ICOCIMS

International student Congress of
Clinical Innovation and Medical Sciences

PROGRAMME & ABSTRACT BOOK

FIRST EDITION

NOV
9 - 11
Parma, Italy

SPONSORS

UNIVERSITÀ DI PARMA

AMBOSS

Barilla
The Italian Food Company. Since 1877.

SUPPORTERS

CIM
CAMICI IN MOVIMENTO

Unilab
SVOLTASTUDENTI

Rotary
Parma

EUROPEAN
MD/PhD
ASSOCIATION

ALUMNI
e AMICI
UNIVERSITÀ DI PARMA

iMSCB

ICOCIMS 2023

TABLE OF CONTENTS

Dear ICOCIMS participants,

We want to express our sincerest thanks for being integral members of the ICOCIMS community during these days.

Our deep appreciation goes out to each and every one of you for your participation in the conference. Recognizing the challenges many of you faced in securing funding, visas, and travel arrangements, and acknowledging the considerable distances many have traveled to join us, we want to express our sincere appreciation. Your commitment to being part of this event is truly commendable. Thank you sincerely for making it possible!

Your presence has brought fresh perspectives, innovative ideas, and valuable viewpoints. We sincerely hope that your participation has contributed to enriching your medical knowledge.

With that said, the chapter of ICOCIMS for this year draws to a close.

In our inaugural first edition, we take pride in presenting an exceptional scientific program that highlighted clinical innovations and advancements in the field of bio and health sciences. This was conveyed through workshops and 11 keynote lectures featuring distinguished speakers from four different countries (Germany, Italy, USA, Taiwan) and prestigious institutions (including the MD Anderson Cancer Center and the University of Taipei).

Moreover, the conference hosted one poster session and five oral sessions, providing a platform for nearly 40 presenters — half of whom coming from outside Italy — to showcase their research.

On top of that, we hope your participation in our social program, including the dinner and after-party, made your participation at the conference an unforgettable one.

All of this became achievable due to your active participation, the invaluable support of our sponsors, and the dedicated involvement of our helpers.

We genuinely hope that you enjoyed your time at ICOCIMS!

– The **Organising Committee**

Acknowledgements

It takes a collective effort to bring ideas to life, and the same goes for our Congress too.

Here, we want to extend our heartfelt gratitude to those who have offered us their expertise, time, and encouragement, and guided us in bringing ICOCIMS to fruition.

- Prof. Elisa Araldi
- Prof. Ovidio Bussolati
- Prof. Gian Paolo Ceda
- Prof. Giancarlo Condello
- Prof. Andrea Errera
- Prof. Marco Falasca
- Prof. Marcello Giuseppe Maggio
- Prof. Pierantonio Muzzetto
- Prof. Paolo Ossola
- Prof. Francesco Potì

We extend our sincere apologies if anyone who supported or endorsed our initiative is not specifically accredited here. Your contributions are truly valued, and we appreciate your understanding.

ORGANISING COMMITTEE

Amandeep Kaur
- Chief Sustainability Officer

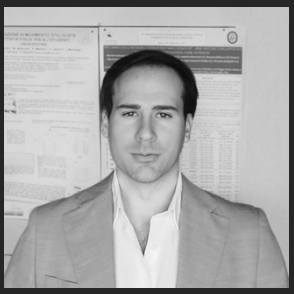
Dario Bottignole
- Co-chair of the Scientific Committee

Emilio Maddalena
- Chief Financial Officer
- Head of the External Relations Committee

Francesco B. Casadei
- Co-chair of the Digital and Media Committee
- Co-chair of the Social Media Committee

Giacomo M. Cerreto
- President
- Head of Logistics team

Olympia Cometa
- Chief Legal Officer
- Chief Diversity, Equity and Inclusion Officer



Riccardo Mazzoli
- Co-chair of the Scientific Committee

Tudor M. Haja
- Co-chair of the Digital and Media Committee
- Co-chair of the Social Media Committee

VOLUNTEERS

Scientific Committee
- Amanda Braga
- Damiano Marchesini
- Elena Morini
- Parsa Mehrkhah
- Samuele Cortellazzi
- Veronica Caselli

Digital & Social Media Commitee
- Giulia Pecoraio
- Jessica Ponti
- Zouhour Fatnassi

Legal Committee
- Alon Dvir

Logistics Committee
- Amitoj Singh
- Simone Mainieri

Crew
- Alessia Mariello
- Alice Adorni
- Beatrice Sampaolo
- Francesca Triscornia
- Giulia Licchelli
- Giulio Righini
- Ilaria Manfredini
- Jasmina Bababusta
- Karla Irene Perez
- Marta Malarini
- Nasim Shabib
- Sadaf Akbari
- Sofia Fiore
- Sophie Jaloux

External Relations Committee
- Veronica Escobar

Photographer
- Kamaldeep Kaur

SPEAKERS

(listed alphabetically by last name)

Prof. Elisa Araldi

- BSc and MSc in Molecular Biology (Italy), PhD in Pathobiology (NYU, USA).
- Postdocs at Yale and ETH Zurich, now Assistant Professor and Group Leader in Computational Systems Medicine at Mainz (Germany), also Assistant Professor in Biochemistry at Parma (Italy).
- Awarded "Early Career Fellowship Programme" grant for groundbreaking project on cholesterol biosynthesis intermediates by Human Technopole.

Cristina Castracani, PhD

- MSc in Biological Sciences, and PhD in Behavioural Biology, University of Parma, Italy. Post-PhD, transitioned to behavioral ecology, exploring ants as bioindicators in Italy.
- Establishing a comprehensive database of Italian ant species and their community structure in diverse ecosystems.
- Citizen Science Advocacy: actively engages in citizen science initiatives, promoting public participation in ecological research.

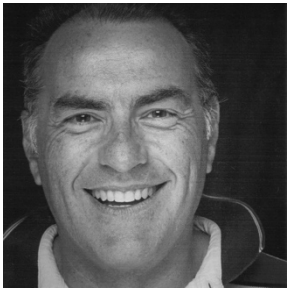
Prof. Simona Colla

- Graduated in Biological Sciences and Molecular Biology from the UniPR, Italy, and pursued Experimental Haematology at the UniMoRe, Italy.
- After research fellowships in Arkansas and Parma, she joined the Dana Farber Cancer Institute before starting her tenure at the University of Texas – MD Anderson Cancer Center.
- Numerous publications, awards, and research grants, including the Harvard Cancer Center Myeloma SPORE Career Development Award.

Prof. Giancarlo Condello

- Bachelor's and Master's in Sports Science and Techniques, and PhD in Exercise Science and Ergonomics at Università degli Studi di Roma.
- Professor at University of Parma, Italy. Project Assistant Professor at University of Taipei (2018-2021) and Visiting Professor at Mahidol University, Thailand (2023).
- Awards from the Ministry of Science and Technology (Taiwan) and University of Taipei (2019-2020), Bengt Nybelius Scholarship (2018), among others.

Prof. Marco Falasca



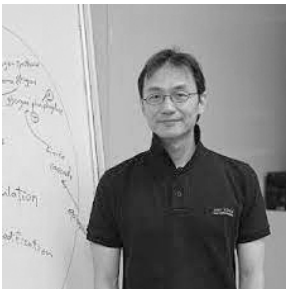
- PhD in Molecular Endocrinology from "Consorzio Mario Negri Sud" (Italy). Postdoc at the Department of Pharmacology, New York University (USA).
- Former Professor at Queen Mary University of London and Senior Lecturer at University College London (UK). Currently, Full Professor in Biochemistry, University of Parma (Italy), and Full Professor in Metabolism, Curtin Medical School (Australia).
- Recognized with numerous awards and honors, reflecting a globally acknowledged role in scientific innovation over the past decades.

Prof. J.Dr. Christian Ferraris

- Juris Doctor (University of Turin, Italy). Master in Management of Healthcare Companies (SDA Bocconi, Milan, Italy).
- Adjunct Professor at San Raffaele University and the University of Milan (Italy).
- Director roles at Assolombardia, AIOP Lombardia, Fondazione Sanità Futura. Member of FASI's administrative council.
  Topic Leader Healthcare, Bocconi Alumni Community.
  Advisory Board Member for Sustainability, 4cLegal (Milan, Italy).

Prof. Vittorio Gallese

- MD and trained neurologist, Professor of Psychobiology at the University of Parma (Italy). Director of the Lab of Social Cognitive Neuroscience.
- Honorary fellow, Institute of Philosophy, School of Advanced Study, University of London (UK). Honorary member, American College of Psychiatrists.
- Cognitive neuroscientist, focuses on the relation between the sensorimotor system and social cognition by investigating intersubjectivity, psychopathology, and language.



Prof. Chia-Hua Kuo

- BA from Fu Jen University (Taiwan). MA in Kinesiology from the University of Texas (Austin, USA). PhD in Exercise Physiology, Biochemistry, and Molecular Biology from the University of Texas.
- Distinguished Professor at the Institute of Sports Sciences, University of Taipei (Taiwan). Chair Professor at Soochow University (China).
- Renowned scientific reviewer and editor for academic journals. Internationally acclaimed for research on human performance, metabolism, sports nutrition, and aging.

Adam R. Marcus, M.A.

- B.A. in History (University of Michigan, USA). M.A. in Science Writing (Johns Hopkins University, USA).
- Editorial Director for Medscape. Lecturer in Science Journalism and Medical Trade Publishing at NYU and CUNY.
- Former editor of Gastroenterology & Endoscopy News, Anesthesiology News, and Pharmacy Practice News. Co-founder of the Center for Scientific Integrity, now RetractionWatch.com.
  Freelance writer published in impactful journals.

Alessandro Pigoni, MD

- Psychiatry Residency, University of Milan (Italy). PhD student in Cognitive Social and Computational Neurosciences, IMT School for Advanced Studies (Lucca, Italy).
- Fellow researcher at Yale Cancer Center (USA). Multiple awards, including WFSBP Young Investigator and ECNP Excellence Awards.
- ECNP Scientific Advisory Panel, Guest Associate Editor for Frontiers in Psychiatry - Neuroimaging, and Frontiers in Psychiatry - Computational Psychiatry, Associate Editor for Minerva Psychiatry Journal.

Jaskirat Singh, BEng

- Bachelor's in Automation and Industrial Mechatronic Systems, ITS Lombardia Meccatronica (Milano, Italy). Bachelor's Degree in Civil & Industrial Engineering, St. Clements University.
- Mechanical & Simulation Engineer, Project Manager at DMD Projects (Tiesse Robot / Kawasaki Robotics, Visano, Italy).
- Collaborative research with CNR (National Research Council, Italy).

OPENING CEREMONY SPEAKERS

(listed alphabetically by last name)

Prof. Stefania Basili,
President of the Italian Conference of MD Program Directors

Prof. Daniele Del Rio,
Deputy Rector for Scientific research, on behalf of the Rector of the University of Parma

Prof. Marcello Giuseppe Maggio,
Director of the University of Parma MD Program (taught in Italian)

Prof. Elena Masselli,
On behalf of Prof. Marco Vitale, Coordinator of the University of Parma at Piacenza MD Program (taught in English)

PROGRAMME

November 09

All times are Italian Time (GMT+1)

Aula Magna, *"Palazzo dell'Università"* of the University of Parma

10:15 - 11:00	Registration
11:00 - 11:45	**Opening Ceremony**
11:45 - 13:00	**Poster Session**
13:00 - 13:30	Lunch break
13:30 - 15:00	**Plenary Oral Session**
15:00 - 15:45	**Keynote Lecture** "Assessing and implementing sustainability in healthcare" by Prof. Dr. C. Ferraris
15:45 - 16:00	Break
15:00 - 15:45	**Keynote Lecture** "Assessing and implementing sustainability in healthcare" by Prof. Dr. C. Ferraris
15:45 - 16:00	Break
16:00 - 16:45	**Plenary Oral Session**
16:45 - 17:00	Break
17:00 - 17:30	**Keynote Lecture** Hematology and Oncology by Prof. S. Colla
17:30 - 18:30	Plenary Oral Session

November 10

All times are Italian Time (GMT+1)

Aule Centrali of the University, at the University Hospital of Parma

9:00 - 9:30	Registration
9:30 - 10:00	**Keynote Lecture** Lifestyle and Metabolic Disorders by Prof. Chia-Hua Kuo (Taiwan)
10:00 - 11:00	**ESS Lab** (Prof. G. Condello) **Cardiovascular Diseases** (UO Cardiology)
11:00 - 11:15	Break
11:15 - 12:15	**Plenary Oral Session**
12:15 - 13:00	**Partners' Presentations** (CIM, EMPA, AMSC, IMSCB, Medicalis)
13:00 - 13:30	Lunch break

13:30 - 14:00	**Keynote Lecture** Mental health and neurosciences by A. Pigoni, MD
14:00 - 15:00	**"Citizen Science"** by C. Castracani, PhD **Plenary Oral Session**
15:00 - 15:45	**Keynote Lecture** "Machine learning for personalised type 2 diabetes treatments" by Prof. E. Araldi
15:45 - 16:00	Break
16:00 - 16:45	**Keynote Lecture** "Research Integrity and Ethics" by A. Marcus, MA
16:45 - 17:00	Break
17:00 - 17:30	**Keynote Lecture** New technologies and socio-economics implications by J. Singh. Beng
17:30 - 18:30	**Plenary Oral Session**

November 11

All times are Italian Time (GMT+1)

Aule Centrali of the University, at the University Hospital of Parma

9:00 - 9:30		Registration
9:30 - 10:15	|	AMBOSS Workshop
10:15 - 11:00	|	Keynote Lecture "Omics-based therapeutical implications" by Prof. M. Falasca
11:00 - 11:15		Break
11:15 - 12:15	|	Keynote Lecture "Neurophysiological basis of empathy" by Prof. V. Gallese
12:15 - 13:00	|	Awards & Closing Ceremony

ORAL SESSION

PRESENTERS

Chiara Maccari
Elia Indrigo
Zuzzanna Wojtozak
Anton Artemyev
Wiktor Kruczek
Maximilian Nuber
Jan Baran
Samuele Cortellazzi
Anna Gagliardi
Ekaterina Timofeeva
Prisca Tamarozzi
Sahar Behzad Khoushgouei
Yekaterina Tychina
Kamil Górecki
Anzor Bairamkulov
Aleksei Staferov
Bogdan-Andrei Borlea
Julia Rafalska
Irina Maria Rusu
Federico Divincenzo
Fabiola Arella
Melika Kolahdoozan
Moses Reji Chandy
Maria Obrycka
Biagio Matera

ORAL SESSION WINNER: Maximilian Nuber

3D-Printed PCL/b-TCP scaffolds for bone regeneration.

Matera B. (1), Meglioli M. (2), Scialoia L.P. (2), Rossi F. (3), Ghezzi B. (2)

1) Laboratorio di biomateriali ed ingegneria tissutale - Centro Universitario di Odontoiatria - Dipartimento di Medicina e Chirurgia - Università di Parma, Parma (Italy)
2) Centro Universitario di Odontoiatria, Dipartimento di Medicina e Chirurgia, Università di Parma, Parma (Italy)
3) Istituto dei Materiali per l'Elettronica ed il Magnetismo, Consiglio Nazionale delle Ricerche, Parma (Italy)

Background Tissue engineering is an ever-growing field which aims to regenerate and reconstruct tissues compromised by degenerative and disruptive diseases by using highly customized scaffolds.
One of the most innovative methods employed to produce scaffolds able to mimic the structure of the native tissue is three–dimensional (3D) printing which, combined with a huge variety of biomaterials, can lead to a great improvement of the regenerative rate.

Methods The fabrication of 3D printed scaffolds composed of polycaprolactone (PCL) and increasing amount of b-tricalcium phosphate (b-TCP) has been performed through a Fused Deposition Modelling system in order to define the higher amount of b-TCP capable to guarantee the ideal PCL/b-TCP combination able to provide good structural features and improved osteogenic properties.
Once defined the best b-TCP concentration, the PCL/b-TCP printing filaments were produced to obtain scaffolds with defined dimensions and topography which have been characterized from a physical(i.e. hydrophilicity, morphology and surface topography) and biological(i.e. adhesion, proliferation and osteoblasts differentiation) point of view.
Two-way ANOVA and the Tukey post-test have been applied(statistical significance when $p<0.05$).

Results Our data showed a great scaffold biocompatibility with a progressive increase of cell viability onto PCL/b-TCP structures. These results were confirmed by scanning electron microscopy which showed that PCL/b-TCP scaffolds provided to a more favorable microenvironment for cell attachment and proliferation. SEM images of the three types of surfaces highlighted that surface roughness was strongly dependent from b-TCP concentration which also affected the scaffold hydrophilic properties making PCL/b-TCP scaffolds more hydrophilic than control. Also, the presence of ceramic powder induced a more marked differentiation which, even if lower at the early stage, was sensibly higher at the end of this period, signal of the essential role of b-TCP in the cellular differentiation process.

Conclusion In this work has been proved that all the samples loaded with ceramic powder showed a greater proliferative and differentiative effect than PCL scaffold, providing for a better microenvironment particularly suitable for cell adhesion, proliferation and osteoblasts differentiation thus representing an ideal candidate for the future development of scaffolds for bone and periodontal regeneration.

A retrospective cohort study evaluating the incidence of Ventilator-Associated Pneumonia (VAP) in adult patients with traumatic brain injury in a tertiary care centre in central Kerala.

Reji Chandy M. (1), Philip S. (1)
1) M.O.S.C. Medical College Hospital, Kolenchery, Kerala (India)

Background Traumatic brain injuries are very common in the present era due to the increase in road traffic accidents, falls and assaults. Most of the traumatic brain injury patients have low Glasgow coma scale(<8) and hence would require intubation and mechanical ventilation so as to prevent hypoxemia, hypercapnia and aspiration.
This exposes the lower respiratory tract to microorganisms which could lead to ventilator associated pneumonia, sepsis and even death. There is a strong brain-lung interaction in patients with traumatic brain injury. Ventilator-associated pneumonia (VAP) is a type of lung infection seen in patients who have been under mechanical ventilation for over 48 hours. VAP has been divided into two types-early onset and late onset VAP. Early onset VAP develops during the first 4 days of intubation and usually has better prognosis and good sensitivity to antimicrobials whereas late onset VAP develops after 4 days of intubation and it has poor prognosis and mostly caused due to multi-drug resistant microbes.

Materials and methods

- Study Design: Retrospective Cohort
- Study Setting: Departments of Anaesthesiology and Critical care, Medical Records
- Duration of the study: 2 Months
- Study Period – Dec 2020 to Dec 2022
- Study tool: Case Study Form
- Sample size (n): 93
- Sampling method: Convenient sampling

The information regarding the age, gender, clinical symptoms, radiological feature, microbiology reports and co-existing medical conditions was collected from the patients record and presence or absence of VAP was recorded. Data entry was done using Excel Spreadsheet and Data Analysis using SPSS and EZR software. The conclusion was made from the above information to know the incidence of VAP. All the categorical variables was summarized using frequency and percentage.
Quantitative variables was summarized using mean and SD if data follows normality assumption else using Median and IQR [Q 1 , Q 3]. Kolmogorov-Smirnov test and Shapiro test was used to check the normality of the data. Robust Poisson regression was used to identify the risk factors associated with early and late VAP. Relative risk along with 95% CI was estimated. The entire analysis was performed using SPSS version 16.

Results Out of the total 93 patients, 50.5 percentage of patients (n=47) developed VAP of which 44.7% had early onset whereas 55.3 % had late onset VAP Among those who developed VAP, K.Pneumoniae (21.9%) was the major causative microorganism for VAP of which 34% were resistant with a lower recovery rate, p-value=0.007. Proportion of patients who recovered were

higher among the younger age group when compared to the older age group, p-value=0.01. Proportion of patients who died with VAP was significantly higher among those who had hypertension when compared to those without any hypertension, p-value=0.04. A borderline significance was also observed in the association between Cardiac diseases and developing VAP, p-value=0.047. Development of early VAP was found to be 4.60 times higher [RR=4.60(95% Ci:3.12,6.78)] among those who had Immunosuppression and proportion of patients developing late VAP was higher (87.1%) among those who had hypertension, p-value=0.03.

Conclusion Incidence of VAP was seen in half of the intubated TBI patients with K. pneumoniae being the most common organism causing VAP. Older patients and patients with hypertension, cardiac diseases, resistant organism had poor prognosis compared to the other. We would like to conclude that it would be of great value: To initiate prophylactic antibiotic measures with proper ventilator care with frequent proper sterile suctioning; changing of HEPA filters and most importantly instilling the requirement of maintaining sterility around these vulnerable population.

Citations:

1) Gururaj - 2005 - Address for Correspondence.pdf [Internet]. [cited 2023 Jan 7]. Available from: https://nimhans.ac.in/wp-content/uploads/2021/02/Traumatic-Brain-Injury-Report.pdf
2) Traumatic brain injury in India: A big problem in need of data Maas Al Neurol India [Internet]. [cited 2023 Jan 7]. Available from: https://www.neurologyindia.com/article.asp?issn=0028-3886;year=2017;volume=65;issue=2;spage=257;epage=258;aulast=Maas
3) Traumatic Brain Injuries (TBIs) WHO Collaborating Centre for Injury Prevention and Safety Promotion – NIMHANS [Internet]. [cited 2023 Jan 7]. Available from: https://nimhans.ac.in/who-collaborating-centre-for-injury-prevention-and-safety-promotion/traumatic-brain-injuries-tbis-who-collaborating-centre-for-injury-prevention-and-safety-promotion/
4) Respiratory Management in Patients with Severe Brain Injury - PubMed [Internet]. [cited 2023 Jan 7]. Available from: https://pubmed.ncbi.nlm.nih.gov/29558976/
5) Host immune response in sepsis due to ventilator-associated pneumonia: how is it different? [Internet]. [cited 2023 Jan 7]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811897/
6) Ventilator-Associated Pneumonia: Diagnosis, Treatment, and Prevention [Internet]. [cited 2023 Jan 7]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1592694/
7) Gao J, Zhou C, Zhang H. Mechanical ventilation in patients with acute ischemic stroke: from pathophysiology to clinical practice. Crit Care. 2020 Apr 7;24:139.
8) Brain–lung interactions and mechanical ventilation in patients with isolated brain injury | Critical Care | Full Text [Internet]. [cited 2023 Jan 7]. Available from: https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03778-0
9) Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia | American Journal of Respiratory and Critical Care Medicine [Internet]. [cited 2023 Jan 7]. Available from: https://www.atsjournals.org/doi/full/10.1164/rccm.200405-644ST
10) Golia S, K T S, C L V. Microbial profile of early and late onset ventilator associated pneumonia in the intensive care unit of a tertiary care hospital in bangalore, India. J Clin Diagn Res JCDR. 2013 Nov;7(11):2462–6.

11) Jovanovic B, Milan Z, Markovic-Denic L, Djuric O, Radinovic K, Doklestic K, et al. Risk factors for ventilator-associated pneumonia in patients with severe traumatic brain injury in a Serbian trauma centre. Int J Infect Dis. 2015 Sep 1;38:46–51.

12) Abdussalam AL. Severe respiratory failure and traumatic brain injuries: What do we know? Qatar Med J. 2017 Feb 14;2017(1):40. 4Mereu L, Dalpra F, Terreno E, Pertile R, Angioni S, Tateo S. Mini-Laparoscopic Repair of Apical Pelvic Organ Prolapse (POP) by Lateral Suspension with Mesh. Facts Views Vis Obgyn. 2018 Sep;10(3):139-145. PMID: 31191848; PMCID: PMC6548408.

A survey of protective effect of melatonin against trifluoperazine-induced genotoxicity in peripheral blood lymphocytes via micronucleus assay.

Behzad Khoushgouei S. (1), Raibee M. (1), Zamani E. (1), Evazalipour M. (1).
1) Guilan University of Medical Sciences, Rasht (Iran)

Background Trifluoperazine is one of the most widely used antipsychotics. Studies show that trifluoperazine may induce genotoxicity and oxidative damage by inducing apoptosis and inhibiting DNA repair and synthesis in long-term exposure. In this study, the protective effects of melatonin, as an antioxidant agent, was evaluated in oxidative-induced genotoxicity by trifluoperazine.

Methods Human lymphocyte samples were obtained from a healthy male volunteer and were divided into negative control, cisplatin, trifluoperazine (50 and 100 µM), trifluoperazine-melatonin (100 µM) groups. Micronucleus assay was performed to determine genotoxicity. Also, oxidative damage was evaluated by lipid peroxidation and glutathione oxidation.

Results The results of this study indicate a significant increase in the amount of micronuclei, glutathione oxidation and lipid peroxidation ($P<0.01$) in the trifluoperazine groups compared to the control group. After treatment with melatonin, a significant decrease in the amount of micronuclei, glutathione oxidation and lipid peroxidation ($P<0/05$) were observed in the mentioned groups.

Conclusions The findings of this study show that trifluoperazine can cause genotoxicity in cells by inducing oxidative stress. It can also be stated that oxidative stress is one of the main pathways used by trifluoperazine to induce genotoxicity and melatonin has a significant effect on reducing oxidative stress and therefore genotoxicity due to its antioxidant effect.

Advantages of a laparoscopic mesh-pectopexy in patients with pelvic organ prolapse.

Tychina Y. (1), Chushkov Y. (2)

1) Sechenov Centre for Motherhood and Childhood, Sechenov University, First Moscow State Medical University, Moscow (Russian Federation)
2) Obstetrics and Gynecology Department, Sechenov University, First Moscow State Medical University, Moscow (Russian Federation)

Background We treated 5 female patients (median age 68 ± 3,5 years) complaining of chronic pelvic pain, symptomatic vaginal bulge, and pelvic muscle spasms. According to Pelvic Organ Prolapse Quantification system (POP–Q), 2 patients were diagnosed with complete uterine prolapse (POP-Q stage IV), and 3 had incomplete uterine prolapse (POP-Q stage III).

Case history Patients A and D have a history of operations for genital prolapse with a subsequent prolapse recurrence.

Investigations During the examination, concomitant pathology of the internal genitalia was revealed in 3 patients: patients A and B had a benign ovarian tumor and patient C had uterine fibroids. Concomitant somatic pathology was detected in 2 patients: C and D.

Treatment All patients underwent laparoscopic mesh-pectopexy. During the operations, polypropylene mesh implant with sizes 6x10 and 4x10 cm were used. The average operation time was 150 ± 42 minutes; blood loss did not exceed 100 ml in all patients; neither intraoperative nor postoperative complications were registered. During the follow–up period (3 months), there were no signs of recurrence of genital prolapse.

Discussion In case of prolapse recurrence or high risks of a recurrence (like in Ehlers-Danlos syndrome), the use of a mesh implant is indicated during surgical treatment [1, 2, 3].
Laparoscopic access allows to assess the condition of the internal genitalia in detail and to identify the presence of a pathology, in particular, to establish the degree of a prolapse. In addition, detailed visualization allows a surgeon to accurately position the mesh implant, fixate it, and assess the degree of its tension as well as the final position of the internal genitalia and pelvic walls after correction [4].

Conclusion Despite the small number of observations, we would like to note the high efficiency and safety of laparoscopic interventions performed using synthetic implants. We confirmed the absence of intra- and postoperative complications, as well as low intraoperative blood loss (100 ml). A common feature of the patients is their elderly age, as well as the presence of somatic diseases. Despite these factors, laparoscopic surgery was possible and was safe. We believe that these advantages will lead to further development of laparoscopic techniques for correction of genital prolapse.

Citations:

1) Ugianskiene A, Davila GW, Su TH; FIGO Urogynecology and Pelvic Floor Committee. FIGO review of statements on use of synthetic mesh for pelvic organ prolapse and stress urinary incontinence. Int J Gynaecol Obstet. 2019 Nov;147(2):147-155. doi: 10.1002/ijgo.12932. Epub 2019 Aug 20. PMID: 31353463.
2) Ng-Stollmann N, Fünfgeld C, Gabriel B, Niesel A. The international discussion and the new regulations concerning transvaginal mesh implants in pelvic organ prolapse surgery. Int Urogynecol J. 2020 Oct;31(10):1997-2002. doi: 10.1007/s00192-020-04407-0. Epub 2020 Jul 21. PMID: 32696186; PMCID: PMC7497328.
3) Nazemi A, Shapiro K, Nagpal S, Rosenblum N, Brucker BM. Pelvic Organ Prolapse in Ehlers-Danlos Syndrome. Case Rep Urol. 2023 Feb 23;2023:6863711. doi: 10.1155/2023/6863711. PMID: 36875296; PMCID: PMC9981282.
4) 4Mereu L, Dalpra F, Terreno E, Pertile R, Angioni S, Tateo S. Mini-Laparoscopic Repair of Apical Pelvic Organ Prolapse (POP) by Lateral Suspension with Mesh. Facts Views Vis Obgyn. 2018 Sep;10(3):139-145. PMID: 31191848; PMCID: PMC6548408.
5) Zhang YA, Wang W, Li XL, Xian-Hui-Zhang, Pan J, Li ZA. The effect evaluation of traditional vaginal surgery and transvaginal mesh surgery for severe pelvic organ prolapse: 5 years follow-up. Open Med (Wars). 2022 Apr 22;17(1):801-807. doi: 10.1515/med-2022-0467. PMID: 35529471; PMCID: PMC9034344.

All that glitters is not gold: assessment of the gastroprotective potential of bee pollen in Wistar rat model.

Górecki K (1), Greluk A. (1), Pacyna K. (1), Ziółko A. (1), Kędzierawski J. (1)

1) Students' Scientific Association at the Department of Histology, Embryology and Cytophysiology, Medical University of Lublin, Lublin (Poland)

Background Among people interested in organic food and healthy lifestyle, bee pollen is a popular diet supplement, especially in countries with developed apiculture. Bee pollen anti-oxidant and gastroprotective effects have been suggested, but the topic is not yet well-researched [1]. It was suggested that polyphenols contained in bee pollen can modulate expression of enzymes such as iNOS, COX-1 and COX-2, that are important for the pathogenesis of diseases of gastric mucosa [2,3,4]. The aim of our study is to evaluate gastroprotective effects of bee pollen supplementation and its effect on iNOS, COX-1 and COX-2 expression in gastric mucosa in vivo.

Methods 30 Wistar rats were divided into 6 groups – 3 running and 3 non-running – among those there was one control, one supplemented with bee pollen and one receiving whey proteins in both levels of physical activity. After 8 weeks of laboratory phase all animals were decapitated and their stomachs were collected, formalin-fixed and paraffin-embedded. 5 µm thick slides were stained with hematoxylin and eosin. Immunohistochemical reactions were performed on other slides, assessing the expression of COX-1, COX-2 and iNOS enzymes. Microscopic images were evaluated for possible changes.

Results Gastric mucosa structure was properly built in control groups and whey protein-supplemented groups. Gastric mucosa was altered in bee pollen supplemented groups, with increased amount of chief cells and lower amount of parietal cells. Expression of iNOS was highest in groups supplemented with bee pollen, while expression of COX-1 in those was lower than in control and whey protein groups. COX-2 expression was similar in all groups.

Conclusion Bee pollen consumption did not result in any visible signs of gastroprotection. Moreover, elevated iNOS levels may suggest a potentially harmful effect that requires further detailed research, as unexpected pro-oxidative effects of bee pollen extracts have previously been described in the literature [2].

Citations:

1) Pérez-Pérez EM, Vit P, Rivas E, Sciortino R, Sosa A, Tejada D, Rodríguez-Malaver AJ. Antioxidant activity of four color fractions of bee pollen from Mérida, Venezuela. Arch Latinoam Nutr. 2012 Dec;62(4):375-80. PMID: 24020258.

2) Moita E, Gil-Izquierdo A, Sousa C, Ferreres F, Silva LR, Valentão P, Domínguez-Perles R, Baenas N, Andrade PB. Integrated analysis of COX-2 and iNOS derived inflammatory mediators in LPS-stimulated RAW macrophages pre-exposed to Echium plantagineum L. bee pollen extract. PLoS One. 2013;8(3):e59131. doi: 10.1371/journal.pone.0059131. Epub 2013 Mar 8. PMID: 23520554

3) Chelucci E, Chiellini C, Cavallero A, Gabriele M. Bio-Functional Activities of Tuscan Bee Pollen. Antioxidants (Basel). 2023 Jan 3;12(1):115. doi: 10.3390/antiox12010115. PMID: 36670977; PMCID: PMC9854628.
4) Hiratsuka T, Futagami S, Tatsuguchi A, Suzuki K, Shinji Y, Kusunoki M, Shinoki K, Nishigaki H, Fujimori S, Wada K, Miyake K, Gudis K, Tsukui T, Sakamoto C. COX-1 and COX-2 conversely promote and suppress ischemia-reperfusion gastric injury in mice. Scand J Gastroenterol. 2005 Aug;40(8):903-13. doi: 10.1080/00365520510015827. PMID: 16170898

Deep Immune Phenotyping of Heart Failure to identify molecular signatures of Metabolically - Induced dysregulations in Peripheral Blood Mononuclear Cells.

Number M. (1), Esenkova E. (1,2,3), Bauer K. (1,2,3), Llavona P (4), Karunanithi S. (4), Köck T. (1,2,3), Pallares Robles A. (1), Wild P. (1,2,3,4,5), Araldi E. (1,2,3).

1) Clinical Epidemiology and Systems Medicine, Center for Thrombosis and Hemostasis (CTH), University Medical Center of the Johannes Gutenberg University Mainz, Mainz (Germany)
2) Preventive Cardiology and Preventive Medicine, Department of Cardiology, University Medical Center of the Johannes Gutenberg University Mainz, Mainz (Germany)
3) German Center for Cardiovascular Research (DZHK), partner site Rhine-Main, Mainz (Germany)
4) Institute of Molecular Biology (IMB), Mainz (Germany)
5) Systems Medicine, Institute of Molecular Biology (IMB), Mainz (Germany)

Background Heart failure (HF) is a multifaceted syndrome characterized by impaired cardiac function, leading to inadequate tissue perfusion. Beyond its primary cardiovascular manifestations, HF is now recognized as a systemic disorder affecting various organ systems, including the immune system and metabolic pathways. Recent studies have unveiled intricate connections between metabolic dysfunction and immune dysregulation, shedding light on their intertwined roles in the pathogenesis and progression of HF. Understanding the complex interplay between metabolism and immunity in HF could pave the way for novel therapeutic strategies targeting both aspects of the disease.

Methods In this work, we aim to explore the intricate relationship between metabolic dysfunction and immunity in HF and highlight their potential implications for the development of innovative treatment approaches. We applied single cell RNA sequencing (scRNAseq) to peripheral blood mononuclear cell (PBMC) samples of 64 individuals with HF with preserved ejection fraction (HFpEF), HF with reduced ejection fraction (HFrEF) and controls from the well-characterized MyoVasc HF cohort. The selection of a spectrum of metabolic dysregulation as a comorbidity to HF allows for the co-analysis of the influence of these conditions on the immune system.

Results & Conclusions In individuals with both HF and metabolic complications, we could identify distinct circulating immune cell types with different abundance compared to controls. In particular, our results point towards a dysregulation CD16+ Natural Killer (NK) and cytotoxic T-cells. They indicate the relevance of the aforementioned cell types for the development of novel therapeutic targets in HF with metabolic complications.

Citations:

1) Bozkurt, B. et al. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. J. Card. Fail. (2021) doi:10.1016/j.cardfail.2021.01.022.

2) Osborn, O. & Olefsky, J. M. The cellular and signaling networks linking the immune system and metabolism in disease. Nat. Med. 18, 363–374 (2012).
3) Halade, G. V. & Lee, D. H. Inflammation and resolution signaling in cardiac repair and heart failure. eBioMedicine 79, e2013374118 (2022).
4) Schiattarella, G. G. et al. Nitrosative stress drives heart failure with preserved ejection fraction. Nature 568, 351–356 (2019).
5) Dick, S. A. & Epelman, S. Chronic Heart Failure and Inflammation: What Do We Really Know? Circ. Res. 119, 159–176 (2016).
6) Koenig, A. L. et al. Single-cell transcriptomics reveals cell-type-specific diversification in human heart failure. Nat Cardiovasc Res 1, 263–280 (2022).
7) Wang, G. et al. Integrating genetics with single-cell multiomic measurements across disease states identifies mechanisms of beta cell dysfunction in type 2 diabetes. Nat. Genet. 1–11 (2023).
8) Obokata, M., Reddy, Y. N. V., Pislaru, S. V., Melenovsky, V. & Borlaug, B. A. Evidence Supporting the Existence of a Distinct Obese Phenotype of Heart Failure With Preserved Ejection Fraction. Circulation 136, 6–19 (2017).

Determination of cortisol as biomarker of stress in cardiovascular diseases in different matrices.

Maccari C. (1), Indrigo E. (2), Magnani G. (2), Niccoli G. (2), Corradi M. (1), Andreoli R. (1).

1) Laboratory of Industrial Toxicology and Advanced Analytical Methods, Department of Medicine & Surgery (DiMeC), University of Parma, Parma (Italy)
2) Division of Cardiology, University of Parma, Parma University Hospital, Parma (Italy)

Background Chronic stress could improve the susceptibility of the individual to developing diseases: in particular, several studies have shown that acute and chronic stress factors could increase the probability to have heart events, such as heart attack.
Cortisol is a steroid hormone commonly known as the "stress hormone". Like all steroid hormones, it is produced from cholesterol. The steps leading to its synthesis take place at the level of the adrenal glands under the control of the hypothalamic-pituitary-adrenal axis. The main factors involved in controlling cortisol secretion are negative feedback, stress-induced stimuli and circadian rhythm. Both rate of cortisol production and its hyper or hyposecretion show high intra- and inter-individual variability, are related to a physiological circadian rhythm and are influenced by environmental factors, psycho-physical stress and involve long-term physiological changes. Normally, cortisol levels were quantified in saliva, urine, or blood, to describe an extemporary, non-specific oxidative status [1].
Hence the interest in the use of cortisol as a biomarker for stress, which could be used as a prognostic marker for many diseases but also as a predictor and therefore applied in the prevention field.

Methods In literature, correlations between cardiovascular diseases and cortisol hypersecretion, measured in biological fluids such as urine, blood or saliva, are described but there are not enough evidences that its levels could be used as prognostic marker because its concentration in related to several factors including sampling time. To reduce the variability of the cortisol levels, hair was used as a matrix [2]. Use hair as a matrix allows to describe the total cortisol production for several weeks or months and it is thought that the amount of cortisol found in hair is proportional to the concentration of systemic cortisol.

Results Since the hair has a growth rate that generally stands around 1 cm/month, the concentration of a compound in a specific hair segment is closely related to the exposure/production suffered by the subject in the period corresponding to the hair growth under examination. For this reason, cortisol levels could be quantified in hair analysis and could be correlated with chronic stress [3].

Citations:

1) Gatti, R., Codemo, C., De Palo, E.F. Biochim. Clin., 34(20109, pp 591-599.
2) Gao, W., Stalder T., Foley, P., Rauh, M., Deng, H., Kirschbaum, C. J. Chromatogr. B. Analyt. Technol. Biomed. LifeSci, 928(2013), pp 1-8.
3) Mayer, S.E., Lopez-Duran, N.L., Sen, S., Abelson, J.L. Psychoneuroendocrinology; 92 (2018), pp 57–65.

Diffusion Tensor Imaging assessment of Pyramidal Pathways in the course of Syringomyelia in Cavalier King Charles Spaniel.

Rafalska J. (1), Wyleżoł O. (1), Tumula K. (1), Banasik A. (2), Wrzosek M. (2)

1) Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Wrocław (Poland)
2) Department of Internal Diseases with a Clinic for Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Wrocław (Poland)

Background The aim of this study was to assess pyramidal pathways damage in the course of syringomyelia using diffusion tensor imaging (DTI) sequence.

Methods Forty Cavalier King Charles Spaniel dogs were qualified for the research. The animals were divided into three groups based on the radiographic changes visible on MRI: dogs with syringomyelia (SM group, 16 dogs), dogs with central canal dilatation (CCD group, 9 dogs), and dogs without radiological symptoms (nonSM group, 15 dogs). All animals underwent the same study protocol that included a clinical and neurological examination followed by MRI examination. DTI was performed with a 1,5 Tesla magnetic resonance scanner (Philips, Ingenia). Two DTI parameters: fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were measured. Measurements of FA and ADC values were made by drawing regions of interest (ROIs) at the level of capsula interna (ROI-1), pyramidal tract in ventral part of the pons (ROI-2), at the junction of medulla oblongata and spinal cord (ROI-3) and in the middle of C2 (ROI4). Image post-processing was done using the Fiber Track package (Philips Ingenia workstation).

Results Statistical analysis showed significant differences in DTI parameters between the nonSM and SM group in FA values in ROI-3 (p=0,0057) and ROI-4 (p=0,0024), also in ADC values in ROI-4 (p=0,02), as well as CCD and SM group in FA values in ROI-3 (p=0,034) and ROI-4 (p=0,0032) also in ADC values in ROI-4 (p=0,02). Findings suggest that the most severe damage to pyramidal pathways in the course of SM occurs at the level of ROI-3 and ROI-4. DTI values measurements may provide more objective spinal cord microstructure.
The lack of differences between the groups in the DTI values in ROI-1 and ROI-2 may suggest that at this level there is no microstructural damage to the piramidal pathways in the course of CM-SM syndrome. At the level of ROI-1 the results could have been influenced by the presence of dilatation and asymmetry of the lateral ventricles in all groups. In the future, we plan to correlate these results with the results obtained in animals without CM-SM syndrome.

Conclusion The results show a significant difference in the DTI parameters in ROI-3 and ROI-4 in the SM group compared to the nonSM and CCD groups. In our opinion, that means that the spinal cord is microstructurally damaged at this level. DTI values measurements may provide more objective spinal cord microstructure.

Citations:

1) Rusbridge C, Greitz D, Iskandar BJ. Syringomyelia: Current Concepts in Pathogenesis, Diagnosis, and Treatment. Journal of Veterinary Internal Medicine (2006) 20:469–479. doi:10.1111/j.1939-1676.2006.tb02884.x
2) Le Bihan D, Mangin J-F, Poupon C, Clark CA, Pappata S, Molko N, Chabriat H. Diffusion tensor imaging: Concepts and applications. J Magn Reson Imaging (2001) 13:534–546. doi:10.1002/jmri.1076
3) Wada M, Hasegawa D, Hamamoto Y, Yu Y, Asada R, Fujiwara-Igarashi A, Fujita M. Comparison of Canine and Feline Meningiomas Using the Apparent Diffusion Coefficient and Fractional Anisotropy. Front Vet Sci (2021) 7:614026. doi:10.3389/fvets.2020.614026
4) Hatem SM, Attal N, Ducreux D, Gautron M, Parker F, Plaghki L, Bouhassira D. Assessment of spinal somatosensory systems with diffusion tensor imaging in syringomyelia. J Neurol Neurosurg Psychiatry. 2009 Dec;80(12):1350-6. doi: 10.1136/jnnp.2008.167858. Epub 2009 Jun 16. PMID: 19535353.
5) Chambers JK, Uchida K, Nakayama H. White matter myelin loss in the brains of aged dogs. Experimental Gerontology (2012) 47:263–269. doi:10.1016/j.exger.2011.12.003

Enhancing the antioxidant activity of alginic acid extracted from Sargassum angustifolium brown algae based on optimizing the extraction.

Kolahdoozan M. (1), Yegdaneh A. (2), Mousavi S.E. (3), Hatamipour M.S. (3)

1) Student Research Committee, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan (Iran)
2) Department of Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan (Iran)
3) Chemical Engineering Department, Faculty of Engineering, University of Isfahan, Isfahan (Iran)

Background An imbalance between the synthesis of reactive oxygen species (ROS) in cells and tissues and the capacity of biological systems to detoxify these reactive products results in a phenomenon known as oxidative stress, which may lead to lifelong diseases. Researchers are always looking for chemicals with antioxidant properties. One of the most significant algal families is Sargassaceae which includes many active compounds. The cell-wall polysaccharide of this brown algae is alginic acid. In order to use this polysaccharide and investigate on its various effects, it must first be isolated from brown algae and the operational parameters of extraction need to be optimized to reach the maximum antioxidant effect.

Methods Algal samples were collected on 2020's winter from Lian Park of Bushehr (Latitude and longitude of28.86◦and50.85◦). The isolation of alginic acid from algae consists of four main steps: preparation, extraction of alginic acid from algae, purification, and determination of yield and structural characterization. The operating parameters of this separation are temperature, time, and the use of new technologies and green extraction methods, such as the use of ultrasound waves during extraction. The effects of changing the parameters (temperature, time, and power of ultrasonic waves) used in the extraction of alginic acid were discussed based on changes in the antioxidant effect. After the separation of alginic acid from brown algae, the extraction efficiency was first calculated, its M/G was measured using 1H NMR spectra, and the antioxidant activity of the extracted alginic acid was examined using the DPPH method.

Results The highest antioxidant effect were observed in sample No.4 with an extraction temperature of 65 °C, extraction duration of 25 min, and 640W of ultrasonication power, whereas the lowest antioxidant effect were observed in sample No.7 at an extraction temperature of 45 °C, extraction duration of 20 min, and 480W ultrasonication power.

Conclusion Increasing the temperature in the range of 35–55°C decreased antioxidant activity. This may be because, at low temperatures, alginic acid blocks with a higher activity level are dissolved in the solvent. However, structural changes due to increasing temperature may cause less activity, whereas the optimum temperature is 65°C, and further investigation is needed to determine the reason. There is no direct relationship between M/G and IC50, and it should be examined along with molecular weight. Increasing the intensity of the waves increased antioxidant activity. Time is not directly and

independently decisive, but an increase in time changes the interaction of other parameters, and the final result changes. Extraction yield can be increased via increasing A/W. It appears that extraction under optimum conditions enhanced the MM block epimer, which may lead to an increase in antioxidant activity.

Citations:

1) Vladkova T, Georgieva N, Staneva A, Gospodinova D. Recent Progress in Antioxidant Active Substances from Marine Biota. Antioxidants. 2022 Feb 22;11(3):439.
2) Wei Q, Zhang YH. Ultrasound-assisted polysaccharide extraction from Cercis chinensis and properites, antioxidant activity of polysaccharide. Ultrason Sonochem. 2023 Apr 29;96:106422.
3) Rizfa MS, Yudiati E, Wijayanti DP. Improving The Antioxidant Activity of Sodium Alginate from Sargassum sp. by Thermal Heating and Chemical Methods. Jurnal Kelautan Tropis. 2020 Nov 14;23(3):284–90.

Evaluation of effectiveness of radioiodine treatment in patients with non-toxic nodular goitre after five years.

Obrycka M (1), Piszcz W. (1), Zawadzka A. (1).
1) Nuclear Medicine Department, Medical University of Bialystok, Bialystok (Poland)

Background Non-toxic nodular goiter is thyroid gland enlargement without disturbance in the hormone function. Over time, however, an asymmetrically enlarged thyroid gland begins to attract patients' attention and cause mental discomfort. Due to the greater self-awareness regarding prevention, goiters are detected more and more often in routine USG examination, but there are no clear recommendations regarding therapy. Studies show insufficient effectiveness of levothyroxine treatment, and surgery is an issue to be discussed. Due to the danger caused by the symptoms of untreated goiter (pressure on adjacent tissues and malignancy) and the need to find the best treatment method, the aim of our study was to evaluate the long-term effectiveness of radioiodine treatment (RIT) in patients with non-toxic goiter.

Methods The study involved 264 patients in euthyreosis aged 18-79, 88% women, 12% men, with a thyroid volume of 46-172 ml, RAIU between 22-44%. Qualifications were based on normal levels of serum fT3, fT4, TSH and characteristic appearance on thyroid scans and ultrasound. Malignant changes were excluded in all nodules by fine needle aspiration biopsy. The activity dose was calculated by Marinelli's formula and ranged between 200-800 MBq. The absorbed dose ranged between 150 and 260 Gy, and was proportional to thyroid volume. Thyroid ultrasonography, and thyroid scan with RAIU at 24 and 48-hours was done before, after 6, 12 months and yearly for the next four years of radioiodine therapy. Follow up control for the evaluation of fT3, fT4, TSH was done every 6 weeks in the first year. Then every 6 months for four years.

Results After 5 years of radioiodine treatment, the average thyroid volume decreased by 51%, euthyroidism was preserved in 89% of patients. All patients were satisfied with the reduction in the visibility of the thyroid gland and the disappearance of symptoms such as cough, shortness of breath and swallowing disorders.

Conclusion Radioiodine treatment is non-invasive, safe and cost effective method of therapy for reduction of large non-toxic goiter and should not be restricted to elderly patients, or ones with high operative risk. Moreover, patients should be informed during the examination about the possibility of non-invasive treatment that can prevent malignancy and ensure both psychological and aesthetic comfort for the patient.

Citations:

1) Cerci C, Cerci SS, Eroglu E, Dede M, Kapucuoglu N, Yildiz M, Bulbul M. Thyroid cancer in toxic and non-toxic multinodular goiter. Journal of Postgraduate Medicine. 2007 Jul-Sep; 53(3): 157-60.

2) Fard-Esfahani A, Emami-Ardekani A, Fallahi B, Fard-Esfahani P, Beiki D, Hassanzadeh-Rad A, Eftekhari M. Adverse effects of radioactive iodine-131 treatment for differentiated thyroid carcinoma. Nuclear Medicine Communications. 2014 Aug; 35(8): 808-17.
3) Hammes J, van Heek L, Hohberg M, Reifegerst M, Stockter S, Dietlein M, Kobe C. Impact of different approaches to calculation of treatment activities on achieved doses in radioiodine therapy of benign thyroid diseases. EJNMMI physics, 2018; 5(1), 1-10.
4) Knobel M. Etiopathology, clinical features, and treatment of diffuse and multinodular nontoxic goiters. Journal of Endocrinological Investigation. 2016 Apr; 39(4): 357-73.
5) Rochau U, Qerimi Rushaj V, Schaffner M, Schönhensch M, Stojkov I, Jahn B, Hubalewska-Dydejczyk A, Erlund I, Thuesen BH, Zimmermann M, Moreno-Reyes R, Lazarus JH, Völzke H, Siebert U. Decision-Analytic Modeling Studies in Prevention and Treatment of Iodine Deficiency and Thyroid Disorders: A Systematic Overview. Thyroid. 2020 May; 30(5): 746-58.
6) Wyszomirska A. Iodine-131 for therapy of thyroid diseases. Physical and biological basis. Nuclear Medicine Review. 2012 Aug 28; 15(2): 120-3.
7) Yildirim Simsir I, Cetinkalp S, Kabalak T. Review of Factors Contributing to Nodular Goiter and Thyroid Carcinoma. Medical Principles and Practice. 2020; 29(1): 1-5.
8) Zheng R, Rios-Diaz AJ, Thibault DP, Crispo JAG, Willis AW, Willis AI. A contemporary analysis of goiters undergoing surgery in the United States. The American Journal of Surgery. 2020 Aug; 220(2): 341-8.

Exploring blood immune cell dynamics to untangle the immunomodulatory effect of radiotherapy in advanced Non-Small Cell Lung Cancer (NSCLC) patients undergoing Immune Checkpoint Inhibitors as first line treatment.

Tamarozzi P. (1), Mazzaschi G. (1), Lorusso B. (2), Verzè M. (1), Pluchino M. (1), Trentini F. (1), Dalla Valle B. (1), Minari R. (1), Perrone F. (1), Bordi P. (1), Leonetti A. (1), Moron Dalla Tor L. (1), Leo L. (1), Milanese G. (3), Balbi M. (3), Buti S. (1), Roti G. (4), Quaini F. (4), Sverzellati N. (3), Tiseo M. (1).

1) Medicine and Surgery, Medical Oncology Unit, University Hospital of Parma, Parma (Italy)
2) Medicine and Surgery, Pathology Unit, University Hospital of Parma, Parma (Italy)
3) Medicine and Surgery, Radiological Science, University Hospital of Parma, Parma (Italy)
4) Medicine and Surgery, Hematology Unit, University Hospital of Parma, Parma (Italy)

Background The role of radiotherapy (RT) in immunotherapy-based (IO) combinatory approaches to advanced NSCLC is still debated, partly due to its dual immune -suppressive and -stimulatory effect. Thus, we performed a longitudinal peripheral blood (PB) analysis to determine the role of radiotherapy (RT) in patients with advanced NSCLC undergoing first-line immune checkpoint inhibitors (ICIs), focusing on the immunological asset and clinical outcomes. The aim of this study is to deepen our understanding on which might be the impact radiotherapy, delivered before or during ICIs, has on patient outcome, by assessing immune status variations following RT and ICI-based treatment.

Methods PB samples were prospectively collected at baseline (T0) and first disease assessment (T1) in patients undergoing Ist line IO-based regimens alone (RTnull) or combined with RT (RTpre, within 4 weeks before ICIs; RTpost, during IO). Flow cytometric analysis included CD3, CD8, CD4, NK, NKT, CD19, CD14 and Treg cells, expression of functional molecules (PD1, Granzyme B [GZB], Perforin [Perf]) and proliferative index (Ki67). PB parameters and their delta variation ([T1-T0/T0] * 100) were correlated with RT administration, while Objective Response Rate (ORR) and Progression-free survival (PFS) were estimated according to the Kaplan Meier method. In accordance with RECIST 1.1 criteria we considered ORR and Disease Control Rate (DCR) as DCR modified: patients with Complete Response (CR), Partial Response (PR) or Stable Disease (SD) for at least 6 months were considered in Clinical Benefit (CB) group, while patients with Progression Disease (PD) and less than 6 months disease stability were included in Non-Responder (NR) group.

Results Among 57 patients, 22 underwent RT either before (RTpre, 32%) or during (RTpost, 68%) ICIs. RT doses ranged from 8 to 54 Gy according to various sites of involvement. No significant differences in ICIs response and survival emerged between RT and RTnull cases. Compared to RTnull, baseline RTpre immune profiles exhibited increased % of CD8, CD19, CD14 and NK cells expressing PD1, reduced CD4+GZB/Perf+ and Tregs. Delta variation revealed that RTpre attenuated the downregulation of PD1 in CD8, CD4 and CD19 cells following ICIs, and favored the circulating release of GZB/Perf+ CD8 and CD4. RTpost reduced CD8 number, proliferation and PD1

expression, while increasing NKT. To explore which lymphocyte populations were mostly affected by RT-induced lymphopenia, we analysed FACS (Fluorescence Activated Cell Sorting Analysis) data of patients who underwent RT before T0 FACS and we interestingly found that the potential lymphopenic effect of RT could be mostly directed against immunosuppressive T cell population, while preserving or even increasing the pool of available PD-1+ Tcells, thereby inducing a higher response to ICIs. We observed a clear trend towards prolonged PFS in RTpre group (median PFS: RTpre= not reached, RTpost= 7.1 mos, RTnull= 5.9 mos) and slightly increased ORR, hinting that the positive cytotoxic (CD8+GZB/Perf+, NK) to suppressive (Tregs) balance triggered by RTpre may result in greater benefit from IO. We investigated indeed the dynamic changes in circulating immune profile and we observed a significantly higher ratio effector/suppressor T cells in patients undergoing RT before ICIs compared to no RT and RT during ICIs cases, likely suggesting a sort of RT preconditioning that favoured a positive effector/suppressor balance following ICI.

Conclusions Our preliminary results suggest the positive imprinting of radiotherapy in patients with advanced NSCLC undergoing first-line ICIs. This evidence might be explained by the different radiotherapy effects on the various cellular subsets involved in the immune response against the tumor. RT timing may impact on clinical outcome of IO-treated NSCLC by shaping immune cells phenotypes and dynamics.

Citations:

1) Mazzaschi, G. et al. Soluble PD-L1 and Circulating CD8+PD-1+ and NK Cells Enclose a Prognostic and Predictive Immune Effector Score in Immunotherapy Treated NSCLC patients. Lung Cancer 148, 1–11 (2020).
2) Cho Y, Park S, Byun HK, Lee CG, Cho J, Hong MH, Kim HR, Cho BC, Kim S, Park J, Yoon HI, Impact of Treatment-Related Lymphopenia on Immunotherapy for Advanced NonSmall Cell Lung Cancer, International Journal of Radiation Oncology • Biology • Physics (2019), doi: https://doi.org/10.1016/j.ijrobp.2019.08.047.
3) Chen, D., Patel, R.R., Verma, V., Ramapriyan, R., Barsoumian, H.B., Cortez, M.A., Welsh, J.W., Interaction between lymphopenia, radiotherapy technique, dosimetry, and survival outcomes in lung cancer patients receiving combined immunotherapy and radiotherapy, Radiotherapy and Oncology (2020), doi: https://doi.org/10.1016/j.radonc.2020.05.051

Hemorrhagic complications after microsurgical treatment for intracranial aneurysms under acetylsalicylic acid: an impact analysis.

Artemyev A. (1), Konovalov A., Grebenev F., Gadzhiagaev V., Pilipenko Y., Okishev D., Manushkova A., Lubnin A., Eliava S.

1) First Moscow State Medical University (MSMU), officially I.M. Sechenov First Moscow State Medical University, Moscow (Russian Federation)

Background According to some studies, the use of ASA in patients undergoing emergency neurosurgical interventions for ruptured aneurysms did not affect intraoperative blood loss or the risk of hemorrhagic complications. Patients with intracranial aneurysms often have comorbidities that require them to take an ASA. In recent years, many patients with aneurysms have been prescribed ASA to prevent aneurysm enlargement. ASA is prescribed to patients with intracranial aneurysms in preparation for surgery using revascularization.

Methods From 2016 to 2021, 64 patients underwent microsurgical aneurysm clipping without revascularization and revascularization group included 20 patients who underwent EC-IC bypass. The following parameters were analysed: the frequency of hemorrhagic complications, the blood loss volume, the duration of surgery and inpatient treatment, the dynamics of hemoglobin (Hb), hematocrit (Ht), erythrocytes, and clinical outcomes according to the modified Rankin scale (mRS).

Results At the time of surgery, the laboratory-confirmed effect of the ASA was registered in 22 patients (main group), and in 42 patients, the ASA did not function (control group). Hemorrhagic complications were noted in two patients in the ASA group. In both cases, the hemorrhagic component did not exceed 15 ml in volume and did not require additional surgical interventions. Statistical analysis showed no significant differences in hemorrhagic postoperative complications.

Conclusions Taking low doses of acetylsalicylic acid during planned microsurgical clipping of cerebral aneurysms does not affect intraoperative blood loss volume, risk of postoperative hemorrhagic complications, length of stay in the hospital, or functional outcomes.

Citations:

1) Altman R, Luciardi HL, Muntaner J, Herrera RN. The antithrombotic profile of aspirin. Aspirin resistance, or simply failure? Thromb J 2004; 2:1–8.
2) Brott TG, Halperin JL, Abbara S, Bacharach JM, Barr JD, Bush RL, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. A report of the American College of Cardiology Foundation/American Hear. Circulation 2011; 124:489–532.

3) Can A, Rudy RF, Castro VM, Yu S, Dligach D, Finan S, et al. Association between aspirin dose and subarachnoid hemorrhage from saccular aneurysms: A case–control study. Neurology 2018; 91:E1175–81.
4) Chalouhi N, Ali MS, Jabbour PM, Tjoumakaris SI, Gonzalez LF, Rosenwasser RH, et al. Biology of intracranial aneurysms: role of inflammation. J Cereb blood flow Metab Off J Int Soc Cereb Blood Flow Metab 2012; 32:1659–76.
5) Dalal KS, Bridgeman MB. Cardiovascular drugs. Nursing (Lond) 2017; 47:63.
6) Devereaux PJ, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, et al. Aspirin in Patients Undergoing Noncardiac Surgery. N Engl J Med 2014; 370:1494–503.
7) Gaziano JM, Brotons C, Coppolecchia R, Cricelli C, Darius H, Gorelick PB, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomized, double blind, placebo-controlled trial. Lancet (London, England) 2018; 392:1036–46.
8) Gerstein NS, Schulman PM, Gerstein WH, Petersen TR, Tawil I. Should more patients continue aspirin therapy perioperatively?: Clinical impact of aspirin withdrawal syndrome. Ann Surg 2012; 255:811–9.
9) Gross BA, Rosalind Lai PM, Frerichs KU, Du R. Aspirin and aneurysmal subarachnoid hemorrhage. World Neurosurg 2014; 82:1127–30.
10) Guo Y, Guo XM, Zhao K, Yang MF. Aspirin and growth, rupture of unruptured intracranial aneurysms: A systematic review and meta-analysis. Clin Neurol Neurosurg 2021; 209
11) Hanalioglu S, Sahin B, Sahin OS, Kozan A, Ucer M, Cikla U, et al. Effect of perioperative aspirin use on hemorrhagic complications in elective craniotomy for brain tumors: results of a single-center, retrospective cohort study. J Neurosurg 2019; 132:1529–38.
12) Hasan D, Hashimoto T, Kung D, Macdonald RL, Winn HR, Heistad D. Upregulation of cyclooxygenase-2 (COX-2) and microsomal prostaglandin E2 synthase-1 (mPGES-1) in wall of ruptured human cerebral aneurysms: preliminary results. Stroke 2012; 43:1964–7.
13) Hasan DM, Mahaney KB, Brown RD, Meissner I, Piepgras DG, Huston J, et al. Aspirin as a promising agent for decreasing incidence of cerebral aneurysm rupture. Stroke 2011; 42:3156–62.
14) Hudson JS, Hoyne DS, Hasan DM. Inflammation and human cerebral aneurysms: current and future treatment prospects. Future Neurol 2013; 815. Korinth MC. Low-dose aspirin before intracranial surgery - Results of a survey among neurosurgeons in Germany. Acta Neurochir (Wien) 2006; 148:1189–96.
15) Li M, Yang S, Liu Q, Guo R, Wu J, Cao Y, et al. Evaluating the safety of early surgery for ruptured intracranial aneurysms in patients with long-term aspirin use: a propensity score matching study. Chinese Neurosurg J 2020; 6
16) Madan GA, Madan SG, Madan G, Madan AD. Minor oral surgery without stopping daily low-dose aspirin therapy: a study of 51 patients. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg 2005; 63:1262–5.
17) Moster M, Bolliger D. Perioperative Guidelines on Antiplatelet and Anticoagulant Agents: 2022 Update. Curr Anesthesiol Rep 2022; 12:286–96.19. Nakamizo A, Michiwaki Y, Kawano Y, Amano T, Matsuo S, Fujioka Y, et al. Impact of antithrombotic treatment on clinical outcomes after craniotomy for unruptured intracranial aneurysm. Clin Neurol Neurosurg 2017; 161:93–7.
18) Oscarsson A, Gupta A, Fredrikson M, Järhult J, Nyström M, Pettersson E, et al. To continue or discontinue aspirin in the perioperative period: a randomized

Innovative biological graft implantation procedures in patients with an infected artificial graft – retrospective analysis.

Kruczek W. (1), Jelonek B. (1), Święszek A. (1)

1) Student Scientific Society, Department of General and Vascular Surgery, Angiology and Phlebology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice (Poland)

Background The development of grafts has revolutionized vascular surgery. One of the primary objectives in saving life and limbs during graft implantation is minimizing the incidence of recurrent infection. Prosthetic infection is an uncommon but severe complication in vascular surgery and is associated with a high mortality and morbidity rate. Biological grafts could be a promising advancement. The aim of our study was to evaluate the safety and efficacy of biological graft implantation and assess crucial re-operation causing risk factors.

Methods The data were retrospectively collected from patients' past medical records. Between 01.2020 and 12.2022, 12 patients underwent reoperation of infected prosthesis using biological graft. Postoperative outcomes - procedural success and complication rates were assessed during the hospital stay and the follow-up period. Long-term outcomes and improvement in patient quality of life were evaluated. Statistical analysis including chi-square test were conducted.

Results The median patients' age was 66,5 years (range, 56-77 years) with 66,7% men and 33,3% women. The comorbidities for infection including systemic infection, hypertension, hypercholesterolemia and smoking were determined as risk factors. 3 types of biological prothesis implantation were performed: femorofemoral crossover bypass, aortofemoral bypass and aortobifemoral bypass. Mean hospital length of stay was 21 days. The mean American Society of Anesthesiologists score for all patients was 3,6 ± 0,1. Statistical analysis including Kaplan–Meier estimator has shown that 3-month post operation period is crucial. A correlation between lower early survival rate and either lower BMI or higher glucose level has been observed. After a 18-month follow up, 33% of our patients with biological grafts survived. The follow up is still pending.

Conclusions Biointegral exhibited durability, elasticity and optimal adaptation of the graft to the patient's tissues. It could be an alternative in the absence of available native vessels. Vascular prosthesis infection is an infrequent but very difficult condition and it is still associated with a high mortality rate. Improving the safety and efficacy of biological grafts, identifying new ways to optimize their performance with awareness of risk factors is a main purpose in further research.

Interplay between Protein Kinase C-ε and Reactive Oxygen Species during Myogenic Differentiation

Cortellazzi S. (1), Pozzi G. (1), Presta V. (1), Masselli E. (1,2), Condello G. (1), Arcari M.L. (1), Micheloni C. (1), Vitale M. (1,2), Gobbi G. (1), Mirandola P. (1), Carubbi C. (1).

1) Anatomy Unit, Department of Medicine & Surgery (DiMeC), University of Parma, Parma (Italy)
2) University Hospital of Parma, Parma (Italy)

Background Reactive oxygen species (ROS) are currently recognized as a key driver of several physiological processes. Increasing evidence indicates that fluctuations of ROS levels can affect myogenic differentiation, but the molecular mechanisms still need to be elucidated [1-2]. Protein kinase C (PKC) epsilon (PKCe) promotes muscle stem cell differentiation and regeneration of skeletal muscle after injury [3]. Recent data describe a tissue-specific role of PKCs in redox biology, some isoforms represent both a target of ROS and an up-stream regulator of ROS production. Based on the observations that ROS and PKCe mutually affect their expression in non-skeletal muscle models [4-5], and that both are involved in myogenic differentiation, in this study, a redox-PKCe crosstalk via Nrf2-Superoxide Dismutase 2 (SOD2) has been unraveled.

Methods To study the PKC-redox axis, an in vitro model of a mouse myoblast cell line (C2C12) was used. In some experiments, knockdown of PKCe was obtained with specific shRNA and siRNA gene silencing. Furthermore, SOD2 immunostaining of formalin-fixed, paraffin-embedded samples of tibialis muscle from wild-type and PKCe-knockout mice was carried out. Intracellular ROS were detected with flow cytometry (FCM) and immunofluorescence (IF) analysis. To assess C2C12 differentiation process, myogenic regulatory factors (MRFs) gene expression analysis through RNA extraction and quantitative RT-PCR was performed. Analysis of PKCe, SOD2, Nrf2 and Myogenin protein was tested with western blot. Also, analysis of PKCe and SOD2 protein content was tested with immunofluorescence. To assess PKCe-SOD2 interaction, a PKCe-Nrf2 co-immunoprecipitation experiment was performed.

Results In this work it has been demonstrated that the transition from myoblast to myotube is typified by increased PKCe protein content and decreased ROS, suggesting that the antioxidant signaling activation is required to prevent ROS accumulation and allow cell differentiation. The expression of SOD2 is significantly higher in the late phases of myogenic differentiation, mimicking PKCe protein content. Furthermore, PKCe inhibition increases ROS and reduces SOD2 protein content while SOD2 silencing did not affect PKCe protein content, advising that the kinase could be an up-stream regulator of SOD2. To support this, it has found that in C2C12 cells, PKCe interacts with Nrf2, whose activation induces SOD2 transcription.

Conclusion Overall, these results indicate that PKCe is capable of activating the antioxidant signaling preventing ROS accumulation in a myotube, eventually promoting myogenic differentiation.

Citations:

1) Barbieri, E.; Sestili, P. Reactive Oxygen Species in Skeletal Muscle Signaling. J Signal Transduct. 2012;2012:982794.
2) Le Moal, E.; Pialoux, V.; Juban, G.; Groussard, C.; Zouhal, H.; Chazaud, B.; Mounier, R. Redox Control of Skeletal Muscle Regeneration. Antioxid Redox Signal. 2017 Aug 10;27(5):276-310.
3) Di Marcantonio, D.; Galli, D.; Carubbi, C.; Gobbi, G.; Queirolo, V.; Martini, S.; Merighi, S.; Vaccarezza, M.; Maffulli, N.; Sykes, S. M.; Vitale, M.; Mirandola, P. PKCε as a novel promoter of skeletal muscle differentiation and regeneration. Exp Cell Res. 2015 Nov 15;339(1):10-9.
4) Di Marcantonio, D.; Martinez, E.; Sidoli, S.; Vadaketh, J.; Nieborowska-Skorska, M.; Gupta, A.; Meadows, J. M.; Ferraro, F.; Masselli, E.; Challen, G. A.; Milsom, M. D.; Scholl, C.; Fröhling, S.; Balachandran, S.; Skorski, T.; Garcia, B. A.; Mirandola, P.; Gobbi, G.; Garzon, R.; Vitale, M. Protein Kinase c Epsilon Is a Key Regulator of Mitochondrial Redox Homeostasis in Acute Myeloid Leukemia. Clin Cancer Res. 2018 Feb 1;24(3):608-618.
5) Cosentino-Gomes, D.; Rocco-Machado, N.; Meyer-Fernandes, J. R. Cell Signaling through Protein Kinase c Oxidation and Activation. Int J Mol Sci. 2012;13(9):10697-10721.

Liquid biopsy and extracellular vesicles (EVs). A new horizon in the precision oncology landscape.

Gagliardi A. (1), Rigalli JP. (2), Weiss J. (2), Barocelli E.(1)

1) School of Specialization in Hospital Pharmacy, Department of Food and Drug Sciences, University of Parma, Parma (Italy)
2) Department of Clinical Pharmacology and Pharmacoepidemiology, UKHD, Heidelberg (Germany)

Background This research aimed at investigating the use of EVs as surrogates for the evaluation of ABC transporters expression in tumour cells. EVs are nanoparticles released by all cell types and contain, among others, ABC-transporters, the most relevant membrane efflux pumps involved in the regulation of drug bioavailability, disposition, therapeutic efficacy and toxicity [1]. In tumour cells, efflux transporter overexpression contributes to resistance to chemotherapy [2] and their quantification in EVs isolated through liquid biopsy could be exploited to predict their expression at cellular level. This could be a starting point for cancer therapy optimisation.

Methods MCF7 (breast cancer), HepG2 (hepatocellular carcinoma), HNO206 (oropharyngeal squamous cell carcinoma) and LS180 (colon adenocarcinoma) cells were used. The expression of ABC transporters was estimated in cell lines and derived-EVs after treatment with different drugs, known to regulate ABC transporters (rifampicin, hypericin, hyperforin, mitotane, enzalutamide and bosentan). EVs were isolated from culture supernatants through size exclusion chromatography. Confirmation of proper isolation was achieved by dynamic light scattering method (Zetasizer NanoZS device). The detection of three surrogate peptides allowed us to quantify the ABC transporters, P-gp, MRP2 and BCRP, in each sample by UPLC-MS/MS analysis (Xevo TQ-XS). One-way ANOVA test followed by Tukey was performed for statistical analysis. *$P<0.05$ was considered as statistically significant.

Results Firstly, rifampicin (48-hour incubation) significantly up-regulated the expression of BCRP in MCF7 cells (20 μM) and of P-gp in LS180 cells (5-20 μM) but not in EVs derived from MCF7/LS180 cells supernatants. At non-cytotoxic concentrations, rifampicin (5, 10 and 20 μM) and hypericin (0.01, 0.1 and 0.5 μM) down-regulated MRP2 in HepG2 cells. Only rifampicin, after longer incubation (72 hour), down-regulated MRP2 expression in HepG2 derived-EVs, leading to the establishment of an association between MRP2 expression in EVs and in the cells of origin.

Conclusions Our study provides the first preliminary evidence of consistent ABC transporter expression changes in a hepatocarcinoma cell line and the corresponding derived EVs after exposure to rifampicin. Further investigations are planned to optimize the experimental conditions extending the search to other cancer cell lines and compounds.

Citations:

1) Achour B, Al-Majdoub ZM, Grybos-Gajniak A, Lea K, Kilford P, Zhang M, Knight D, Barber J, Schageman J, Rostami- Hodjegan A. Liquid Biopsy Enables Quantification of the Abundance and Interindividual Variability of Hepatic Enzymes and Transporters. Clin Pharmacol Ther. 2021 Jan;109(1):222-232.
2) Holohan, C., Van Schaeybroeck, S., Longley, D. et al. Cancer drug resistance: an evolving paradigm. Nat Rev Cancer 13, 714–726 (2013).

Modern Concepts of the use of Meshes for Hernioplasty and Trends in their Development.

Tychina Y. (1)

1) Department of Faculty Surgery N°2, Sechenov University, First Moscow State Medical University, Moscow (Russian Federation)

Background Approximately 1 million meshes are used every year during operations [1]. According to the structure of the mesh, they are divided into three groups. First–generation meshes (from one biopolymer); second-generation meshes: composite (a combination of biopolymers or biopolymer with anti-adhesive molecules) and biological (decellularized tissues of farm animals, most often porceline) [2]. The Aim of Study. To establishing modern concepts of the use of meshes for hernioplasty and trends in their development.

Methods An analysis of the PubMed articles database was carried out for the key queries “hernia mesh biomaterials” and “synthetic and biological meshes” (timeline 2020-2023).

Results As of 2021, the number of first-generation commercial meshes in the USA was 16 from 7 manufacturers (Ethicon, B-Braun, Gore, Tricomed, Covidien, BARD, Medtronic). The number of composite meshes is 15 from 9 manufacturers (Ethicon, BARD, PFM, FEG Textiltechnik, Medtronic, Lotus, Genzyme, Atrium). The number of biological meshes on the US market is 4 from 3 manufacturers (Davol, Covidien, LifeCell) [2].
Polypropylene remains the main polymer for creating meshes; however, priority is given to the second generation – composite meshes. Titanium, chitosan, polyglycolide, hyaluronic acid, carboxymethylcellulose and collagen are the leaders among the modifying materials for reducing adhesion. The current trends on mesh modification are antibacterial activity and nanodiamod coating [3, 4].
Systematic reviews of comparative studies of the difference in the use of synthetic and biological meshes indicate the inconsistency of their results. More than 80% of studies have an imperfect design according to the IDEAL criteria and 75% of ROBINS-I studies identified a high risk of bias [5].

Conclusions Because of incorrect statistical processing and imperfect design of the study, the results of clinical studies comparing biological and synthetic meshes are ambiguous. This raises the question of the need for more high-quality clinical trials and systematic reviews. It is also relevant to increase the research activities in the field of mesh modifications to improve their biocompatibility and reduce the frequency of complications.

Citations:

1) Elango, S., Perumalsamy, S., Ramachandran, K., & Vadodaria, K. (2017). Mesh materials and hernia repair. BioMedicine, 7(3).
2) Turlakiewicz K, Puchalski M, Krucińska I, Sujka W. The Role of Mesh Implants in Surgical Treatment of Parastomal Hernia. Materials (Basel). 2021 Feb 24;14(5):1062. doi:

10.3390/ma14051062. Erratum in: Materials (Basel). 2021 Jun 24;14(13): PMID: 33668318; PMCID: PMC7956701.

3) Pérez-Köhler B, Linardi F, Pascual G, Bellón JM, Eglin D, Guillaume O. Efficacy of antimicrobial agents delivered to hernia meshes using an adaptable thermo-responsive hyaluronic acid-based coating. Hernia. 2020 Dec;24(6):1201-1210. doi: 10.1007/s10029-019-02096-3. Epub 2019 Nov 28. PMID: 31781966.
4) Houshyar S, Sarker A, Jadhav A, Kumar GS, Bhattacharyya A, Nayak R, Shanks RA, Saha T, Rifai A, Padhye R, Fox K. Polypropylene-nanodiamond composite for hernia mesh. Mater Sci Eng C Mater Biol Appl. 2020 Jun;111:110780. doi: 10.1016/j.msec.2020.110780. Epub 2020 Feb 26. PMID: 32279794.
5) Kamarajah SK, Smart NJ, Daniels IR, Pinkney TD, Harries RL. Bioabsorbable mesh use in midline abdominal wall prophylaxis and repair achieving fascial closure: a cross-sectional review of stage of innovation. Hernia. 2021 Feb;25(1):3-12. doi: 10.1007/s10029-020-02217-3. Epub 2020 May 24. PMID: 32449096; PMCID: PMC7867504.

Phenotypic and genotypic characterization of paediatric osteosarcoma patient-derived cell lines.

Divincenzo F. (1), Marini E. (1), Banche Niclot A.G.S. (1), Proto C.F. (2), Ferrero I. (2), Pinnetta G. (2), Tirtei E. (3), Dorin Asaftei S. (3), Cereda M. (4), Peirone S. (4), Fagioli F. (1,2), Mareschi K. (1,2)

1) Department of Public Health and Paediatrics, University of Turin, Turin (Italy)
2) Stem Cell Transplantation and Cellular Therapy Laboratory, Paediatric Onco-Haematology Division, Regina Margherita Children's Hospital, City of Health and Science of Turin, Turin (Italy)
3) Pediatric Oncology Department, Regina Margherita Children's Hospital, City of Health and Science of Turin, Turin (Italy)
4) Department of Biosciences, University of Milan, Italy & Italian Institute for Genomic Medicine, c/o IRCCS, Candiolo (Italy)

Background Osteosarcoma (OS) is the most frequent Bone Sarcoma that mainly affects the paediatric population. Prognosis remains poor when it metastasises in the lung, representing an unmet clinical need. The aim of this study is to produce in vitro patient-derived cell line models that would allow the discovery of new treatment strategies in a preclinical setting. [1]

Methods The tumour samples were obtained from biopsies of paediatric patients enrolled in the SAR-GEN_ITA trial (id: NCT04621201) [2]. The tumour fragments were enzymatically and mechanically homogenised. Cell suspensions were plated with Dulbecco Modified Eagle Medium + L-GLUT and Penicillin-Streptomycin (1%) + 10% of Human Platelet Lysate. The cells were first plated in 2D and subsequently in 3D conditions (Spheroids). The expression of stem and osteoblastic markers were compared, using Real-Time PCR, with a pool of bone marrow mesenchymal cells (healthy donors) in order to exclude any expansion of the stromal component. At the third step, the tumorigenicity test (Soft Agar Assay) was carried out. Furthermore, immunophenotypic (IP) analysis was done. To confirm the correspondence between the expanded cells and the primary tumour, Short Tandem Repeats analysis (STRs) and Whole Exome Sequencing (WES with NovaSeq6000, Illumina) were performed.

Results 30 OS fragments were used to set up primary cell lines. 8 cell lines grew in 2D until 10th step with a success rate of 27% and 3 of them also in 3D (38%). 2 of the latter formed clones in Soft Agar (67%). The phenotypic and genotypic profile was studied on a cell line derived from lung metastasis: an osteoblastic OS (ST-054). The IP of ST-054 showed high expression of CD105, 90, 73, 29 and 44. The Real-Time PCR analysis showed a higher expression of the genes Nanog, Oct-4, Sox-2 and RUNX2 in ST-054 compared to the mesenchymal control.
The match between primary tumour and ST-054 cell line was 97% and 85% respectively for somatic mutations and Copy Number Alterations. Also the fraction of neoplastic cells and the ploidy analysed showed a perfect match. Based on all these results ST-054 represents a patient-derived cell line with metastatic characteristics of OS primary tumour.

Conclusion The expansion and selection of this cell line represents a tool for studying tumour cells with a crucial role in progression and invasion. Combination of the IP and the genetic expression could be used to find new targets and therapeutic approaches for a personalised and effective therapy.

Citations:

1) Harris, M. A., & Hawkins, C. J. (2022). Recent and Ongoing Research into Metastatic Osteosarcoma Treatments. International Journal of Molecular Sciences, 23(7), 3817. https://doi.org/10.3390/ijms23073817
2) Genomic Profiles Analysis in Children, Adolescents and Young Adult With Sarcomas (SAR-GEN_ITA): a Multicenter Prospective Study

Presence of Ixodes ricinus and risk of Lyme Disease in city parks in Wrocław, Poland.

Baran J. (1), Al-Ameri S. (1), Będkowska D. (1), Ozierańska N. (1), Karwańska M. (2), Siedlecka M. (2), Miszczak M. (2), Pacoń J. (2), Bierowiec K. (2).

1) Faculty of Veterinary Medicine, Department of Epizootiology and Clinic of Birds and Exotic Animals, Students' Scientific Society EZA, Wrocław University of Environmental and Life Sciences, Wrocław (Poland)
2) Faculty of Veterinary Medicine, Department of Epizootiology and Clinic of Birds and Exotic Animals, Division of Infectious Diseases and Veterinary Administration & Division of Parasitology, Department of Internal Medicine and Clinic of Diseases of Horses, Dogs and Cats, Wrocław University of Environmental and Life Sciences, Wroclaw (Poland)

Background Ticks of the species Ixodes ricinus are common parasitic arachnids in Poland. They have a great importance as a reservoir and vector of pathogens such as Borrelia burgdorferi, which is the cause of Lyme disease in humans and animals. The aim of the study was to determine the habitat of I. ricinus and the frequency of the B. burgdorferi carriage among them.

Methods During the period from May to October 2022, a total of 236 I. ricinus ticks were collected in three of the largest and most frequently visited Wrocław city parks. During the next stage of the research, the presence of B. burgdorferi genetic material was detected using the real-time PCR method.

Results The research determined the B. burgdorferi prevalence of 38.30% (CI 95%; 28.47% - 48.13%) among the I. ricinus ticks. Prevalence of this pathogen was similar in different developmental forms with 37.84% (CI 95%; 22.21% - 53.47%) in nymphs, and 38.60% (CI 95%; 25.96% - 51.23%) in adult forms of the species. Occurrence of the ticks was seasonal, with the most of I.ricinus collected in the month of July (n=139).

Conclusions Research shows that a tick bite in a city park carries a real risk of B. burgdorferi infection in humans and animals. The research was co-financed by the Student Activity Fund (FAST 2022) of the Wrocław City Hall.

Citations:

1) Hansford KM, Wheeler BW, Tschirren B, Medlock JM. Questing Ixodes ricinus ticks and Borrelia spp. in urban green space across Europe: A review. Zoonoses Public Health. 2022 May;69(3):153-166. doi: 10.1111/zph.12913. Epub 2022 Feb 4. PMID: 35122422; PMCID: PMC9487987.
2) Rauter C, Hartung T. Prevalence of Borrelia burgdorferi sensu lato genospecies in Ixodes ricinus ticks in Europe: a metaanalysis. Appl Environ Microbiol. 2005 Nov;71(11):7203-16. doi: 10.1128/AEM.71.11.7203-7216.2005. PMID: 16269760; PMCID: PMC1287732.

Prospective study of Prostate Cancer detection with mpMR/US Fusion, Standard and Saturation biopsy.

Timofeeva E. (1), Bazarkin A. (1), Morozov A. (2), Taratkin M. (2), Ganzha T. (2), Danilov S. (2), Chernov Y. (2), Abdusalamovich A. (2), Amosov A. (2), Enikeev D. (2), Krupinov G. (2).

1) Institute for Clinical Medicine named after N.V. Sklifosovsky, Sechenov University, Moscow (Russian Federation)
2) Institute for Urology and Reproductive Health, Sechenov University, Moscow (Russian Federation)

Background Currently, about 80% of men with low-grade prostate cancer (ISUP 1) are underwent radical treatment. Overdiagnosis of low-grade cancer is associated with the use of systematic biopsy methods (standard transrectal, saturation). According to the European Association of Urology, patients with prostate cancer suspicion should have a multiparametric MRI before a biopsy. Indication for both primary and secondary MR-targeted biopsies is the presence of a suspicious lesion on mpMRI. The most common method of MR-targeted biopsy in clinical practice is mpMR/US fusion biopsy. There is contradictory data in recently published studies on detection rate of clinically significant prostate cancer with systematic and MR-targeted biopsies.

Methods Inclusion criteria were following: PSA>2 ng/mL and/or a positive DRE, and/or a suspicious lesion on TRUS, and PI-RADSv2.1 lesion ≥3. At first, the ""unblinded"" urologist performed a transperineal mpMR/US-fusion and saturation biopsy. Then the “blinded” urologist obtained transrectal standard biopsy. Clinically significant cancer was defined as ISUP ≥2.

Results We enrolled 96 patients. Median age was 63 years, prostate volume – 47 cm3 and PSA – 6.82 ng/mL. MpMR/US-fusion, saturation and standard biopsies were comparable in regard to the detection rate of clinically significant (21.0%, 19.0%, 16.0%; p=0.751), clinically insignificant cancer (15.0%, 19.0%, 17.0%; p=0.818) and overall detection rate (38.0%, 39.0%, 36.0%; p=0.385). The number of positive cores among mpMR/US fusion, saturation and standard biopsies was 33.0%, 10.0% and 13.0% respectively (p<0.01). At the same time, no statistically significant difference was found with respect to maximum cancer core length (6.4 mm, 6.35 mm, 5.1 mm, respectively; p=0.7).

Conclusions The detection rate of clinically significant, clinically insignificant and overall detection of prostate cancer is comparable when performing both systematic biopsy methods and mpMR/ultrasound fusion biopsy.

Citations:

A. A. Aizer et al., “Cost Implications and Complications of Overtreatment of Low-Risk Prostate Cancer in the United States,” J. Natl. Compr. Cancer Netw., vol. 13, no. 1, pp. 61–68, Jan. 2015, doi: 10.6004/JNCCN.2015.0009.

1) P. C. Albertsen, J. A. Hanley, and J. Fine, "20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer," JAMA, vol. 293, no. 17, pp. 2095–2101, May 2005, doi: 10.1001/JAMA.293.17.2095.
2) "European Association of Urology - Uroweb." https://uroweb.org/ (accessed Sep. 06, 2022).
3) G. Eure, D. Fanney, J. Lin, B. Wodlinger, and S. Ghai, "Comparison of conventional transrectal ultrasound, magnetic resonance imaging, and micro-ultrasound for visualizing prostate cancer in an active surveillance population: A feasibility study," Can. Urol. Assoc. J., vol. 13, no. 3, pp. E70–E77, Mar. 2019, doi: 10.5489/CUAJ.5361.
4) S. Loeb et al., "Overdiagnosis and overtreatment of prostate cancer," Eur. Urol., vol. 65, no. 6, pp. 1046–1055, 2014, doi: 10.1016/J.EURURO.2013.12.062.
5) F. M. E. Wagenlehner et al., "Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, a prospective multinational multicentre prostate biopsy study," Eur. Urol., vol. 63, no. 3, pp. 521–527, Mar. 2013, doi: 10.1016/J.EURURO.2012.06.003.
6) S. Loeb et al., "Systematic review of complications of prostate biopsy," Eur. Urol., vol. 64, no. 6, pp. 876–892, Dec. 2013, doi: 10.1016/J.EURURO.2013.05.049.
7) G. Ploussard et al., "Risk of repeat biopsy and prostate cancer detection after an initial extended negative biopsy: longitudinal follow-up from a prospective trial," BJU Int., vol. 111, no. 6, pp. 988–996, May 2013, doi: 10.1111/J.1464-410X.2012.11607.X.
8) S. A. Ahyai et al., "The presence of prostate cancer on saturation biopsy can be accurately predicted," BJU Int., vol. 105, no. 5, pp. 636–641, Mar. 2010, doi: 10.1111/J.1464-410X.2009.08744.X.
9) V. Scattoni, A. Zlotta, R. Montironi, C. Schulman, P. Rigatti, and F. Montorsi, "Extended and saturation prostatic biopsy in the diagnosis and characterisation of prostate cancer: a critical analysis of the literature," Eur. Urol., vol. 52, no. 5, pp. 1309–1322, Nov. 2007, doi: 10.1016/J.EURURO.2007.08.006.
10) P. Pepe and F. Aragona, "Morbidity after transperineal prostate biopsy in 3000 patients undergoing 12 vs 18 vs more than 24 needle cores," Urology, vol. 81, no. 6, pp. 1142–1146, Jun. 2013, doi: 10.1016/J.UROLOGY.2013.02.019.
11) V. Kasivisvanathan et al., "MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis," N. Engl. J. Med., vol. 378, no. 19, Mar. 2018, doi: 10.1056/NEJMOA1801993.
12) W. Baccaglini, F. P. A. Glina, C. L. Pazeto, W. M. Bernardo, and R. Sanchez-Salas, "mpMRI-targeted biopsy versus systematic biopsy for clinically significant prostate cancer diagnosis: a systematic review and metaanalysis," Curr. Opin. Urol., vol. 30, no. 5, pp. 711–719, Sep. 2020, doi: 10.1097/MOU.0000000000000801.
13) M. van der Leest et al., "Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study," Eur. Urol., vol. 75, no. 4, pp. 570–578, Apr. 2019, doi: 10.1016/J.EURURO.2018.11.023.
14) N. L. Hansen et al., "Multicentre evaluation of targeted and systematic biopsies using magnetic resonance and ultrasound image-fusion guided transperineal prostate biopsy in patients with a previous negative biopsy," BJU Int., vol. 120, no. 5, pp. 631–638, Nov. 2017, doi: 10.1111/BJU.13711.
15) M. Kroenig et al., "Diagnostic Accuracy of Robot-Guided, Software Based Transperineal MRI/TRUS Fusion Biopsy of the Prostate in a High Risk Population of Previously Biopsy Negative Men," Biomed Res. Int., vol. 2016, 2016, doi: 10.1155/2016/2384894.

Rotational atherectomy improves clinical outcomes of percutaneous coronary intervention (PCI) in comparison to only balloon-dilatable PCI.

Stefanov A. (1), Staferov A. (1).

1) First Moscow State Medical University, named after I.M. Sechenov, Moscow (Russian Federation)
2) Federal Research and Clinical Center Federal Medical-Biological Agency of Russia (Russian Federation)

Background Coronary artery disease (CAD) became a 21st century pandemic which causes deaths of approximately 9,5 million people worldwide annually. Advancements in cardiology allow physicians to treat CAD in minimally invasive way via percutaneous coronary intervention (PCI) with further implantation of drug-eluting stents (DES) , which doesn't require to make traumatically severe incisions and sternotomy. Nonetheless, severely calcifications often cause post procedural complications after PCI and worsens clinical outcomes. Recently new technique called "Rotational atherectomy" (RA) emerged, it allows to cut hard calcified plaques from the inside of the vessel, therefore theoretically improving the results. Our research is designed to prove that RA improves clinical outcomes of PCI.

Methods We examined clinical outcomes of 127 patients who underwent treatment from 2016 to 2022. Categorical variables were described as percentages and were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation or median unless otherwise specified and were compared using the t-test or Wilcoxon rank-sum test, as appropriate. A two-sided p value of 0.05 was considered statistically significant.

Results Two groups were formed depending on treatment strategy – only balloon-dilated PCI (62 patients) and RA-assisted PCI (65 patients). 82,3% and 80,0% of patients in both groups were men, mean age was 68,2±9,5 and 70,1±8,2 respectively. Duration of intervention was 78,6±18,5 and 55±14,5 minutes ($p<0,05$), on average 2,5±0,8 and 2,7±1,1 DES were implanted (p=NS), technical success was in 90,3% and 98,5% ($p<0,05$). Major adverse cardiac events (MACE) rate was 6,5% and 6,2% ($p<0,05$) in Group 1 and Group 2 respectively.

Conclusion The use of RA was associated with a higher rate of technical success and lower risk of MACE, shorter duration of intervention despite more complex lesion variants and, based on the findings, can be considered as the preferred initial strategy in patients with calcified native coronary artery lesions.

Shoulder-Neck Syndrome.

Bairamkulov A. (1), Tychina Y. (1), Kalinsky E. (1), Lychagin A. (1).

1) First Moscow State Medical University, named after I.M. Sechenov, Moscow (Russian Federation)

Background This abstract is to demonstrate shoulder-neck syndrome: definition, clinical evaluation, diagnostics, prevention and treatment.

Methods The study includes the analysis of 5 groups and controls (n~938): group #1 (n=938)—follow up (1 and 2 years) via VAS (Visual Analogue Scale), UCLA (University of California Los Angeles shoulder rating scale), SPADI (Shoulder Pain and Disability Index), DASH (Disability of the Arm, Shoulder and Hand Outcome Measure), NDI (Neck Disability Index), SF-36 (Short Form-36); group #2 (n=686)— clinical evaluation with physical stress-tests; group #3 (n~400)— postural spine radiography; group #4 (n=95)— robotic assessment of shoulder biomechanics ("CON-TREX"). Based on the results of this study, we developed a new treatment and rehabilitation protocol for patients with shoulder trauma: the ""shoulder"" block" and the ""neck"" block. Group #5 (n=41) was created to present the efficiency of this new protocol. It consist of patients that underwent new protocol in early post-traumatic / posop period: 3-4 weeks after conservative treatment / 4-6 weeks after surgical treatment.

Results We have found Shoulder-neck syndrome in 73% of patients. All patients that underwent the new treatment / prevention protocol demonstrated a significant improvement in UCLA, SPADI, DASH and NDI scales by the first year of follow up, as well as the reduction of the average pain score by 3 times and get a 14.4-point increase in SF-36 scale. The application of our new protocol leads to decreasing of c-spine disorders in 40% and combined disfunctions in 36.8% of cases. We didn't find any evidence of Shoulder-neck syndrome in 40.5% in group #5.
Thus, according to our findings, the Shoulder-neck syndrome should be defined as a combination of pain and dysfunction in the neck and shoulder, which affect each other in a single kinematic system.

Conclusion Thus, the close relationship of the shoulder and the cervical spine can be considered proven. The use of the new protocol has demonstrated the undeniable advantage in prevention and treatment of the Shoulder-neck syndrome and should be recommend for widespread use in clinical practise.

Citations:

1) The relationships between shoulder pain, range of motion, and disability in patients with shoulder dysfunction / S. Anwer, A.H. Alghadir, E.S. Al-Eisa, Z.A. Iqbal // Journal of Back and Musculoskeletal Rehabilitation. – 2018. – Vol. 31. – No 1. – P. 163–167.
2) The Responsiveness of Patient- Reported Outcome Tools in Shoulder Surgery Is Dependent on the Underlying Pathological Condition / R.Z. Unger, J.M. Burnham, L. Gammon [et al.] // The American Journal of Sports Medicine. – 2019. – Vol. 47. – No 1. – P. 241–247.

3) The Rotator Cuff and the Superior Capsule: Why We Need Both / C.R. Adams, A.M. DeMartino, G. Rego [et al.] // Arthroscopy: The Journal of Arthroscopic & Related Surgery: Official Publication of the Arthroscopy Association of North America and the International Arthroscopy Association. – 2016. – Vol. 32. – No 12. – P. 2628–2637.

State-of-the-art In Situ Laser Fenestration in the endovascular treatment of aortic arch pathologies using two types of aortic arch stent graft systems.

Wojtczak Z. (1), Maciąg R., Gałązka Z., Matsibora V., Sajdek M., Wretowski D., Leszczyński J., Stępkowski K., Januszewicz M., Rowiński O.

1) Medical University of Warsaw, Warsaw (Poland)

Background Laser in situ fenestration (LISF) is an innovative alternative for arch vessel revascularization in endovascular aortic arch repair. With low complication and mortality rate, it allows the management of various complex aortic pathologies including acute aortic syndromes. This study aimed to present early patient outcomes of endovascular arch repair combined with an emergent method of LISF performed in the foremost centre in Poland.

Methods From 2020 to 2023, 8 patients underwent aortic arch repair with LISF combined with aortic arch stentgraft systems (6 Nexus Endospan off-the shelf system, 2 COOK custom-made arch branch stentgrafts) in the 2nd Department of Clinical Radiology MUW. Vascular accesses (femoral artery, common carotid artery, superficial temporal artery, radial artery, subclavian artery, axillary artery) were appropriately selected for patients' anatomical conditions. The treatment was applied with two different stent graft systems and the Turbo-Elite laser atherectomy catheter 0,9-2,3 mm. Balloon expandable covered stents in combination with self-expandable nitinol stents were deployed. All patients were followed up regularly and imaging examinations were performed.

Results LISF was successful in all of the patients. Indications included chronic dissection(5), atherosclerotic aneurysm(3). There was 1 case with aortic kinking causing an issue with main module positioning(NEXUS system), which was resolved intraoperative. No patient developed major complications, such as strokes, transient ischemic attacks, spinal cord ischemia. During the 1-12 months follow-up 1 case of endoleak was detected(type I or III). Control angiography demonstrated false lumen thromboses, consecutive positive remodeling of the aorta, and patent in situ laser-fenestrated arteries.

Conclusions While LISF in aortic arch stentgrafts remains an off-label technique, it was shown to be an effective and promising state-of-the-art treatment option for urgent patients, patients unfit for open surgical repair, or with anatomical anomalies. However, long-term data remain scarce. Preoperative evaluation of the anatomy of intracranial arteries is essential.

Citations:

1) Planer D, Elbaz-Greener G, Mangialardi N, Lindsay T, D'Onofrio A, Schelzig H, Chaykovska L, Hill A, Holden A, Antonello M, Tan KT, Orrico M, Ronchey S, Marmur Y, Pecoraro F, Lachat M. NEXUS Arch: A Multicenter Study Evaluating the Initial Experience With a Novel Aortic Arch Stent Graft System. Ann Surg. 2023 Feb 1;277(2):e460-e466. doi: 10.1097/SLA.0000000000004843. Epub 2023 Jan 10. PMID: 33714965.

2) Kärkkäinen, Jussi & Tenorio, Emanuel & Jain, Akhilesh & Mendes, Bernardo & Macedo, Thanila & Pather, Keouna & Gloviczki, Peter & Oderich, Gustavo. (2020). Outcomes of target vessel endoleaks after fenestrated-branched endovascular aortic repair. Journal of Vascular Surgery. 72. 10.1016/j.jvs.2019.09.055.
3) Qin J, Zhao Z, Wang R, Ye K, Li W, Liu X, Liu G, Cui C, Shi H, Peng Z, Yuan F, Yang X, Lu M, Huang X, Jiang M, Wang X, Yin M, Lu X. In Situ Laser Fenestration Is a Feasible Method for Revascularization of Aortic Arch During Thoracic Endovascular Aortic Repair. J Am Heart Assoc. 2017 Apr 21;6(4):e004542. doi: 10.1161/JAHA.116.004542. PMID: 28432073; PMCID: PMC5532990.

The efficacy of Limosilactobacillus reuteri D-Lactate in modulating macrophage cell lipid metabolism in Non-Alcoholic Fatty Liver Disease (NAFLD).

Arella F. (1)
1) iMed Cell Function and Therapeutic Targeting, Faculty of Pharmacy, University of Lisbon

Background Non-alcoholic fatty liver disease (NAFLD) comprises a wide spectrum of liver alterations ranging from simple steatosis to hepatocellular carcinoma (1). Due to a westernized diet, NAFLD is becoming the most common chronic liver disease and its association with gut microbiota dysbiosis has been demonstrated (2). Changes to the microbiome can also cause gut inflammation explaining the important role of innate immunity and its cells (3). Nowadays, there is an increasing interest in the use of probiotics to alleviate NAFLD outcomes. The laboratory of Prof. André Fernando Anastácio dos Santos has recently shown that mice supplemented with the probiotic Limosilactobacillus reuteri (L. reuteri) were protected from liver disease, partially via D-lactate production (4). Given the ability of L. reuteri to modulate gut homeostasis and dysbiosis, impacting liver disease, we hypothesized that D-lactate metabolites may directly modulate macrophages to ameliorate NAFLD pathology.

Methods Firstly, we aimed to unveil the role of D-lactate in macrophage lipid metabolism and inflammation by exposing macrophages to sodium palmitate (PA) in the presence/absence of sodium D-Lactate. We next assessed mRNA levels of genes related to fatty acid uptake (Cd36), lipid biosynthesis (Dgat2 and Pparγ), and inflammation (IL-10 and Tgf-β).

Results The results showed that modulation with D-lactate reduced significantly mRNA expression levels of Pparγ, Cd36, and Dgat2. Our findings indicate that in the presence of a pro-inflammatory stimulus PA, D-lactate can restore mRNA levels of Tgf-β which could attenuate liver fibrosis and that Il-10 mRNA expression, was significantly higher compared with the control group. This led us to assume that, even with a pro-inflammatory stimulus, D-lactate exacerbated the expression of Il-10.
Further, we indagate the protein production in macrophages for DLDH, PPARγ, STAT3 and pSTAT3 by Western blot. In addition, a Nile Red assay demonstrated that D-lactate protected against lipid accumulation. Finally, we evaluated if D-lactate has the ability to modulate human monocyte-differentiated macrophages in ex vivo steatosis model by Flow cytometry. our finding revealed an initial distinction between monocyte-derived macrophages that were differentiated with M-CSF and those differentiated with GM-CSF. Curiously, we can observe in the population resulting from GM-CSF a significant decrease in CD80 and CD14 markers in the population treated with PA 125 µM and D-lactate 5 mM compared to the control D-lactate. Overall, we can distinguish two clear populations between the control and the MDM supplemented with D-lactate thus indicating that D-lactate can modulate the differentiation of monocytes even in the presence of a pro-inflammatory stimulus.

Conclusion In conclusion, understanding the metabolic pathways behind D-lactate modulation in macrophage response to lipid accumulation may unveil the role of L. reuteri in NAFLD improvement. We provide new insights into how microbiota-derived metabolites affect host metabolic homeostasis, focusing on the role of D-lactate in the regulation of liver metabolism while hinting at novel therapeutics.

Citations:

1) Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: Trends, predictions, risk factors and prevention. Nat. Rev. Gastroenterol. Hepatol. [Internet]. 2018;15:11–20. Available from: http://dx.doi.org/10.1038/nrgastro.2017.109
2) Ofosu A, Ramai D, Reddy M. Non-alcoholic fatty liver disease: Controlling an emerging epidemic, challenges, and future directions [Internet]. Ann. Gastroenterol. 2018;31:288–295. Available from: www.annalsgastro.gr
3) Kazankov, K., Jørgensen, S. M. D., Thomsen, K. L., Møller, H. J., Vilstrup, H., George, J., Schuppan, D., & Grønbæk, H. (2019). The role of macrophages in nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Nature Reviews Gastroenterology and Hepatology, 16(3), 145–159. https://doi.org/10.1038/s41575-018-0082-x
4) Santos AA, Afonso MB, Ramiro RS, Pires D, Pimentel M, Castro RE, et al. Host miRNA-21 promotes liver dysfunction by targeting small intestinal Lactobacillus in mice. Gut Microbes [Internet]. 2020;12:1–18. Available from: https://www.tandfonline.com/doi/abs/10.1080/19490976.2020.1840766

The role of miR-708 in NSCLC: expression level and target genes.

Rusu I.M. (1), Raduly L. (2), Zanoaga O. (2), Budisan L. (2), Harangus A. (3), Ciocan C. (2), Braicu C. (2), Simon M. (3), Borlea B. (1)

1. Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca (Romania)
2. The Research Center for Functional Genomics, Biomedicine and Translational Medicine - Iuliu Hateiganu University of Medicine and Pharmacy
3. Leon Daniello Pneumology Hospital, Cluj-Napoca (Romania)

Background Non-small cell lung cancer (NSCLC) comprises 85% of lung cancers. NSCLC has a high incidence and mortality. The present study aimed to investigate the role of miR-708-5p and analyze the relationship between target coding genes and their signalling pathways.

Methods To identify the expression level of the miR-708-5p, we collected tissue samples (tumor and nontumoral adjacent tissues - matched paired biological samples). All patients were diagnosed with NSCLC (lung adenocarcinoma and lung squamous cell carcinoma) in stages III and IV.

Results miR-708-5p was identified as overexpressed in an NSCLC patient cohort of 32 males. The present study has demonstrated the potentially critical role of miR-708 in regulating several key pathways (extracellular matrix-receptor interaction, adherence junctions and Hippo signaling) in the progression of NSCLC. Additional confirmation of the overexpression of miR-708-5p was done in the male patient cohort (from The Cancer Genome Atlas Program).

Conclusion miR-708-5p are promising candidates for further investigation in NSCLC, specifically in male patients. Understanding their specific roles, target genes, and clinical implications could lead to novel therapeutic strategies and improved patient management.

Citations:

1) Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49.
2) Monteleone NJ, Lutz CS. miR-708-5p: a microRNA with emerging roles in cancer. Oncotarget. 2017;8(41):71292-316
3) O'Brien J, Hayder H, Zayed Y, Peng C. Overview of MicroRNA Biogenesis, Mechanisms of Actions, and Circulation. Front Endocrinol (Lausanne). 2018 Aug 3
4) Jang JS, Jeon HS, Sun Z, Aubry MC, Tang H, Park CH, et al. Increased miR-708 expression in NSCLC and its association with poor survival in lung adenocarcinoma from never smokers. Clin Cancer Res. 2012;18(13):3658-67

The use of biofeedback training in treating depressive symptoms: a medical review.

Borlea B. (1), Armean S. (1), Rusu I.M. (1), Monea S. (1)

1) Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca (Romania)

Background Biofeedback (BF) is a self-regulation technique through which the patient learns to voluntarily control brain activity. It uses different imaging techniques, such as electroencephalogram (EEG), in which case it's called neurofeedback, functional magnetic resonance imaging (fMRI), but also heart-rate measuring devices, that are able to convert their respective stimuli into meaningful visual or auditory cues. A trained practitioner will then guide the therapy session. BF training is becoming increasingly popular, especially in cases where medication is contraindicated, or the patient is intolerant, as it has been shown that 10-30% of patients with major depression don't respond to antidepressant treatment. We decided to write this study to assess the efficiency of BF training in treating depressive symptoms.

Methods For assessing the efficiency of BF, we selected articles published between 2013-2023 in the PubMed database, based on a search strategy using the key terms (""Biofeedback, Psychology""[Mesh]) AND ""depression""[Mesh]. Out of 67 articles, we included only clinical trials and randomized controlled trials and we excluded articles not written in English. We calculated the power of the studies using G*Power. PRISMA guidelines were used for data synthesis and the bias risk was not evaluated.

Results We analyzed 10 articles, with a total of 491 participants. All 10 selected studies provided positive results, supporting the idea that BF may be an effective technique in treating depression, although one of the studies found no significant differences between BF and self-guided psychological strategies ($p>0.05$). It should be noted that most of the studies suffer from the same limitations: small sample sizes potentially leading to analysis bias, short follow-up periods, the lack of a placebo group and the lack of an objective assessment of depressive symptoms. We found that 9 out of the 10 studies were underpowered, 1- <0.80. There are also very few prior studies as BF is a relatively new concept, which seems to have been gaining popularity in the last few years, hitting a peak in 2021.

Conclusion Current studies seem to show that BF training is efficacious in the treatment of depressive symptoms, however, larger studies and more rigorous study designs are needed in order to confirm these results. Until then, BF may still provide a valuable alternative to current methods.

Citations:

1) Hou Y, Zhang S, Li N, Huang Z, Wang L, Wang Y. Neurofeedback training improves anxiety trait and depressive symptom in GAD. Brain Behav. 2021 Mar;11(3):e02024. doi: 10.1002/brb3.2024. Epub 2021 Jan 27. PMID: 33503332; PMCID: PMC7994677.

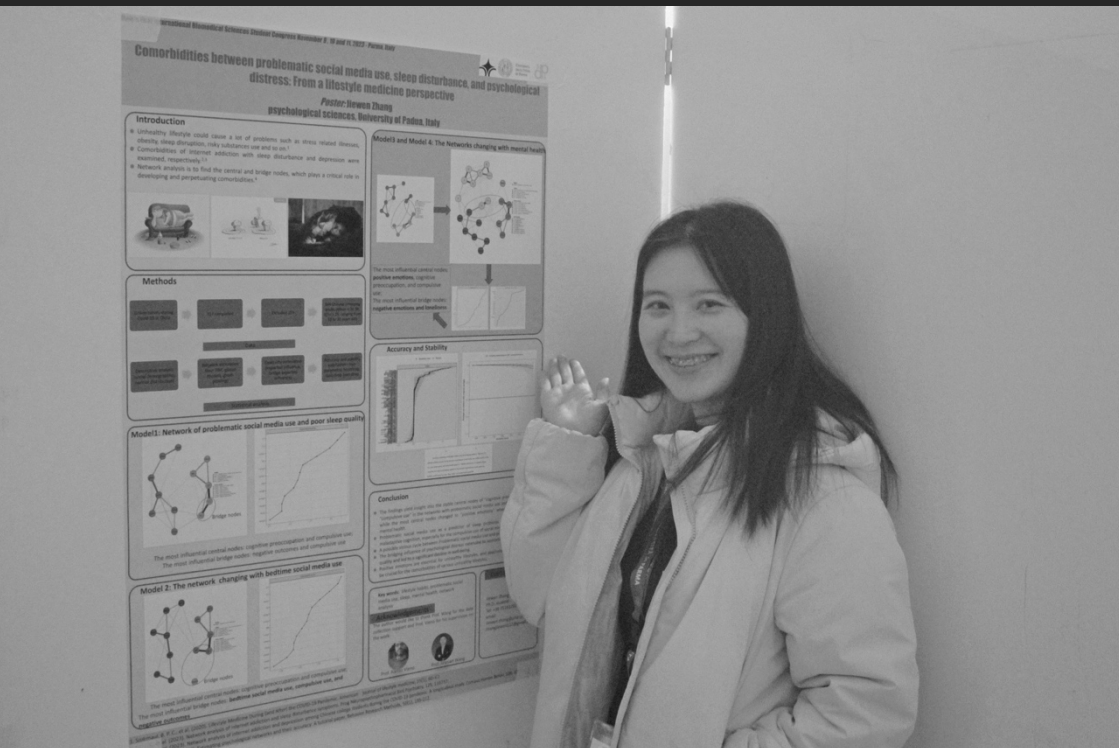
2) Choobforoushzadeh A, Neshat-Doost HT, Molavi H, Abedi MR. Effect of neurofeedback training on depression and fatigue in patients with multiple sclerosis. Appl Psychophysiol Biofeedback. 2015 Mar;40(1):1-8. doi: 10.1007/s10484-014-9267-4. PMID: 25362584.
3) Compère L, Siegle GJ, Riley E, Lazzaro S, Strege M, Pacoe E, Canovali G, Barb S, Huppert T, Young K. Enhanced efficacy of CBT following augmentation with amygdala rtfMRI neurofeedback in depression. J Affect Disord. 2023 Oct 15;339:495-501. doi: 10.1016/j.jad.2023.07.063. Epub 2023 Jul 16. PMID: 37459978; PMCID: PMC10530481.
4) Jaeckle T, Williams SCR, Barker GJ, Basilio R, Carr E, Goldsmith K, Colasanti A, Giampietro V, Cleare A, Young AH, Moll J, Zahn R. Self-blame in major depression: a randomised pilot trial comparing fMRI neurofeedback with self-guided psychological strategies. Psychol Med. 2023 May;53(7):2831-2841. doi: 10.1017/S0033291721004797. Epub 2021 Dec 2. PMID: 34852855; PMCID: PMC10235657
5) Guleken Z, Eskikurt G, Karamürsel S. Investigation of the effects of transcranial direct current stimulation and neurofeedback by continuous performance test. Neurosci Lett. 2020 Jan 18;716:134648. doi: 10.1016/j.neulet.2019.134648. Epub 2019 Nov 22. PMID: 31765731.
6) Tsuchiyagaito A, Misaki M, Kirlic N, Yu X, Sánchez SM, Cochran G, Stewart JL, Smith R, Fitzgerald KD, Rohan ML, Paulus MP, Guinjoan SM. Real-Time fMRI Functional Connectivity Neurofeedback Reducing Repetitive Negative Thinking in Depression: A Double-Blind, Randomized, Sham-Controlled Proof-of-Concept Trial. Psychother Psychosom. 2023;92(2):87-100. doi: 10.1159/000528377. Epub 2023 Jan 11. PMID: 36630946; PMCID: PMC10238612.
7) Maynart WHDC, Albuquerque MCDS, Santos RCS, Sarmento PA, Silva JJD, Costa CSG, Santos JDDS, Pontes CO, Barros MCDS, Belo FMP, Costa CRB, Cabral Júnior CR. The use of biofeedback intervention in the improvement of depression levels: a randomised trial. Acta Neuropsychiatr. 2021 Jun;33(3):126-133. doi: 10.1017/neu.2020.46. Epub 2021 Jan 11. PMID: 33427129.
8) Hsieh HF, Huang IC, Liu Y, Chen WL, Lee YW, Hsu HT. The Effects of Biofeedback Training and Smartphone-Delivered Biofeedback Training on Resilience, Occupational Stress, and Depressive Symptoms among Abused Psychiatric Nurses. Int J Environ Res Public Health. 2020 Apr 22;17(8):2905. doi: 10.3390/ijerph17082905. PMID: 32331460; PMCID: PMC7215829.
9) Yen CF, Chou WP, Hsu CY, Wu HC, Wang PW. Effects of heart rate variability biofeedback (HRVBFB) on sleep quality and depression among methamphetamine users. J Psychiatr Res. 2023 Jun;162:132-139. doi: 10.1016/j.jpsychires.2023.05.029. Epub 2023 May 2. PMID: 37149922.
10) van der Zwan JE, de Vente W, Huizink AC, Bögels SM, de Bruin EI. Physical activity, mindfulness meditation, or heart rate variability biofeedback for stress reduction: a randomized controlled trial. Appl Psychophysiol Biofeedback. 2015 Dec;40(4):257-68. doi: 10.1007/s10484-015-9293-x. PMID: 26111942; PMCID: PMC4648965.
11) Al-Harbi KS. Treatment-resistant depression: therapeutic trends, challenges, and future directions. Patient Prefer Adherence. 2012;6:369-88. doi: 10.2147/PPA.S29716. Epub 2012 May 1. PMID: 22654508; PMCID: PMC3363299."

POSTER SESSION

PRESENTERS

Andrea Graziani
Dorota Szydłowska
Jiewen Zhang
Anzor Bairamkulov
Milica Mladenovic
Renata Mangione
Silvia Mastromarino
Aleksei Staferov
Anna Incerti-Tinterri

POSTER SESSION WINNER: Jiewen Zhang



"BRAIN WALKING GREEN": A pilot study on a preventive protocol of combined physical activity and cognitive stimulation in a group of older adults coming from Marche.

Mastromarino S (1), Cipollari S. (2), Capponi L. (3)

1) University of Parma, Department of Medicine and Surgery (Italy)
2) IRCCS Santa Lucia, Rome (Italy)
3) University of Turin, Turin (Italy)

Background Today we live more, but not necessarily better. The percentage of elderly people in the general population increases year by year, and the importance of adopting a bio-psycho-social approach in both treatment and prevention is becoming significant in preventing neurodegenerative conditions to broaden the concept of well-being and considering health not as “absence of disease”, but as the quality of life experienced and perceived. The present work aims to test the efficacy of a preventive intervention protocol consisting in multiple sessions of combined cognitive stimulation and Nordic Walking training within a group of healthy elders coming from central Italy (Macerata, Marche). The program is called: “Brain Walking Green”, and it strives to improve cognitive performance, quality of life, physical wellness, satisfaction of the present living status and, in general, well-being.

Methods Subjects coming from the central Italy (Macerata, Marche) followed 90 minutes of intervention two times per week across a month. It consisted of 45 minutes of Nordic Walking training and 45 minutes of cognitive stimulation tasks. Pre and post-operative evaluations were carried out using 7 tools, aimed at evaluating general cognition, health and quality of life (QoL): 1) Addenbrooke’s Cognitive Examination (ACE-R); 2) Cognitive Reserve Index questionnaire (CRIq); 3) Free and Cued Selective Recall Reminding Test (FCSRT); 4) Geriatric Depression Scale (GDS); 5) World Health Organization Quality of Life Scale (WHOQOL-BREF); 6) Short Form Healthy Survey (SF-12); 7) Motivation for Change - Physical Activity (MAC2-AF). Physical state was assessed with the following tools: 1) Tinetti scale; 2) Conley scale; 3) 6-minutes’walk test, adapted for this study testing 1 minute only. The study included an inactive control group.

Results Cognitive outcomes resulted to be significantly modified by the intervention. Significant improvements were reported in general cognitive performance in the experimental group, while memory performance resulted to be improved in both experimental and control group. Post-training blood pressure values resulted significantly decreased only in the experimental group. No significant differences were detected in other secondary outcomes. Even if there were not reported significant differences between pre and post intervention, participants revealed themselves as more confident and engaged after the protocol. General mood, trust, and self-awareness raised at the end of the intervention.

Conclusion The study doesn't lack of limitations, principally due to the presence of an unbalanced small sample. Few significant results emerged on the protocol efficacy in this study. However, participating in multimodal interventions appeared to enhance the quality of life and the general motivation towards well-being and social engagement. Future research could include more participants, balancing gender, enlarge the total number of sessions, evaluate the role of individual differences, and test the effect of an active control group.

Citations:

1) Figueiredo, S., Finch, L., Mai, J., Ahmed, S., Huang, A., & Mayo, N. E. (2013). Nordic walking for geriatric rehabilitation: a randomized pilot trial. Disability and Rehabilitation, 35(12), 968-975. https://doi.org/10.3109/09638288.2012.717580
2) Cucinotta, D. (2007). Prevention of pathological aging by comprehensive clinical, functional, and biological assessment. Archives of Gerontology and Geriatrics, 44, 125-132. https://doi.org/10.1016/j.archger.2007.01.019
3) Morris, J. C., Cummings, J. (2005). Mild cognitive impairment (MCI) represents early-stage Alzheimer's disease. Journal of Alzheimer's Disease, 7(3), 235-239. https://doi.org/10.3233/JAD-2005-7306
4) Rikli, R. E., Jones, C. J. (1998). The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. Journal of Aging and Physical Activity, 6(4), 363-375. https://doi.org/10.1123/japa.6.4.363
5) Siciliano, M., Raimo, S., Tufano, D., Basile, G., Grossi, D., Santangelo, Trojano., F., Santangelo, G. (2016). The Addenbrooke's Cognitive Examination Revised (ACE-R) and its sub-scores: normative values in an Italian population sample. Neurological Sciences, 37(3), 385-392. https://doi.org/10.1007/s10072-015-2410-z

Investigation of the Epstein-Barr virus serological status in the adult population of Serbia.

Mladenovic M. (1), Knezevic A. (1)

1) Faculty of Medicine University of Belgrade, Institute of Microbiology and Immunology, Belgrade (Serbia)

Background Epstein-Barr virus (EBV) is a ubiquitous virus (1), with a seroprevalence >90% of the world population (2, 3). The virus establishes primary and then latent infection with occasional reactivation (1). Because of its oncogenic potential, there exists an association with numerous malignancies (e.g. Hodgkin lymphoma, etc.) (5). Data on the EBV seroprevalence in Serbia is scarce, hence the aim of this study is the investigation of the EBV serological status in the adult population by detecting specific antibodies against viral antigens.

Methods Serum samples of 58 individuals (age: 30.8±13.7 years; gender: M=41.4%, F=58.6%) were tested with commercial ELISA kits for the presence of four antibodies against EBV (anti-VCA-IgM, anti-VCA-IgG, anti-EA-IgG, anti-EBNA-IgG). Based on literature data, every patient was, depending on serology results, classified in an appropriate profile of EBV infection (primary, latent, reactivation) (6, 7). Statistical analysis was performed with Easy R software.

Results In the 89.5% serum samples, antibodies against EBV were detected, with increasing trend of seropositive patients with age: from 87% in population 18-30 years, to 100% in the elderly population. The significant difference was not found ($p>0.05$) in the number of EBV seropositive samples between genders nor between age groups. Indicator of primary infection is anti-VCA-IgM with or without positive anti-VCA-IgG and anti-EA-IgG (7). This profile matched 3.4% of the studied population as expected since examined population were healthy individuals (8). Markers of latent infection are anti-VCA-IgG and anti-EBNA-IgG antibodies, and this profile was found in 81% of samples, which correlates with knowledge that most infections with EBV occur in young adulthood (2, 9). Reactivated infection is characterized by positive anti-VCA-IgG and anti-EA-IgG (indicator of active virus replication) and was found in 3.4% samples (10). People with reactivated infection should be monitored for early detection of malignancies associated with EBV (11). Samples positive only on anti-EBNA-IgG were sorted in an unknown profile and were found in 1.7% of examinees. Most probably these people have latent infection (7).

Conclusion Since 89.5% of samples were seropositive, we conclude that the studied population has a high grade of EBV infection. Follow-up investigation is indicated in order to monitor the number of reactivated infections and malignancies associated with EBV.

Citations:

1) Sarwari NM, Khoury JD, Rojas Hernandez CM, Chronic Epstein Barr virus infection leading to classical Hodgkin lymphoma. BMC Hematology. 2016; 16:19
2) Smatti MK, Al-Sadeq DW, Ali NH, Pintus G, Abou-Saleh H, Nasrallah GK, Epstein-Barr Virus Epidemiology, Serology, and Genetic Variability of LMP-1 Oncogene Among Healthy Population: An Update. Frontiers in Oncology. 2018; Vol. 8, art. 211
3) Figuera-Silva CM, Pereira FE, Prevalence of Epstein-Barr virus antibodies in healthy children and adolescents in Vitoria, State of Espirito Santo, Brazil. Revista da Sociedade Brasileira de Medicina Tropical. 2004; 37(5):409-412
4) Odumade OA, Hogquist KA, Balfour HH, Progress and Problems in Understanding and Managing Primary Epstein-Barr Virus Infections. Clinical Microbiology Reviews. 2011; Vol. 24, No. 1, pp. 193-209
5) Tempera I, Lieberman P, Epigenetic regulation of EBV Persistence and Oncogenesis. Semin Cancer biol. 2014; 0:22-29
6) Brkic S, Jovanovic J, Preveden T, Vukobratov Z, Seroloski profil Epstein-Barr virusne infekcije u akutnoj infektivnoj mononukleozi. Med Pregl. 2003; LVI(1-2):7-16
7) Klutts JS, Ford BA, Perez NR, Gronowski AM, Evidence-Based Approach for Interpretation of Epstein-Barr Virus Serological Patterns. Journal of Clinical Microbiology. 2009; p.3204-3210
8) Smatti MK, Yassine HM, AbuOdeh R, AlMarawani A, Taleb SA, Althani A, et al. Prevalence and molecular profiling of Epstein Barr virus (EBV) among healthy blood donors from different nationalities in Qatar. PloS ONE. 2017; 12(12): e0189033
9) Abrahamyan S, Eberspaccher B, Hoshi M-M, Aly L, Luessi F, Groppa S et al. Complete EpsteinBarr virus seropositivity in a large cohort of patients with early multiple sclerosis. J Neurol Neurosurg Psychiatry. 2020; 91:681-686
10) Jiang Y, Zilioli S, Stowe R, Rubinstein R, Peek K, Cutchin M, Perceived social support and latent herpesvirus reactivation: Testing main and stress-buffering effects in an ethnically diverse sample od adults. Psychosom Med. 2021; 83(7):767-776
11) Sausen DG, Bhutta MD, Gallo ES, Dahari H, Borenstein R, Stress-Induced Epstein-Barr Virus Reactivation. Biomolecules. 2021; 11, 1380

Two faces of immunotherapy - severe hepatotoxicity and long-term response - in patients with advanced melanoma.

Szydłowska D. (1), Piątek M. (1)
1) University of Opole (Poland)

Background Immunotherapy (IT), by triggering an anti-tumor immune system response, can improve survivability of cancer patients. Unfortunately, its use can cause a variety of side effects, including immune-mediated hepatitis, also with a severe course.

Case history A 46-year-old man was diagnosed with cutaneous melanoma in 2019. After surgical treatment (excision of the lesion and surrounding lymph nodes), the stage was set at pT4bpN1acM0. Complementary IT with pembrolizumab was administered. Seven months after its completion, PET/CT scan showed focal lesions in the lungs and pancreas. EUS with pancreatic biopsy was performed and the presence of melanoma metastases confirmed. IT nivolumab+ipilimumab was implemented. After 3 doses, CTC grade G2 hyperthyroidism was noted, requiring pharmacotherapy. After the 4th dose, an increase in aminotransferases >500U/L (grade G3) was seen. A thick-needle biopsy of the liver revealed lesions consistent with autoimmune hepatitis. High-dose steroid therapy was implemented, with no improvement after 4 days. Mycophenolate mofetil was used as a second-line treatment with normalization of liver parameters after 4 weeks. IT was definitively terminated. Follow-up imaging studies showed a complete response, sustained for about a year now.

Conclusion IT is an innovative treatment, but it can cause life-threatening complications. Early recognition of side effects and prompt implementation of appropriate management is crucial. Even after treatment is discontinued, the patient may benefit in the long term, underscoring the value of IT in the treatment of cancer patients.

Summary We report a 46-year-old-man who presented with cutaneous melanoma. After anti-PD1 monoclonal antibody therapy, he failed to achieve full therapeutic success. The implementation of combination anti-PD1 and anti-CTLA4 immunotherapy, despite causing severe autoimmune hepatitis, resulted in long-term remission, highlighting the potential of this innovative treatment for cancer patients.

Citations:

1) Rutkowski P, Wysocki PJ, Nasierowska-Guttmejer A et al. Cutaneous melanoma — diagnostic and therapeutic guidelines in 2016. Oncol Clin Pract 2015; 11: 216–231;
2) Rutkowski P, Wysocki PJ, Nasierowska-Guttmejer A et al. Cutaneous melanomas. Oncol Clin Pract 2019; 15. DOI: 10.5603/OCP.2018.0055.

Comorbidities between problematic social media use, sleep disturbance, and psychological distress: From a lifestyle medicine perspective.

Zhang J. (1)

1) Dipartimento di Psicologia dello Sviluppo e della Socializzazione, University of Padua (Italy)

Background There has been a growing body of evidence pointing to the negative impacts of social media use, such as problematic social media use (PSMU), on healthy habits and mental health. However, the key individual symptoms contributing to these outcomes remain unclear from the perspective of network analysis. Thus, the present study aims to conceptualize the associations between PSMU, sleep disturbance, and well-being as interacting between nodes to identify the most influential central and bridge domains that come into play.

Methods The analysis included a total of 564 Chinese emerging adults (Mean = 24.59, SD = 3.25, ranging from 18 to 30 years old). Network analysis was employed by using EBICglasso model and examining expected influences within various associations: between PSMU and sleep disturbance, between PSMU, bedtime social media use (BSMU), and sleep disturbance, between PSMU and well-being, and among PSMU, BSMU, sleep disturbance, and well-being. Accuracy and stability measures were further calculated to ensure the robustness of the networks.

Results “Cognitive preoccupation” demonstrated a consistent central role in all the networks. Followed by the central symptom of “compulsive use” in the relationship between PSMU and sleep disturbance. While “positive emotions” took on a central role both between the networks of PSMU and well-being, and among PSMU, BSMU, sleep disturbance, and well-being.
Furthermore, the “negative outcomes” symptom of PSMU served as a bridging factor connecting PSMU and sleep disturbance communities. However, in this context, when BSMU was added, BSMU played the primary bridging role, and then “compulsive use” and “negative outcomes between PSMU, BSMU, and sleep disturbance.
Moving on, within the networks depicting the relationships with well-being, the well-being symptoms of “negative emotions” and “loneliness” played crucial bridging roles. They primarily exerted their influence through interactions with “negative outcomes”, “preference for online social interaction”, “positive emotions”, “health”, and “daytime dysfunction” acting as key touchpoints.

Conclusion Our study reveals a strong network connection among PSMU, BSMU, sleep disturbance, and well-being. The PSMU symptoms of “cognitive preoccupation” and ""positive emotions"" in well-being are pivotal, offering key targets for addressing maladaptive thinking and fostering positive emotions at the same time. We also emphasize the role of BSMU symptoms and compulsive social media use, contributing to sleep disturbance in problematic users. Addressing psychological distress, like negative

emotions and loneliness, is crucial to breaking the cycle between PSMU, BSMU, sleep issues, and lower well-being.

Citations:

1) Epskamp, S., Borsboom, D., & Fried, E. I. (2018). Estimating psychological networks and their accuracy: A tutorial paper. Behavior Research Methods, 50(1), 195-212. https://doi.org/10.3758/s13428-017-0862-1
2) Epskamp, S., Cramer, A. O., Waldorp, L. J., Schmittmann, V. D., & Borsboom, D. (2012). qgraph: Network visualizations of relationships in psychometric data. Journal of Statistical Software, 48, 1-18. https://doi.org/10.18637/jss.v048.i04
3) Zhang, J., Marino, C., Canale, N., Charrier, L., Lazzeri, G., Nardone, P., & Vieno, A. (2022). The Effect of Problematic Social Media Use on Happiness among Adolescents: The Mediating Role of Lifestyle Habits. International Journal of Environmental Research and Public Health, 19(5), 2576. https://doi.org/10.3390/ijerph19052576
4) Zhao, Y., Qu, D., Chen, S., & Chi, X. (2023). Network analysis of internet addiction and depression among Chinese college students during the COVID-19 pandemic: A longitudinal study. Comput Human Behav, 138, 107424.
5) Lu, J. X., Zhai, Y. J., Chen, J., Zhang, Q. H., Chen, T. Z., Lu, C. L., Jiang, Z. L., Guo, L., & Zheng, H. (2023). Network analysis of internet addiction and sleep disturbance symptoms. Prog Neuropsychopharmacol Biol Psychiatry, 125, 110737. https://doi.org/10.1016/j.pnpbp.2023.110737
6) Zhang, J., Marci, T., Marino, C., Canale, N., Vieno, A., Wang, J., & Chen, X. (2023). Factorial validity of the problematic social media use scale among Chinese adults. Addictive behaviors, 148, 107855. Advance online publication. https://doi.org/10.1016/j.addbeh.2023.107855

Endoprosthetics of the shoulder joint using additive technologies.

Bairamkulov A. (1), Kalinsky E. (1), Tychina Y. (1), Staferov A. (1), Chomaeva K. (1)
1) First Moscow State Medical University named after I.M. Sechenov (Russia)

Background The aim of this study is to introduce the case of a 54-year-old male patient with osteoarthritis who was hospitalized at University Hospital. From the age of 51 he complained of constant pain and was diagnosed with osteoarthritis.

Case history The onset of pain more than 10 years ago; unknown severe trauma of the shoulder. From the age of 51 the patient complained of constant pain and was diagnosed with osteoarthritis grade 3. At the age of 54 the patient was hospitalized at Sechenov University Hospital for total shoulder arthroplasty.

A physical examination showed combined contracture of the shoulder joint and hypotrophy of the deltoid muscle in the right shoulder. The patient suffered from severe pain and a decrease in range of motion, leading to a reduction in quality of life. VAS (visual analogue scale): 90; SF-36 (short form 36): 20%; UCLA (University of California, Los Angeles): 22. Computer tomography detected a significant reduction in the surface area of the glenoid fossa of the scapula.

The patient underwent endoprosthetics of the shoulder joint using additive technologies: the individual design glenoid augment and exact copy of the damaged scapula were manufactured by 3-D printer for preoperative planning and restoration the bearing surface of the articular part. The observation period was 12 months; before the operation and at follow-up visits at 3, 6, and 12 months, a survey, physical examination, range of motion assessment, and objective evaluation of the patient's condition using VAS, SF-36, and UCLA questionnaires were performed.

We restored the supporting surface for the placement of a shoulder prosthesis. This procedure restored the retroversion of the shoulder head and the introversion of the glenoid, and the functions of the right shoulder joint were resumed with the desired amplitude and volume of movements, significantly improved the patient's quality of life, reduced the pain syndrome. Results of the patient’s scales after 12 months: VAS: 0; SF-36: 85%; UCLA: 100.

Conclusion This case is to demonstrate the capabilities of additive technologies in the treatment of orthopedic patients and the effectiveness of a modern personalized approach. These methods allow a simple and convenient way to achieve less deviation and higher accuracy during surgery, reduce radiation load and blood loss, as well as accelerate the patient's recovery and return to the former quality of life.

Citations:

1) Cherkasskiy L., Caffrey J.P., Szewczyk A.F. Patient-specific 3D models aid planning for triplane proximal femoral osteotomy in slipped capital femoral epiphysis. J Child Orthop. 2017 Apr;11(2):147–153.
2) Kalenderer Ö, Erkuş S, Turgut A, İnan İH. Preoperative planning of femoral head reduction osteotomy using 3D printing model: A report of two cases. Acta Orthop Traumatol Turc. 2019 May;53(3):226-229. doi: 10.1016/j.aott.2019.01.002. Epub 2019 Jan 29. PMID: 30709647; PMCID: PMC6599387.
3) Won Tak Man, Jin Jimmy, Lau Tak Wing. The use of three-dimensional printing technology in orthopaedic surgery: a review. J Orthop Surg. 2017 Jan;25(1):1–7.

N-acetyl cysteine rescues cortical glial cell populations and results in functional improvements in a mouse model of primary autosomal recessive microcephaly 17 (MCPH17).

Incerti Tinterri A. (1), Khastkhodaei Ardakani M. (1), Astigiano C. (1), Ferrini F. (2), La Rosa C. (3), Bovetti S. (3), Buffo A. (1), Boda E. (1)

1) Dept. of Neuroscience and Neuroscience Institute Cavalieri Ottolenghi, Università degli Studi di Torino, Torino (Italy)
2) Dept. of Veterinary Sciences, Università degli Studi di Torino, Torino (Italy)
3) Dept. of Life Sciences and Systems Biology and Neuroscience Institute Cavalieri Ottolenghi, Università degli Studi di Torino, Torino (Italy)

Background Primary autosomal recessive microcephaly 17 (MCPH17) is a rare neurodevelopmental disorder caused by mutations in the CIT gene, which encodes for the Citron Kinase (CIT-K), a kinase involved in DNA repair and cytoskeletal dynamics. Patients with MCPH17 show reduced brain volume, intellectual disability, motor deficits, epilepsy, and early mortality. Cit-k KO mice recapitulate MCPH17 phenotype. In the Cit-k KO mouse brain, DNA damage and reactive oxygen species (ROS) accumulation is accompanied by neural progenitor apoptosis and glial cell alterations, including oligodendroglia and astroglia reduction, hypomyelination, and increased numbers of microglia presenting dysmorphic features.

Methods To identify pharmacological treatments that can reduce cellular damage accumulation and improve the functional phenotype of Cit-k KO mice, we chronically treated Cit-k KO mice during the first 2 postnatal weeks with an FDA-/EMA-approved antioxidant drug N-acetylcysteine (NAC), which can pass the blood-brain-barrier.

Results NAC treatment reduced brain ROS levels and slightly increased Cit-k KO mouse life span. Treated mice showed motor improvement and reduction of epileptic myoclonus. Deposition of perineuronal nets around cortical parvalbumin-positive interneurons was significantly rescued by NAC treatment, suggesting a positive effect on the maturation/function of inhibitory neurons. Although NAC did not rescue Cit-k KO mouse hypomyelination, cortical oligodendrocytes and astrocytes significantly increased in numbers, while microglia density and dysmorphic features decreased.

Conclusion Our data suggest that in the Cit-k KO mouse cortex, NAC-induced functional improvements may be at least in part mediated by the correction of Cit-k KO glial cell dysfunctions. Ongoing analyses will unveil the functional bases of NAC effects.

Citations:

1) Bianchi, F. T., Tocco, C., Pallavicini, G., Liu, Y., Vernì, F., Merigliano, C., … Di Cunto, F. (2017). Citron Kinase Deficiency Leads to Chromosomal Instability and TP53-Sensitive Microcephaly. Cell Reports, 18(7), 1674–1686. https://doi.org/10.1016/j.celrep.2017.01.054
2) Boda, E., Lorenzati, M., Parolisi, R. et al. Molecular and functional heterogeneity in dorsal and ventral oligodendrocyte progenitor cells of the mouse forebrain in response to DNA damage. Nat Commun 13, 2331 (2022). https://doi.org/10.1038/s41467-022- 30010-6
3) Muzzi, P., Camera, P., Di Cunto, F., & Vercelli, A. (2009). Deletion of the citron kinase gene selectively affects the number and distribution of interneurons in barrelfield cortex. Journal of Comparative Neurology, 513(3), 249–264. https://doi.org/10.1002/cne.21927

Reassessment of biological subtype- key to appropriate management of recurrent breast cancer.

Szydłowska D. (1), Sitek L. (1), Raźniewska D. (1).
1) University of Opole (Poland)

Background In breast cancer, hormone receptor expression levels and HER2 status determine the biological subtype and have predictive significance. In recurrent disease, it is possible to change the biological features of breast cancer. We present the fate of a patient in whom reassessment of the biological subtype in a metastatic focus contributed to a change in the therapeutic decision.

Case history A 55-year-old female patient was diagnosed with a left breast tumor on mammography, BIRADS 5. Thick-needle biopsy diagnosed G-2 stage breast cancer, and immunohistochemistry showed: ER(+++), PR (+++), HER2 negative (1+), Ki67 about 90% of cells. The clinical stage was set at cT2N0M0. The patient underwent left simple breast amputation with sentinel lymph node biopsy. Histopathological examination of the postoperative material diagnosed G-3 ductal carcinoma and metastasis in one of the lymph nodes (pT2N1a(sn)). Follow-up treatment included chemotherapy, followed by radiotherapy to the chest wall and axilla, and hormone therapy with an aromatase inhibitor. After 2 years of hormone therapy, a right femoral metastasis was found on an MRI performed for pain. The patient underwent radiotherapy, followed by palliative hormone therapy with fulvestrant. Follow-up imaging showed progression of bone lesions and liver metastasis. Systemic treatment was changed and abemacyclib with an aromatase inhibitor was used. Due to progression, a biopsy of the liver metastasis was performed, where a triple-negative breast cancer metastasis was diagnosed. This prompted a change in treatment to cisplatin, and further progression prompted another modification of therapy to the modern sacituzumab conjugate Govitecan.

Conclusion Differences in the biological subtype of distant metastatic breast cancer and primary tumor occur with variable frequency. Reassessment of hormone receptor expression and HER2 status is recommended by scientific societies. It should be pursued in clinical practice, as it can significantly change therapeutic management.

Citations:

1) Potemski P, Czyżykowski R. Supportive care. Neutropenia. Oncol Clin Pract 2020; 16. DOI: 10.5603/OCP.2020.0009
2) Breast cancer Jassem J, Krzakowski M. Onkol Prakt Klin Edu 2020;6(5):297-352.

Treatment of an oncological patient with Coronary Artery Disease.

Staferov A. (1), Bairamkulov A. (1), Zolotarev A. (1), Prutkoglyadova A. (1)

1) First Moscow State Medical University named after I.M.Sechenov, Moscow (Russian Federation)

Background The aim of this study was to present a 51 years old patient with concomitant oncological and cardiovascular pathologies.

Case history Patient D., 51 years old, male was diagnosed with T3NxM0 colorectal cancer 3 months prior to admission to our center. He also had a cardiac history of myocardial infarction and percutaneous coronary interventions (PCI) of right coronary artery (RCA) and left anterior descending artery (LAD) with bare-metal stents 15 years ago. Subsequently, his cardiovascular health has worsened, and he exhibits symptoms of 3rd class (according to CCS) angina, stage 2 arterial hypertension. He also has type 2 diabetes mellitus.

Basic cardiovascular diagnostics was performed. ECG showed regular normal sinus rhythm, echocardiogram showed hypokinesia of anterior and anterolateral wall and preserved ejection fraction of 53%. Invasive coronary angiogram (ICA) showed restenosis of LCA, distal RCA and stenosis of distal left main (LM), diagonal branch (DB) and diffuse lesion of proximal RCA.

Cardio-oncology team (COT) decided that preferred method of revascularization would be PCI and it should be treated immediately, with double antiplatelet therapy consisting of clopidogrel and acetylsalicylic acid (ASA) for 4 months, followed by anterior colectomy with switch to ASA monotherapy. PCI of RCA was performed firstly, and it was successful. But early post-operative period was complicated by a massive hemorrhage. Hemostatic therapy and fresh-frozen plasma were administered, eventually bleeding was stopped. It was decided to perform next PCI and surgical resection of the tumor as soon as possible. After that PCI of LCA was performed followed by surgical resection of tumor. Adjuvant 6-month long FOLFLOX-6 chemotherapy was prescribed.

After 4,5 years there were no major adverse cardiovascular events and complications related to oncology. He presented to our center with unstable angina ICA revealed stenosis of middle part of RCA and it was treated with PCI without subsequent complications.

Conclusion This case demonstrates challenges which COT may face during the treatment of patients: either related to hemorrhage after prescription of antiplatelet drugs or thrombotic events associated with insufficient therapy or systemic inflammation caused by cancer. Chemotherapy prescribed to patients can also be cardiotoxic, therefore worsening the results.

Citations:

1) Giza, D. E., Marmagkiolis, K., Mouhayar, E., Durand, J. B., & Iliescu, C. (2017). Management of CAD in Patients with Active Cancer: the Interventional Cardiologists' Perspective. Current cardiology reports, 19(6), 56. https://doi.org/10.1007/s11886-017-0862-x
2) Battisti, N. M. L., Welch, C. A., Sweeting, M., de Belder, M., Deanfield, J., Weston, C., Peake, M. D., Adlam, D., & Ring, A. (2022). Prevalence of Cardiovascular Disease in Patients With Potentially Curable Malignancies: A National Registry Dataset Analysis. JACC. CardioOncology, 4(2), 238–253. https://doi.org/10.1016/j.jaccao.2022.03.004
3) Doolub, G., & Mamas, M. A. (2022). Percutaneous Coronary Angioplasty in Patients with Cancer: Clinical Challenges and Management Strategies. Journal of Personalized Medicine, 12(9), 1372. MDPI AG. Retrieved from http://dx.doi.org/10.3390/jpm12091372
4) Radmilovic, J., Di Vilio, A., D'Andrea, A., Pastore, F., Forni, A., Desiderio, A., Ragni, M., Quaranta, G., Cimmino, G., Russo, V., Scherillo, M., & Golino, P. (2020). The Pharmacological Approach to Oncologic Patients with Acute Coronary Syndrome. Journal of clinical medicine, 9(12), 3926. https://doi.org/10.3390/jcm9123926
5) Koo, C.Y., Tai, BC., Chan, D.K.H. et al. Chemotherapy and adverse cardiovascular events in colorectal cancer patients undergoing surgical resection. World J Surg Onc 19, 21 (2021). https://doi.org/10.1186/s12957-021-02125-5

We, the Organizing Committee, would like to sincerely thank everyone who was a part, in any capacity or role, of the first edition of ICOCIMS.

We hope it was educational, and you had a great time.

See you next year!

First Edition Or.Co. (left to right): Amandeep Kaur, Emilio Maddalena, Dario Bottignole, Giacomo M. Cerreto, Tudor M. Haja, Riccardo Mazzoli, Olympia Cometa, Francesco B. Casadei

UPCOMING PARTNERS EVENTS

- **IMSCB**
  International Medical Students' Congress of Bucharest
  December 6th – 10th, 2023

- **Medicalis**
  International Congress for Medical Students and Young Health Professionals in Cluj-Napoca
  March 14th – 17th, 2024

- **AMSC**
  Antwerp Medical Students' Congress
  September 9th – 12th, 2024

Check their websites and social media to stay updated on news, deadlines, and participation details!

Mark your calendar for

ICOCIMS

SECOND EDITION

Next edition will take place on
November 7th, 8th and 9th, 2024

see you there!