italy.
1988 Master (Laurea) in Physics, University Federico II, Naples, Italy

CURRENT POSITION(S)
2008 – Full Professor of Physics, Technische Universität Darmstadt, Institut für Festkörperphysik, Darmstadt, Germany
2018 – Department Director, GSI Helmholtzzentrum für Schwerionenforschung, Biophysics Department, Darmstadt, Germany

PREVIOUS POSITIONS (selected)
2015 – 2018 Director – Trento Institute for Fundamental Physics and Applications (TIFPA), National Institute of Nuclear Physics (INFN), Trento, Italy
2007 – 2015 Department Director, GSI Helmholtzzentrum für Schwerionenforschung, Biophysics Department, Darmstadt, Germany

TEACHING ACTIVITIES (sel.)
2018 - 2008 Medical Physics and Radiation Biophysics, Master in Physics, TU Darmstadt, Germany

INSTITUTIONAL RESPONSIBILITIES (sel.)
2016 – 2020 Member of the ESA Human spaceflight and Exploration Science Advisory Committee (HESAC), ESTEC, The Netherlands
2015 – 2020 Chair of the ESA Life Sciences Working Group, ESTEC, The Netherlands
2014 – Member of the Technical-Scientific Committee (CTS) of the Centro Nazionale Adroterapia Oncologica (CNAO), Pavia, Italy
2011 – 2018 Chair of the ESA Topical Team on Space Radiation Research
2023 - Chair of the ESA Topical Team on radiation in lunar exploration

Reviewer (sel.)
Reviewer for EU-Horizon 2020 projects, for ESA IBER projects and for NASA projects
Member of several Program Advisory Commettee (PAC): IThemba accelerator (Cape Town), LNS-INFN (Catania), GANIL (Caen)

Grants (sel.)
PI or local PI of 9 ongoing projects (EU ERC, EU H2020, EU-Horizon Space, ESA, Helmholtz Gemeinschaft)

Publication details:
Orcid unique identifier: 0000-0002-4615-553X
Citation report: 492 papers, 14985 citations; h-index=61 (Scopus, July 2023)
Expertscape Rank #1 in radiobiology

More information on:
https://www.gsi.de/biophysik
https://en.wikipedia.org/wiki/Marco_Durante_(physicist)

Pubblicazioni

1. M.Durante, J. Debus and J.S. Loeffler, Physics and biomedical challenges of cancer therapy with accelerated heavy ions. Nat. Rev. Phys. 3 (2021) 777-790 IF=31

2. M. Durante and H. Paganetti, Nuclear physics in particle therapy: a review. Rep. Prog. Phys. 79 (2016) 096702. IF=17.

3. M. Durante and F.A. Cucinotta, Physical basis of radiation protection in space travel. Rev. Mod. Phys. 83 (2011) 1245-1281. IF=54

4. M. Durante, R. Orecchia and J.S. Loeffler, Charged particles in the clinical setting: status and perspectives. Nat. Rev. Clin. Oncol. 14 (2017) 483-495. IF=66

5. T. Kamada, H. Tsujii, E.A. Blakely, J. Debus, W. De Neve, M. Durante, O. Jäkel, R. Mayer, R. Orecchia, R. Pötter, S. Vatnitsky and W.T. Chu, Twenty-years of carbon-ion radiotherapy in Japan: a re-evaluation of the clinical experience. Lancet Oncol. 16 (2015) e93-e100.

IF=54.

Membri gruppo di ricerca straniero

Cognome	Nome	Data Nascita	Qualifica
Weber	**Uli**	**15/03/1066**	**Staff Scientist**
Schuy	**Christoph**	**24/04/1983**	**Staff Scientist**
Boscolo	**Daria**	**16/04/1987**	**Staff Scientist**
Sokol	**Olga**	**19/07/1991**	**Staff Scientist**
Vandevoorde	**Charlot**	**19/10/1987**	**Staff Scientist**
Tinganelli	**Walter**	**18/12/1978**	**Staff Scientist**

Descrizione delle attività in programma

Sintesi

Cancer is the second cause of death in Europe (Eurostat report 2023) and one of the expanding and effective cures for solid tumors is ion therapy. The Treatment Planning Systems (TPS) that are currently used contain accurate knowledge of the interaction of the ion with the human body, but for what regards the microscopic level there is a consistent lack of data, especially on nuclear interactions and nuclear fragmentation. This forces the TPS to stay on the safe side and deliver the "safe" amount of dose, considering the known uncertainties.
The current proposal aims to measure the double differential cross sections for Oxygen on a Carbon and a Polyethylene targets as a function of the produced fragment charge, mass, production angle and kinetic energy with a 5% accuracy. With these measurements, performed in an energy range compatible with the one from ion therapy, it will be possible to elucidate part of the nuclear processes happening during proton and carbon ion treatments. This will allow to increase the accuracy of the TPS, increasing (in the long run) the number of patients treated each year on the same machine.
The proposal starts from the tools, knowledge and detectors available to the FOOT collaboration, that has developed in recent years two set-ups devoted to the measurement of the fragmentation processes. We will use the GSI infrastructure for the availability of a well tunable Oxygen-16 beam.
In the two year span foreseen for the project, it will be possible to:
1 - tune the detectors for the measurements;
2 - build the nuclear emulsion spectrometers needed;
3 - perform the needed Monte Carlo Simulations;
4 - acquire the data at the GSI;
5 - analyze the data, providing the cross section measurements.

Obiettivi

Cancer treatment with ion beams (70–500 MeV/u), thanks to the Bragg peak in a depth-dose profile, is highly effective and precise and can replace conventional radiotherapy for the treatment of tumors located in close vicinity of sensitive organs (e.g. eyes, brain, neck) as well as pediatric cases and radioresistant tumors. A limit to the precision achievable with this technique is the nuclear fragmentation process of both the beam particles and the target nuclei of the human body (mostly H, C and O), which modify significantly the dose map expected in the case of pure electromagnetic interactions of the primary ions with the patient body [2,3]. Cross sections for fragment production, their dependence on energy, production angle and isotopic composition are not known for most of the relevant energy range and ion types [5]. In order to improve the TPSs for ion therapy, the FOOT collaboration is developing dedicated detectors to perform these measurements with proton, carbon and oxygen beams [1].
The MOFFIITS proposal aims to use the FOOT detectors to measure the double differential fragmentation cross sections of a 16O beam in processes as O+C, O+O and O+H useful to improve and validate TPS for oxygen beams. Furthermore the O+H reaction, using an indirect kinematics approach, will provide the fragmentation cross section of an oxygen target by a proton beam (target fragmentation), useful to improve the RBE knowledge of proton beams in the entrance channel during a proton therapy treatment. To this purpose oxygen beams in the range 200-500 MeV/u will be needed. In Italy there are no facilities that provide this kind of beam, while the GSI laboratory is one of few places in the world that allows for this type of measurement. At the same time, to perform these measurements specific detectors are needed and FOOT, with its electronic and nuclear emulsion table-top set-ups [4] (both based in Italy), is practically the only one currently available.

Metodologia prevista

The double differential fragmentation cross-section measurement as a function of fragments kinetic energy and angle requires a complete knowledge of the beam characteristics, an accurate identification of the produced fragments, high precision in the measured quantities and control of all background sources. All these features are provided by the detectors and technologies developed in the framework of the FOOT collaboration [1].
The FOOT detector is a fixed target experiment composed of an “upstream region” with pre-target detectors, used to monitor the impinging beam, and a downstream region for fragments tracking and identification. As expected from Monte Carlo simulations and previous fragmentation measurements, heavier fragments ($Z > 2$) are forward peaked within a 10 degrees polar angle and with a kinetic energy per nucleon peaked around the corresponding primary beam value. Light fragments (n and H), instead, have wider angular and kinetic energy distributions. Such distributions led to the development of two different set-ups, as they define the detector geometrical acceptance:
1 - a magnetic spectrometer, with detectors for tracking and identification of fragments heavier than 4He. Such set-up covers an angular acceptance up to about 10 degrees with respect to the beam axis;
2 - a nuclear emulsion spectrometer, optimized for the identification of low Z fragments emitted at large polar angles, that extends the angular acceptance up to about 45 degrees.
In order to measure the fragmentation cross sections for the processes of interest for MOFFIITS, oxygen beams in the 200-500 MeV/u range (relevant for particle therapy) will irradiate simple and composite targets (C and C2H4). Using a well known subtraction method, it will be possible to extract the cross section of the O+H process from the direct measurement of the cross sections in the O+C and O+C2H4

interactions.
Applying a suitable Lorentz boost to the kinematic quantities related to the projectile fragments generated in the O+H process, the cross section of the oxygen fragmentation induced by a proton beam is obtained. This measurement is of great interest in ion therapy in order to understand the implication of the target fragmentation on the ion RBE.

The work will be structured in four work packages:
WP1: Nuclear emulsion set-up. The team, led by G. Galati, will be responsible for detector preparation (first year), its exposure to the beam, nuclear emulsion development, data acquisition and analysis, leading to the measurements of low charge fragments (Z<=3) cross section during the second year.
WP2: Electronic set-up. The team, led by P. Cerello, will be responsible for detector updates (addition of neutron detectors and Si beam monitors), their tuning and calibration during the first year, and actual data taking in the second year.
WP3: Simulation and data analysis. The team, led by S. Muraro and M. Toppi, will be responsible for all Monte Carlo simulations and of the reconstruction programs during the first year, while during the second year will work on the analysis of data taken with the electronic set-up, dedicated to fragments with higher charge (Z>=2).
WP4: Beam delivery. The GSI team, led by M. Durante, will be responsible for the delivery of high quality, low divergence and low intensity oxygen-16 beam, mainly to be performed in the second year.
Coordination among the different work packages will be led by M. Villa.

Risorse finanziarie e umane di entrambi i Paesi

German side:
- Facility: GSI accelerator complex, allowing to have Oxygen-16 beam in the kinetic energy range between 100 and 700 MeV/u. Used in the second year of the project.
- Personnel: 2 months each participant, mainly in the second year of the project.

Italian side:
- Facility: Electronic set-up of the FOOT collaboration. To be used in the first year for calibration and performance studies and in the second year for data taking.
- Facility: nuclear emulsion spectrometer darkroom at National Gran Sasso Laboratories and nuclear emulsion film development and scanning with fast automated optical microscopes in Naples.
- Facility: Computing farm at CNAF (Bologna) used for Monte Carlo simulations and data analysis.
- Personnel: 4 months each participant, both in the first and in the second year of the project.

Risultati attesi

Oxygen fragmentation cross sections in the interaction with a proton or a carbon target will be measured with an accuracy of 5%, as a function of the fragment type, energy and scattering angle. No measurements of this type are available today in the energy range relevant for hadrontherapy (E < 500 MeV/u). With an accurate set of fragmentation measurements (WP1, WP2 and WP4) and the related data analysis (WP3) it will be possible to:
- Update current Treatment Planning systems (TPS) and therefore evaluate with improved accuracy the expected enhancement in the dose delivery (and the related cell killing) in the tumor target volume and in the nearby volumes (healthy tissues or organs at risk). More precise TPSs will allow a more precise dose delivery on the tumor, sparing surrounding healthy tissues and, for a given total dose, will reduce the treatment time or the number of treatment sessions. This will improve the overall efficacy of the treatment facility, allowing more patients to be cured. It is well known, indeed, that the main limitation in hadrontherapy centers for what regards the number of patients that can be treated is the machine-time availability [2].

- Test and Update the interaction models of nucleus-nucleus collisions [5]. Measurements with 16O ions in the 10-500 MeV/u range are important for the development of interaction models of nucleus-nucleus collisions, in a transition regime where the simplifications of the few body systems and the thermodynamics treatment of high-A nuclei cannot be used. The existing phenomenological models, usually adopted in general purpose Monte Carlo codes, are affected by significant uncertainties, highlighting the necessity of experimental data for effective model benchmarking. Details about the produced ion species (isotopic composition) and the angular dependence of cross sections are sensitive parameters in phenomenological models.

Collaborazioni

The FOOT collaboration [1] is an international team which already involves research groups from Italy, Germany, France and Japan. The implementation of the MOFFIITS scientific program will be an opportunity to further promote the relevance of fragmentation measurements, strengthening the existing link between the Italian and German partners. The FOOT collaboration has already performed measurements at GSI on an Oxygen beam with a partial version of the electronic apparatus and with the nuclear emulsions set-up [4]. The new measurements with the full electronic apparatus, allowing unprecedented isotopic identification of oxygen fragments, will improve the knowledge of fragmentation processes relevant for the development of hadrontherapy Treatment Planning System. Institutes performing hadrontherapy in Italy, namely CNAO in Pavia and the Proton Therapy center in Trento, as well as in Germany such as GSI (Darmstadt) and the Heidelberg Ion Therapy center (Heidelberg), can profit directly from the results of this project.
Furthermore, the dissemination of our scientific results in the particle therapy community at large would also be an opportunity to start new projects based on our current set-ups (mainly built and residing in Italy) and the GSI, given the vast options of ion types and the extended energy range that makes it a unique infrastructure in Europe.

Bibliografia

[1] G. Battistoni et al, Measuring the Impact of Nuclear Interaction in Particle Therapy and in Radio Protection in Space: the FOOT Experiment, Frontiers in Physics, 8 (2021), 568242.

[2] M. Durante, J. Debus and J.S. Loeffler, Physics and biomedical challenges of cancer therapy with accelerated heavy ions. Nat. Rev. Phys. 3 (2021) 777-790.

[3] M. Durante and H. Paganetti, Nuclear physics in particle therapy: a review. Rep. Prog. Phys. 79 (2016) 096702.

[4] M.C. Montesi et al, Ion charge separation with new generation of nuclear emulsion films, Open Physics 17 (2019) 233 - 240.

[5] M. De Napoli et al, Carbon fragmentation measurements and validation of the Geant4 nuclear reaction models for hadrontherapy, Physics in Medicine and Biology 57 (2012) 7651 - 7671.

PIANO ECONOMICO - FINANZIARIO

TABELLA 1: PREVENTIVO					
DESCRIZIONE		Numero	Importo unitario (€)	Totale (€)	
a. Viaggi e soggiorni ricercatori stranieri in Italia	1° ANNO	0	0	**0**	
	2° ANNO	0	0	**0**	
	3° ANNO	0	0	**0**	
	TOTALE	**0**		**0**	
b. Viaggi e soggiorni ricercatori italiani all'estero	1° ANNO	0	0	**0**	
	2° ANNO	9	3.000	**27.000**	
	3° ANNO	0	0	**0**	
	TOTALE	**9**		**27.000**	
c. Prestazioni professionali e/o di terzi	1° ANNO	0	0	**0**	
	2° ANNO	0	0	**0**	
	3° ANNO	0	0	**0**	
	TOTALE	**0**		**0**	
d. Contratti per personale non strutturato	1° ANNO	2	28.000	**56.000**	
	2° ANNO	1	28.000	**28.000**	
	3° ANNO	0	0	**0**	
	TOTALE	**3**		**84.000**	
e. Workshops	1° ANNO			7.500	
	2° ANNO			9.500	
	3° ANNO			0	
	TOTALE			**17.000**	
f. Pubblicazioni o altre forme di disseminazione	1° ANNO			4.000	
	2° ANNO			6.000	
	3° ANNO			0	
	TOTALE			**10.000**	
g. Materiale consumabile (max 40,00% di SUBTOTALE COSTI)	1° ANNO			30.000	28,44%
	2° ANNO			23.000	24,34%
	3° ANNO			0	0,00%
	TOTALE			**53.000**	
h. Materiale inventariabile (max 10,00% di SUBTOTALE COSTI)	1° ANNO			8.000	7,58%
	2° ANNO			0	0,00%
	3° ANNO			0	0,00%
	TOTALE			**8.000**	
i. Altro	1° ANNO			0	
	2° ANNO			1.000	
	3° ANNO			0	
	TOTALE			**1.000**	
SUBTOTALE COSTI	1° ANNO			**105.500**	
	2° ANNO			**94.500**	
	3° ANNO			**0**	
	TOTALE			**200.000**	
j. Costi di personale strutturato (min 30,00% - max 40,00% di TOTALE COSTI)	1° ANNO			70.000	34,06%
	2° ANNO			70.000	35,99%
	3° ANNO			0	0,00%
	TOTALE			**140.000**	
k. Costi indiretti (max 20,00% della somma SUBTOTALE COSTI + voce j)	1° ANNO			30.000	17,09%
	2° ANNO			30.000	18,24%
	3° ANNO			0	0,00%
	TOTALE			**60.000**	
TOTALE COSTI	1° ANNO			**205.500**	

	2° ANNO		**194.500**	
	3° ANNO		**0**	
	TOTALE		**400.000**	

TABELLA 2: FONTI DI FINANZIAMENTO		
DESCRIZIONE	IMPORTO (€)	%
A. Cofinanziamento Ente Proponente	**200.000**	50,00%
B. Cofinanziamento richiesto al MAECI	**200.000**	50,00%
TOTALE FINANZIAMENTI	**400.000**	

(1) Elenco materiale consumabile

- Layers and chemical components for nuclear emulsion films (20 k€)
- Neutron and Si detectors, front-end electronics included (21 k€)
- Mechanics (12 k€)

(2) Elenco materiale inventariabile

- Computing farm extension for data storage and processing (8k€ inclusive of disk space and server blade)

(3) Elenco altre spese

- Transportation (about 800kg for the setups, van rental: 1 k€)

Dichiaro che tutti i partecipanti al progetto, italiani e stranieri, sono a conoscenza e concordano con la presentazione di questa domanda.

Autorizzo il trattamento dei miei dati personali ai sensi della vigente normativa sulla privacy. Specifico altresì di non avere in alcun modo indicato dati sensibili (relativi, in particolare, a salute, convinzioni religiose e opinioni politiche). In ogni momento mi saranno consentite la rettifica, l'integrazione e la cancellazione dei miei dati personali come previsto dall'art. 7 D.Lgs. 196/03.

