Decreto Rettore Università di Roma "La Sapienza" n. **1611/2022** del **10.05.2022**

CRISTINA NOCELLA Curriculum Vitae

Place: Rome Date: 07/07/22

Part II - Education

| Туре | Year | Institution | Notes (Degree, Experience) |
|--------------------------|-----------|-----------------------------|---|
| University graduation | 2006/2007 | Sapienza University of Rome | Bachelor degree in Biological Sciences. Mark: 110/110 with Honours Title of thesis: <i>Determinazione</i> <i>tramite citofluorimetria della</i> <i>proteina pro-aterogena CD40L:</i> <i>ruolo el TNFα</i> Tutor: Francesco Violi |
| University graduation | 2009/2010 | Sapienza University of Rome | Master Degree in "Biology applied to biomedical research". Mark: 110/110 with Honours Title of thesis: <i>Effetto degli</i> <i>omega n-3 sullo stress</i> <i>ossidativo in pazienti affetti da</i> <i>scompenso cardiaco.</i> Tutor: Pasquale Pignatelli |
| PhD | 2017 | Sapienza University of Rome | PhD in "Immunological, Hematological and Rheumatological Sciences". Title of thesis: <i>Gut-derived</i> <i>lipopolysaccharide</i> and <i>platelet</i> <i>activation: implications for</i> <i>patients at risk of</i> <i>cardiovascular disease</i> Tutor: Giacomo Frati |

Part III - Appointments

IIIA – Academic Appointments

| Start | End | Institution | | | | Position |
|-------|------|-----------------------|-----------------------------|------------|------------------|---|
| 2011 | 2013 | Sapienza Departmer | University nt of Interna | of al M | Rome, edicine | Research Fellow (L. 240/2010) Reaserch Title: |

ALL. B

| | | and Medical Specialties | "The role of phisical exercise on inflammation and oxidative stress in patients with metabolic syndrome" |
|------|-------------|---|---|
| 2013 | 2014 | Sapienza University of Rome, Department of Internal Medicine and Medical Specialties | Research Fellow (L. 240/2010) Reaserch Title: <i>"The role of phisical exercise on inflammation and oxidative stress in patients with metabolic syndrome".</i> |
| 2019 | In progress | Sapienza University of Rome, Department of Clinical, Internal, Anesthesiologic and Cardiovascular Sciences | RTDA. Reaserch Title: "Role of lipopolysaccharide in platelet activation during the atherothrombotic process". |

IIIB – Other Appointments

| 2018 | 2019 | IRCCS Neuromed, Department of Angiocardioneurology, Pozzilli (IS) | Post-doc scholarship Reaserch Title: "The role of authophagy as a protective mechanism in cardiovascular disease: new insights into oxidative stress modulation and cardiovascular regeneration" |
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Part IVa – Teaching experience

| Year | Institution | Lecture/Course |
|----------------------|---|------------------|
| From 2019 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of | Hygiene |
| | Policlinico Umberto I L/SNT1 | |
| 2019/2020 | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) ROME - Degree Course A - Azienda Policlinico Umberto I L/SNT1 | Epidemiology |
| From 2020 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) - Degree Course O - Frosinone ASL Frosinone Umberto I L/SNT1 | Medical Genetics |
| From 2020 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) - Degree Course W - ASL Latina | Histology |

| | Formia - Gaeta L/SNT1 | |
|----------------------|--|-----------------|
| From 2021 | Sapienza University of Rome, | Human anatomy |
| to date | of Nurse) - Degree Course W - ASL Latina Formia - Gaeta L/SNT1 | |
| From 2020 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) - Degree course U - Molise Region - IRCCS Neuromed Pozzilli L/SNT1 | Oncology |
| From 2021 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) - Degree course U - Molise Region - IRCCS Neuromed Pozzilli L/SNT1 | Blood Diseases |
| From 2021 to date | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) - Degree course Q – ASL Latina L/SNT1 | Applied Biology |

Part IVb - Degree Theses Supervision

| 2020/2021 | Sapienza University of Rome, Nursing (qualifying for the health profession of Nurse) ROME - Degree Course A - Azienda Policlinico Umberto I L/SNT1 | Thesis Supervisor Thesis title: "La corsa dell'epatite a: dall'Europa alla Campania". Student: Cosimo Cusano |
|----------------------|---|---|
| 2021/2022 | Sapienza University of Rome, Pharmaceutical Chemistry and Technology ROME - Single cycle master's degree | Thesis Co-Supervisor Thesis title: "Microbiota intestinale e malattie cardiovascolari: ruolo del TAK- 242 (Resatorvid) come inibitore del TLR4". Student: Chiara Felici |
| From 2020 do date | Sapienza University of Rome, Pharmaceutical Chemistry and Technology ROME - Single cycle master's degree | Thesis Co-Supervisor Thesis title: <i>"Studio della permeabilità intestinale in pazienti pre e post trattamento con inibitore del PCSK9"</i> . Student: Francesca Trastulli |
| From 2022 | Sapienza University of Rome, Pharmaceutical Chemistry and Technology ROME - Single cycle master's degree | Thesis Co-Supervisor Thesis title: <i>"Ruolo della rifaximina nella riduzione dei livelli di LPS derivante dal microbiota intestinale"</i> . Student: Barbara Zuin |

| Year | Title |
|-------------------|--|
| From 2017 to date | Member of the Italian Society of Pathology and Translational Medicine (SIPMeT) |
| From 2019 to date | Member of the Italian Society of Atherosclerosis Study (SISA) |
| From 2022 | Member of the Italian Society for the Study of Haemostasis and Thrombosis (SISET) |
| 2019 | Travel grant, 33° Congresso Nazionale SISA |
| 2020 | Eligible to be appointed as associate professor for the "Settore Concorsuale 06/N1", from 22/06/2020 to 22/06/2029 |

Part Vb - Selection for Oral Presentation at national and international conferences

| 2011 | Selected speaker at 12° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: <i>"LDL oxidation by platelets enhances</i> <i>platelet isoprostanes formation: a novel mechanism of platelet activation".</i> |
|------|---|
| 2012 | Selected speaker at 13° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: <i>"Effetto immediato dell'atorvastatina</i> <i>su stress ossidativo e funzionalità piastrinica: ruolo della NOX2".</i> |
| 2013 | Selected speaker at 14° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: <i>"Lipopolysaccharide and platelets: new</i> <i>insight into platelet activation"</i> . |
| 2014 | Selected speaker at 23° National Congress of "Società Italiana per l'emostasi e la trombosi, SISET". Oral presentation title: "Bacterial lipopolysaccharide amplifies platelet aggregation by common agonists via overproduction of thromboxane A2 and isoprostane 8-iso-PGF2 α -III". |
| 2015 | Selected speaker at 16° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: <i>"Endotoxemia as mechanism for</i> <i>platelet aggregation via eicosanoids formation in patients with</i> <i>pneumonia".</i> |
| 2015 | Selected speaker at International Congress of "American Heart Association". Oral presentation title: <i>"Endotoxemia As Mechanism For</i> <i>Platelet Aggregation In Patients With Pneumonia"</i> |
| 2017 | Selected speaker at International Congress of "Società Italiana di Patologia e Medicina Traslazionale, <i>SIPMeT</i> ". Oral presentation title: <i>"Lipopolysaccharide as trigger of platelet aggregation via eicosanoid</i> <i>over-production".</i> |
| 2018 | Selected speaker at 19° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: <i>"Lipopolisaccaride intestinale e</i> <i>attivazione piastrinica nei pazienti HIV: ruolo di diversi modelli di carica</i> <i>virale".</i> |
| 2018 | Selected speaker at 35° National Cardiology Congress of "Conoscere e curare il cuore". Oral presentation title: "Localization of lipopolysaccharide from Escherichia coli into human atherosclerotic plaque" |

| 2019 | Selected speaker at 20° National congress "Gruppo di Studio delle Piastrine". Oral presentation title: "Low-Grade Endotoxemia Enhances Artery Thrombus Growth Via Toll-Like Receptor 4. Implication for Myocardial Infarction". |
|------|---|
| 2019 | Selected speaker at 36° National Cardiology Congress of "Conoscere e curare il cuore". Oral presentation title: <i>"Digoxin and platelet activation in atrial fibrillation patients: in vivo and in vitro study"</i> |
| 2020 | Selected speaker at International Congress of "International Society on Thrombosis and Haemostasis (ISTH)". Oral presentation title: "Low-Grade Endotoxemia Enhances Artery Thrombus Growth Via Toll-Like Receptor 4. Implication for Myocardial Infarction" |
| 2020 | Selected speaker at 37° National Cardiology Congress of "Conoscere e curare il cuore". Oral presentation title: " <i>Lipopolisaccaride intestinale e attivazione piastrinica nei pazienti HIV: ruolo di diversi modelli di carica virale</i> ". |
| 2020 | Selected speaker at 34° National Congress of "Società Italiana Studio Aterosclerosi (SISA)". Oral presentation title: " <i>Gut Permeability-Related</i> <i>Toll-Like Receptor 4-Primed Platelets in Myocardial Infarction</i> ". |
| 2020 | Invited speaker at Regional Congress of "Società Italiana Studio Aterosclerosi (SISA)". Oral presentation title: " <i>LPS e aterosclerosi in pazienti con STEMI</i> ". |

Part Vc - Selection for Poster at national and international conferences

| 2017 | Selected Poster at 7th International Conference on " <i>Coagulation in Liver Disease</i> ". Poster title: " <i>Low-grade endotoxemia and platelet activation in cirrhosis</i> ". |
|------|--|
| 2018 | Selected poster at 25° National Congress of "Società Italiana per l'emostasi e la trombosi, SISET". Poster title: <i>"Serum albumin is inversely associated with portal vein thrombosis in cirrhosis".</i> |
| 2019 | Selected poster at 34° National Congress of "Società Italiana Studio Aterosclerosi (SISA)". Poster title: " <i>Lipopolysaccharide induces platelet activation in HIV patients: the role of different viral load patterns</i> ". |
| 2021 | Selected poster at 35° National Congress of "Società Italiana Studio Aterosclerosi, SISA". Poster title: <i>"Aging-Related Decline of Autophagy in Patients with Atrial Fibrillation. A post-hoc analysis from the ATHERO-AF study".</i> |

Part Vd - Editorial Board

| From 2021 to | Member of the Editorial Board as Academic Editor of "Oxidative | | |
|--------------|--|--|--|
| date | medicine and cellular longevity" IF: 7.310 | | |
| 2021 | Guest Editor of the Special Issue ""Dietary Bioactives and | | |
| | Atherosclerotic Cardiovascular Disease", Nutrients IF: 4.546. | | |

Part Ve - Reviewer

| | Reviewer for the following international scientific journals: "Antioxidant; IF: 7.675", "Oxidative medicine and cellular longevity IF: 7.31", "Nutrition, IF: 4.893", "Thrombosis and Haemostasis; IF: 6.681". | | |
|------|--|--|--|
| 2021 | Invited reviewer for grant proposal for the National Science Center, Poland. Funding scheme: SONATA BIS-11 Institution: Medical University of Warsaw | | |
| 2021 | Invited reviewer for grant proposal for the National Science Center, Poland. Funding scheme: OPUS-21 Institution: Jagiellonian University in Cracow | | |

Part VI - Research Activities

| Keywords | | Brief Description |
|--|--------------------------------|---|
| Mechanisms of platelet activation Gut-derived LPS | | In these years, my research interest has been the study of the mechanisms of platelet activation, which plays a role in the onset of cardiovascular disease. Among mechanisms that elicit platelet activation, oxidative stress plays a major role favouring platelet hyperactivity. Indeed, upon stimulation by physiological agonists, human platelets generate and release several types of reactive oxygen species (ROS) by NOX2 activation. More recently, I studied other mechanisms of platelet activation such as during an inflammatory response. In these pathological conditions, platelet activation could be mediated by different promoting factors such as LPS. Indeed, colleague and I demonstrated that LPS, at a concentration similar to that we found in human circulation, could trigger platelet aggregation and activation. LPS could be derived from gut microbiota as a consequence of dysbiosis. Therefore, we studied the role of gut-derived LPS on platelet activation and thrombus formation and demonstrated that LPS promotes thrombus growth by the amplification and propagation of platelet aggregation suggesting that the reduction of circulating LPS levels could represents a strategy potentially useful reducing the inflammatory or the thrombotic process in different process in different process in the second platelet activation for the thrombotic process in different process in the second platelet activation activation. |
| • | NOX2-mediated oxidative stress | I studied, in cardiovascular diseases, the role of NADPH oxidase and in particular its isoform NOX2, the most important ROS- |
| • | NOX2 regulation mechanisms | producing enzyme. Specifically, I evaluated the relationship between NOX2 and metalloproteinase 2 (MMP2), a zinc- and calcium-dependent endopeptidase involved in the degradation and remodeling of the extracellular matrix during several physiological and pathological processes, hypothesizing an involvement of MMP2 in the regulation of NOX2 function. The |

| | | study showed that MMP2 could play a new role in modulating oxidative stress by regulating NOX2 activity in platelets and polymorphonuclear cells. This result is evidenced by 1) a decrease in ROS production and NOX2 activity after 20 minutes of cell stimulation and 2) persistent ROS production in cells treated with an MMP2 inhibitor. This result suggests that MMP2 could represent a new tool to reduce NOX2 activation in contexts characterized by an overproduction of ROS derived from NOX2 |
|---|---|--|
| | | activation such as in cardiovascular diseases. |
| • | Antioxidant treatment Nutraceutic approach | Oxidative stress is a common feature of many human disorders, such as cardiovascular disease. Many of the risk factors, including smoking, hypertension, hypercholesterolemia, diabetes, and obesity, are associated with an increased risk of developing cardiovascular disease, involving an elevated oxidative stress burden (either due to enhanced ROS production or decreased antioxidant protection). There are many therapeutic options to treat oxidative stress-associated cardiovascular diseases. Numerous studies have focused on the utility of antioxidant supplementation. However, whether antioxidant supplementation has any preventive and/or therapeutic value in cardiovascular pathology is still a matter of debate. Therefore, I evaluated the |
| | | effect of some antioxidant demonstrating that 1) a high adherence to the Mediterranean diet reduces oxidative stress in patients with NAFLD; 2) specific components of extra-virgin olive oil (EVOO) such as oleuropein, improves the post-prandial glycemic profile in diabetic patients; 3) a Mix of polyphenols (catechin and epicatechin) and threalose, a disaccharide, reduce the impact of risk factors on the onset of cardiovascular disease. |

Part VII – Summary of Scientific Achievements

| Product type | Number | Data Base | Start | End |
|--------------------|--------|--|-------|------|
| Papers | 111 | Scopus | 2011 | 2022 |
| [international] | | | | |
| Patents | 2 | 1)https://patentscope.wipo.int/s earch/en/detail.jsf?docId=W020 19111142 2) Patent deposited 12/06/2017, n° 102017000064897. | | |
| Books [scientific] | 1 | ISBN 978-953-51-6072-4 | | |

| Total Impact factor | 558,33 |
|-------------------------------|--------|
| Total Citations | 2685 |
| Average Citations per Product | 24,2 |
| Hirsch (H) index | 31 |
| Normalized H index* | 2.82 |

*H index divided by the academic seniority.

Link to Bibliographic-scientometric parameters of Cristina Nocella -link to Pubmed: https://pubmed.ncbi.nlm.nih.gov/?term=Nocella+C&sort=date&filter=dates.2011-2022 - link to Scholar: https://scholar.google.com/scholar?hl=it&as_sdt=0%2C5&q=Cristina+Nocella&oq= - link to Scopus: https://www.scopus.com/authid/detail.uri?authorId=38961782000

Part VIII- Selected Publications

List of the publications selected for the evaluation. For each publication report title, authors, reference data, journal IF (if applicable), citations, press/media release (if any).

- 1. Violi F, Cammisotto V, Bartimoccia S, Pignatelli P, Carnevale R, **Nocella C**. Gut-derived lowgrade endotoxaemia, atherothrombosis and cardiovascular disease. Nature Review Cardiology. 2022. doi: 10.1038/s41569-022-00737-2. **IF: 49.421; citations: 0**
- D'Amico A, Cavarretta E, Fossati C, Borrione P, Pigozzi F, Frati G, Sciarretta S, Costa V, De Grandis F, Nigro A, Peruzzi M, Miraldi F, Saade W, Calogero A, Rosa P, Galardo G, Loffredo L, Pignatelli P, Nocella C* (corresponding authors), Carnevale R*. Platelet Activation Favours NOX2-Mediated Muscle Damage in Elite Athletes: The Role of Cocoa-Derived Polyphenols. Nutrients. 2022;1:1558. IF: 6.706; citations: 0
- Carnevale R*, Nocella C* (equal contribution), Schiavon S, Cammisotto V, Cotugno M, Forte M, Valenti V, Marchitti S, Vecchio D, Biondi Zoccai G, Rubattu S, Martinelli O, Pignatelli P, Violi F, Volpe M, Versaci F, Frati L, Frati G, Sciarretta S. Beneficial effects of a combination of natural product activators of autophagy on endothelial cells and platelets. Br J Pharmacol. 2021;178:2146-2159. IF: 9.473; citations: 5
- 4. **Nocella C** (corresponding author), Mezzaroma I, Cammisotto V, Castellani V, Milito C, Rugova A, Frati G, Pignatelli P, Violi F, Pastori D, Carnevale R. Lipopolysaccharide induces platelet activation in HIV patients: the role of different viral load patterns. HIV Med. 2021;22:434-444. **IF: 3.094; citations: 1**
- 5. **Nocella C**, Bartimoccia S, Cammisotto V, D'Amico A, Pastori D, Frati G, Sciarretta S, Rosa P, Felici C, Riggio O, Calogero A, Carnevale R, SMiLe Group. Oxidative Stress in the Pathogenesis of Antiphospholipid Syndrome: Implications for the Atherothrombotic Process. Antioxidants (Basel). 2021;10:1790. **IF: 7.675; citations: 0**

- Carnevale R, Sciarretta S, Valenti V, di Nonno F, Calvieri C, Nocella C, Frati G, Forte M, d'Amati G, Pignataro MG, Severino A, Cangemi R, Arrivi A, Dominici M, Mangieri E, Gaudio C, Tanzilli G, Violi F. Low-grade endotoxaemia enhances artery thrombus growth via Tolllike receptor 4: implication for myocardial infarction. Eur Heart J. 2020;41:3156-3165. IF: 29.983; citations: 25
- 7. Nocella C, Cammisotto V, Bartimoccia S, Castellani V, Loffredo L, Pastori D, Pignatelli P, Sanguigni V, Violi F, Carnevale R. A novel role of MMP2 in regulating platelet NOX2 activation. Free Radic Biol Med. 2020;152:355-362. IF: 7.376; citations: 7
- Del Ben M, Nocella C* (equal contribution), Loffredo L, Bartimoccia S, Cammisotto V, Mancinella M, Angelico F, Valenti V, Cavarretta E, Carnevale R, Violi F. Oleuropein-enriched chocolate by extra virgin olive oil blunts hyperglycaemia in diabetic patients: Results from a one-time 2-hour post-prandial cross over study. Clin Nutr. 2020;39:2187-2191. IF: 7.324; citations: 8
- 9. Nocella C, Cammisotto V, Pigozzi F, Borrione P, Fossati C, D'Amico A, Cangemi R, Peruzzi M, Gobbi G, Ettorre E, Frati G, Cavarretta E, Carnevale R; SMiLe Group. Impairment between Oxidant and Antioxidant Systems: Short- and Long-term Implications for Athletes' Health. Nutrients. 2019;11:1353. IF: 4.546; citations: 42
- 10. Nocella C, Biondi-Zoccai G, Sciarretta S, Peruzzi M, Pagano F, Loffredo L, Pignatelli P, Bullen C, Frati G, Carnevale R. Impact of Tobacco Versus Electronic Cigarette Smoking on Platelet Function. Am J Cardiol. 2018;122:1477-1481. IF: 2.843; citations: 35
- 11. Carnevale R*, **Nocella C*** (equal contribution), Cammisotto V, Bartimoccia S, Monticolo R, D'Amico A, Stefanini L, Pagano F, Pastori D, Cangemi R, Violi F. Antioxidant activity from extra virgin olive oil via inhibition of hydrogen peroxide-mediated NADPH-oxidase 2 activation. Nutrition. 2018;55-56:36-40. **IF: 3.591; citations: 9**
- 12. Carnevale R*, **Nocella C*** (equal contribution), Pignatelli P, Bartimoccia S, Stefanini L, Basili S, Novo M, D'Amico A, Cammisotto V, Pastori D, Violi F. Blood hydrogen peroxide break-down activity in healthy subjects and in patients at risk of cardiovascular events. Atherosclerosis. 2018;274:29-34. **IF: 4.255; citations: 9**
- 13. Carnevale R*, Nocella C* (equal contribution), Petrozza V, Cammisotto V, Pacini L, Sorrentino V, Martinelli O, Irace L, Sciarretta S, Frati G, Pastori D, Violi F. Localization of lipopolysaccharide from Escherichia Coli into human atherosclerotic plaque. Sci Rep. 2018;8:3598. IF: 4.011; citations: 50
- 14. Pastori D*, **Nocella C*** (equal contribution), Farcomeni A, Bartimoccia S, Santulli M, Vasaturo F, Carnevale R, Menichelli D, Violi F, Pignatelli P; ATHERO-AF Study Group.

Relationship of PCSK9 and Urinary Thromboxane Excretion to Cardiovascular Events in Patients With Atrial Fibrillation. J Am Coll Cardiol. 2017;70:1455-1462. **IF: 16.834; citations: 42**

- 15. Carnevale R, Raparelli V, Nocella C, Bartimoccia S, Novo M, Severino A, De Falco E, Cammisotto V, Pasquale C, Crescioli C, Scavalli AS, Riggio O, Basili S, Violi F. Gut-derived endotoxin stimulates factor VIII secretion from endothelial cells. Implications for hypercoagulability in cirrhosis. J Hepatol. 2017 Nov;67(5):950-956. IF: 14.911; citations: 54
- 16. **Nocella C**, Carnevale R, Bartimoccia S, Novo M, Cangemi R, Pastori D, Calvieri C, Pignatelli P, Violi F. Lipopolysaccharide as trigger of platelet aggregation via eicosanoid overproduction. Thromb Haemost. 2017;117:1558-1570. **IF: 4.952; citations: 35**
- 17. Pagano F*, **Nocella C*** (equal contribution), Sciarretta S, Fianchini L, Siciliano C, Mangino G, Ibrahim M, De Falco E, Carnevale R, Chimenti I, Frati G. Cytoprotective and Antioxidant Effects of Steen Solution on Human Lung Spheroids and Human Endothelial Cells. Am J Transplant. 2017;17:1885-1894. **IF:6.493; citations: 13**
- 18. Raparelli V, Basili S, Carnevale R, Napoleone L, Del Ben M, **Nocella C**, Bartimoccia S, Lucidi C, Talerico G, Riggio O, Violi F. Low-grade endotoxemia and platelet activation in cirrhosis. Hepatology. 2017;65:571-581. **IF:14.079; citations: 61**
- 19. Carnevale R, Sciarretta S, Violi F, **Nocella C**, Loffredo L, Perri L, Peruzzi M, Marullo AG, De Falco E, Chimenti I, Valenti V, Biondi-Zoccai G, Frati G. Acute Impact of Tobacco vs Electronic Cigarette Smoking on Oxidative Stress and Vascular Function. Chest. 2016;150:606-612. **IF:6.147; citations: 184**
- 20. Pignatelli P, Carnevale R, Pastori D, Cangemi R, Napoleone L, Bartimoccia S, **Nocella C**, Basili S, Violi F. Immediate antioxidant and antiplatelet effect of atorvastatin via inhibition of Nox2. Circulation. 2012;126:92-103. **IF:15.202; citations: 121**

Luogo e data

Roma, 07/07/2022

Firma

(non soggetta ad autentica ai sensi dell'art. 39 del D.P.R. 28.12.2000, n. 445)