Book of abstracts Young Scientists' Forum 2.0

Poznań
December 6th, 2024

Organizer: Greater Poland Cancer Centre

wielkopolskie centrum onkologii

Invitation

Dear Colleagues,

We would like to cordially invite you to participate in the next edition of the Young Scientists' Forum 2.0, which will be held on the 6th of December, 2024 in Poznań.

YSF 2.0 is a conference aimed at young scientists and students below 35 years of age, specializing in oncology-related sciences (including basic sciences such as biology, medical physics, genetics, biotechnology, pharmacy), as well as young clinicians, pathomorphologists, medical physicists and radiographers interested in therapy and diagnostics.

The forum is an ideal place not only to present one's work but also to exchange professional experiences and form brand new international cooperation networks.

The conference will be conducted in English in a hybrid form: on-line and on-site on the premises of the Greater Poland Cancer Centre.

The Forum is under the honorary scientific patronage of Professor Julian Malicki - the Director of the Greater Poland Cancer Centre.
The Forum has a competitive character. Abstracts submitted by participants will be evaluated by the Jury and reviewed by experts in basic and clinical sciences.

Submissions approved for the oral part will be presented in the form of a multimedia presentation and discussed with the Jury. All parts of the presentation are equally evaluated - the idea, the results of the study and the skills of scientific debate.

We kindly encourage you to submit your work - abstracts are to be sent in English at the latest by the 15th of November, 2024.

Registration will be available between the 1st of September and 15th of November, 2024.

The registration fee is 100 PLN and must be paid by the 20th of November, 2024.

Awards to support career and scientific development, including travel to congresses and courses, are to be received by the authors of the three best abstracts and presentations.

We sincerely invite you to participate!

On behalf of the Scientific and Organizational Committee

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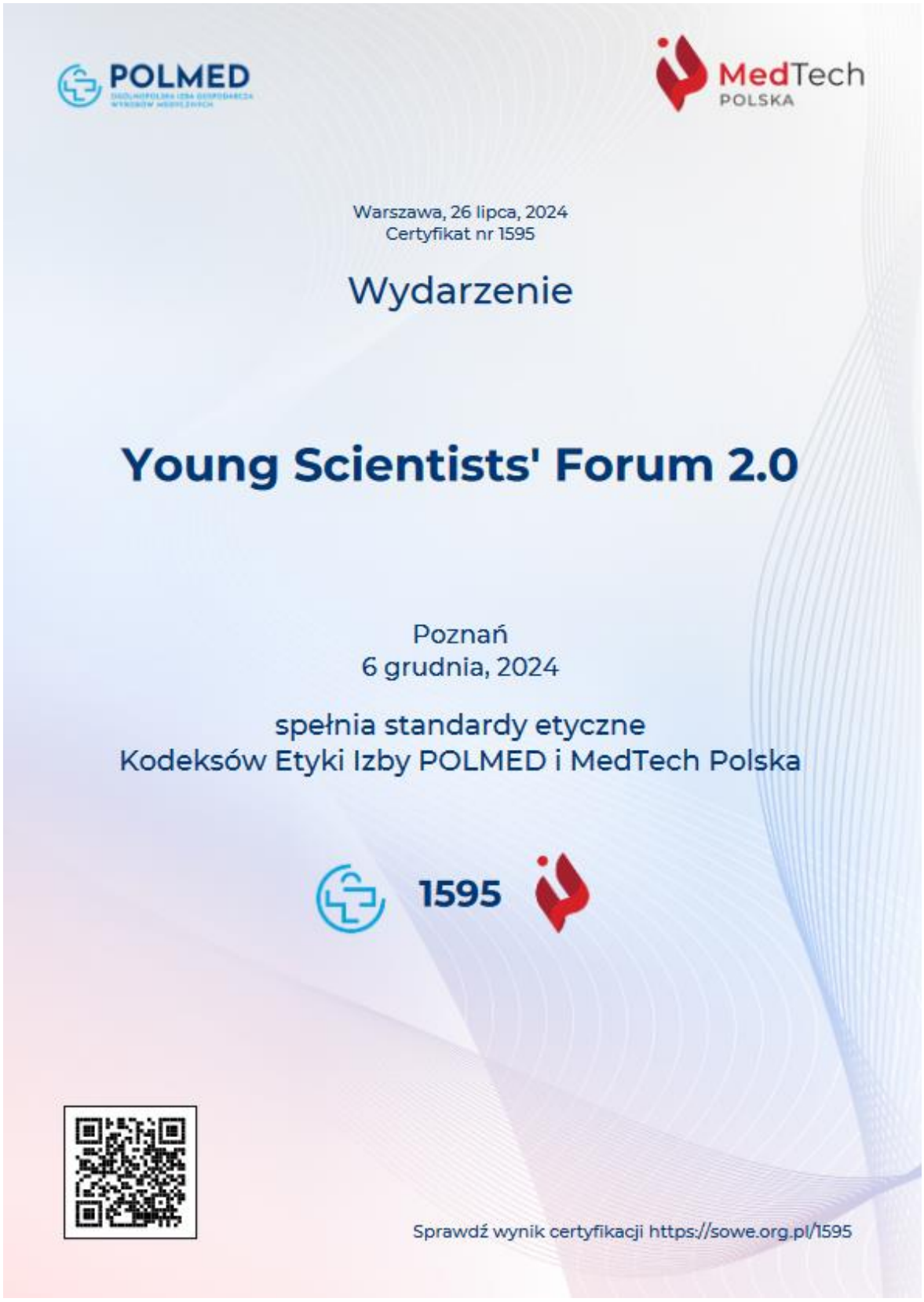

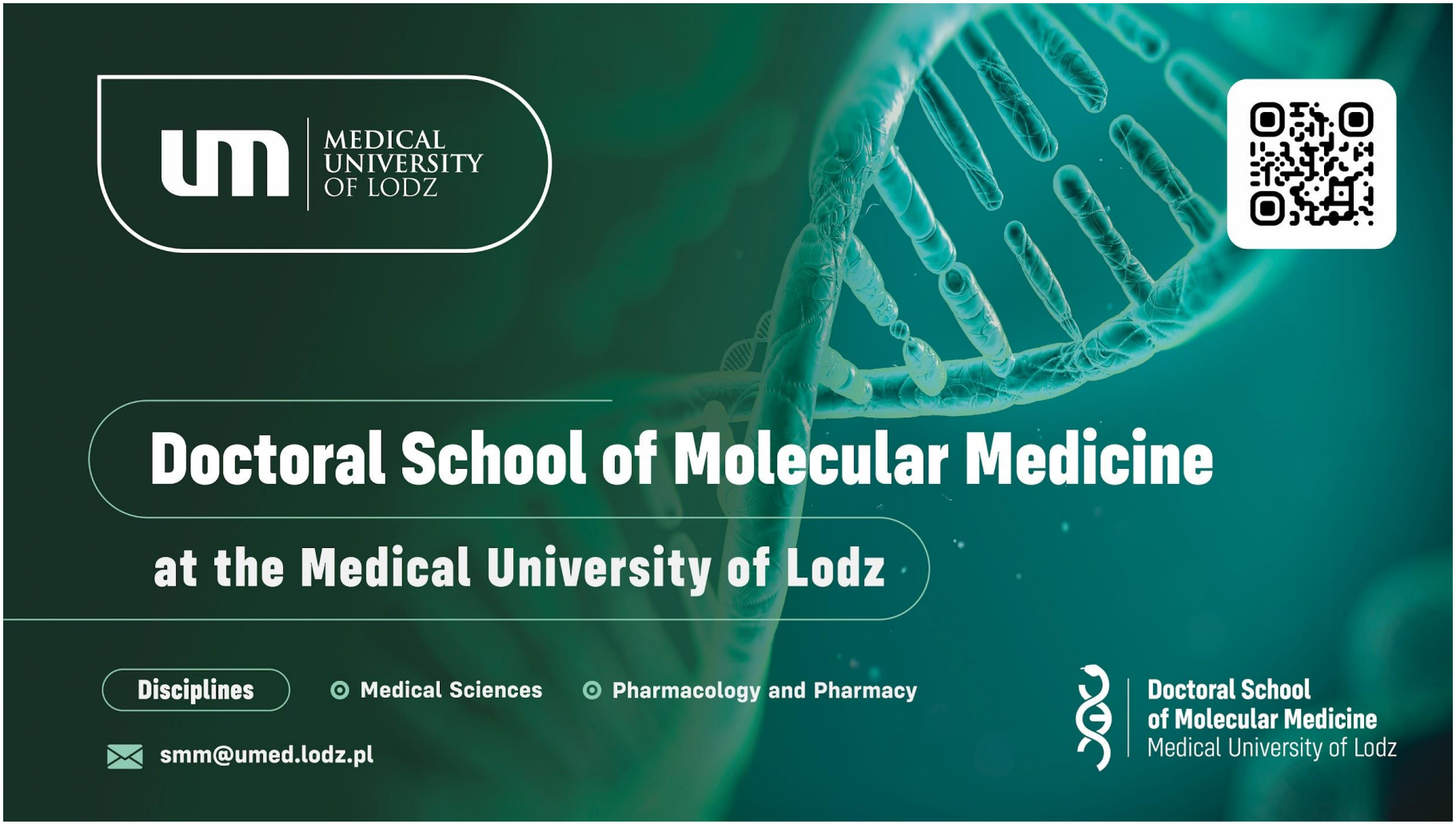
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Programme

8.30 - 8.45	Opening ceremony	
8.45 - 10.15	**PANEL A. Physics & Clinics**	
8.45 - 9.00	*The influence of the length of the irradiated optical fiber on the Cherenkov radiation value during small-field dosimetry using Exradin W2 scintillators*	Ewelina Nowak
9.00 - 9.15	*UKB-UnPAC: Image extraction pipeline for filtering UK Biobank Magnetic Resonance Imaging (MRI) data for radiomics analysis of peri-prostatic adipose tissue*	Ryan O'Keeffe
9.15 - 9.30	*Introduction of film dosimetry into the clinical practice of a proton therapy center*	Kinga Graczyk
9.30 - 9.45	*Retrospective evaluation of radiation doses received by Cardiac Implantable Electronic Devices (CIED) in patients undergoing radiotherapy*	Karolina Rapczyńska
9.45 - 10.00	*AI-assisted algorithms for HER2 assessment can predict HER2 amplification*	Mateusz Maniewski
10.00 - 10.15	*AI-powered virtual assistant and personal health knowledge graph for effective data curation in breast cancer*	Wenjie Liang
10.20 - 10.50	**INAUGURATION LECTURE** **Prof. Bożena Kamińska-Kaczmarek** **Nencki Institute of Experimental Biology of the Polish Academy of Sciences, Warsaw**	
10.50 -11.10	Coffee break & time for sponsors	
11.10 - 13.10	**PANEL B. Radiobiology & Clinics**	
11.10 - 11.25	*Stroma-mediated energy metabolism plasticity enhance resistance to imatinib and is a potential therapeutic target in chronic myeloid leukemia*	Nikodem Kasak
11.25 - 11.40	*Impact of regorafenib on the pharmacokinetics of trametinib in a rat model*	Filip Otto
11.40 - 11.55	*SIRT-1 inhibition in combination with ionizing radiation exposure enhances impairment of cell proliferation in HPV+ cell lines*	Lorenzo Coltro
11.55 - 12.10	*Is the omission of the external iliac or upper pelvic lymph nodes from elective irradiation safe in selected anal canal squamous cell cancers?*	Bartłomiej Skrzypiec
12.10 - 12.25	*The pursuit of novel head and neck cancer biomarkers – tumor and blood expression of chloride intracellular channels family*	Bartosz Wojtera
12.25 - 12.40	*The prevalence and location of positive surgical margins in patients undergoing open, laparoscopic, and DaVinci robot-assisted radical prostatectomy*	Jędrzej Borowczak

12.40 - 12.55	*Nephrotic syndrome during treatment with Sunitinib for kidney cancer, case report*	Krzysztof Michalak
12.55 - 13.10	*Intraoperative radiotherapy changes the composition of surgical wound fluids after breast cancer surgery, inducing immune cell cytotoxicity*	Igor Piotrowski
13.10 - 14.10	Lunch & time for sponsors	
14.10 - 16.10	**PANEL C. Basic Science**	
14.10 - 14.25	*3D Exploration of CAF-Macrophage Interactions in Breast Cancer Spheroids*	Oliwia Piwócka
14.25 - 14.40	*Silk spheres for targeted delivery of oligonucleotide therapeutics to HER2-positive cancer cells*	Sara Molenda
14.40 - 14.55	*Kinetin Riboside-Induced Multi-Faceted Cell Death in Hepatocellular Carcinoma cells via Purine Biosynthesis Disruption, Metabolic Stress, and Autophagy*	Marta Orlicka-Płocka
14.55 - 15.10	*miR-27b-5p: a novel player in the biology of head and neck squamous cell carcinoma*	Joanna Kozłowska--Masłoń
15.10 - 15.25	*Sonodynamic therapy as a potentiation of photodynamic therapy: a promising strategy to combat MRSA*	Aleksandra Sztych
15.25 - 15.40	*Species-Selective Detection of β-Galactosidase Activity*	Kaja Jaskot
15.40 - 15.55	*Association between BRG1 and ERβ in colorectal cancer*	Julia Lipowicz
15.55 - 16.10	*ERK2 Silencing as a Therapeutic Strategy in Head and Neck Squamous Cell Carcinoma: Impact on Cell Survival, Proliferation, and Cycle Arrest*	Julia Ostapowicz
16.10 - 17.10	Coffee break & time for sponsors	
16.10 - 17.00	Jury deliberations	
17.00 - 18.30	Closing ceremony & awards	

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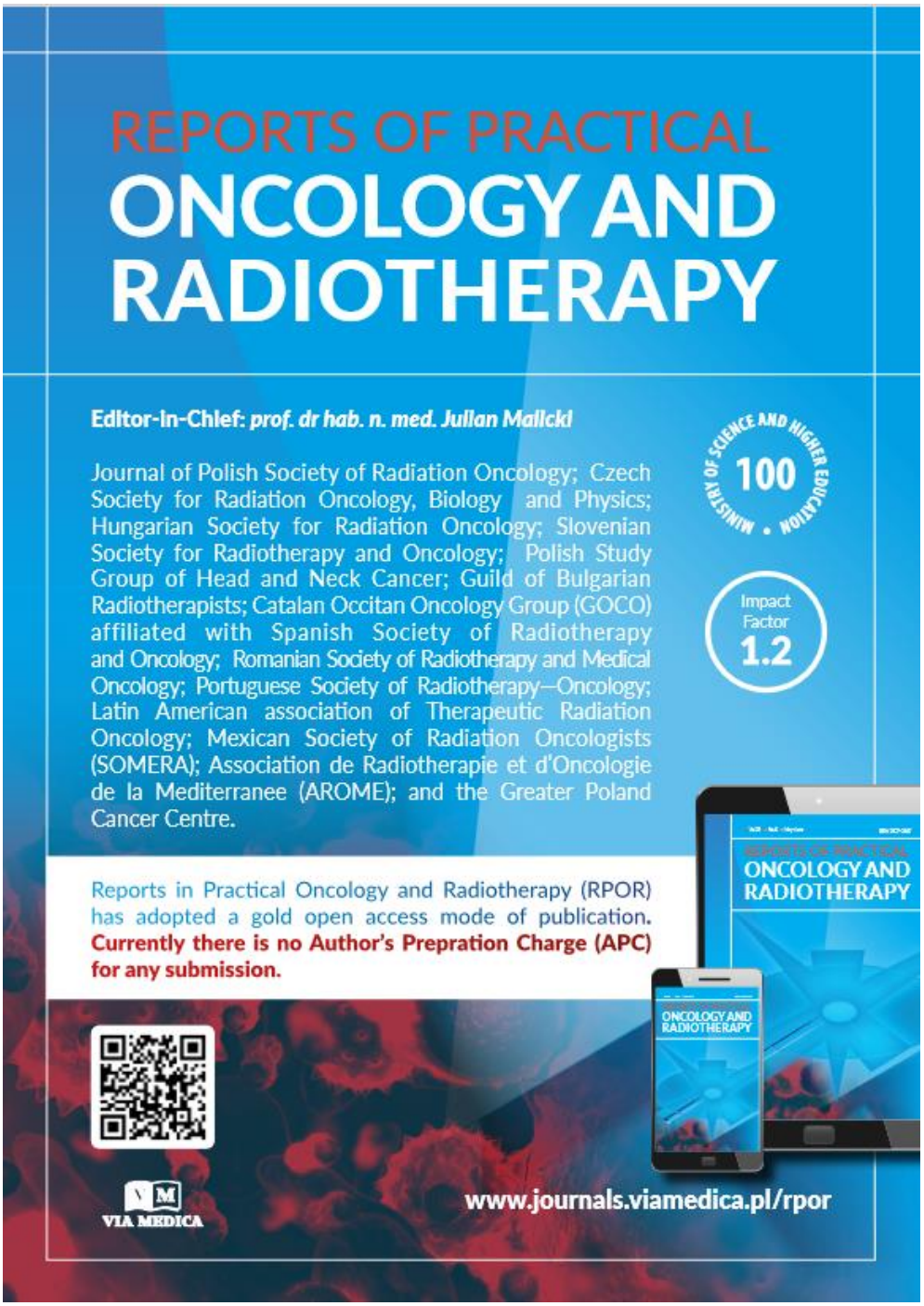

Oral Session

O1

UKB-UnPAC: Image extraction pipeline for filtering UK Biobank Magnetic Resonance Imaging (MRI) data for radiomics analysis of peri-prostatic adipose tissue

O'Keeffe, R.(1), Leech, M 1. & O'Neill, A.G.M (1)

1. Applied Radiation Therapy, Discipline of Radiation Therapy, School of Medicine, Trinity College Dublin, Trinity St. James's Cancer Institute, Dublin, Ireland.

Introduction
The UK Biobank (UKB) is a large-scale biomedical database and research resource containing health information from approximately half a million UK participants recruited between 2006 and 2010. The sheer volume of data and quantity of variables available for download requires careful selection and filtering to limit time spent on data screening and cleaning, however with no option to automate this process, selection and filtering for big-data type studies could take months. An in-house Python package was developed that would allow the researcher to select data of interest and automate its acquisition.

Materials and methods
This presentation describes an automated method developed for curating a large volume download (Approx 32'500 patients) of UKB Dixon weighted magnetic resonance (MR) images and related data for analysis within a study investigating the link between periprostatic adipose tissue and aggressive prostate cancer. The package was developed in the Python programming language. Images were visually checked and inspected in 3D-Slicer.

Results
4 key processes were identified: Unzipping, Parsing, Acquiring, and Converting. Associated scripts were developed that allow concise data selection with minimal input from the researcher. UnPAC is able to perform the entire process in 11seconds/patient, with a 33 fold reduction in required data storage.

Conclusions
We present an automated methodology for the extraction of large scale data from the UK-Biobank, which can be used to increase the feasibility of "big-data" type studies. Our methodology is quicker, requires less data storage, and requires minimal technical expertise. It is also freely available and open-source.

Keywords: maging research, Python, DICOM, UK Biobank

Funding: The world Cancer Research Fund

O2

Retrospective evaluation of radiation doses received by Cardiac Implantable Electronic Devices (CIED) in patients undergoing radiotherapy

Karolina Rapczyńska (1)

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Introduction
Cardiac implantable electronic devices (CIEDs) are increasingly used in patients with cardiovascular diseases. However, the use of radiotherapy in patients with CIEDs, particularly in the thoracic region, poses a risk of device malfunction due to ionizing radiation exposure. This study retrospectively evaluates radiation doses received by CIEDs during radiotherapy in cancer patients.

Materials and methods
The study included 91 patients with CIEDs treated with radiotherapy at the Greater Poland Cancer Centre between 2017 and 2023. Dose distributions were analyzed based on treatment plans for head, neck, and thoracic regions. Techniques such as 3D-CRT, IMRT, and VMAT were evaluated for their impact on radiation doses received by the CIEDs.

Results
Patients receiving radiotherapy to the left breast had the highest mean doses to their CIEDs, reaching up to 50.4 Gy, with a mean dose of 2.39 Gy across all cases. Techniques like VMAT and IMRT demonstrated significantly lower doses to the devices compared to 3D-CRT, ensuring better device protection.

Conclusions
Advanced radiotherapy techniques, especially VMAT and IMRT, are more effective in minimizing radiation exposure to CIEDs. The findings underscore the importance of treatment planning to reduce the risk of device malfunction, particularly for patients with CIEDs near the radiation field.

Keywords: CIED, radiotheraphy, dose

Funding: Funded as part of scientific activities in the Poznan University of Medical Sciences.

O3

AI-assisted algorithms for HER2 assessment can predict HER2 amplification

Mateusz Maniewski (1,2,3), Jędrzej Borowczak(4), Justyna Durślewicz (1,5), Hanna Andrusewicz (1), Jakub Dzierżawski(1), Jarosław Starzyński (1), Marek Zdrenka (1), Pamela Chudzińska (6), Łukasz Szylberg (1,2)

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Introduction

Human Epidermal Growth Factor Receptor 2 (HER2) is a crucial predictive marker in breast cancer, with overexpression linked to aggressive disease and targeted therapy options. While immunohistochemistry (IHC) is widely used for HER2 assessment, ambiguous results necessitate further molecular testing. This study explored the potential of artificial intelligence (AI) to enhance HER2 evaluation.

Materials and methods

153 formalin-fixed, paraffin-embedded (FFPE) breast cancer tissues were analyzed, including 50 cases each with HER2 2+ and negative or positive amplification, and 53 HER2 3+ controls. IHC was performed per ASCO 2018 guidelines, with 2+ cases undergoing confirmatory CISH or FISH. Two AI algorithms, uPath and VMscope, analyzed digitized IHC slides, and their performance was compared to assessments by expert pathologists.

Results

Significant discrepancies were observed between initial IHC and AI-based assessments. uPath classified 30% of cases as HER2 2+ and 70% as 3+, while VMscope classified 8% as 1+, 26% as 2+, and 66% as 3+. uPath demonstrated 100% sensitivity and 9.09% specificity in predicting HER2 amplification, compared to 89.8% and 80.0% for VMscope, respectively. Notably, both algorithms were more likely to classify amplified cases as HER2 3+ compared to pathologists.

Conclusions

These findings suggest that AI algorithms offer high sensitivity in detecting HER2 amplification and provide consistent results. AI-assisted diagnosis may expedite HER2 assessment and potentially reduce the need for FISH testing, leading to faster treatment decisions. However, further validation is crucial to ensure accurate identification of all patients eligible for HER2-targeted therapies.

Keywords: artificial intelligence, breast cancer, HER2, cancer, treatment

Funding: None.

O4

AI-powered virtual assistant and personal health knowledge graph for effective data curation in breast cancer

Wenjie Liang (1), Remzi Celebi (2), Ensar Emir Erol (2), Isabelle de Zegher (3), Katerina Serafimova (4), Todor Primov (4), Svetla Boytcheva (4), Andre Dekker (1), Aiara Lobo Gomes (1), Petros Kalendralis (1)

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Introduction
Electronic health records (EHRs) contain valuable information for breast cancer management. However, integration of heterogeneous personal health data from EHRs requires tedious curation efforts. In this study, we aim to leverage Artificial Intelligence (AI) curation tools to support automated health data transformation into an interoperable and reusable personal health knowledge graph (PHKG), using direct identifiable data of Breast Cancer (BC) patients. This study is in scope of the AI-powered Data Curation & Publishing Virtual Assistant (AIDAVA) project.

Materials and methods
The virtual assistant was developed by integrating multiple AI techniques supporting automated curation. First, breast cancer-related patient data were extracted from the EHR systems of MAASTRO Clinic and ingested into the AIDAVA system. Data items were standardized, annotated into classes and mapped with a pre-defined ontology. Next, internally developed AI tools were triggered to support data transformation into the PHKG. Finally, the PHKG was assessed using a Shapes Constraint Language (SHACL)-based validator to evaluate and improve the mapping process. From the validated PHKG, a SPARQL query was developed to form a BC registry.

Results
A first version of the prototype was developed to semi-automatically curate EHR data and publish breast cancer-related patient information. It confirmed the feasibility of the approach while crystallizing the value of data transformation to support mapping and multilingual NLP and LLM tools to maximize automation.

Conclusions
The proposed prototype is an effective approach for automating patient data curation and knowledge graph construction. Moreover, it provides a potential solution to improve personal health data reuse.

Keywords: breast cancer, personal health knowledge graphs, data curation, artificial intelligence, semantic representation

Funding: This work was supported by the European Union's Horizon Europe research and innovation programme under grant agreements No. 101057062 (AIDAVA).

O5

The pursuit of novel head and neck cancer biomarkers – tumor and blood expression of chloride intracellular channels family

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Introduction
The chloride intracellular channels (CLICs) family includes six ion channels encoded by CLIC1-CLIC6 genes. CLIC1 overexpression was reported in oral and nasopharyngeal cancer tissues and blood plasma. However, the expression patterns of other CLICs in head and neck cancer (HNC) remain unclear. Our study aims to assess the expression of the CLIC family in the tumor tissue and the blood of HNC patients.

Materials and methods
We examined 99 tumor samples, including squamous cell carcinoma of the oral cavity and larynx, 85 tissue samples harvested from the free margin of surgical resection, and blood collected from 38 oral cancer patients and 8 healthy individuals. We analyzed tumor CLICs expression on the mRNA level with RT-qPCR, on the protein level with Western Blot, and CLICs blood expression with ELISA.

Results
We found higher expression of CLIC1 ($p=0,038$) and lower expression of CLIC2, CLIC3, and CLIC5 genes ($p=0,0493$, $p<0.0001$, $p<0.0001$, respectively) in the tumors compared to normal tissue on the mRNA level, whereas, on the protein level, we found lower expression of CLIC3 in the tumors ($p<0,0001$). In the blood serum of HNC patients, we found higher expression of CLIC1 and CLIC3 proteins ($p=0,023$, $p<0,0001$, respectively) and lower expression of CLIC4 and CLIC6 proteins ($p=0,0122$, $p=0,0015$, respectively) compared to the control group.

Conclusions
Our results indicate that CLICs may be novel HNC blood biomarkers potentially used in early diagnosis. Furthermore, differences between cancerous and normal tissue expression suggest that CLICs may play a role in HNC pathogenesis.

Keywords: oral cancer, laryngeal cancer, CLIC, cancer biomarker, liquid biopsy

Funding: Greater Poland Cancer Centre Grant - grant number 10/2022 (262) Poznan University of Medical Sciences Doctoral School Grant - grant number SDUM-DGB 15/04/23.

O6

The prevalence and location of positive surgical margins in patients undergoing open, laparoscopic, and DaVinci robot-assisted radical prostatectomy

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Introduction
Positive surgical margins (PSM) influence the prognosis and risk of biochemical recurrence in prostate cancer patients. We investigated the location and prevalence of PSM among patients undergoing open, laparoscopic, and robot-assisted radical prostatectomy in our institution.

Materials and methods
We retrospectively analyzed clinical and histopathological data of 153, 126, and 243 patients undergoing open, laparoscopic, and DaVinci robot-assisted radical prostatectomy, respectively. Only patients with T2/T3 tumors, no lymph node or distant metastasis, and no history of prior therapy were included.

Results
PSM rates were 35.8%, 32.54%, and 50.98% for robot-assisted, laparoscopic, and open radical prostatectomy, respectively. The PSM rate was significantly higher than in the other group, with no differences in PSM rated between robot-assisted and laparoscopic surgeries. The most frequent location of PSM in the DaVinci group was the right prostate love($p = 0.02$). We found significant differences in the percentage of apex margin positivity between analyzed groups ($p = 0.0001$). PSM were associated with higher odds of biochemical recurrence in the DaVinci (OR 3.14 [1.14-8.69]; p=0.027), laparoscopy (6.05 [1.08-33.96]; p=0.041), and open surgery groups (OR 2.74 [1.03-7.29], p=0.044).

Conclusions
DaVinci robot-assisted prostatectomy achieved lower PSM rates than open surgery and potentially reduce the risk of early biochemical recurrence. Robot-assisted prostatectomy showed similar results to laparoscopy, while also offering a short learning time. While PSM increased the odds of early biochemical recurrence, neither the extensity of PSM nor its location were associated with patients prognosis.

Keywords: radical prostatectomy, DaVinci, positive surgical margins, pathology, prostate cancer

Funding: none.

O7

Nephrotic syndrome during treatment with Sunitinib for kidney cancer, case report

Krzysztof Michalak (1)

1. Faculty of Medicine, University of Opole, Opole, Poland

Introduction
Molecularly targeted treatment is one of the fastest growing areas of oncology. Tyrosine kinase inhibitors such as sunitinib are used in the treatment of kidney cancer. However, the late complications associated with this treatment, and methods of treating them, are still unknown to us.

Materials and methods
A 70-year-old man was referred to the Nephrology Department, for suspected nephrotic syndrome. History of kidney cancer, status post right nephrectomy, disseminated disease. Patient treated with Sunitinib, secondary to treatment proteinuria. Laboratory tests revealed: creatinine 1.81mg/dl, eGFR 37ml/min, proteinuria 5g/day, leukocytes 3.2tys./µl, haemoglobin 10.7g/dl, platelets 83tys./mm³. After discontinuation of sunitinib, laboratory tests showed regression of proteinuria 2 g/day, renal impairment at a similar level. At follow-up one week later: proteinuria 2.7g/day, creatinine 1.96mg/dl, eGFR 36ml/min, haemoglobin 11.5g/dl.

Results
Nephrotic syndrome was diagnosed as a complication of sunitinib treatment. Currently, there are no indications for other treatments, no clear recommendations in this type of complication, most often withholding therapy until proteinuria falls below 2.5 g/day. In view of the resolution of proteinuria from nephrotic to non-nephrotic, it was proposed to reinstate treatment with sunitinib at a reduced dose, or at higher intervals with observation of renal failure parameters and proteinuria.

Conclusions
We currently have no standards of treatment when nephrological complications occur during molecularly targeted treatment. The nephrotic syndrome could have resulted from a direct effect of sunitinib, primary membranous nephropathy, or secondary membranous nephropathy in the course of malignancy. Haematoonconefrology is perhaps the direction of the future.

Keywords: Sunitynib, nephrotic syndrome, proteinuria, kidney cancer

Funding: University of Opole, Medical faculty.

O8

Intraoperative radiotherapy changes the composition of surgical wound fluids after breast cancer surgery, inducing immune cell cytotoxicity

Igor Piotrowski (1), Wiktoria Maria Suchorska (1,2), Janusz Wasiewicz (3), Katarzyna Kulcenty (1)

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Introduction
Breast-conserving surgery (BCS) modifies the local wound environment to be more favourable for regrowth of breast cancer cells. Surgical wound fluid (SWF) which is produced in the wound following BCS was shown to increase growth and aggressive phenotype of cancer cells in vitro. Recent research demonstrated that intraoperative radiotherapy (IORT) delivered directly after breast-conserving surgery (BCS) modifies the pro-tumorigenic composition of SWF, and impairs its ability to induce cancer cell growth and aggressive phenotype in vitro. SWF is also rich in immune-related cytokines, which is why we decided to investigate the profile of those cytokines following IORT, and their impact on the activity of immune cells.

Materials and methods
We collected wound fluids from patients after BCS alone (WF), and after BCS followed by IORT (RT-WF). We measured the concentration of immune-related small molecules in WF, and assessed the phenotype of human peripheral blood mononuclear cells (PBMC), macrophages, and NK cells stimulated in vitro with SWF.

Results
The composition of SWF differed depending on therapy and molecular subtype of the tumour. When used to stimulate PBMCs, SWF from RT-WF group increased the population of anti-tumour T cells and decreased the population of naïve T cells. Additionally IORT enhanced SWF-induced NK cell cytotoxicity.

Conclusions
The present study demonstrates a distinct molecular makeup of wound fluids collected following BCS or IORT. We determined that the SWF impacts the populations of mononuclear blood cells differently depending both on the therapy used and the molecular subtype of the tumour with IORT causing enrichment in populations showing anti-tumour effects.

Keywords: breast cancer, intraoperative radiotherapy, wound healing, immune cells, tumour microenvironment

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O9

3D Exploration of CAF-Macrophage Interactions in Breast Cancer Spheroids

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Introduction
Tumor-associated macrophages (TAMs) and cancer-associated fibroblasts (CAFs) are key components of the tumor microenvironment, driving breast cancer progression and invasion. Their interactions facilitate tumor growth and metastasis through changes in cell phenotype and signaling within the tumor stroma. This study aims to investigate the cross-talk between CAFs and macrophages in breast cancer, using a 3D spheroid model to mimic the complexity of the in vivo microenvironment and assess potential therapeutic strategies to disrupt these interactions.

Materials and methods
3D spheroids were generated using the BT474 breast cancer cell line, CAFs isolated from patient samples, and macrophages. Resveratrol (RSV) was applied to assess its effect on macrophage polarization and invasion. Flow cytometry analyzed shifts in M1 and M2 macrophage populations. Invasion assays and RT-qPCR were used to evaluate invasive capacity and EMT-related pathways.

Results
Co-cultures of BT474 cells, CAFs, and macrophages led to an increase in M2 macrophage populations compared to BT474-macrophage spheroids alone. RSV treatment promoted a shift toward M1 macrophages, with a notable reduction in M2 markers. Invasion assays demonstrated that spheroids containing both CAFs and macrophages exhibited significantly greater invasive capacity compared to BT474-only spheroids, while RSV treatment reduced invasion. RT-qPCR results suggested that RSV influenced pathways associated with EMT, migration, and survival.

Conclusions
CAFs and macrophages play critical roles in promoting breast cancer invasiveness. Modulating these interactions through agents like RSV could alter macrophage polarization and reduce invasion. This 3D model provides an innovative platform to study stromal-immune cell interactions and investigate potential therapeutic interventions targeting the tumor microenvironment.

Keywords: cancer-associated fibroblasts, tumor microenvironment, spheroids, 3D cancer model, breast cancer

Funding: The National Science Centre Poland funded this research (grant number: 2019/35/B/NZ7/04342).

O10

Kinetin Riboside-Induced Multi-Faceted Cell Death in Hepatocellular Carcinoma cells via Purine Biosynthesis Disruption, Metabolic Stress, and Autophagy

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Introduction
N6-furfuryladenosine (kinetin riboside, KR), an adenosine derivative, inhibits cancer cell proliferation, with cytotoxicity modulated by adenosine kinase. Complementary cellular assays were used to trace the metabolic pathway of intermediate metabolites generated from the enzymatic transformation of [13C]KR in hepatocellular carcinoma (HepG2) cells, revealing multiple, extensive modifications. KR was found to cause metabolic disruptions, purinosome assembly, and ultimately cell death. This aligns with the dependence of cancer cell metabolism on the Crabtree effect, where glucose-induced inhibition of cellular respiration restricts oxidative phosphorylation, intensifying the impact of metabolic disruptions. Replacing glucose with galactose in culture media, forced cancer cells to rely on OXPHOS, increasing sensitivity to mitochondrial disruption by KR.

Materials and methods
Cellular proliferation, programmed cell deaths, mitochondrial parameters and energy phenotype were assessed using flow cytometry, Seahorse analyzer, confocal microscopy, proteomic analysis and HPLC.

Results
The data indicate that all three pathways—de novo, salvage, and catabolic—contribute to purine metabolism and regulation in cancer cells. Further analysis confirmed that KR disrupts multiple levels of cancer cell metabolism, leading to energy imbalance, oxidative stress, and reduced proliferation. KR selectively targets pathways essential for cell growth and apoptosis by disrupting mitochondria, generating ROS, and acting as a potent mitotoxic agent. Moreover, KR exerts effects at multiple levels of cellular organization, while the autophagy process increases the stress threshold required to induce cell death through various mechanisms.

Conclusions
These findings suggest that KR, by interfering with intracellular purine metabolism and disrupting purine biosynthesis enzymes, has potential as a natural anticancer agent, comparable to established mitochondrial toxins.

Keywords: purine derivative, mitochondria, cancer cell metabolism, programmed cell death, Crabtree effect

Funding: NCN 2014/13/B/NZ7/02291.

O11

miR-27b-5p: a novel player in the biology of head and neck squamous cell carcinoma

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Introduction
Head and neck squamous cell carcinoma (HNSCC) is one of the most common and fatal cancers worldwide. Recently, non-coding RNAs were described as molecules with therapeutic or diagnostic potential in different malignancies. One of them - miR-27b-5p is a mature strand of a well-known epithelial-to-mesenchymal transition (EMT) modulator.

Materials and methods
Expression and patients' clinicopathological data were downloaded from the UCSC and the cBioPortal database. The miR-27b-5p level, survival curves, patients' immune profiles, and gene enrichment were studied. MicroRNA (miRNA) potential targets were examined using online databases and tools. Finally, two cancer cell lines were modified with a miR-27b expressing plasmid or control one and subjected to functional tests. Irradiation and chemotherapy response were assessed with apoptosis and proliferation assay, respectively. Additionally, expression profiles of obtained cell lines were investigated using RNA-seq analysis.

Results
In patients, miR-27b-5p higher expression was linked with absent perineural invasion, HPV(+) status, and better overall survival. Analysis of patients' immune profiles indicated substantial differences in tumor infiltration degree, the composition of the infiltrating fraction, and other immune features. Low miRNA levels were associated with overexpression of genes implicated in processes promoting cancer development - EMT, angiogenesis, or hypoxia. Induced overexpression of miR-27b in cancer cell lines negatively affected their cell cycle, growth, and migration ability. Moreover, it was linked with a lower proliferation rate after the cisplatin administration and, interestingly, was associated with a worse response to applied irradiation and doxorubicin therapy.

Conclusions
Based on the above data, we emphasize the complex and pivotal impact of miR-27b-5p on HNSCC biology.

Keywords: miR-27b-5p, miRNA, ncRNA, HNSCC, head and neck cancers

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O12

Sonodynamic therapy as a potentiation of photodynamic therapy: a promising strategy to combat MRSA

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Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) infections are an escalating global health issue due to increasing antibiotic resistance. Traditional treatment options are often ineffective, necessitating alternative therapeutic strategies. This study investigates a dual synergistic approach combining photodynamic therapy (PDT) and sonodynamic therapy (SDT) using two sensitizers, rose bengal (RB) and chlorin e6 (Ce6), to enhance bactericidal effectiveness against MRSA.

Materials and methods

The study evaluated the stability of RB and Ce6 under ultrasound and light exposure. RB served as a sonosensitizer, activated by ultrasound, while Ce6 functioned as a photosensitizer, activated by light. MRSA cultures were treated with RB and Ce6 separately and in combination under different excitation conditions. Bacterial reduction was measured to assess the synergistic effect of the combined therapies at varying molar ratios of RB to Ce6.

Results

The results showed that RB was more efficient than Ce6 in generating ROS under ultrasound activation, contributing to increased antibacterial activity. The combined use of RB and Ce6 at molar ratios of 1:1 and 1:3 produced a greater than 3-log reduction in MRSA, significantly surpassing the effectiveness of each sensitizer used individually. This synergistic interaction allowed for effective bacterial destruction at lower sensitizer concentrations.

Conclusions

The dual application of PDT and SDT with RB and Ce6 demonstrates a promising non-antibiotic approach to combating MRSA. The observed synergistic effects suggest that this combined therapy could offer a safer and more effective alternative, especially in cases where antibiotic resistance limits traditional treatment options.

Keywords: SDT, synergism, rose bengal, chlorins, MRSA

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O13

Species-Selective Detection of β-Galactosidase Activity

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Introduction
Elevated β-galactosidase (β-gal) activity is a widely recognized biomarker for detecting cellular senescence associated with cancer. Fluorescein di-β-D-galactopyranoside (FDG) is a fluorogenic substrate for detecting β-galactosidase (β-gal) activity. FDG is non-fluorescent, consisting of fluorescein-conjugated to two galactose groups. β-gal cleaves the glycosidic bonds, releasing free fluorescein, which can be easily detected using fluorescence-based methods. To improve substrate delivery and enhance detection in various cellular contexts, different versions of probes based on fluorescein have been developed. This study investigates 5-(Pentafluorobenzoylamino) Fluorescein Di-β-D-Galactopyranoside (PFB-FDG) as a species-selective substrate, providing new insights into cellular senescence.

Materials and methods
Human U251 and HEK293T cells, alongside E. coli. Fluorescence activation was analyzed using an Imaging Flow Cytometry. Cell lysates and purified β-gal enzymes were tested to validate species-specific probe activation. Molecular docking simulations were conducted using AutoDock Vina and analyzed in UCSF Chimera and LigPlot+. The crystal structures of human and E. coli β-galactosidases were used to model interactions and assess steric clashes, revealing structural features underlying PFB-FDG's selectivity for human β-gal.

Results
PFB-FDG selectively detected human β-gal activity without cross-reactivity with E. coli β-gal. While FDG was activated by both human and bacterial β-gal. Molecular docking revealed steric hindrance in E. coli β-gal's binding pocket, preventing effective substrate activation.

Conclusions
These novel properties highlight the potential of PFB-FDG for a wide range of applications enhancing targeted drug delivery systems in medical treatments. Consequently, our research paves the way for developing more precise and species-specific detection methodologies, with significant implications for fundamental research and clinical practice.

Keywords: Cellular Senescence, β-Galactosidase Activity, Species-Selectivity, Fluorogenic Probe

Funding: This study was supported by grant OPUS 22 2021/43/B/NZ3/01454 from the National Science Centre, Poland.

O14

ERK2 Silencing as a Therapeutic Strategy in Head and Neck Squamous Cell Carcinoma: Impact on Cell Survival, Proliferation, and Cycle Arrest

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Introduction
One key pathway in cancer progression is ERK-mediated signaling (Extracellular Signal-regulated Kinases), a group of MAPK proteins that regulate processes like gene expression, cell division, and motility. Overexpression of ERK2 is strongly associated with cancer initiation, progression, metastasis, and therapy resistance. Targeting ERK2, a critical player in this pathway, holds promise for cancer therapy. This study investigates ERK2's role in head and neck squamous cell carcinoma (HNSCC) by silencing its expression in cell lines, hypothesizing that ERK2 knockdown will reduce cancer cell survival, proliferation, and migration.

Materials and methods
Established HNSCC cell lines (H103 and Detroit-562) with stable ERK2 gene knockdown (ERK2 CRISPRi) were obtained with CRISPR-Cas9 system. Further, cell viability, proliferation, migration ability, clonogenic formation and cell cycle distribution were analyzed in comparison to controls (cells transduced with control sgRNA). The normality of the observed data distribution was assessed using the Shapiro–Wilk test. The one-way ANOVA was conducted for multiple comparisons. Statistical analysis was performed with the GraphPad Prism 10.0.2 software, and $p<0.05$ was considered statistically significant.

Results
ERK2 silencing influences a decrease in cell proliferation and viability in both examined cell lines. Moreover, ERK2 knockdown causes a reduction of the clonogenic formation ability of HNSCC cells compared to the control. Additionally, in the Detroit-562 cell line, ERK2 silencing leads to changes in cell cycle distribution by cell arrest in the G1 phase.

Conclusions
ERK2 depletion leads to a reduction in the aggressiveness of HNSCC cells, suggesting its potential for targeted cancer therapy

Keywords: HNSCC, ERK2, gene silencing, cancer research

Funding: The research was supported by the intramural grant number 14/03/2023/PRB/WCO/007 of the Greater Poland Cancer Centre.

O15

Impact of regorafenib on the pharmacokinetics of trametinib in a rat model

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Introduction
The development of resistance by tumor cells is a common challenge in oncology, often leading to treatment failure. One strategy to counteract this issue is the combination of multiple drugs targeting different pathways, such as regorafenib (REG) and trametinib (TRA). This approach can enhance anticancer efficacy at both pharmacodynamic (PD) and pharmacokinetic (PK) levels, thereby facilitating the attainment of higher concentrations in the bloodstream and tissues. The aim of the study was to determine how the PK parameters of TRA would change in the presence of REG.

Materials and methods
Male Wistar rats were assigned to two groups: the IREG+TRA group (n = 6) received oral doses of REG (20 mg/kg b.w.) and TRA (3 mg/kg b.w.), while the IITRA group (n = 6) received TRA alone (3 mg/kg b.w.). Blood samples were collected over 72 hours, and TRA concentrations were analyzed using UPLC-MS/MS following plasma protein precipitation. PK parameters were evaluated via non-compartmental analysis with MonolixSuite v2024R1, and statistical analysis was conducted with SAS 9.4., including the Student's t-test and Mann–Whitney test.

Results
The TRA analysis method was rapid, taking only 5 minutes and requiring 20 µL of plasma. REG co-administration significantly increased TRA's Cmax by 250% and AUC0-∞ by 326%, while decreasing tmax, CL/F, and Vd/F by 64%, 35%, and 46%, respectively ($p < 0.05$).

Conclusions
The UPLC-MS/MS method allows for rapid drug concentration determination using a small amount of biological material. REG co-administration significantly increased TRA exposure, which may support developing new regimens that enhance therapeutic efficacy while considering adverse event risks.

Keywords: trametinib, regorafenib, pharmacokinetics, drug-drug interaction

Funding: The study was designed and executed with the support of institutional statutory funding.

O16

Association between BRG1 and ERβ in colorectal cancer

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Introduction
SWI/SNF complexes regulate gene expression through nucleosome remodeling and their components, including BRG1 (SMARCA4), have been shown to cooperate with nuclear receptors. One of these is estrogen receptor β (ERβ, gene ESR2) whose low expression has been associated with poorer overall survival of CRC patients. It has been shown ERβ interacts with BRG1 in breast cancer. Limited data describe the epigenetic background of ERβ-dependent pathways in CRC. Therefore, we conducted a study to assess the relationship between ERβ and BRG1 in CRC cells.

Materials and methods
Established CRC cell lines, obtained from ATCC, were transduced using lentiviral system with full-length ERβ1, control construct and BRG1 shRNAs. Cells overexpressing full-length ERβ1 and control construct underwent RNA-seq to assess the transcriptomic profile. Expression levels of selected genes, including ESR2 and SMARCA4 were evaluated using qPCR, western blot and immunofluorescence.

Results
RNA-seq data presented reduced expression of SWI/SNF complex components, including BRG1, in ERβ-expressing CRC cells. Cells overexpressing ERβ were characterized with significantly reduced BRG1 expression level compared to control. The effect was more robust with the receptor-activating ligand present (DPN). Immunofluorescence assay likewise showed ERβ-dependent decrease in BRG1 abundance.

Conclusions
Our findings reveal a possible new connection between ERβ and BRG1, demonstrating that ERβ downregulates BRG1 expression in CRC cells.

Keywords: epigenetics, colorectal cancer, BRG1, ERβ

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Poster Session

P1

3D-Printed Bolus for Total Scalp Irradiation: A case study of a 71-year-old woman with metastatic cancer

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Introduction
A 71-year-old woman under oncological surveillance for invasive lobular carcinoma, previously treated with mastectomy and chemotherapy, presented in our clinic with multiple scalp metastases. Given the need for effective management of the symptom and improvement of her quality-of-life, total scalp irradiation was recommended as a palliative treatment option.

Materials and methods
Between June 3rd and June 20th, 2024, the patient underwent total scalp irradiation, receiving a total dose of 39Gy across 13 fractions. Treatment planning employed four full arcs, ensuring that 95% of the planning target volume received 98.85% of the prescribed dose. Imaging was performed using a Siemens SOMATOM go.Top scanner. The resulting DICOM files were processed with 3D Slicer and custom 3D-printed bolus cap was designed to optimize radiation delivery to the scalp.

Results
The treatment plan achieved a conformity index of 0.95, ensuring precise dose distribution while maintaining acceptable maximum doses to organs at risk. Daily imaging was used to monitor air gap volumes. These while the computed tomography simulation scan revealed an initial air gap volume of 127.7 cm^3, which serves as a baseline reference for subsequent cone beam computed tomography (CBCT) acquired during treatment sessions. Over the course, the recorded air gap volumes varied between 97.1 cm^3 and 138.7 cm^3, indicating constant size fluctuations. This variability suggests that factors like patient positioning or anatomical dynamics may influence the air gap.

Conclusions
The custom 3D-printed bolus cap significantly improved treatment efficacy, aiding symptom relief. This case study underscores the importance of personalized treatment planning in palliative care for metastatic cancer patients.

Keywords: 3D printing, scalp irradiation, treatment planning, palliative radiotherapy

Funding: None.

P2

Albumin-Based Nanoparticles as a Novel Approach for Systemic Lutein Delivery

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Introduction
Lutein is an antioxidant carotenoid with anticancer potential established in cell studies. However, its poor water solubility poses a challenge to effective systemic administration, limiting its therapeutic application. In this study, we developed albumin-based nanoparticles as a delivery system for lutein. Albumin nanoparticles are a recognized pharmaceutical formulation in cancer therapy, enabling intravenous administration of poorly soluble compounds while reducing adverse effects compared to conventional anticancer treatments.

Materials and methods
Lutein-loaded nanoparticles were synthesized using a modified nab technology and characterized in terms of particle size, polydispersity index (PDI), and zeta potential. To enable long-term storage, nanoparticles were freeze-dried, then assessed for particle characteristics upon reconstitution. Additionally, lutein content and entrapment efficiency were evaluated, and stability was examined across various dilutions to assess controlled release potential.

Results
The synthesized nanoparticles demonstrated a mean particle size of 133.50 ± 2.84 nm, a polydispersity index of 0.194 ± 0.014, and a zeta potential of -28.13 ± 1.79 mV. Upon rehydration, lyophilized particles retained similar size (132.63 ± 3.18 nm), PDI (0.195 ± 0.014), and zeta potential (-27.24 ± 4.89 mV). Lutein content in the formulation reached 4.39 ± 0.13 %, with an entrapment efficiency of 89.74 ± 2.83 %. Size stability across dilutions indicated a potential for controlled lutein release upon intravenous administration.

Conclusions
Albumin-based nanoparticles present a promising intravenous delivery system for lutein, enhancing its bioavailability and controlled release. Further studies are needed to determine lutein's crystallinity and release conditions from nanoparticles to fully harness its therapeutic potential.

Keywords: lutein, albumin nanoparticles, intravenous delivery, anticancer, controlled release

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P3

Comparison of the safety profiles of CDK4/6 inhibitors used in hormone receptor-positive breast cancer - a survey study

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Introduction
CDK4/6 inhibitors (palbociclib, riboiclib and abemaciclib) are a modern group of drugs used in combination with hormone therapy for the treatment of hormone-dependent, HER2-negative breast cancer. Despite their comparable antitumor efficacy, there are clear differences between them in terms of toxicity profile and their potential for interaction. These characteristics could serve as a criterion for selecting a ciclib for a patient as part of treatment personalization.

Materials and methods
The study was conducted by questionnaire method in a group of 157 patients diagnosed with hormone-dependent breast cancer, in which 106 patients were qualified for treatment with one of three CDK4/6 inhibitors in combination with hormone therapy, and 49 patients as the control group using hormone therapy alone.

Results
There was a lower chance of adverse reactions of any kind in the ciclib plus hormone therapy group compared to the control group ($OR < 1$; $p < 0,05$). The highest chance of an adverse reaction occurred in the order abemaciclib > ribociclib > palbociclib ($p < 0,05$). The chance of adverse effects in the abemaciclib group was more pronounced in the subgroup with $BMI < 30$ than $BMI \geq 30$.

Conclusions
CDK4/6 inhibitors improve tolerability of breast cancer hormone therapy. The greatest chance of adverse effects occurs in patients taking abemaciclib. In patients with a $BMI \geq 30$, the pharmacological activity of abemaciclib may be reduced. Patients taking ciclibes should be eligible for drug review in terms of summation of side effects with concomitant therapies, and in terms of ciclib-dependent cytochromes and membrane transporters modification.

Keywords: CDK4/6 inhibitors, hormone-dependent breast cancer, adverse drug reactions, drug interactions

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P4

Development and validation of the RP-HPLC method for quantitative determination of phytosterols in intravenous lipid emulsions

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Introduction
Intravenous lipid emulsions are the primary energy source in parenteral nutrition, supporting energy balance and supplying essential unsaturated fatty acids. Most emulsions are derived from vegetable oils, which are rich in phytosterols. Since these compounds are not fully metabolized by the human body, they are excreted via the hepato-biliary system. The presence of phytosterols is linked to alterations in liver function test results and is considered a contributing factor in the pathogenesis of intestinal failure-associated liver disease (IFALD).

Materials and methods
The main aim of the conducted research was to develop and validate a method for the simultaneous separation and quantification of two phytosterols, stigmasterol and β-sitosterol, using RP-HPLC. Optimal separation was achieved with an octadecylsilane column and a mobile phase consisting of methanol and acetonitrile in a 15:85 ratio with a flow rate of 1.0 mL/min. Chromatograms were recorded at 202 nm.

Results
The calibration curves were linear over a concentration range of 0.001 - 0.1 mg/mL for both analyzed phytosterols. The LOD and LOQ were 1.07 and 3.25 µg/mL for stigmasterol and 0.89 to 2.75 µg/mL for beta-sitosterol. The method demonstrated acceptable precision, with relative standard deviation values below 1%. Accuracy was assessed through recovery percentages, which were within the acceptable range of 99.64 – 100.56%.

Conclusions
In conclusion, the developed method was comprehensively validated for linearity, precision, and accuracy in alignment with current guideline requirements, demonstrating its reliability and suitability for stigmasterol and β-sitosterol quantification in intravenous lipid emulsions.

Keywords: phytosterols, RP-HPLC, validation, intravenous lipid emulsions

Funding: This work was funded by grant LIDER/17/0092/L-12/20/NCBR/2021 from the National Centre for Research and Development, Poland.

P5

Development of 3D Cell Culture Models for Translational Research and Immunotherapy Studies

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Introduction
In the ever-evolving landscape of biomedical research, 3D Cell Culture (3DCC) systems have become essential for replicating in vivo environments and promoting more physiologically cellular interactions and microenvironment. 3DCC models can be beneficial in preclinical studies by reducing drug testing costs and minimizing the excessive use of animal models.

Materials and methods
In our experiments we used RL95-2 (endometrial carcinoma) cells in the 3D co-culture with PBMCs in the presence of immune checkpoint inhibitors: atezolizumab, ipilimumab, onvatilimab. We provide 3DCC for CFPAC-1, MiaPaca-2, and PANC-1 cells in the presence of drugs from clinical treatment. 3D cell cultures were provided on the LifeGel®. Cell viability was measured using CellTiter-Blue® using the protocol optimized for 3D cell culture.

Results
We demonstrate a new in vitro model for verifying the potency of immune checkpoint inhibitors. We propose a co-culture with PBMCs in the presence of tested biologics, where the viability of 3D structures is evaluated. Moreover, we develop an innovative platform for testing the efficacy of anti-pancreatic cancer drugs. We demonstrate that young and old 3DCC structures exhibit completely different responses to drug treatments, a phenomenon that cannot be observed in 2D cell culture conditions!

Conclusions
In the realm of cancer research, 3D cell cultures showcase a predictive power in assessing the mechanistic effects and anticancer effects of drugs that rivals traditional in vivo research models. LifeGels® biophysical parameters can be modified: hardness, density and elasticity, creating an environment adapted to every characteristic of cancer cells, and making them accessible to immune cells evasion and biologics penetration.

Keywords: anti-cancer therapies, drug development, 3D cell culture, viability assays

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P6

Differential response of human acute myeloid leukemia cells to selective MCL-1 inhibitor S63845

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Introduction
Myeloid cell leukemia-1 (MCL-1) is an anti-apoptotic protein from the BCL-2 family that prevents cell death by interacting with pro-apoptotic proteins. Its overexpression is crucial for the survival and growth of acute myeloid leukemia (AML) cells and contributes to treatment resistance. This led to the development of the selective MCL-1 inhibitor, S63845. The aim of this study was to evaluate the effect of S63845 on AML cells.

Materials and methods
The study was conducted in vitro on a panel of human AML cell lines that represent different AML subtypes, such as KG-1, HL-60, NB-4, and ML-1 cell lines. The Presto Blue assay was used to assess concentration-dependent cell viability and determine the IC50 value for each leukemia cell line. The expression levels of MCL-1 protein before and after cell treatment with S63845 were analyzed using Western Blot technique. Apoptosis induction was analyzed with a cytometric annexin V/propidium iodide assay.

Results
Results demonstrated that S63845 reduced cell viability in a concentration-dependent manner and increased apoptosis. A correlation was found between MCL-1 expression levels and cell sensitivity to S63845: KG-1 and ML-1 cells, which exhibited higher MCL-1 expression, were more resistant, whereas HL-60 and NB-4 cells, with lower MCL-1 levels, were more sensitive. Significantly, MCL-1 protein levels in AML cells decreased after treatment with S63845.

Conclusions
These findings indicate that S63845 effectively induces apoptosis and lowers MCL-1 expression, positioning it as a promising agent for targeted AML therapy. Further studies are needed to explore the detailed anti-cancer mechanisms of S63845 and its potential clinical applications.

Keywords: acute myeloid leukemia, BCL-2 protein family, MCL-1 inhibitors, S63845, apoptosis

Funding: The study was supported by the grant from Polpharma Scientific Foundation.

P11

Dosimetric verification of point doses for I-125 implants designed by different manufacturers in prostate brachytherapy

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Introduction
The purpose of this study is to determine the effect of the type of I-125 radioactive source on dose distribution in the planning process of ultra-low dose rate (uLDR) prostate brachytherapy.

Materials and methods
7 patients who had undergone brachytherapy in our center were included in the study. Dose in five geometrical points were analyzed for 12 types of implants that are available on the market. The plans were originally calculated for S17plus implant model (Eckert & Ziegler Medical). Point dose calculations were performed using RadCalc(LAP) software.

Results
The differences in doses for individual points were significant. The largest differences were observed at the point located in the center of the patients' urethra and between BestMedical 2301 (highest doses for each point) and IsoStar (lowest doses) implants.

Conclusions
The choice of implant manufacturer strongly influences what dose distribution will be obtained for the prostate. It is possible to obtain satisfactory plans that meet the dosimetric criteria for each type of implant, but the positioning of each source will vary significantly.

Keywords: brachytherapy, iodine seeds, prostate cancer, dose verification

Funding: None.

P12

Drug-related problems in oncologic patients based on retrospective analysis of medical records

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Introduction
The aim of the study was to analyze DRPs among patients hospitalized at the Greater Poland Center in Poznan between 01/01/2022 and 31/01/2023. In this regard the characteristics of the patient with the highest risk of DRP was determined, and the most common cause of DRP was identified. Thus areas of priority for clinical pharmacists were established.

Materials and methods
Pharmacotherapy was assessed retrospectively from the medical records of 31 patients, including anthropometric data, laboratory and microbiological results. PCNE V.9.1- 2020 classification was used to clasify DRPs. Shapiro-Wilk, Mann-Whitney and Kruskal-Wallis tests were used for statistical analysis.

Results
DRPs occurred in 94% of patients. The most common DRPs in the study group were adverse drug reactions (possibly) occurring (62%), unnecessary drug therapy (18%), especially with proton-pump inhibitors and suboptimal treatment effect (16%). The drug classes with the highest number of DRPs were antimicrobials, especially amikacin (18%), drugs for acid related disorders and psycholeptics. More DRPs occured in non-surgical wards, maliny radiotherapeutic ones, than in surgical wards (p=0.0031). There was a higher risk of DRP in patients with eGFR<60 ml/min. than in those with eGRF>60 ml/min. (p=0,0374). 99% of identified DRPs were preventable.

Conclusions
Implementation of a routine clinical pharmacy service for pharmacological consultation is justified, especially for patients treated with radiation therapy and patients with reduced renal function. Antibiotic therapy should be consulted by a multidisciplinary team. Given the difficult staffing situation in health care, training on recommendations for monitored therapy, indications for PPIs and proper antibiotic therapy is recommended.

Keywords: pharmacotherapy, drug-related problems

Funding: None.

P13

Efficacy of the combination of venetoclax and MAPK pathway inhibitor in acute myeloid leukemia cells

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Introduction
Acute myeloid leukemia (AML) is a fast-progressing bone marrow malignancy marked by the buildup of abnormal cells of the myeloid lineage. Due to the complexity and molecular heterogeneity of AML, its treatment is challenging. In the recent years, the development of targeted therapies focusing on proteins of signaling pathways involved in cell growth, proliferation and cell death has become increasingly significant. Among them, BCL-2, an antiapoptotic protein from the BCL-2 family, and mitogen-activated protein kinase (MAPK) are overexpressed in AML, contributing to the excessive cell proliferation and chemoresistance, making them promising candidates for new therapies. This study evaluated the effects of the MAPK pathway inhibitor, PD98059 (PD) and the BCL-2 inhibitor, venetoclax (ABT-199) on the AML HL-60 cell line.

Materials and methods
To assess the impact of PD, ABT-199, and their combination on leukemia cell viability, the Prestoblue assay was used. HL-60 cell viability was measured and compared in both 2D and 3D culture models, the latter prepared using PuraMatrix Peptide Hydrogel. Changes in leukemia cell count were determined with Coulter method. Additionally, cytotoxicity of the tested agents was analyzed through cell cycle progression (propidium iodide staining) and apoptosis (annexin V/propidium iodide assay).

*Re*sults
Results showed that the combination of PD and ABT-199 decreased HL-60 cell viability compared to each compound alone, with stronger effects observed in the 2D culture. These inhibitors together significantly increased apoptosis and disrupted the cell cycle in HL-60 cells.

Conclusions
Study highlights the synergy of PD and ABT-199 and the importance of the MAPK and BCL-2 in AML.

Keywords: acute myeloid leukemia, BCL-2 protein family, venetoclax, MAPK signaling pathway, targeted therapy

Funding: The study was supported by the grant from Polpharma Scientific Foundation.

P14

HtrA1 expression and its potential connection to chemotherapy resistance in breast cancer

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Introduction
Breast cancer (BC) is the most commonly diagnosed cancer in women worldwide. Despite advancements in treatment, chemotherapy resistance remains a significant challenge, impacting patient outcomes. Recent studies suggest that the serine protease HtrA1 regulates cellular processes related to stress response, mitochondrial function, and apoptosis. HtrA1 is often downregulated in cancers, indicating its potential role as a tumour suppressor. While limited research has focused on HtrA1 in BC, some studies show reduced HtrA1 expression correlates with more aggressive disease and worse prognosis. This study explores the relationship between HtrA1 expression and chemotherapy response in BC.

Materials and methods
Four BC cell lines representing different molecular subtypes were studied: triple negative (TN) BC (MDA-MB-231), HER2+ (SKBR3), luminal A (T47D), and luminal B (BT474). IC50 for cisplatin and paclitaxel was measured using the MTT assay. HtrA1 expression was quantified using qPCR on material collected from in vitro cultures.

Results
Significant differences in HtrA1 expression were observed among the cell lines, with TNBC showing the highest and HER2+ the lowest expression. The highest resistance to cisplatin was shown for TNBC, while the HER2+ cells were the most sensitive. HER2+ cells were also the most sensitive to paclitaxel, while luminal B cells were the most resistant. No correlation between HtrA1 expression and drug sensitivity was found.

Conclusions
BC cell lines showed significant differences in HtrA1 expression and chemotherapeutics sensitivity depending on the molecular subtype, however, more research needs to be done to prove whether there is a correlation between expression and resistance to chemotherapy.

Keywords: HtrA1, cisplatin, paclitaxel, chemosensitivity, breast cancer

Funding: Greater Poland Cancer Centre

P15

Hypercoagulability State Combined with Post-Treatment Hypofibrinolysis in Invasive Breast Cancer: A Seven-Year Follow-Up Evaluating DFS and OS

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Introduction
Cancer treatment, including chemotherapy, endocrine therapy, targeted therapy and radiotherapy, has been identified as an important independent risk factor for venous thromboembolism in cancer patients. The aim of the study was to evaluate the effect of adjuvant therapy on the coagulation and fibrinolysis components in invasive breast cancer.

Materials and methods
Tissue factor pathway inhibitor (TFPI), tissue factor (TF), tissue plasminogen activator (t-PA), plasminogen activator inhibitor-1 (PAI-1) antigen (concentration) and TFPI and TF activities were examined in the blood samples of 60 breast cancer patients treated by adjuvant chemotherapy, endocrine therapy, radiotherapy and immunotherapy. Blood samples were taken 24 h before primary surgery and 8 months after tumour removal surgery.

Results
Adjuvant therapy administrated to breast cancer patients significantly increased the concentration of plasma TF, the PAI-1 antigen and also the activity of TFPI and TF, but significantly decreased the level of the t-PA antigen. Combined chemotherapy and endocrine therapy, but not monotherapy, has an important effect on haemostatic biomarker levels.

Conclusions
Breast cancer patients receiving adjuvant therapy have an elevated risk of developing a hypercoagulability and hypofibrinolysis state leading to venous thromboembolism.

Keywords: breast cancer, adjuvant treatment, hemostasis, cancer therapy-associated thrombosis

Funding: None.

P16

Inhibition of HSF1 activity reduces the proliferation of estrogen-positive breast cancer cells and increases the effectiveness of hormone therapy

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Introduction
Breast cancer is the most common malignant tumor in women. About 70% of cases are positive for estrogen receptor (ER) expression. They are first treated with hormonal therapy using ER antagonists (e.g. tamoxifen) or inhibitors of estrogen synthesis. However, 20-40% of patients develop metastases. Recently we found the potential role of Heat Shock Factor 1 (HSF1) in the growth of ER+ breast cancer. HSF1 is a well-known transcription factor regulating the cell response to stress. It is also activated by estrogen in ER+ breast cancer cells. We decided to study the effect of HSF1 inhibition on ER+ breast cancer cells and their response to tamoxifen.

Materials and methods
We used ER+ breast cancer cells corresponding to luminal A (MCF7, T47D) and luminal B (BT-474) types and non-tumorigenic mammary epithelial MCF10A cells. We tested the effect of three commercially available HSF1 inhibitors (CCT251236, KRIBB11, DTHIB) on cell proliferation, HSF1-dependent gene expression, and response to tamoxifen.

Results
We established the IC50 for tested compounds for all used cell lines. We found that each inhibitor reduced HSF1-dependent gene expression and cell proliferation at compound concentrations around the IC50 with accompanying changes in the cell cycle. Unlike CCT251236 and KRIBB11, DTHIB was the most effective in reducing HSF1 and ESR1 (ERα) levels. The tested compounds also increase the sensitivity of breast cancer cells to 4-hydroxytamoxifen (the active metabolite of tamoxifen).

Conclusions
Our results indicate that HSF1 inhibition may affect the growth of ER+ breast cancer cells and increase their sensitivity to tamoxifen.

Keywords: breast cancer, HSF1, HSF1 inhibitors, estrogen receptor, tamoxifen

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P17

Irradiation of uveal melanoma cells in 2D and 3D in vitro models

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Introduction
Uveal melanoma (UM) is the most common eye cancer. It is characterized by high mortality due to metastases, which affect about 50% of patients. Metastases are difficult to treat due to the lack of effective therapies. 3D spheroid model allows modeling of the tumor microenvironment and studying the interactions between different types of cells and their response to treatment. In our study we focus on cellular response to radiation of UM cells in the 2D and 3D in vitro models.

Materials and methods
We have used Mel270 UM cell line from primary tumor together with normal human Hepatic Stellate Cells and Human Microvascular Endothelial Cells to form spheroids. They were prepared by the hanging drop method. Cells and spheroids were irradiated by 1-20 Gy of X-Ray radiation using Xstrahl irradiator.

Results
Already 3 Gy led to growth inhibition of 2D Mel270 cells. However, in 3D model slightly higher doses were required to inhibit proliferation. The morphological structure of spheroids remained unchanged even at 20Gy.

Conclusions
Our study shows that 2D and 3D models of uveal melanoma cells differ in their response to radiotherapy, which highlights the need for more complex in vitro models. In the 2D model, inhibition of cell growth was observed at low doses of radiation, whereas in the 3D model, the spheroid structure remained stable even at higher doses, but their growth and migration were inhibited. The use of a 3D model may contribute to the development of more effective therapeutic strategies that take into account the specific properties of the microenvironment.

Keywords: irradiation, uveal melanoma, in vitro, spheroids, 3D

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P18

Liposomal Delivery of Natural Compounds for Glioblastoma Multiforme Therapy: Stability and Cytotoxicity Analysis

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Introduction
Glioblastoma multiforme (GBM) is an aggressive brain cancer with limited treatment and a 5-year survival rate of 4-5% (1). Natural compounds such as cannabidiol and naringenin have anticancer properties but limited bioavailability (2) (3). Using liposomes, self-assembling nanostructures comprising a lipid bilayer represent an innovative delivery of natural compounds to tumor cells (4) (5).

Materials and methods
The study demonstrated that cannabidiol (CBD), naringenin (NG), and their combination (CBD+NG) can be encapsulated in negatively charged liposomes using thin lipid film hydration. The CBD, NG, and POPC phospholipids were dissolved and evaporated to create a dry lipid film. This film was hydrated to form a heterogeneous group of liposomes, which were extruded to obtain a homogeneous population. Nanoformulations were evaluated for particle size, polydispersity index (PDI), zeta potential, and shelf life for 15 days (2-4°C and 22°C). Their anticancer potential against GBM cell lines was tested in vitro using the MTT assay.

Results
The liposomes demonstrated an average particle size of <151 nm (T0) and <184 nm (throughout the experiment), a PDI <0.3, and a negative zeta potential. Nanoformulations against U87 and UMG138 cells showed exhibited at IC50>25 μM. The most potent cytotoxic effect was observed with CBD+NG on the U87 glioma cell line.

Conclusions
The nanoformulations were homogeneous and stable for 15 days regardless of their storage temperature, as evidenced by a narrow particle size distribution, a low PDI <0.3, and a negative zeta potential. Moreover, liposomes <200 nm were produced, crucial for the effective compound delivery into the tumor microenvironment.

Keywords: cancer, glioblastoma, cannabidiol, naringenin, liposomes

Funding: None.

P19

lncRNA EGOT is the marker of HPV infection and a prognostic factor for HNSCC patients

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Introduction
High-risk human papillomavirus (HPV) contributes to oropharyngeal cancers through mechanisms involving the deregulation of host cell functions by oncoproteins E6 and E7. Changes in the epigenome, particularly involving long non-coding RNAs (lncRNAs), are crucial for understanding HPV-related carcinogenesis.

Materials and methods
This study aimed to analyze the expression levels of lncRNAs in HPV-related head and neck squamous cell carcinoma (HNSCC) to determine their biological and clinical significance, addressing the current gap in clinically validated biomarkers for early screening and therapeutic interventions.

Results
The study highlights the significant overexpression of the EGOT gene in HPV-positive HNSCC samples, suggesting its potential as a marker to distinguish between HPV-negative and HPV-positive cases. Furthermore, high EGOT expression correlates with better overall survival (OS) and indicates possible resistance to 5-fluorouracil (5-FU) therapy, making it a valuable prognostic factor.

Conclusions
These findings underscore the potential of incorporating EGOT expression analysis in clinical practice for improved patient stratification and treatment outcomes in HNSCC.

Keywords: EGOT, HNSCC, lncRNAs, HPV

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P20

Parenteral Nutrition Lipid Emulsions as Carriers for Cyanidin and Tangerine Oil

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Introduction
Cyanidin and tangeretin (present in tangerine oil) are polyphenolic compounds recognized for their anti-inflammatory, antioxidant, and anticancer properties. However, their limited water solubility restricts practical applications. Nanoemulsions provide a promising delivery system for these compounds, improving their bioavailability and effectiveness. This study aimed to formulate emulsions with selected polyphenols and assess their physicochemical properties.

Materials and methods
In the initial step, individual core emulsions were prepared for each compound by combining the aqueous and lipid phases through ultrasonic homogenization. These samples were subsequently incorporated into commercial emulsions: Lipofundin, Lipidem, and Smoflipid and subjected to ten cycles of high-pressure homogenization followed by heat sterilization. The resulting samples were then assessed for their physicochemical properties.

Results
All polyphenol-enriched emulsions demonstrated pH and osmolarity levels within acceptable ranges. The mean droplet diameter varied between 200 and 322 nm for cyanidin emulsions and 180 to 313 nm for tangerine oil emulsions. The critical PFAT5 parameter (0.05%) was not exceeded in samples containing tangerine oil. For cyanidin emulsions, the PFAT5 value also remained below 0.05% when combined with Lipidem and Smoflipid but exceeded this threshold with Lipofundin.

Conclusions
In conclusion, cyanidin emulsions prepared with Lipidem and Smoflipid demonstrated favorable physicochemical properties, while all tangeretin emulsions consistently complied with pharmacopoeial standards throughout the study period.

Keywords: nanoemulsion, anticancer, drug delivery, cyanidin, tangerine oil

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P21

Protein nanoparticles loaded with active compounds from Magnolia officinalis

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Introduction
Nanotechnology has been widely applied in pharmaceutical sciences, particularly in the synthesis of drug nanocarriers. This approach enables the use of compounds previously limited by unfavorable physicochemical properties. Due to their biocompatibility, non-toxicity, biodegradability, and non-immunogenicity, albumins are commonly used in nanoparticle synthesis. This study aimed to develop albumin-based nanocarriers loaded with honokiol and magnolol, which possess well-documented anticancer, anti-inflammatory, and antioxidant properties.

Materials and methods
The selected compounds were dissolved in a suitable organic solvent and added to the albumin solution. All samples were stirred on the magnetic stirrer for 10 min, centrifuged, and subjected to manual and ultrasonic homogenization (two-step process) or only ultrasonic homogenization (one-step process). Organic solvents were then evaporated on a rotary evaporator under reduced pressure. Particle size and zeta potential were measured immediately after sample preparation.

Results
The albumin nanoparticles synthesized through a two-step process exhibited average sizes of 90.53 nm for magnolol and 197.0 nm for honokiol, with zeta potentials of -19.8 mV and -38.7 mV, respectively. Conversely, when only ultrasonic homogenization was applied, the nanoparticles measured 111.5 nm for magnolol and 30.51 nm for honokiol, with average zeta potentials of -18.8 mV and -17.0 mV, respectively. Regardless of the synthesis method, albumin nanoparticles containing polyphenols displayed heterogeneity, with the presence of fractions II and III observed across all samples.

Conclusions
The studies conducted suggest that albumin-based nanocarriers hold promise as an effective delivery system for magnolol and honokiol. However, additional research is needed to confirm their stability and safety for application.

Keywords: albumins, polyphenols, nanotechnology, nanoparticles, anticancer

Funding: This work was funded by grant OPUS No. 2022/45/B/NZ7/01056 from the National Science Centre, Poland

P22

Senescence in head and neck squamous cell carcinoma: link between senescence-associated secretory phenotype (SASP) expression and clinicopathological features

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Introduction
Cellular senescence is a state where cells cease to divide and become resistant to apoptosis. In the context of cancer, senescence can be activated by oncogenes or induced through therapeutic interventions. Although cellular senescence is thought to play a protective role against tumor formation, the excessive buildup of senescent cells can promote cancer development by releasing pro-inflammatory factors collectively known as the senescence-associated secretory phenotype (SASP).

Materials and methods
We analyzed the mRNA expression levels of selected cellular senescence markers (p16 and LMNB1) and SASP factors (IL-6, IL-1b, CXCL-1, and TNF-α) in 72 cancerous and 64 normal tissue samples from patients with head and neck squamous cell carcinoma (HNSCC) of the larynx and oral cavity, and correlated these findings with clinical follow-up data.

Results
Our results indicate higher levels of selected SASP factors in cancerous compared to normal tissues. We presented the relationship between SASP factors expression at the transcript level and the progression of the disease. Moreover, we proposed CXCL1 as a candidate biomarker differentiating normal tissues from cancerous ones and IL1b expression as a molecular factor related to increased TNM stage.

Conclusions
Our initial study suggests that SASP expression may be linked to certain clinicopathological features. However, further in-depth research is required to clarify the specific roles of senescence-related mechanisms and SASPs, particularly regarding tumor response to therapy and the condition of the patient's immune system.

Keywords: cellular senescence, head and neck cancer, SASP

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P23

The drug development in Europe vs U.S.: special focus on Theranostics

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Introduction
The evolving radioisotope diagnosis and therapy demand rapid drug development. While the availability of novel radiotracers is limited worldwide, the United States (U.S.) Food and Drug Administration (FDA) and the European Medicines Agency (EMA) seem to share one goal: to make novel radiotracers accessible reality.

Materials and methods
Several documents, including the U.S. FDA and EMA's regulations, European Union (EU) Commission projects, as well as the most recent clinical trials and scientific reports, were analyzed to evaluate the current status and future perspectives of the U.S. and EU drug development. Focusing on Theranostics, the timeline of the novel radiocompounds' release and registration in the EU and U.S. was analyzed and compared to present the differences, common denominators and expected outcomes.

Results
Since 2019, when the U.S. government released an official regulatory document defining the term diagnostic and therapeutic radioisotope agents available for commercial use, the EU has focused on rapid drug development without strictly establishing clinical application goals. In May 2021, the EU announced the European Programme for Medical Radionuclides (PRISMAP) and PRISMAP consortium opening, aiming to synthesize and test high-purity radionuclides for diagnosis and therapy, focusing on Theranostics. As a result, multiple novel radionuclides have been introduced to nearly thirty medical centres in EU countries, including alpha-emitters, which are currently considered the future of Theranostics.

Conclusions
The EU pre-clinical studies constantly evolve while the U.S. NM industry focuses on clinical testing and formal registration, ensuring future radiopharmaceuticals' commercial availability.

Keywords: drug development, nuclear medicine, oncology, radiopharmaceuticals, theranostics

Funding: None.

P24

The impact of hypoxia on m6A RNA signatures in HNSCC pathogenesis

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Introduction
Hypoxia is a common feature of solid tumors, including head and neck squamous cell carcinoma (HNSCC) and it is considered as hallmark of cancer. HIF1α (Hypoxia- inducible factor 1α) is a main transcriptional factor mediating metabolic changes in tumor microenviroment in response to lower oxygen supplies. N6-methyladenosine (m6A) as the most abundant and conserved epigenetic modification of eukaryotic mRNA, plays a role in development of hypoxic, hypoglycemic and acidic TME by regulating HIF protein expression. However, m6A RNA and hypoxia both influence similar events in cancer cells.

Materials and methods
RNA from HNSCC Fadu and Detroit-562 cell lines cultured in normoxic (21% O2) and hypoxic (1%O2) conditions were collected after 24, 48 and 72 hours to further analysis - The real-time quantitative polymerase chain reaction (RT-qPCR) was performed to quantify mRNA level of: HIF1A gene to establish hypoxic conditions in vitro and m6A RNA related genes- METTL3 (writer), FTO (eraser), YTHDF2 (reader) and YTHDC2 (reader)

Results
In FaDu cell line, the relative transcript levels of METTL3, FTO , and YTHDC2 were significantly higher in hypoxic conditions in comparison to normoxia ($p < 0.05$). Similarly, in the Detroit 562 cell line, the relative mRNA levels of METTL3, YTHDF2, and YTHDC2 were significantly higher under hypoxia in comparison to normoxia ($p < 0.05$).

Conclusions
Our study reaveals changes in m6A RNA- related genes expression in hypoxic conditions in comparison to normoxia in head and neck cancer cell lines. This suggest that hypoxia and m6A RNA methylation may interact and act simultaneously in tumor progression.

Keywords: head and neck cancer, hypoxia, hypoxia inducible factors, m6A RNA methylation

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P25

The importance of Endocrine Disturbing Factors in relation to breast cancer- Review Case

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Introduction
Endocrine Disturbing Factors are substances present in the air, soil and water supply. They're used in personal care products, as well as preservation of vegetables and fruits and are also present in plastic containers such as water bottles. There are many allegations about carcinogenic effects and possible long-term effects of these compounds. In this review case, we will take a closer look to xenoestrogens in correlation with breast cancer.

Materials and methods
There was total of 53 178 articles related to the phrase" Breast cancer", 78 related to "EDCs induced breast cancer" and 4 090 results related to "EDCs" searched on Pubmed platform. The possible or proven role of EDCs in the process of carcinogenesis in chosen articles, were highlighted.

Results
The results of the study included a list of compounds that are related to the carcinogenesis of breast cancer and a list of mechanisms in which they contribute to the disruption of endocrine functions in the body. Moreover, in addition to reports on breast cancer, the paper also included references to their other long-term effects. The substances that got included in the research were: PCBs, Parabens, Phenols, Organochlorine Pesticides, TCDD, DEHP, BPA, mycotoxins, phytoestrogens.

Conclusions
The topic of EDCs causing breast cancer has recently started to arouse interest and more reports on this topic have started to appear. However, the compounds to which the research relates are few and far between. With this work, we hope to draw attention to breast cancer and the EDCs that accumulate in the body and exert carcinogenic effects.

Keywords: breast cancer, EDCs, review case

Funding: None.

P26

Verification of the usefulness of the VarianESAPI-EQD2Converter script in clinical practice

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I*ntroduction*
The usefulness of the EQD2 (Equivalent Dose in 2Gy Fractions) formula is that the resulting doses are additive (on the same scale and therefore summable), which is useful for normalizing a diverse group of fractionated treatment regimens for analysis of their outcomes by clinicians.

Materials and methods
My work aimed to test the performance of a VarianESAPI-EQD2Converter script created to convert nominal dose distributions to EQD2 for use in the Eclipse treatment planning system. This tool is very useful in everyday practice, as Eclipse cannot independently calculate the patient's EQD2.

Results
In the first stage of my research, I studied 25 patients with glioma (60Gy/2Gy) to assess the accuracy of EQD2 calculations for three critical structures: the brainstem, eye lens, and inner ear, which do not overlap. I selected three different α/β values for each structure based on the literature. When a 3 mm margin was applied, the EQD2 calculations matched my results. However, without the margin, results varied with different α/β values (ear σ: 0.36-0.45Gy, brainstem σ: 0.50-0.67Gy, eye σ: 0.21-0.52Gy). Overall, higher α/β values led to smaller differences between script-calculated EQD2 and my values. In the second stage, I analyzed 15 prostate cancer patients (70.2Gy/2.6Gy) to compare EQD2 calculations using two overlapping region approaches: "increasing" and "decreasing" by α/β. The "increasing" approach yielded higher EQD2 values for the rectum (σ=0.52Gy) and bladder (σ=0.56Gy) compared to the "decreasing" approach.

Conclusions
In conclusion, the script is a valuable clinical tool. Differences stem from the computation grid and algorithms used.

Keywords: EQD2, eclipse, α/β

Funding: None.

P27

What is the landscape of the uterine, vaginal, and gut microbiome in patients with gynecological cancers?

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Introduction
Nowadays, human microbiome studies have broadened dramatically, providing insights into contributions to various cancer incidents. Altered gut microbiome initiates an inflammatory response through microorganism-associated molecular patterns, leading to intensified steroidogenesis. Additionally, bacteria secrete the enzyme β-glucuronidase and may increase the level of circulating estrogen. Unfortunately, gynecological cancers still lack clear conclusions due to the hard availability of sampling. This study aimed to describe the composition of microbiomes in patients with endometrial and ovarian cancers. Niches of interest were gut, uterus, and vagina.

Materials and methods
The laboratory workflow consists of DNA extraction from swab samples, PCR, and 16S rRNA sequencing. Compositional data analysis was performed including ordination based on the variance and differential abundance analysis. Complementary, top taxa charts and alpha-diversity measures were conducted.

Results
83 patients and 52 healthy women were recruited. 1355 different taxa were identified. Anorectal subset had the highest diversity, evenly distributed within the diagnoses. Uterine and vaginal samples indicated slightly higher diversity for patients with endometrial pathologies than ovarian. The healthy uterus microbiome was dominated by Lactobacillus. However, it consists of much more diverse taxa in the ovarian cancer group than others.

Conclusions
Coexisting microbiomes differ strongly within the body sites. The gut microbiome consists of a population of genera highly differentiated, remaining signals of healthiness. The opposite in the vagina, higher diversity was associated with pathology occurrence. Continuously in the uterus, a low-abundant site exposed to the maintenance of potential predatory species. Demanding further investigations and discussions, gynecological microbiomes remained the double nature of the invader and the guard.

Keywords: microbiome, gynecological cancers, nanopore sequencing, immunology, microbiology

Funding: PhD Minigrants 102, Initiative of Excellence - Research University – ‘Skład mikrobioty macicznej u kobiet z patologiami ginekologicznymi’, 102/13/SNP/0001, 10.2023 – 12.2024

P28

Assessment of genetic predisposition in patients with neuroendocrine pancreatic tumors, treated at the National Institute of Oncology, the Gliwice Branch

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Introduction
Pancreatic neuroendocrine tumours are rare diseases of unknown etiology. However, it is known that they can develop due to a genetic predisposition, for example, as components of neoplasm syndromes, such as multiple endocrine neoplasia syndrome MEN1 or von Hippel-Lindau syndrome (VHL). The aim of the study is to analyse how often patients with pancreatic neuroendocrine tumours treated at the National Institute of Oncology, Branch in Gliwice show a genetic predisposition to MEN1 and VHL syndromes and whether this predisposition affects the course of the disease.

Materials and methods
The study included 134 patients who presented with the diagnosis or suspicion of pancreatic neuroendocrine tumour between 1994 and 2023. In order to select this group of patients, the records of 200 patients treated at the National Institute of Oncology, Branch in Gliwice, were retrospectively reviewed.

Results
Genetic tests were performed in 114 of them, including MEN1 mutation in 14 cases and VHL mutation in 5 cases. The article will present the types of mutations in both genes and an analysis of the severity of the disease.

Conclusions
The presented analysis clearly indicates that when diagnosing pancreatic neuroendocrine tumours, the possibility of an existing genetic predisposition is insufficiently taken into account. According to ASCO recommendations, genetic testing for an existing predisposition should always be performed if this predisposition covers 10% of cases or more. This study was also presented at conference “Studenckie Onkoforum” organized by National Research Institute of Oncology in Warsaw, in May 2024.

Keywords: endocrine, pancreas, MEN1, VHL, NET

Funding: None.

P29

Analysis of cancer-related differentially expressed genes in subcutaneous muscles of a Huntington's disease mouse model

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Introduction:
A reduced incidence of cancer has been observed among patients with Huntington's disease (HD). In light of the underlying cause of HD, namely the abnormal huntingtin protein, it seems plausible to suggest that its effect on cancer-specific gene expression may be a potential avenue of investigation. Due to the strong association of the extracellular matrix with the nature of the tumor, we proceeded to test whether changes in the expression of tumor-associated genes were present in the subcutaneous muscles (SMs) of the R6/2 mouse model of HD.

Material and methods:
SMs were harvested from R6/2 mice and controls. After RNA isolation from those tissues, they were subjected to microarray analysis. The data obtained were used for bioinformatics analyses to determine changes in gene expression.

Results:
A total of thirty genes exhibited decreased expression and seven genes demonstrated increased expression in the SM of R6/2 mice compared to the control group. Sh2d4a, Eln, Col12a1, Thbs1, Fos, Tnc, Hp, Lep, and Angptl7 exhibited an expression profile which was contrary to that observed in tumors documented in the literature.

Conclusion:
The results of our study demonstrated a distinct expression profile of selected genes in the SM, which exhibited a notable divergence from that observed in cancer. This finding suggests the potential involvement of an altered form of huntingtin in regulating the expression of these genes, thereby exerting characteristics of an anti-tumor effect. However, further detailed studies involving HD patients are required to confirm these findings.

Keywords: Huntington’s disease, gene expression profile, cancers, mouse model, microarray

Funding: Poznan University of Medical Sciences Doctoral School grant number (154 / 2024 / MGB) financed from the statutory funds.

P30

Assessment of postbiotics as radiotherapy adjunctive agents on glioblastoma in vitro models treated with ionizing radiation

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Introduction
Glioblastoma (GB), one of the most common brain tumors remains an incurable cancer. It is characterised by molecular and cellular heterogeneity, along with frequent inherent or acquired chemo- and radioresistance. Gut microbiota dysbiosis is common in cancer patients, who often undergo aggressive medical treatment. Postbiotics are metabolic products and macromolecules produced by probiotic bacteria, mainly lactic acid bacteria. Plenty metabolites, such as short-chain fatty acids or nucleic acids, have been confirmed to cross the blood-brain barrier and exert beneficial effects on the central nervous system cells and have selectively cytotoxic action towards cancer cells. In the current study, postbiotics' radiosensitising properties were assessed in vitro on patient-derived and commercially available glioblastoma cell lines while the cytoprotective action was examined on commercially available normal cell line.

Materials and methods
Lacticaseibacillus rhamnosus and Lactiplantibacillus plantarum derived postculture media were applied to patient-derived and commercially available GB in vitro models and normal human fibroblasts, that then underwent ionizing irradiation treatment. Cell viability analysis was conducted using the Presto Blue assay (ThermoFisher); apoptosis and necrosis processes were verified by flow cytometry on cells stained with Annexin V and propidium iodide (BD Biosciences); cellular proliferation was assessed by 5-ethynyl-2'-deoxyuridine incorporation assay.

Results
Tested postbiotics show anti-neoplastic potential against GB cells in vitro and may increase GB sensitivity to radiotherapy with varied susceptibility of patient-derived cell lines. The cytoprotective activity of postbiotics toward normal fibroblasts in the presence of ionizing radiation was observed.

Conclusions
Postbiotics' possible implementation as nutraceuticals supporting the standard anticancer therapy is worth further examination.

Keywords: glioblastoma, postbiotics, lactic acid bacteria, ionizing radiation

Funding: The costs of the investigation were supported by the statutory funds of Medical University of Lodz, Poland 503/6-086-01/503-61-001.

P31

Cancer immunotherapy by activation of cGAS-STING and RIG-I/MAVS pathways with oligonucleotides delivered via functionalized silk nanospheres

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I*ntroduction*
The cGAS-STING and RIG-I/MAVS pathways are components of the innate immune system. Oligonucleotide agonists like 2'3'cGAMP and M8 can induce cancer cell apoptosis and interferon expression, activating an anti-tumor immune response. However, their instability and lack of cell specificity highlight the need for a targeted drug delivery system for their transport.

Materials and methods
The 2'3'cGAMP (cGAS-STING agonist) and M8 (RIG-I/MAVS agonist) were analyzed using HER2+ ovarian cancer SKOV3 cells in 2D and 3D cell cultures. Functionalized silk was produced via a bacterial expression system and purified with concentrated propionic acid. Oligo-therapeutics were delivered by lipofectamine or HER2-targeted silk nanospheres. Pathway activation was assessed using qRT-PCR and Western Blot.

Results
In 2D SKOV3 cultures, 2'3'cGAMP and M8 delivered by lipofectamine increased IFN-beta expression compared to controls, while in 3D conditions, only the M8 molecule showed activity. The M8 molecule in the 2D assay demonstrated over 1000 times higher potential for IFN-beta induction compared with 2'3'cGAMP. Moreover, functionalized silk was produced to form spherical carriers. In 2D culture, targeted delivery of 2'3'cGAMP using silk spheres increased IFN-beta expression in SKOV3 cells by 1.5 times compared to lipofectamine delivery. Preliminary WB analysis confirmed the presence of proteins of both pathways in SKOV3 cells.

Conclusions
The oligotherapeutics 2'3'cGAMP and M8 activated the cGAS-STING and RIG-I/MAVS pathways, increasing IFN-beta expression, and 2'3'cGAMP targeted delivery using silk spheres increased its efficacy. This approach could advance cancer immunotherapy development.

Keywords: bioengineered silk, drug delivery, cancer therapy, oligonucleotide-based therapeutics, STING pathway

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P32

Immunological disorders and incidence of infections in pediatric survivors of acute lymphoblastic leukemia (ALL) - a single-center study

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Introduction
Leukemia is the most common childhood cancer, with survival rates of 83–94% for pediatric ALL. While infections are major cause of early mortality during treatment, less is known about infection risks after therapy. Children who have completed therapy for leukemia may be at particularly higher risk of infections following therapy completion as prior laboratory studies have shown persistent immune dysfunction for months to years after chemotherapy. This study explores the link between immune markers—lymphocyte subpopulations and IgG levels—and infection rates in pediatric ALL survivors to identify candidates for immunoglobulin prophylaxis.

Materials and methods
Eighteen children treated for ALL (2020-2024) were evaluated through a survey on infection severity and frequency, combined with laboratory assessments of lymphocyte subpopulations and immunoglobulin G levels at five points of time: at therapy completion, and at 3, 6, 12, and 24-36 months post-treatment. The results of the patients were compared with age-appropriate norms. Additionally, a review of the available literature related to the topic of infections in children after the end of treatment was conducted.

Results
The study included 6 girls and 12 boys (median diagnosis age: 6 years). Infection rates exceeded those of the general population in 67% of patients, with 28% requiring frequent antibiotic therapy. Infections lasted an average of 5–6 days, leading to 5–7 days of school absences. Up to two years post-treatment some patients have deviations in lymphocyte subpopulations, which may correlate with increased infection rates. Immunoglobulin G levels were within the normal range in 80% of patients.

Conclusions
Infections are significant post-treatment complication in pediatric ALL.

Keywords: acute lymphoblastic leukemia, children, infections, immunology, reatment

Funding: The research was carried out in connection with a doctoral thesis.

P33

Integration of radiomic-based nomograms for prediction of axillary lymph node metastasis in breast cancer: A Systematic Review and Meta-Analysis

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Introduction
Axillary lymph node metastasis (ALNM) significantly influences the staging, treatment, and prognosis of breast cancer patients. Radiomic-based nomograms, which integrate imaging-derived radiomic features with clinical data, have emerged as innovative, non-invasive tools for predicting ALNM. This review evaluates their diagnostic performance and clinical applicability.

Materials and methods
A systematic search of PubMed, EMBASE, Scopus, IEEE Xplore, Wiley, Google Scholar, and Web of Science databases was conducted up to 20 October 2024. Studies reporting diagnostic performance metrics such as sensitivity, specificity, and area under the curve (AUC) were included. The quality of the studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 tool. RevMan 4.0 and R-Package software were used for statistical analysis.

Results
A total of 23 studies with 10,611 patients were included. The pooled diagnostic accuracy in the training set was sensitivity 0.86 (95% CI, 0.82-0.88), specificity 0.79 (95% CI, 0.73-0.84), and AUC 0.90. Validation set results were similar: sensitivity 0.83, specificity 0.77, and AUC 0.88. Subgroup analyses highlighted that integrating machine learning improved diagnostic performance, with AUC reaching 0.85. Heterogeneity was attributed to clinical factors, modelling methods, regions, and imaging modalities ($P<0.05$).

Conclusions
Radiomic-based nomograms offer high diagnostic accuracy for predicting ALNM and represent a promising adjunct to existing methods. Standardized methodologies and prospective studies are essential for clinical translation.

Keywords: breast cancer, axillary lymph node metastasis, radiomics, normogram

Funding: None.

P34

Machine learning guided eccDNA prediction

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Introduction
EccDNA (extrachromosomal circular DNA) is located in cell nuclei. They can carry many different types of sequences, including oncogenes (https://doi.org/10.1016/j.bbcan.2020.188392, https://doi.org/10.1186/s40364-022-00399-9). They are believed to be a main driver of copy number variation (https://doi.org/10.1038/s41467-018-03369-8). However, experimental studies of eccDNA are difficult and expensive. Our goal is to help eccDNA research by providing a reliable way of predicting which sequences are more likely to be eccDNA.

Materials and methods
Based on literature and existing experimental data, we have identified a set of factors that, we believe, can be used to identify eccDNA sequences. We performed a statistical analysis on human genes to verify the importance of these factors, and using data collected for that analysis, we have created a machine learning model capable of predicting the probability of a gene being eccDNA.

Results
Using the machine learning model, we have been able to predict the probability of human genes being eccDNA, and have been able to create a set of genes with an above-average probability of members being eccDNA, that contains 72% of known genes contained within eccDNA. Additionally, we used machine learning coefficients, we have been able to compare the importance of different factors and thus can, for example, say that a miRNA gene that is intronic is less important to eccDNA biogenesis than the presence of tandem repeats.

Conclusions
Machine learning can be successfully applied in bioinformatics for prediction of eccDNA based on factors of the genomic context.

Keywords: eccDNA, machine learning, prediction, cnv, oncogenes

Funding: This work was supported by a grant by the polish Ministry od Education and Science (MEIN) [0054/DIA/2014/43].

P35

Selective CDK2/5 Inhibitors: A Novel Approach to Developing Effective and Safe Glioma Therapies

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Introduction
The complexity of mechanisms underlying cancer development opens doors to innovative therapeutic approaches. One promising strategy targets cyclin-dependent kinases (CDKs), which normally regulate the cell cycle but whose overactivity can drive tumor growth. For safety reasons, current strategies for developing CDK inhibitors focus on identifying selective compounds targeting specific isoforms. These efforts have so far led to the approval of three drugs for clinical use, all based on the selective inhibition of CDK4/6 isoforms. Most CDK inhibitors are based on a heterocyclic aromatic core with distinct molecular fragments, and the introduction of even minor modifications can significantly affect the selectivity of the compound.

Materials and methods
We synthesized two series of compounds using classical methods of organic synthesis. Then, we performed kinase enzymatic radiometric study to evaluate the potency and selectivity of the developed molecules. Selected structures were tested on U118 and H4 glioma cell lines.

Results
In our research, we proposed a new class of CDK inhibitors structurally based on a novel heterocyclic core. Among the tested compounds, we identified Compound 1, which potently inhibited CDK2 (IC50 = 20 nM) and CDK5 (IC50 = 20 nM). These high activities were accompanied by excellent selectivity toward other isoforms.

Conclusions
Since both CDK2 and CDK5 are implicated in the etiopathogenesis of gliomas, we evaluated the effect of compound 1 on glioma cell lines. The results demonstrated a significant reduction in cell viability at concentrations of 10 μM and 100 μM. Moreover, compound 1 showed higher potency compared to temozolomide, the current gold standard for glioma treatment.

Keywords: cyclin-dependent kinase (CDK), glioma, CDK inhibitors, cancer therapy, selective inhibition

Funding: The study was supported by Jagiellonian University Medical College grants: N42/DBS/000378.

P36

Target Volume and Toxicity: Does a Larger Volume Mean Higher Toxicity in Prostate Cancer Radiotherapy?

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Introduction
This study evaluated the impact of target volume (clinical-CTV and planning-PTV) on the incidence and severity of early radiation-induced bladder (GU) and rectal (GI) toxicity in prostate cancer patients treated with moderately hypofractionated radiotherapy (MHRT).

Materials and methods
Sixty-eight consecutive patients irradiated with MHRT (70 Gy in 28 fractions) in 2022-2023 were included in the study. Toxicity was evaluated using a modified RTOG scale, with grade 2 (G2) divided into G2a (mild symptoms, pharmacological preventive treatment) and G2b (more severe symptoms, pharmacological treatment and/or modifications necessary). Statistical analysis included logistic regression and ROC curves.

Results
Median CTV was 85cm3 (IQR 64-102cm3) and PTV was 176cm3 (IQR 154-211cm3). Early ≥G2b GU toxicity occurred in 14 patients (20.6%) and early ≥G2b GI toxicity in 2 patients (2.9%). A borderline significant association was observed between CTV and ≥G2b GU toxicity (p=0.054), with a significant association for PTV (p=0.018). ROC analysis indicated a threshold volume of CTV >112cm3 (p=0.064) and PTV >218cm3 (p=0.028) best differentiated patients with early ≥G2b symptoms. Incidence of ≥G2b GU toxicity was 14.5% for CTV ≤112cm3 and 46.1% for CTV >112cm3. Due to the low incidence of severe early GI toxicity (G2b), a detailed volume-effects analysis for the rectum was not conducted.

Conclusions
1) The risk of ≥G2b GU early toxicity depends on the target volume. 2) CTV >112 cm3 resulted in ≥G2b GU early toxicity in nearly half of the patients. 3) Moderately hypofractionated radiotherapy resulted in low incidence of early GI toxicity.

Keywords: prostate cancer, hypofractionated radiotherapy, bladder toxicity, rectal toxicity, target volume

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P37

What's inside the uterus? The reveal of a healthy uterine microbiome composition

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Introduction
According to current research, the uterus is colonized by microorganisms. Studies on the composition of the endometrial microbiome increased, exposing the challenge of sampling and data analysis. The presumptions of the bacteria's role concern fertility and cancer occurrence. The importance emerges from associations with inflammation and steroidogenesis. This study aimed to describe the diversity of the healthy uterine microbiome. Tested factors of potential influence included age, menopausal status, number of pregnancies, and day of the menstrual cycle.

Materials and methods
The laboratory workflow consists of DNA extraction from swab samples, PCR, and 16S rRNA nanopore sequencing. Compositional data analysis was performed including ordination based on the variance and differential abundance analysis. Complementary, top n taxa charts and alpha-diversity measures were conducted.

Results
34 healthy patients were recruited for the study. 600 different taxa were identified. The most abundant taxa in healthy endometrium were Lactobacillus crispatus, L. jensenii, L. Gasseri, Faecalibacterium prausnitzii, and Streptococcus agalactiae. A complementary analysis of factors modulating bacterial composition showed that the genus Dialister was more frequent in postmenopausal women than in menstruating. This could suggest that postmenopausal women's uteruses are more susceptible to the colonization of unfavorable bacteria.

Conclusions
The healthy uterus microbiome composition differs and remains under further investigation including bacteria-derived factors. On the other hand, the obtained variety may suggest a few beneficial variants for healthiness. Considering the numerous reports on the association of bacteria with cancer, it is promising to conclude a healthy uterine microbiome with a prevention opportunities attitude.

Keywords: microbiome, uterus, nanopore sequencing, reproductive health, microbiology

Funding: PhD Minigrants 102, Initiative of Excellence - Research University – 'Skład mikrobioty macicznej u kobiet z patologiami ginekologicznymi', 102/13/SNP/0001, 10.2023 – 12.2024

P38

The miRecc database containing miRNA sequences potentially encoded by eccDNA

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Introduction
Circular extrachromosomal DNA (eccDNA) are covalently closed, circular single-stranded and double-stranded nuclear DNA. These have been detected in both healthy and cancerous tissues. Studying eccDNA is both challenging and costly, as they constitute only about 5% of the total genomic mass and are highly unstable after extraction. The goal of the miRecc database is to facilitate access to information about miRNA gene sequences that are overexpressed in cancer and potentially encoded by eccDNA.

Materials and methods
This project used a data mining workflow, and machine learning techniques (logistic regression) were used to determine the probabilities. Technologies such as Python, Flask, and SQLite were utilized to create the interface.

Results
The probability that a given miRNA gene sequence is carried by eccDNA was calculated. Genomic context and the source information are also included in each entry's card. All entries are stored in a SQL database. A web application was developed to process and present the results, as well as a REST (Representational State Transfer) API was also implemented to enable seamless data sharing and further analysis.

Conclusions
A database containing miRNA sequences can effectively serve as one of the first tools for predicting eccDNA for miRNA oncogenes.

Keywords: eccDNA, oncogenes, prediction, database

Funding: This work was supported by a grant by the polish Ministry od Education and Science (MEIN) [0054/DIA/2014/43]

P39

Cellular senescence and autophagy in colon cancer cell chemoresistance and stemness: role of hypoxic environment and autophagy inhibition

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Introduction
Chemotherapy of colorectal cancer displays limited therapeutic efficacy due to chemoresistance. Autophagy and therapy-induced senescence (TIS) are suspected chemoresistance mechanisms, with TIS believed to induce phenotype changes also present in cancer stem cells.

Materials and methods
In vitro experiments were performed using two cell culture variants: in normoxia (21% O2) and hypoxia (1% O2) to determine if autophagy inhibition coupled with oxygen deprivation has a senolytic effect or hinders the ability of senescent cells to divide/produce progeny. The main phenotype-testing experiments were performed on HCT116 cell line treated with irinotecan (IRINO) to induce senescence, and with hydroxychloroquine (HCQ) as well as bafilomycin A1 (BAFA1) to inhibit autophagy.

Results
IRINO was capable of pharmacologically inducing senescence, based on increased proportion of polyploid and G2/M phase-arrested cells as well as SA-β-gal positive cells. This coincided with decreased expression of several, surface markers (CD44, CD133, CD166) upon senescence induction. qPCR experiments in HCT116 cell line depict the changes in the level of expression of proliferation- and metabolism-related genes in hypoxic condition and upon treatment with HCQ as well as BAFA1. Additionally, BAFA1 induced a senolytic effect on the senescence-escape HCT116 cell line. Moreover, hypoxia may be a contributing factor for accelerated escape from senescence based on β-gal staining/qPCR results.

Conclusions
Both regulation of autophagy and hypoxia display an effect in regulating both senescent state and stem features with hypoxia allowing for senescence escape, and autophagy inhibitors having a senolytic effect in specific cases. This indicates the need to consider the role of new physicochemical parameters in personalized medicine.

Keywords: colon cancer, senescence, hypoxia, autophagy

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P40

Optimization of high-pressure homogenization process of magnolol-enriched intravenous lipid emulsion

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Introduction
Intravenous lipid emulsions (ILEs) can be utilized as delivery systems for lipophilic drugs. Enriching ILEs with active substances helps enhance drug solubility and bioavailability. One notable example is magnolol, a lipophilic compound derived from Magnolia officinalis, which demonstrates anticancer activity through complex, multi-level molecular mechanisms. It is essential that ILEs meet strict criteria to ensure both efficacy and safety. For instance, the United States Pharmacopeia (USP) specifies that the mean droplet diameter (MDD) should not exceed 500 nm, and droplets larger than 5 μm (PFAT5) should constitute no more than 0.05% of the emulsion. The study aimed to optimize the homogenization process and to develop magnolol-loaded ILE that meets the USP requirements for safe intravenous administration. A stability study of the prepared ILEs was conducted under three different storage conditions

Materials and methods
Two systems were designed and prepared: NE-B (as a blank) and NE-MAG (as a magnolol-enriched ILE). Homogeneous systems were obtained using high-shear homogenization followed by high-pressure homogenization (HPH).

Results
The optimal HPH conditions were achieved at 800 bar with ten cycles. ILEs exhibited a MDD between 197 and 212 nm and a PFAT5 value below 0.02%. Short-term stability tests conducted at 4°C, 25°C, and 35°C (±1°C) demonstrated satisfactory stability of the ILEs over a 30-day storage period.

Conclusions
In conclusion, the optimized HPH process enabled the preparation of a ILE with favorable physicochemical properties and stability. Furthermore, the intravenous administration parameters obtained for NE-MAG highlight its significant potential, positioning it as a promising candidate for further research and development in cancer therapy.

Keywords: magnolol, optimization, cancer, emulsion, intravenous

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P41

Role of blood-brain barrier disruption in brain cancer development in stroke survivors

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Introduction
The BBB is a selective border of cells that regulates the transport of various substances and cells between the central nervous and circulatory systems. It consists of endothelial cells (creating tight junctions), astrocytes and pericytes, which together maintain the brain's delicate environment. Brain tumours can lead to strokes by narrowing the diameter of blood vessels. Nevertheless there are few articles investigating stroke being a risk factor for primary and secondary brain tumours. Recent studies suggest that ischemic stroke patients have higher risk of developing a tumour compared to the general population. Although some studies indicate a potential link between brain cancer and stroke, the exact nature of their relationship remains under investigation.

Materials and methods
We conducted a retrospective literature review to identify plausible causes of this phenomenon.

Results
We found that strokes can lead to disruption of blood-brain barrier through various mechanisms, such as degradation of tight junction proteins, oxidative stress and neuroinflammation. This in turn, may allow cancer cells to develop and metastasise into the brain.

Conclusions
We propose that one possible link between stroke and cancer is the disruption of the blood-brain barrier (BBB), a key protective structure in the central nervous system.

Keywords: blood brain barrier, stroke, brain cancer, metastasis, BBB disruption

Funding: This research was supported by the NCN OPUS 21 grant (UMO-2021/41/B/ST4/02000)

P42

The influence of the length of the irradiated optical fiber on the Cherenkov radiation value during small-field dosimetry using Exradin W2 scintillators

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Introduction
Modern dosimetry in radiotherapy, driven by SRS and SBRT, focuses on precise small-field measurements. Scintillators, among the most accurate dosimeters, convert ionizing radiation into light, but Cherenkov radiation in optical fibers affects accuracy. The MAX SD system (Standard Imaging, Middleton, USA) addresses this issue using an electrometer algorithm analyzing two fiber configurations. This study examines Cherenkov radiation correction's impact based on field size and fiber irradiation using the CyberKnife S7 accelerator (Accuray, Sunnyvale, USA).

Materials and methods
The experiment used a MicroDiamond detector (PTW, Freiburg, Germany) for reference and calibrated scintillator with collimator sizes from 5 mm to 60 mm. To enhance accuracy, an alternative calibration method adjusting the irradiated fiber length was developed. The study analyzed how fiber length during calibration influenced results compared to MicroDiamond measurements, highlighting the method’s impact on dosimetric precision.

Results
The results demonstrate that CLR (Cherenkov Light Ratio) calibration method recommended by the manufacturer is inadequate for field sizes below 12,5 mm. The method in which the calibration geometry was changed reduced the discrepancy between the measured and reference dose values for small fields. It prompted further analysis of the length of the exposed optical fiber on the obtained CLR values.

Conclusions
CLR coefficients were measured following the manufacturer’s method, revealing discrepancies between scintillator and MicroDiamond measurements. The method proved unsuitable for very small fields. Adjusting the geometry significantly improved results, indicating the manufacturer's approach is inadequate for the smallest fields. It is suggested that the modified method may substantially enhance measurement accuracy.

Keywords: scintillators, small fields, dosimetry, cherenkov

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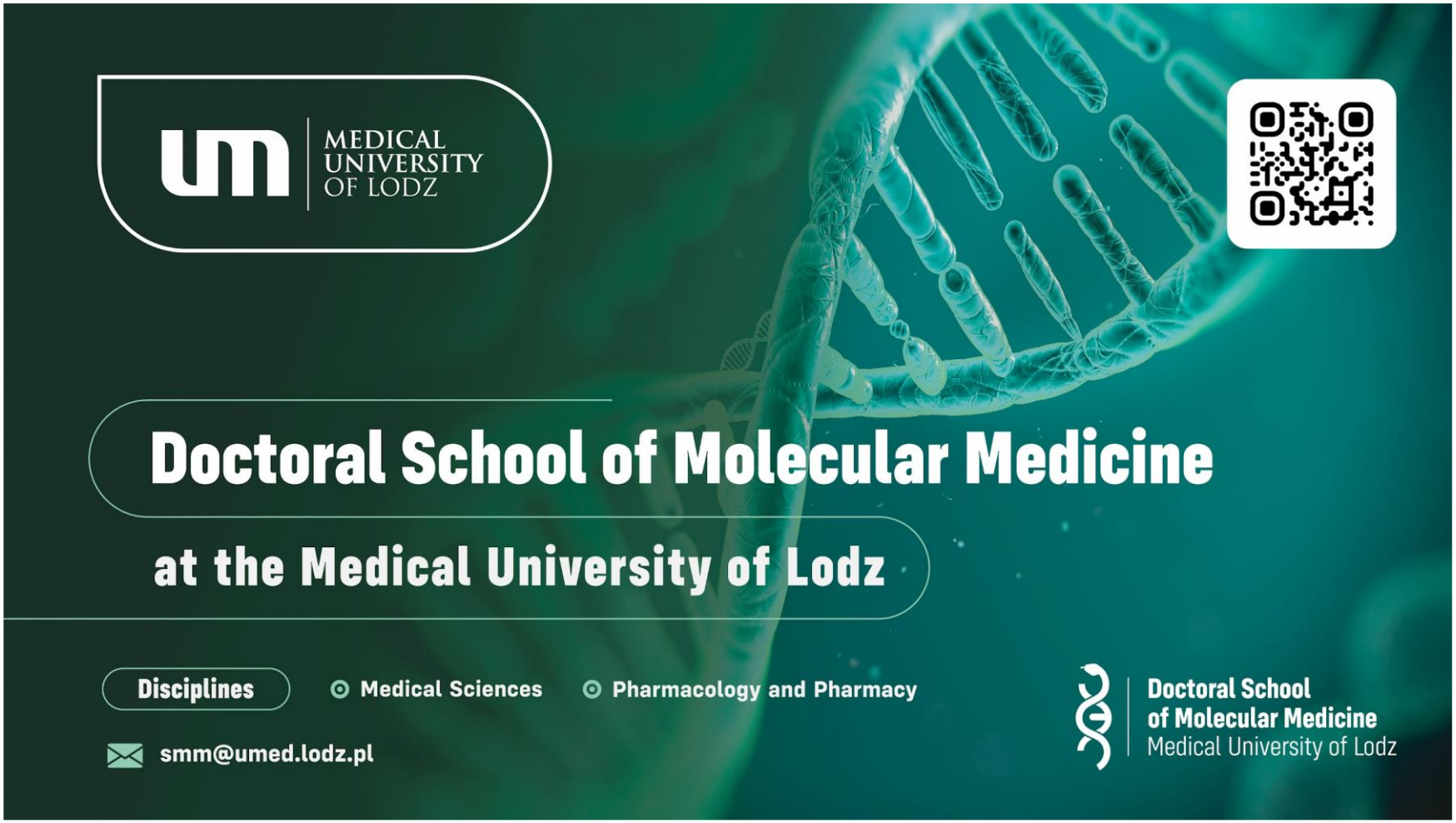
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