# Courses (XXXIX cycle)

| Course | Year | Teacher | Curriculum | Frontal lessons (cfu/ hrs) | Guided exercises (cfu/ hrs) | Assisted study (cfu/ hrs) | SSD | Topic |
|---|---|---|---|---|---|---|---|---|
| **Aging and frailty: from biology to clinic** | I year | Prof. Patrizia Mecocci | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 2 cfu<br>24 hrs | 2 cfu<br>36 hrs | MED/09 | 1 |
| **Atherosclerotic vascular disease: from pathophysiology to therapeutic management** | I year | Prof. Matteo Pirro | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 2 |
| **Diagnostics of preclinical atherosclerotic vascular damage** | I year | Prof. Gaetano Vaudo | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 3 |
| **Synaptopathies and clinical neurochemistry in neuroscience** | I year | Prof. Massimiliano Di Filippo | Neurosciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/26 | 4 |
| **"Target" Surgery** | I year | Prof. Piero Covarelli | Surgical Sciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/18 | 5 |
| **Target therapy, immunotherapy, and therapy cellular therapy in hematological malignancies** | I year | Prof. Maria Paola Martelli<br>Dr. Roberta La Starza | Biotechnology in Human Bone Marrow Transplantation | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/15 | 6 |
| **Radiobiology and Applied Radiotherapy** | I year | Prof. Cynthia Aristei | Radiotherapy in Oncology | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/36 | 7 |
| **Covid19. Session 1** | I year | Prof. Antonella Mencacci | All curricula | 3 cfu<br>18 hrs | - | - | MED/07 | 8 |
| **Aging and frailty: from biology to clinic** | II year | Prof. Patrizia Mecocci | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 2 cfu<br>24 hrs | 2 cfu<br>36 hrs | MED/09 | 1 |
| **Atherosclerotic vascular disease: from pathophysiology to therapeutic management** | II year | Prof. Matteo Pirro | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 2 |
| **Diagnostics of preclinical atherosclerotic vascular damage** | II year | Prof. Gaetano Vaudo | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 3 |
| **Synaptopathies and clinical neurochemistry in neuroscience** | II year | Prof. Massimiliano Di Filippo | Neurosciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/26 | 4 |
| **"Target" Surgery** | II year | Prof. Piero Covarelli | Surgical Sciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/18 | 5 |
| **Target therapy, immunotherapy, and therapy cellular therapy in hematological malignancies** | II year | Prof. Enrico Tiacci | Biotechnology in Human Bone Marrow Transplantation | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/15 | 6 |
| **Radiobiology and Applied Radiotherapy** | II year | Prof. Cynthia Aristei | Radiotherapy in Oncology | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/36 | 7 |

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| **Covid19. Session 2** | II year | Prof. Antonella Mencacci | All curricula | 3 cfu<br>18 hrs | - | - | MED/07 | 8 |
| **Aging and frailty: from biology to clinic** | III year | Prof. Patrizia Mecocci | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 2 cfu<br>24 hrs | 2 cfu<br>36 hrs | MED/09 | 1 |
| **Atherosclerotic vascular disease: from pathophysiology to therapeutic management** | III year | Prof. Matteo Pirro | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 2 |
| **Diagnostics of preclinical atherosclerotic vascular damage** | III year | Prof. Gaetano Vaudo | Pathology and Clinical Studies of Athero-sclerosis and Aging | 1 cfu<br>6 hrs | 1 cfu<br>12 hrs | 1 cfu<br>18 hrs | MED/09 | 3 |
| **Synaptopathies and clinical neurochemistry in neuroscience** | III year | Prof. Massimiliano Di Filippo | Neurosciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/26 | 4 |
| **"Target" Surgery** | III year | Prof. Piero Covarelli | Surgical Sciences | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/18 | 5 |
| **Target therapy, immunotherapy, and therapy cellular therapy in hematological malignancies** | III year | Prof. Antonio Pierini | Biotechnology in Human Bone Marrow Transplantation | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/15 | 6 |
| **Radiobiology and Applied Radiotherapy** | III year | Prof. Cynthia Aristei | Radiotherapy in Oncology | 3 cfu<br>18 hrs | 4 cfu<br>48 hrs | 4 cfu<br>72 hrs | MED/36 | 7 |
| **Covid19. Session 3** | III year | Prof. Antonella Mencacci | All curricula | 3 cfu<br>18 hrs | - | - | MED/07 | 8 |

**Each Curriculum provides: 14 cfu/year (3-year: 36 cfu) distributed in the following frontal and alternative teaching activities:**

**- 6 credits/year (three-year course: 18 credits) - Lectures (1 credit = 6 hours)**

**- 4 credits/year (three-year course: 12 credits) - Guided exercises (1 credit = 12 hours)**

**- 4 credits/year (three-year course: 12 credits) - Assisted study (1 credit=18 hours)**

1. The progressive aging of the population means that social and healthcare systems find themselves having to manage elderly patients more and more frequently, characterized by clinical complexity, intrinsic vulnerability, and risk of adverse events such as increasingly seriously compromising their quality of life. There has been a significant increase in life expectancy; however, this increase has not translated into an extension of the years spent in good health but rather into an increase in the years lived with disability. In this scenario, a review of traditional healthcare models is necessary to respond to new needs. The biological, clinical, and psycho-social complexity of the old age person is a very current topic in the geriatric and gerontological world. It has oriented its research toward defining the aspects that lead to the appearance, evolution, and/or frailty regression. Aging is associated with the reduction of the functional reserves of multiple organs and systems of the organism, universally for some aspects which expose the individual to a greater risk of disease, but heterogeneous and modulable for others, which makes it plausible and achievable to increase a healthy active life expectancy. The term "frailty" identifies precisely this condition of vulnerability, which is sometimes challenging to recognize given that the determinants of this process are very different, intrinsic and extrinsic to the person, as well as dynamic. Identifying and measuring frailty is a fundamental and necessary step for clinicians to acquire awareness of the real care urgency of the complex patient and to consequently plan a personalized intervention on the individual and with precision on the person and not on the diseases, unlike what happens with traditional medicine. Once frailty has been identified, thanks to the Geriatric Multidimensional Assessment (VMD) tool, the clinical intervention model to be adopted is the one oriented and derived from VMD, capable of allowing the clinical, functional, and social problems of the person with fragility, practicable in clinical routine and scientifically validated to improve the health outcomes and quality of life of the old age patient.

2. During the course, consolidated and emerging aspects relating to the pathophysiology of atherosclerotic vascular damage will be explored in depth. In particular, the molecular, cellular, biochemical, and hemodynamic mechanisms of insult affecting the different components of the arterial wall will be covered, as well as the processes involved in the repair phase of arterial damage. The analytical methodologies for evaluating the "burden" of determinants and indicators of atherosclerotic risk, the different diagnosis strategies of subclinical and clinically manifest atherosclerotic disease, as well as the methods of prognostic stratification of cardiovascular risk will be explored in depth. The various strategies, acquired and under development, for preventing and treating causal factors, risk, and determinants of atherosclerotic disease will also be outlined.

3. The importance of the correct preclinical diagnosis of atherosclerotic damage lies precisely in being able to highlight early signs of vascular disease in extremely early stages. Through various methods, such as the evaluation of the flow-mediated vasoactivity (VFM) of the brachial artery using an ultrasound method combined with digital image analysis, it is possible to reveal the earliest alteration, that of the loss of the capacity for vasodilation to insults represented by the factors of cardiovascular risk. It is also possible to document functional and morphological vascular damage through the study of the stiffness of the aortic wall, using an application tonometer, stiffness which, if present, constitutes the initial moment of organ damage, especially at the cardiac level. Finally, the documentation of the preclinical morphological damage is completed through the digitalized ultrasound measurement of the intima-media thickness (IMT) of the main conduction arteries (carotid, femoral) combined with the possibility of studying the constitutional qualitative aspects as well as aspects induced by the extent of stenosis by atheromatous plaques in different districts

4. This course involves the study of the pre-clinical aspects of degenerative and inflammatory diseases of the CNS through the use of a wide range of biomarkers that can be determined in the cerebrospinal fluid, which reflect the different molecular mechanisms involved in the pathogenesis of such diseases. We will discuss the molecular mechanisms underlying basis of alterations in synaptic transmission, of neuronal plasticity and neuronal damage in experimental models of neurological diseases, neurodegenerative and neuroinflammatory diseases, and also in models of ischemia brain and hyperexcitability of neurons. The objective of such curricular activity is to characterize, by means of electrophysiology methods, the synaptic and neurons present in different regions of the central nervous system, such as the nucleus striatum and the hippocampus, underlying the pathogenesis and alterations cognitive-behavioral of degenerative diseases (such as Parkinson's disease and Alzheimer's disease) and inflammatory diseases (such as multiple sclerosis) of the Central Nervous System In addition, we will explore the aspects related to the interaction between the immune system and the nervous system under physiological conditions and during neuroinflammatory processes, with the aim of understanding the role played by neuro-immune cross-talk in the alteration of the mechanisms underlying cognitive and social activities in patients with CNS diseases.

5. This Curriculum aims to introduce PhD students to the most innovative aspects of the application of surgical therapy in oncological field, starting with studies in molecular biology, which are indispensable to guide the development of advanced surgical techniques functional to the implementation of a "Target Therapy" to be complementary to pharmacological therapy. Aspects of oncological diseases affecting various districts (breast, lung, intestine, central nervous system, prostate, ovary, others...) and treatment pathways will be addressed, with special reference to national and international reference guidelines. Aspects of choosing and/or combining surgical therapy with neoadjuvant or adjuvant post-surgical therapy will be discussed. The most advanced technological aspects in the treatment of localized forms of lung, breast and liver malignancies will also be covered.

6. The course is aimed at examining in depth all the biological and clinical-hematological aspects necessary to adopt a "personalised" therapeutic approach defined on the basis of the genotypic and phenotypic characteristics of the disease, and the possibility of modulating the immune response. Specific topics will be covered over the three years, taught by teachers who are experts in the sector. Aspects of the so-called "target" therapy will be covered, largely represented by inhibitory molecules that selectively affect cells in which certain genetic alterations are present (Prof. Maria Paola Martelli, Dr. Roberta La Starza), monoclonal Abs (Prof. Enrico Tiacci), CAR-T and cellular therapies (Prof. Antonio Pierini). For these last aspects, ample space will be dedicated to immunological reconstitution post-bone marrow transplant, and to the development and use of monoclonal antibodies in diagnostics and therapy, starting from production methods, to their use for disease diagnosis and follow-up, and therapeutic applications. Examples of therapeutic applications and translational research will be discussed.

7. The course will cover the following topics: clinical, dosimetric and biomolecular predictive features of outcome in patients treated with Total Marrow/Lymphoid Irradiation; quantitative analysis of data extracted from methods of imaging for the development of predictive models of outcome in patients undergoing radiation treatment; translational research on the role of the microbiota in radiotherapy. The course will be structured to pursue the following objectives: deal with the Basics of Radiotherapy and Radiobiology; acquire the most advanced techniques in radiation therapy oncology; Quality Assurance; address the critical issues related to the treatment plan treatment and treatment. These issues will be discussed in relation to the methods that are used for the precise identification of the tumor target(s), with concomitant sparing of surrounding healthy tissues, and preservation of organs and their function, and reduction of treatment duration.
1st year: Basic radiobiology; 5 Rs of radiobiology; Multitarget model; Quadratic linear model; Dose fractionation in radiation therapy; Treatment-related toxicity: etiopathogenesis, risk factors, prevention and management; Integration between systemic therapies and radiation therapy in onco-hematology; Integration of radiotherapy with biomolecular markers and new treatments.
2nd year: Radiotherapy equipment. External Beam Radiation Therapy Brachytherapy. Stereotactic radiotherapy Radiotherapy in the conditioning for haematopoietic stem cell transplantation (Total Body Irradiation and Total Marrow/Lymphoid Irradiation). Radiotherapy as a bridge treatment in patients who will receive CAR T therapy. Clinical, dosimetric and biomolecular parameters predictive of outcome in patients treated with Total Marrow/Lymphoid Irradiation.
3rd year: Clinical, dosimetric and biomolecular parameters predictive of outcome in patients treated with Total Marrow/Lymphoid Irradiation. Development of radiomics tools to predict response to radiation treatments and treatment-related toxicity. Translational research: the microbiota in radiotherapy.

8. The impact of the pandemic on the various disciplines in the curricula is addressed from various perspectives including: laboratory implications of covid infection and post-covid syndrome in malignant hemopathies; in immunocompromised individuals; in non-neoplastic individuals; in the cardiovascular, respiratory, dermatological and neurology systems. We will also focus on the clinical impact in unfit patients as well as fit patients. A continuos update on epidemiological and virological state of art will be provided.

# Bioethics course (1st year of the course, September/October period)

| Course | Year | Teacher | Curriculum | Frontal Lessons (cfu/hrs) | Topic |
|---|---|---|---|---|---|
| Preliminary foundations for an ethics of science and scientific research | I year | Prof. Marco Moschini | All | 2 hrs | Considerations on the preliminary foundations for an ethics of science and scientific research<br>- Rediscover the ethical foundation of relationships in today's time<br>- The ethical problems posed by an era of science and technology<br>- For an ethics of medical research: morally repositioning deontology |
| What is bioethics? | I year | Prof. Antonio Allegra | All | 2 hrs | Philosophical introduction. Brief history of bioethics. Some examples of direct medical interest: care and treatment, attention to the person, communication and transparency |
| Practice and theory of University Bioethics Committees (CUB): defining the indefinable. | I year | Prof. Gianluca Cardinali | All | 2 hrs | Type of cases that can be addressed by the CUB, general principles for the bioethical opinion, prejudicial nature of the scientific quality of the project . |
| Introduction to human trials. The Regional Ethics Committee (CER). | I year | Dr. Cristina Pedini (Segreteria Comitato Etico Regionale - CER) | All | 2 hrs | Introduction to human trials.<br>The role of the Ethics Committee in the approval of Pharmacological Studies and Observational Studies on drugs Objectives: Reference regulations, ethical standards, evaluation methods and procedures. |
| Genetics and Ethics | I year | Dr. Paolo Prontera | All | 2 hrs | Ethical aspects of genetic investigations. Regulations for the use and conservation of biological samples for genetic tests, in diagnostics and in scientific research. Focus on informed consent and information. |
| Bio-law | I year | Avv. Francesco Vitelli | All | 2 hrs | The rights of freedom, performance and participation in medicine. Self-determination between conventional protection and balancing needs; a new orientation from a medical and ethical-juridical point of view. |