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PESQUISAS CLÍNICAS - 2° CONGRESSO CANCERTHERA EM CONJUNTO COM O 18° SIMPÓSIO EDWALDO CAMARGO

EFFECTS OF A CONVENTIONAL CHELATOR-MODIFIED ANTI-INTEGRIN PEPTIDE ON GLIOBLASTOMA CELL PROLIFERATION AND MIGRATION

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A B S T R A C T

Introduction/Justification: Glioblastoma (GB) is the most aggressive brain tumor, with high morbidity and mortality rates. The overall survival of GB patients is only 14 months, not improved by the traditional or latest therapeutic options, as surgical resection, temozolomide chemoradiation or gefitinib. FAPESP-founded "Cancer Innovation Center with Emphasis on Metals and Theranostics" (CancerThera) is dedicated to the development of new metallopharmaceuticals and radiopharmaceuticals for tumor diagnosis and treatment. Among these developments, an anti-integrin peptide modified by a conventional spacer (C6) and chelator (DOTA) was evaluated as a potential treatment of GB. Overexpressed in GB, integrins are transmembrane proteins that play essential roles in cell proliferation and migration. Therefore, integrin inhibition may be a potential targeted therapy for GB patients. **Objectives:** The study aimed to evaluate the effects of the DOTA-C6-anti-integrin peptide on GB cell lines proliferation and migration, as an initial step for GB theranostic development. **Materials and Methods:** The anti-proliferative activity of the DOTA-C6-anti-integrin peptide (0.01 nM - 100 μM) was evaluated in human GB (U87, U118, and U251), murine GB (GL261), and non-tumoral cell lines (HaCaT), by considering the cell amounts at baseline and 48h after exposure (two untreated control groups). Cells were fixed with 50% trichloroacetic acid and stained with sulforhodamine B. Spectrophotometric absorbance was performed at 540nm in a microplate reader. Cell migration was assessed in U118, U251, and Gl261 cells treated with the DOTA-C6-anti-integrin peptide (1 μM - 100 μM) using the wound-healing assay. Wound cells were photographed immediately (0h) and after 24h. Images were analyzed by the ImageJ software (National Institutes of Health). For statistical analysis, samples did assume normal distribution in Shapiro-Wilk's test, thus we used t test to compare the groups using SPSS 21 software (SPSS Incorporation). Resultados: At the tested concentration range, the DOTA-C6-anti-integrin peptide did not affect proliferation of GB and HaCaT cell lines. In U118 cells, we observed that treatment with the DOTA-C6-anti-integrin peptide had no effect on cell migration at any of the tested concentrations. In contrast, in U251 cells, the treatment significantly inhibited migration compared to untreated cells at a concentration of 100 μM ($p = 0.03$). In Gl261 cells, the treatment significantly inhibited migration compared to untreated cells at concentrations of 1 μM and 0.1 μM ($p = 0.04$). **Conclusion:** Despite the lack of anti-proliferative effect, the DOTA-C6-anti-integrin peptide inhibited migration in GB cell lines, U251 and Gl261. An invasive pattern being a GB hallmark, our data suggests that the DOTA-C6-anti-integrin peptide may aid in developing a GB theranostic agent. **Acknowledgements:** The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #429463/2018-9), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2023/09738-4, FAPESP #2023/012810-9, Cancer Theranostics Innovation Center (CancerThera), CEPID FAPESP #2021/10265-8), and International Atomic Energy Agency (IAEA) technical cooperation projects for development of

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Keywords: Anti-integrin peptide, Cell migration, Glioblastoma.

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COMPETITION RESPONSE OF PSMA-I&T RADIOLABELED WITH LUTETIUM-177 TO LNCAP, PC-3 AND RWPE-1 CELLS

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A B S T R A C T

Introduction/Justification: 177Lu-PSMA-I&T stands out as a promisor radiopharmaceutical for therapy of prostate cancer based on the specific bind of Glu-urea-Lys pharmacophoric group prostate-specific membrane antigen (PSMA), anchored in the epithelial prostate cell membrane, overexpressed in prostate cancer and increased in metastatic castration-resistant prostate cancer (mCRPC). To study the affinity of 177Lu-PSMA-I&T to target receptor, in vitro competition assay is frequently evaluated. **Objectives:** The purpose of this study was to compare the binding of 177Lu-PSMA-I&T in competition assay to three cell lines. LNCaP and PC-3 are the most used in vitro cell lines studies of prostate cancer research and LNCaP cells are known to have a mutated androgen receptor (AR) (T877A), PC3 is negative for AR expression, and RWPE-1 is frequently used as non-cancerous control. **Materials and Methods:** Radiochemical purity (%RP) of radiolabeling 177Lu-PSMA-I&T was determined by High Performance Liquid Chromatography (HPLC) and Thin Layer Chromatography (TLC) with results of > 95% of main peak and < 3% of free 177Lu, respectively. In vitro assays were performed with LNCaP (ATCC® CRL- 1740, American Type Culture Collection), RWPE-1 and PC-3 (LIM55, FMUSP) cell lines, cultivated in RMPl 1640 medium (Life Technologies, MD, USA) plus 10% v/v Fetal Bovine Serum (FBS) with 100 UI/mL of penicillin and 300 μg/mL of streptomycin. 6-well plates were used, and to each well 2×105 cells. For the total binding, cell incubation medium was removed and replaced with 1 mL of 177Lu-PSMA-I&T (2.22 MBq (60 μCi), approximately 0.076 nmol of peptide, diluted with RMPl 1640 medium/10% v/v FBS) and 1 mL of RMPl 1640 medium, per well. The plates were incubated for 1 h at 37 °C. Cells were washed two times with 1 mL of 0.1 M PBS pH 7.4, followed by an incubation step of 5 minute at room temperature with 1mL ice-cold glycine buffer (0.05 M glycine pH 2.8) and lysed with 2 mL of 1 M sodium hydroxide and incubation step of 10 minutes at room temperature. The same procedure was repeated replacing 1 mL of RMPl 1640 medium with 1mL of competitor (PSMA I&T, molar excess of 7.6 nmol in RMPl 1640 medium). To have the same geometry, the tubes were filled to the same volume (1mL) at each step. An automatic gamma counter with NaI (TI) crystal (D5002 Cobra II, Packard) was used to measure the radioactivity (as cpm) at each tube, and the concentration of 177Lu-PSMA-I&T bonded to the cells was determined in fmol. The assays were performed in quintuplicate for each cell. **Results:** The binding of 177Lu-PSMA-I&T to LNCaP cells showed 1309.3 $\pm$ 176.8 fmol without competitor and 928.5 $\pm$ 84.7 fmol in the presence of competitor, with significant difference (P= 0.0152, GraphPad Prism®). PC-3 cell line showed 28.8 $\pm$ 15.2 fmol without competitor and 25.3 $\pm$ 6.2 fmol with competitor, showing no significant variation (P = 0.6599). The results of binding with RPWE-1 cell line showed 74.3 $\pm$ 6.2 fmol without competitor and 37.9 $\pm$ 7.7 fmol with competitor, a significant difference ($P \leq 0.0001$). **Conclusion:** These results demonstrated the affinity of 177Lu-PSMA-I&T for binding receptors in LNCaP cells and low uptake by PC-3 cells due to the lack of expression of specific receptors. RWPE-1 cell line is positive for AR/PSA mRNA/protein and sensitive to androgens. However, it expresses low levels of PSMA, which likely explains the reduced binding of the radiopharmaceutical.

Keywords: Binding, Lutetium-177, PSMA-I&T, Radiopharmaceutical;.

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SYNTHETIC QUINAZOLINONES AS NEW ANTILEUKEMIC AGENTS

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A B S T R A C T

Introduction/Justification: Acute leukemias are aggressive malignancies characterized by the uncontrolled proliferation of hematopoietic progenitor cells in the bone marrow, leading to impaired production of normal blood cells. Nitrogen heterocycles have attracted the attention of researchers from various fields, with an extensive list of different biological activities. Among the heterocycles, quinazolines stand out, which have been widely investigated for the development of new drugs. **Objectives:** Evaluation of the anticancer activity of quinazolinones against acute leukemic cell lines. **Materials and Methods:** The quinazolinones (A1-A20) were synthesized in the Laboratory of Synthesis of Natural Products and Drugs (Institute of Chemistry, Unicamp). In total 2×104 cells of T cell acute lymphoblastic leukemia (T-ALL), Jurkat, and acute promyelocytic leukemia (APL), NB4, per well were seeded in a 96-well plate in the appropriate medium in the presence of vehicle or different concentrations of compounds (ranged

from 0.8 to 50 μM) for 72 h. Leukemic cells were exposed to the presence of vehicle or different concentrations of compounds (ranged from 0.8 to 50 μM) for 24, 48 and 72 h. Next, 10 μl methylthiazoletetrazolium (MTT, Sigma-Aldrich) solution (5 mg.mL^{-1}) was added and incubated at 37°C, 5% CO2 for 4 h. The reaction was stopped using 100 μL 0.1 N HCl in anhydrous isopropanol. Cell viability was evaluated by measuring the absorbance at 570 nm. IC50 values were calculated using non-linear regression analysis in GraphPad Prism 5 (GraphPad Software, Inc., San Diego, CA, USA). SwissADME and pkCSM software were used to predict the properties of the compounds. **Results:** Of the compounds synthesized, A1, A2, A3 and A4 showed antileukemic activity. Compounds A1 and A4 were the least cytotoxic for both cell lines. A2 showed strong activity against Jurkat cells. The best compound in the study, A3, showed strong activity against both Jurkat and NB4 cells. In the investigation of apoptosis by flow cytometry, the baseline cell viability was greater than 85%, which indicates a good quality cell culture and reliability in the data obtained. A2 showed greater efficacy, but still limited in Jurkat cells compared to NB4 cells. Compound A4 was the most effective in both models tested. For Log P (consensus), all the molecules are within the molecular filters, with A3 having the highest value, 3.79. The final analysis of all those described in this study indicates that all the quinazolinones synthesized meet the parameters for oral bioavailability. **Conclusion:** In this study, we prepared a series of quinazolinones that exhibited antiproliferative activities in T-ALL and APL. The most promising result of the study was A3 for both T-ALL and APL cells, respectively. In the analysis of apoptosis by flow cytometry, the highlight was also A3, which was the most effective against both cell lines.

Keywords: Antileukemic, Jurkat, NB4, Quinazolinone.

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NEW FUNCTIONALIZED QUINAZOLINES AS POTENTIAL AGENTS AGAINST HEAD AND NECK AND LUNG CANCER

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A B S T R A C T

Introduction/Justification: Lung cancer (LC) and head and neck cancer (HNC) are high incidence tumors around the world. Patients with the tumors have been treated for years with cisplatin alone or in combination with other agents. More recently, hyperexpression of the epidermal growth factor receptor (EGFR) has been identified in most LC and HNC, and anti-EGFR agents have been incorporated into the treatment of tumor carriers. However, a substantial number of patients with tumors still die, which justifies the search for new antineoplastic agents. **Objectives:** Evaluate the antiproliferative activity of new functionalized quinazolines against FaDu, HaCat, SCC-25 and NCI-H460 cell lines. **Materials and Methods:** The quinazolines (Q1-Q6) were synthesized in the Laboratory of Synthesis of Natural Products and Drugs (Institute of Chemistry, Unicamp). Non-small cell lung cancer (NCI-H460), squamous cell pharyngeal cancer (FaDu), squamous cell carcinoma of the tongue (SCC-25), and epidermal keratinocytes (HaCaT) were selected for this study, and all cell lines comply with the International Organization for Standardization (ISO 10993-5 and ISO 10993-1). The cytotoxicity of each compound in the cell lines was determined by the MTT (3-(4,5-dimethylthiazol-2-yl)-2-5 diphenyl tetrazolium bromide) assay. Cisplatin and gefitinib were used as positive controls. MTT is captured by cells and reduced intra-cellularly in a mitochondrion-dependent reaction to yield a formazan product. The ability of cells to reduce MTT provides an indication of their intactness and mitochondrial activity that serves as a measure of viability. After a 48 h incubation with compounds (seven concentrations on a logarithmic scale from 1 to 1000 μg.mL-1), the plates were centrifuged to pellet the cells, the supernatant was removed, and 10 μL of MTT (Sigma, M5665) dissolved in 100 μL of phosphate-buffered saline (Sigma P4417) was added followed by incubation for 4 h at 37°C in a humid, 5% CO_2 atmosphere. After this period, the plates were centrifuged again, the supernatant was removed, and the insoluble formazan crystals were dissolved in 150 μL of Isopropyl alcohol. The absorbance was read in a Synergy ELISA plate reader (Bio Tek Instruments, Highland Park, Winooski, USA) at 570 nm. The results were expressed as percentage inhibition relative to control cells (considered as 100%). **Results:** Compounds Q1 and Q6 showed no cytotoxic activity. The synthetic intermediate, Q2 and the target compound Q3 showed an unexpected but interesting cytotoxic activity for the HaCat cells. Compound Q4 showed strong and selective cytotoxic activity against the FaDu cells. Analyzing the NCI-H460 cells, compound Q5 showed strong and selective cytotoxic activity. **Conclusion:** Compounds Q2 and Q3 deserve attention as potential agents for the treatment of actinic keratosis patients. The Q4 and Q5 compounds emerge as new potential agents for the treatment of patients with HNC and LC, respectively. Studies focusing on response and toxicity to agents in animal models are necessary to verify the efficacy and safety of agents before starting studies in humans.

Keywords: Antiproliferative, Lung cancer, Quinazoline.

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GOLD(I)-BASED COMPLEX AUDMAP: A PROMISING ANTIPROLIFERATIVE AGENT FOR MELANOMA TREATMENT

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A B S T R A C T

Introduction/Justification: Melanoma is the most aggressive type of skin cancer, with increasing global incidence. Platinum-based chemotherapy, particularly cisplatin, remains a standard treatment, but its effectiveness is often limited by drug resistance and severe side effects. Gold-based complexes have gained attention as potential alternatives due to their greater chemical stability, selective cytotoxicity against platinum-resistant cells, lower systemic toxicity, and immunomodulatory effects. Previous studies from our group demonstrated the antiproliferative activity of AuDMAP, a gold(I)-based complex, in the UACC-62 melanoma cell line. Building on these findings, this study investigates the antiproliferative effects, cytotoxicity, and selectivity of AuDMAP in SK-MEL-28 and A-375 melanoma cells, as well as its impact on cell migration and potential anti-metastatic properties in comparison to cisplatin. **Objectives:** To evaluate the antiproliferative activity and cell death mechanisms induced by the AuDMAP complex in SK-MEL-28 and A-375 melanoma cell lines, as well as determining its toxicity against non-tumoral HaCaT cells. **Materials and Methods:** Melanoma and non-tumor cells were cultured in DMEM + 10% FBS + 1% penicillin-streptomycin and treated with AuDMAP (0.78–100 μM) for 48h, with cisplatin as a control. Sulforhodamine B (SRB) and Thiazolyl Blue Tetrazolium Bromide (MTT) assays were performed to determine cell viability, antiproliferative activity, and IC50 values. The wound healing assay assessed migration, and flow cytometry will be conducted to explore cell death mechanisms and cell cycle effects. **Results:** AuDMAP exhibited strong antiproliferative activity, inhibiting ~80% of cell proliferation at 6.25 μM in melanoma cells - 15x more effective than cisplatin for SK-MEL-28 and 3.3x for A-375. IC50 values were 2.61 μM (SK-MEL-28), 2.50 μM (A-375), and 1.81 μM (HaCaT), yielding a low Selectivity Index (0.69–0.72). Migration assays revealed that AuDMAP significantly reduced wound closure, suggesting anti-metastatic potential. In A-375, wound closure was -8.5% with AuDMAP vs. 62.8% with cisplatin (6.25 μM), while in SK-MEL-28, closure was 4.6% vs. -13.5%, respectively. Given these promising results, further studies will focus on cell cycle analysis and death mechanisms to better understand the biological effects of AuDMAP. **Conclusion:** AuDMAP is a gold(I)-based complex that demonstrates potent antiproliferative and antimigratory effects in melanoma cells, with efficacy significantly superior to cisplatin in the tested models. The inhibition of cell proliferation and migration suggests its potential as a promising anticancer agent, possibly disrupting tumor progression and metastasis. However, the low selectivity index observed indicates that its cytotoxic effects extend to non-tumor cells, raising concerns about the safety profile in intravenous administration. To further explore its therapeutic viability, future studies will investigate its mechanisms of action at the molecular level, focusing on cell cycle modulation and programmed cell death pathways. These findings contribute to the growing interest in gold(I) compounds as novel candidates for melanoma treatment, particularly for topical administration. **Acknowledgements:** This study was supported by grants from the Brazilian Agencies FAPESP (2021/10265-8 Cancer Theranostics Innovation Center - CEPID), and Program (PPPD) at the University of Campinas (UNICAMP, ID Number 325141).

Keywords: AuDMAP, Cell proliferation, Melanoma, Skin cancer.

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EVALUATION OF ANTIPROLIFERATIVE OF A POTENTIAL THERAPEUTIC ASSOCIATION OF SILVER COMPLEXES WITH LIMONENE IN SQUAMOUS CELL CARCINOMA AND MELANOMA CELL LINES

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A B S T R A C T

Introduction/Justification: Skin cancer, strongly associated with UV exposure, is the most common malignancy worldwide, including squamous cell carcinoma (SCC), and cutaneous melanoma (CM). Although cisplatin and 5-FU are standard treatments for SCC and CM, the development of new therapeutic alternatives is crucial. Silver complexes have shown promising anticancer potential, while the monoterpene limonene has demonstrated efficacy in enhancing skin permeation, supporting its application in topical drug delivery. **Objectives:** Our study aimed to evaluate the in vitro antiproliferative effects of silver complexes and limonene, isolated and in association. **Materials and Methods:** The silver complexes identified as I and II were synthesized at the Institute of Chemistry of University of Campinas. The pure substances R-(+)-limonene and S-(-)-limonene were acquired from Merck. Pharyngeal SCC (FaDU) and melanoma (A-375, SK-MEL-28) cells (4×10^3 cells/mL) were treated with complexes I e II (0.4–400 μM) or their combination with R-(+) and S-(-) limonene (4 μM). Cisplatin and 5-FU (100 μL/well, 0.4 to 400 μg/mL, in triplicate) were used as positive controls. Before (T0) and after (T1) sample addition, cells were fixed with 50% trichloroacetic acid (TCA, 50 μL/well), and were then resuspended in Tris base for subsequent absorbance at 540 nm with a microplate reader spectrophotometer (VersaMax, Molecular Devices). The difference between T0 and T1 absorbance values represented 100% cell growth. Effective concentration representing the sample concentration required to

promote 50% growth inhibition (IC50) for each cell line was calculated by sigmoidal regression using Origin 8.0 software. The Combination Reduction Index (CRI) was calculated as IC 50 of the metal complex + monoterpene / IC 50 of the metal complex alone. **Results:** Both silver complexes exhibited potent antiproliferative activity. The antiproliferative effect of silver complex I ranged from 4 μM to 10 μM in SCC and CM cell lines, whereas the antiproliferative effect of silver complex II ranged from 1 μM to 6 μM in the same cell lines. The association of silver complex I in combination with S-(-)-limonene resulted in synergism effect in the FaDu cell line with IC50 < 2 μM, CRI = 0.4. The association of silver complex II with both enantiomers demonstrated a partial synergistic effect in the FaDu and SK-MEL-28 cells, with IC50 <1.5 μM and CRI = 0.5. **Conclusion:** Silver complexes are promising candidates for in vivo studies as potential alternatives for the treatment of patients with SCC and CM. Additional experiments are necessary to evaluate their mechanism of action and toxicity. The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2016/07729-4; #2023/09738-4 and Cancer Theranostics Innovation Center, (CancerThera), CEPID FAPESP #2021/10265-8).

Keywords: Combination, Limonene, Melanoma, Silver complexes, Squamous cell carcinoma.

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ROLE OF GENETIC VARIABILITY IN METABOLIC PATHWAYS ON CISPLATIN-INDUCED KIDNEY INJURY IN HEAD AND NECK CANCER PATIENTS

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A B S T R A C T

Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is a prevalent malignancy responsible for approximately 5.0% of global cancer deaths. The standard treatment for locally advanced HNSCC involves cisplatin (CDDP)-based chemotherapy and radiotherapy, which can lead to significant adverse effects, particularly nephrotoxicity. It is already well known that the efficacy of CDDP as well as its side effects vary in distinct patients with HNSCC, and single nucleotide variants (SNVs) in genes that act in CDDP metabolism constitute a plausible explanation for this finding. **Objectives:** To investigate the roles of SNVs GSTM1, GSTT1, GSTP1 c.313A>G, XPC c.2815A>C, XPD c.934G>A and c.2251A>C, XPF c.2505T>C, ERCC1 c.354C>T, MLH1 c.93G>A, MSH2 c.211+9C>G, MSH3 c.3133A>G, EXO1 c.1765G>A, TP53 c.215G>C, CASP3 c.-1191A>G and c.-182-247G>T, FAS c.-1378G>A and c.-671A>G, and FASL c.-844C>T SNVs on kidney function outcomes in HNSCC patients undergoing CDDP treatment. **Materials and Methods:** A total of 109 patients with locally advanced HNSCC treated with CDDP were included in the study. Genotypes were determined using polymerase chain reaction (PCR). Renal function was assessed by calculating estimating glomerular filtration rate (eGFR) using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, before treatment initiation and 30 days post-treatment. The percentage variation in kidney function was calculated by determining the difference between baseline (pre-chemotherapy) and follow-up (post-chemotherapy) values for eGFR divided by the pre-chemotherapy value and represented as ΔeGFR. **Results:** Patients with the GSTT1 present and ERCC1 c.354CT or TT isolated genotypes presented a decline in kidney function of 4.94% and 8.94%, respectively. A decline of 17.67% in renal function post-CDDP treatment was observed in patients with the GSTT1 present combined with TP53 c.215CC genotype. Patients with the GSTP1 c.313AG or GG and ERCC1 c.354CT or TTC>T (17.57%), MLH1 c.93GA or A (12.49%), or MSH3 c.3133AG or GG (12.19%) combined genotypes showed a reduction in renal function after CDDP treatment. Renal function declines of 18.85% and 13.38% were observed in patients with ERCC1 c.354CT or TT and MLH1 c.93GA or AA or MSH3 c.3133AG or GG combined genotypes, respectively. **Conclusion:** Our data indicates, for the first time, preliminary evidence that combined inherited abnormalities, SNVs that act in CDDP metabolism, act as independent factors for nephrotoxicity in HNSCC patients and can be used to select patients for personalized treatments that promote renal protection and reduced nephrotoxicity. **Acknowledgements:** The study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (grant number 88887.513947/2020-00), the Postdoctoral Program (PPPD) at the University of Campinas (UNICAMP) (Postdoctoral ID number: 326285), and the Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP) Cancer Theranostics Innovation Center (CancerThera) (FAPESP 2021/10265-8).

Keywords: Cisplatin, Head and neck squamous cell carcinoma, Nephrotoxicity, Single nucleotide variants.

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KIF13B C.*3163G>A SINGLE NUCLEOTIDE VARIANT ON OROPHARYNGEAL SQUAMOUS CELL CARCINOMA SUSCEPTIBILITY AND TUMOR CHARACTERISTICS

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A B S T R A C T

Introduction/Justification: Oropharyngeal squamous cell carcinoma (OPSCC) is a subtype of head and neck cancer with high mortality rates and aggressive behavior. Smoking, alcohol consumption, and HPV infection are well-established risk factors in carcinogenesis of the tumor. Genetic inherited variations can influence OPSCC susceptibility and tumor characteristics by altering gene expression. The KIF13B gene encodes a kinesin motor protein involved in intracellular transport, and sequence variations in its regulatory regions may affect gene expression. However, the impact of the KIF13B c.*3163G>A single nucleotide variant (SNV) on OPSCC risk and tumor features remains unclear. **Objectives:** To evaluate whether distinct genotypes of the SNV KIF13B c.*3163G>A influence the risk and tumor characteristics of OPSCC, as well as the expression of the KIF13B gene and the microRNA (miRNA) let-7e-3p in controls, and to functionally assess the interaction between let-7e-3p and the SNV region in the 3'-UTR of KIF13B. **Materials and Methods:** We evaluated 250 OPSCC patients and 250 controls seen at the Clinical Oncology Services of the General Hospital of University of Campinas. The genomic DNA was obtained from peripheral blood leukocyte samples from patients and controls entered the study. The KIF13B c.*3163G>A SNV genotypes were identified by polymerase chain reaction (PCR). The RNA was obtained from peripheral blood leukocyte samples from controls. The gene and let-7e-3p expression were evaluated by quantitative PCR. Interaction between let-7e-3p and the 3'-UTR of KIF13B was evaluated by luciferase reporter assay in FaDu and Detroit 562 pharyngeal cell lines. **Results:** KIF13B c.*3163GG genotype was more common in OPSCC patients than in controls (42% versus 32%; P = 0.03); individuals with KIF13B c.*3163GG genotype were under 1.73-fold increased risk of OPSCC than others. KIF13B c.*3163GG genotype was more common in patients with greater tumor extension (46% versus 28%, P = 0.01) than others and in patients with greater tumor extension than in controls (46% versus 32%; P = 0.004); individuals with KIF13B c.*3163GG genotype were under 2.47-fold increased risk of aggressive OPSCC than others. Individuals with KIF13B c.*3163GG genotype showed lower levels of KIF13B mRNA (1.02 arbitrary units (AUs) ± 0.35 standard deviation (SD) versus 1.28 AUs ± 0.53 SD, P = 0.05). The expression level of miRNA let-7e-3p was similar in individuals with distinct genotypes KIF13B c.*3163G>A SNV (0.52AUs ± 0.31DP versus 0.48AUs ± 0.26DP versus 0.55AUs ± 0.39DP, respectively; P= 0.85). The let-7e-3p miRNA exhibited more efficient binding to the 3'-UTR of the ancestral G allele compared to the variant A allele in the FaDu (p = 0.004) and Detroit 562 (p = 0.04) cell lines. **Conclusion:** Our data present, for the first time, evidence that KIF13B c.*3163G>A SNV is associated with increased risk of OPSCC possibly due to the variation of KIF13B gene expression, modulated by the miRNA let -7e-3p.
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Keywords: KIF13B, Oropharyngeal squamous cell carcinoma, Risk, Single nucleotide variants.

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ASSOCIAÇÃO ENTRE SINTOMAS DE DEPRESSÃO E UMA VARIANTE NO GENE DA CHAPERONA ERP29 ASSOCIADA A PROCESSOS INFLAMATÓRIOS EM PACIENTES COM CÂNCER DE CABEÇA E PESCOÇO

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R E S U M O

Introdução/Justificativa: O câncer de cabeça e pescoço (CCP) é um problema de saúde global, frequentemente acompanhado de reações emocionais, incluindo a depressão. Genes que regulam as vias de resposta inflamatória ao estresse desempenham um papel importante nos processos depressivos. O gene ERP29 codifica uma proteína chaperona envolvida no enovelamento e secreção de proteínas no retículo endoplasmático. Estudos conduzidos pelo nosso grupo demonstraram que a supressão do ERP29 em linhagens de células de tumores de cabeça e pescoço está associada ao aumento da expressão de genes das vias MAPK e Akt, conhecidas por seu envolvimento em processos inflamatórios. Além disso, uma variante genética de base única (SNV) no ERP29 (rs7114, A>G) foi associada a um maior risco de desenvolvimento de CCP e à redução da expressão do gene. No entanto, a relação dessa SNV com os sintomas depressivos ainda não foi estabelecida. **Objetivos:** O presente estudo teve como objetivos: 1) investigar se os sintomas depressivos em pacientes com CCP estão associados a

características clínicas e do tumor, e 2) avaliar a relação entre os genótipos da SNV ERP29 rs7114 e os sintomas depressivos. **Materiais e Métodos:** Foram avaliados 70 pacientes com CCP (57 homens, 13 mulheres, idade média de 60 anos, 59 tabagistas e 54 etilistas) atendidos até dois anos após o diagnóstico no Hospital de Clínicas da UNICAMP. Os sintomas depressivos foram avaliados por meio do Inventário de Depressão de Beck (BDI-II) que contém 21 questões abordando aspectos como humor depressivo, culpa, ideação suicida, isolamento social, alteração na imagem corporal, distúrbios do sono, fadiga e perda de libido. Cada item é pontuado de zero (ausência de sintoma) a três (sintoma grave) e a soma total reflete a gravidade dos sintomas depressivos. Os genótipos da SNV ERP29 rs7114 (AA, AG ou GG) foram identificados por meio da reação em cadeia da polimerase em tempo real com sondas TaqMan (Life Technologies) e os reagentes do kit TaqMan Universal PCR Master Mix (Applied Biosystems), seguindo as recomendações do fabricante. O significado estatístico das diferenças entre os grupos foi calculado por meio do teste de Mann-Whitney com os resultados apresentados em mediana e intervalo interquartil (IQR). **Resultados:** As características clínicas dos pacientes (sexo, estado civil, tabagismo e etilismo) e os aspectos do tumor (localização e estágio TNM) não influenciaram os sintomas depressivos desses pacientes com CCP. No entanto, observamos que os pacientes mais jovens (< 60 anos) apresentaram sintomas depressivos mais intensos (22 (IQR: 18,0) vs. 16 (IQR: 14), p = 0,02). Além disso, pacientes com os genótipos AG ou GG da SNV rs7114 (A>G) no ERP29 tiveram pontuações mais altas de sintomas depressivos em comparação com aqueles com o genótipo AA (28 (IQR: 14,5) vs. 18 (IQR: 13), p = 0,02). **Conclusão:** Nossos resultados sugerem que a variante genética rs7114 no ERP29 pode estar associada a sintomas depressivos de pacientes com CCP. Esses resultados demonstram a importância de investigar fatores genéticos na manifestação de sintomas emocionais em pacientes oncológicos. Estudos futuros, com ampliação da casuísta e análise de marcadores inflamatórios, são necessários para confirmar essa associação. Agência financiadora: CNPq.

Palavras-chave: Câncer de cabeça e pescoço, Depressão, ERP29, Variante genética.

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COMPARISON BETWEEN MANUAL AND AUTOMATIC SEGMENTATION OF THE WHOLE-BRAIN AND CEREBELLUM

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A B S T R A C T

Introduction/Justification: 18F-FDG PET/CT is widely used to quantify brain metabolic activity and plays a key role in studying various diseases. Segmentation method choice can significantly influence standardized uptake value (SUV) measurements, thereby affecting the accuracy of the analysis. The Beth Israel Plugin in ImageJ allows both manual and automatic segmentation, making it relevant for evaluating differences in brain and cerebellum analysis. **Objectives:** This study aims to compare the mean, maximum, and peak SUVs obtained through manual and automatic (Grow Mask) segmentation of the brain and cerebellum, assessing the relative percentage differences and variations between the methods. **Materials and Methods:** Seventy-three multiple myeloma (MM) patients who underwent 18F-FDG PET/CT were included in the study, comprising 43 men (58.9%) with a mean age of 64.2 ± 11.4 years. Brain segmentation was performed in FIJI using two methods: (1) manual segmentation (MS) consisting of a spherical volume of interest (VOI) of 6.7 mL for the cerebellum and 377 mL for the brain and (2) auto-segmentation (AS) using a Grown Mask algorithm. Manual cropping of PET images was performed before AS to exclude non-cerebellar regions. The relative percentage difference between the two methods was calculated as (1 - MS/AS). Mean, maximum and peak SUVs (SUVmean, SUVmax and SUVpeak, respectively), as well as maximum and minimum variation ranges of SUVs between MS and AS, were recorded. **Results:** For the brain, SUVs were higher for AS compared to MS: SUVmean = 4.19 ± 0.02 (MS) vs. 5.99 ± 0.03 (AS), corresponding to 30.05% difference (range: 10.21% to 41.39%); SUVpeak = 8.07 ± 0.05 (MS) vs. 9.05 ± 0.06 (AS), 10.83% difference (range: 0% to 40.59%); and SUVmax = 10.76 ± 0.06 (MS) vs. 11.75 ± 0.07 (AS), 8.43% difference (range: 0% to 55.46%). For the cerebellum, a greater variability between MS and AS SUVs were found: SUVmean = 6.00 ± 0.03 (MS) vs. 5.47 ± 0.02 (AS), corresponding to -9.69% difference (range: 0% to 53.51%); SUVpeak = 7.06 ± 0.03 (MS) vs. 7.29 ± 0.03 (AS), 3.15% difference (range: 0% to 32.96%); SUVmax = 8.23 ± 0.04 (MS) vs. 9.20 ± 0.04 (AS), 10.54% difference (range: 0% to 42.57%). **Conclusion:** The choice of segmentation method significantly impacts SUV values. AS yielded higher brain SUVs, while cerebellum MS showed greater variability due to manual adjustments and VOI selection. The differences between methods stem from segmentation techniques: MS used a spherical VOI, sometimes excluding the highest SUV point, whereas AS encompassed the full structure, capturing the true SUVmax. Thus, spherical VOI is less precise for whole-organ analysis but useful for quick regional calculations. Standardizing segmentation methods is crucial for reliable comparisons in clinical and research settings.

Keywords: 18F-FDG PET/CT, Cerebellum, Segmentation, SUV, Whole-Brain.

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FDG PET/CT AND PSMA PET/CT IN MUSCULOSKELETAL SOFT TISSUE SARCOMAS

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A B S T R A C T

Introduction/Justification: Soft tissue musculoskeletal sarcoma (STS) is a rare and varied class of mesenchymal-derived malignancies. Due to its histopathological heterogeneity and presence in different body locations, its diagnosis and treatment continue to present a significant medical challenge. In nuclear medicine, 18F-FDG PET/CT (FDG PET/CT) has been used to grade sarcomas, predict their prognosis, and assess therapy response. Although prostate-specific membrane antigen (PSMA) has been mainly used to detect prostate cancer metastases with PSMA PET/CT imaging and treat with 225Ac/177Lu-PSMA, this antigen has been shown to accumulate in non-prostatic tissues, including several types of sarcomas. **Objectives:** Evaluate the potential of PSMA PET/CT in diagnosing different types of STSs compared to FDG PET/CT, with the aim of expanding the clinical management of these patients and the potential of a Theranostics strategy with radiolabeled PSMA. **Materials and Methods:** Forty-four participants (20 females) with STS were prospectively enrolled and submitted to FDG PET/CT and PSMA PET/CT for primary staging, with a 48-hour interval between studies. SUVmax values were obtained in both studies of the primary STS lesion, locoregional lymph node metastases (LRLNs), distant lymph node metastases (DLNs), and bone metastases. SUVmax values among FDG PET/CT and PSMA PET/CT studies were normalized using the mediastinum SUVmax as a standard reference. The number of metastases detected by FDG PET/CT and PSMA PET/CT were also compared, as well as the absolute SUVmax values. **Results:** The absolute SUVmax values were higher on PSMA PET/CT compared to FDG PET/CT, respectively for the primary STS lesions (18.5 vs 12.8), for LRLNs (8.0 vs 4.5) and bone metastases (8.7 vs 3.2), while these values were similar for DLNs (3.0 vs 4.0). When the SUVmax values were normalized using the mediastinum as a reference the ratio comparing PSMA PET/CT to FDG PET/CT showed, respectively: 10.3 vs 5.3 for the primary STS; 4.7 vs 2.0 for LRLNs; 4.8 vs 2.9 for bone metastases; and 1.7 vs 1.7 for DLNs. PSMA PET/CT detected more LRLNs compared to FDG PET/CT (10 patients vs 7 patients, respectively) and more bone metastases (5 patients vs 3 patients). The detectability of DLNs was equal in both studies (7 patients). **Conclusion:** Our preliminary findings indicate that PSMA PET/CT is a potential diagnostic tool for staging sarcomas patients. Due to the high uptake in the primary STS lesions and metastases, there is a potential for a theranostics approach. This study received financial support from the São Paulo State Foundation for Teaching and Research Support (Cancer Theranostics Innovation Center, (CancerThera), CEPID FAPESP #2021/10265-8).

Keywords: 18 F-PSMA PET/CT, 18F-FDG PET/CT, Sarcoma, Theranostics.

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ACHADOS METABÓLICOS PÓS VACINAÇÃO PARA COVID-19 EM PET-CT COM 18F-FDG

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R E S U M O

Introdução/Justificativa: O processo de vacinação em massa contra a COVID-19 levou ao surgimento, nos exames de PET-CT com 18F-FDG, de hipermetabolismo glicolítico nos linfonodos de drenagem regional do sítio de injeção. Nesse contexto, em função da dificuldade de diferenciação diagnóstica desses achados reacionais com lesões secundárias linfonodais, podem ser solicitados exames complementares confirmatórios (como seguimento por Ultrassonografia ou Tomografia) ou iniciados tratamentos baseados em eventuais falso-positivos. Nesse sentido, estudos e revisões passaram a indicar o reagendamento de PET-CT com 18F-FDG para até 6 semanas após a imunização. O presente estudo se justifica pela necessidade de uma melhor caracterização de tais efeitos morfometabólicos da imunização contra o SARS-CoV-2, observados no PET-CT com 18F-FDG, o que pode otimizar a diferenciação de achados caracteristicamente reacionais de outras hipóteses. **Objetivos:** O presente estudo tem o propósito de descrever os padrões de imagem observados ao PET-CT com 18F-FDG associados à resposta inflamatória que surge após a vacinação, com diferentes tipos de imunizantes contra o SARS-CoV-2, bem como investigar a incidência de linfonodos de drenagem regional com hipermetabolismo glicolítico de natureza reacional relacionados, alterações de forma dos mesmos, além da duração e magnitude de tais alterações. **Materiais e Métodos:** Foram avaliados, retrospectivamente, os exames de PET-CT com 18F-FDG e prontuários eletrônicos de 87 pacientes vacinados contra COVID-19, no ano de 2021, na cidade do Rio de Janeiro, sobretudo os imunizantes ChAdOxnCoV-19 (AstraZeneca – 36 pacientes) e Coronavac (Sinovac – 16 pacientes), quanto à forma do linfonodo de drenagem regional (normal x alterado), seus níveis metabólicos ao PET-CT, sua natureza (falso positivo para malignidade x reacional pós-vacina x normal) e a relação desses achados com o tempo desde a imunização, a idade e o tipo de

imunizante. **Resultados:** Houve o surgimento de graus variados de hipermetabolismo glicolítico em linfonodos de drenagem regional após a vacinação contra a COVID-19, em 27,6 % dos pacientes, com relação inversa do SUVmax ao número de dias desde a imunização (rs= -0,590 e p-valor ≤ 0,001 para o sítio de injeção; rs = -0,416 e p-valor = 0,013 para o linfonodo axilar) e à idade do imunizado (rs= -0,376; p-valor = 0,024).; evidencia ainda que tais achados foram extremamente infrequentes após 4 semanas de imunização. Ademais, os resultados do estudo demonstram menor incidência de achados metabólicos pós-vacinais (6,3%), naqueles pacientes vacinados com o imunizante Coronavac, sem nenhum achado equívoco para natureza reacional inflamatória ou neoplásica, para este grupo. **Conclusão:** O presente estudo demonstrou o surgimento de achados metabólicos reacionais pós-vacinais em PET-CT com 18F-FDG em pacientes imunizados contra o SARS-CoV-2, com relação inversa à idade e ao número de dias desde a imunização, bem como é um dos únicos a demonstrar menor repercussão da vacinação com o imunizante Coronavac nos estudos de PET-CT, uma vez que não levou a nenhum achado metabólico equívoco entre natureza reacional inflamatória e metabólica. Por fim, o trabalho demonstrou que a análise conjunta dos dados clínicos com os aspectos morfometabólicos observados ao PET-CT com 18F-FDG permite otimizar o diagnóstico diferencial de achados de natureza reacional e secundária.

Palavras-chave: 18F-FDG PET/CT, COVID-19, Vacinação.

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INDUCTION CHEMOTHERAPY IN ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA: A REAL-WORLD DATA STUDY

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A B S T R A C T

Introduction/Justification: Approximately 60% of HNSCC patients are diagnosed at a locally or locoregionally advanced stage. Patients with locally or locoregionally advanced stage and not amenable to surgical resection receive chemoradiotherapy (CTRT) as definitive treatment, or induction chemotherapy (ICT) followed or not by CTR. In the last scenery, docetaxel plus cisplatin (TP) and docetaxel plus cisplatin plus 5-fluorouracil (TPF) followed by CTRT were first described as effective ICTs regimens with acceptable safety profile. Despite the superiority of TPF over TP in response rate, loco-regional control, and survival of patients with advanced HNSCC, unequivocal disadvantages have been attributed to the regimen, as grade 3 or above adverse events, and the need of infusion devices or inpatient beds for continuous 5-fluorouracil infusion, which clearly increases the costs of treatment. **Objectives:** The current study aimed to analyze patients with locoregionally advanced HNSCC treated with TPF or TP followed by CTRT at the General Hospital of the University of Campinas, with the purpose of developing an ICT protocol applicable to services with limited resources. **Materials and Methods:** Patients with HNSCC at stage III or IVA-B (T4 and/or N2b, N2c or N3) treated with ICT using TPF or TP followed by CTRT from January 14 th, 2015, to November 24 th, 2021, were included in the study. The choice between TPF and TP as induction chemotherapy (ICT) was based on the clinical judgment of the responsible oncologist, considering patient-specific factors such as performance status, comorbidities, and tolerance to intensive regimens. Additionally, the availability of a hospital bed for the continuous intravenous infusion of 5-fluorouracil was a practical determinant. Toxicity, response rate, and event-free survival (EFS) and overall survival (OS) were evaluated in patients of both groups. Event-free survival (EFS) and overall survival (OS) were assessed using the Kaplan-Meier curves and the log-rank test. The impact of clinicopathological characteristics on patients' survival was assessed through univariate and multivariate Cox regression. **Results:** Eighty-seven patients with HNSCC were treated with ICT, being 38 with TPF and 49 with TP. An excess of ECOG 0 or 1 was seen in TPF group and an excess of males in TP group, but no significant differences in age, smoking and alcohol intake, body mass index, tumor location, grade and TNM stage, toxicities grade 3 or above, treatment response, and cycles interval, were seen in patients treated with TPF and TP. The median follow-up time was 22.6 months (range: 1.2 to 93.8). The two-year and five-year EFS rates of patients of the total group were 33.8% and 25.3%, respectively. ICT regimens did not alter response to ICT, and patients' EFS and OS. Cox multivariate analysis identified stable or progressive disease (HR: 5.56) and interval between cycles ≥ 28 days (HR: 2.79) as predictors of lower EFS, and ECOG ≥ 1 (HR: 3.42), stable or progressive disease (HR: 4.67), and interval between cycles ≥ 28 days (HR: 2.73) as predictors of lower OS. **Conclusion:** Our findings indicate TP as a good treatment option for locoregionally advanced HNSCC, especially in socioeconomically limited settings.

Keywords: Head and neck squamous cell carcinoma (HNSCC), Induction chemotherapy, Response rate, Survival, Toxicity.

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PET/CT WITH 68GA-FAPI46 FOR THE DETECTION OF PRIMARY AND METASTATIC LESIONS IN PATIENTS WITH DIFFERENT TYPES OF CANCER. INITIAL EXPERIENCE

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A B S T R A C T

Introduction/Justification: Fibroblast activation protein (FAP), a transmembrane glycoprotein, is over expressed by cancer-associated fibroblasts in the tumor microenvironment. Radiolabeled fibroblast activation protein inhibitors (FAPI) are currently being investigated for PET imaging. **Objectives:** To evaluate the diagnostic efficacy of PET/CT with fibroblast activation protein inhibitor (FAPI) labeled with gallium 68 (68Ga-FAPI46) for detecting primary and metastatic lesions in patients with different types of cancer. **Materials and Methods:** Patients with different types of cancer confirmed by histopathological study were evaluated with PET/CT with 68Ga-FAPI46 for initial staging or to detect tumor recurrence. The results of PET/CT were compared to the findings of conventional imaging methods such as computed tomography and magnetic resonance imaging and with FDG PET/CT and anatomopathological studies. **Results:** Thirty patients were evaluated, twenty two of whom were diagnosed with lung carcinoma, five with soft tissue sarcoma, one patient with each of the following tumors: gastric, breast and neuroendocrine carcinoma. High expression of FAPI was observed in most primary tumors. The diagnostic performance was high due to a favorable physiological organ distribution and low background signal leading to the detection of most metastatic lesions especially in lymph nodes, pleura, peritoneum, skeleton, liver and central nervous system. By contrast, there was false-positive 68Ga-FAPI46 uptake in inflammatory and infectious processes. **Conclusion:** PET/CT with 68Ga-FAPI46 is a promising imaging modality for the detection of primary and metastatic lesions of many types of cancer.

Keywords: FAPI, gallium68, PET/CT.

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INFLUÊNCIA DE VARIANTES GENÉTICAS EM VIAS INFLAMATÓRIAS MODULADAS PELO EGFR NO CÂNCER DE OROFARINGE

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R E S U M O

Introdução/Justificativa: A superexpressão do gene EGFR ocorre na maioria dos carcinomas de células escamosas de orofaringe (CCEOF) e seus inibidores são utilizados no tratamento desses pacientes. A ativação do EGFR estimula a produção de citocinas (IL1A, IL1B e IL32) e proteínas inflamatórias (CCND1) envolvidas na origem e progressão do CCEOF. Indivíduos expostos a fatores ambientais relacionados ao CCEOF apresentam riscos distintos de desenvolver a doença, assim como pacientes com características clínico-patológicas semelhantes podem evoluir de maneiras diferentes. Variantes de nucleotídeo único (SNVs) em genes de vias inflamatórias moduladas pelo EGFR parecem influenciar essas diferenças. **Objetivos:** Nosso objetivo foi avaliar o papel das SNVs nos genes IL1A (rs2856836, G>A), IL1B (rs1143627, G>A), IL32 (rs4786370, C>T) e CCND1 (rs7177, A>C; rs678653, C>G) no risco, nas características clínico-patológicas e no prognóstico de pacientes com CCEOF. **Materiais e Métodos:** Foram analisados 476 pacientes com CCEOF (412 homens, 64 mulheres, média de idade: 58 anos, 413 tabagistas, 381 etilistas) diagnosticados entre janeiro de 2001 e maio de 2006: 100 no Hospital de Clínicas da USP, 66 no Hospital AC Camargo e 310 no Hospital de Clínicas da UNICAMP. Como grupo controle, investigamos 575 indivíduos saudáveis (511 homens, 64 mulheres, média de idade: 42 anos, 185 tabagistas, 290 etilistas), compostos por doadores de sangue do Hemocentro da UNICAMP. As informações clínicas e tumorais foram obtidas a partir dos prontuários e questionários específicos. As SNVs foram genotipadas por PCR em tempo real com sondas TaqMan (Life Technologies) e reagentes do kit TaqMan Universal PCR Master Mix (Applied Biosystems), seguindo as recomendações do fabricante. As diferenças entre os grupos foram avaliadas pelos testes de Fisher ou qui-quadrado (χ^2). A regressão logística múltipla foi utilizada para estimar razões de chance (ORs), ajustadas por idade e tabagismo. A análise de sobrevida incluiu apenas pacientes da UNICAMP, utilizando os métodos de Kaplan-Meier e regressão de Cox. Valores de $p < 0,05$ foram considerados significativos. **Resultados:** Os genótipos das SNVs apresentaram frequências similares entre pacientes e controles. Indivíduos com os distintos genótipos estiveram sob risco similares de apresentarem o CCEOF. Entretanto, algumas SNVs foram associadas a características específicas: IL1A rs2856836 (GG ou GA) foi mais frequente em tabagistas (59,3% vs. 39,0%, $p = 0,003$). IL1A rs2856836 (GG) foi mais comum em tumores avançados (T3 ou T4) (96,5% vs. 88,1%, $p < 0,001$). CCND1 rs678653 (CG ou GG) foi mais prevalente em pacientes com linfonodos acometidos (68,7% vs. 53,9%, $p = 0,003$) e IL1B rs1143627 (GG ou GA) foi mais frequente em tumores HPV-positivos (95,9% vs. 79,1%, $p = 0,01$). Nenhum dos genótipos das SNVs influenciou a SLE e a SG desses pacientes. **Conclusão:** Nossos resultados sugerem que SNVs em vias inflamatórias moduladas pelo EGFR podem influenciar a progressão tumoral, especialmente em subgrupos específicos de pacientes. No entanto, análises do microambiente tumoral e estudos funcionais são necessários para confirmar os nossos achados.

Palavras-chave: Câncer de orofaringe, Processos inflamatórios, Variantes genéticas.

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PROTOCOL OF A RANDOMIZED PILOT STUDY ON SURVIVAL IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS UNDERGOING CHEMORADIATION VERSUS COMBINED CHEMORADIATION WITH INTRANASAL PERILLYL ALCOHOL

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A B S T R A C T

Introduction/Justification: Glioblastoma multiforme (GBM) is a highly aggressive type of brain tumor and remains one of the most challenging cancers to treat. This tumor is characterized by rapid progression and unfavorable prognosis. After undergoing surgery, radiotherapy (RT), and chemotherapy (CT) with temozolomide (TMZ), patients generally exhibit low survival rates. Perillyl alcohol (POH) is a hydroxylated monoterpene with antitumor, anti-angiogenic, and pro-apoptotic properties, inhibiting RAS oncogene-mediated signaling. In vitro and in vivo studies showed POH's cytotoxicity to both TMZ-resistant and sensitive cells, and its effectiveness as a radiosensitizer in malignant glioma cell lines. In phase I/II trials with oral POH in advanced, refractory cancer patients, nausea and other gastrointestinal toxicities led to study discontinuation. Currently, POH is being studied as an inhaled anticancer agent, showing no toxicity and promising activity with increased survival in patients with recurrent gliomas, however, these studies were not randomized, and to date, these investigations have been conducted exclusively in patients with recurrent gliomas. **Objectives:** This study presents a protocol from the University of Campinas, developed by experts across multiple fields, to evaluate the effects of intranasal POH in GBM patients. **Materials and Methods:** Patient's will be recruited from the Oncology Service at the General Hospital of the University of Campinas (UNICAMP) after tumor resection, with a total of 40 participants. Adult individuals of any gender will be included. Through randomization, participants will be randomly assigned to two groups: the control group (RT+CT) and the intervention group (RT+CT + POH inhalations). Block randomization of four patients will ensure balance between groups during recruitment. The randomization sequence was generated at www.randomization.com. The control group will undergo RT and CT with TMZ: 75 mg/m^2 of TMZ daily for 6 weeks during RT (2 Gy/day for 5 days a week, totaling 60 Gy), followed by 150 or 200 mg/m^2 of TMZ for 5 days per cycle in 28-day cycles for 6 cycles. The participants in the intervention group will receive the same treatment plus 0.3% POH inhalations (55 mg in 3 mL of water, 4 times daily, with 6-hour intervals). They will undergo 6 weeks of RT + TMZ + POH, followed by 6 cycles of TMZ + POH (5 days of TMZ + POH, followed by 23 days of POH only). Cranial MRIs will be analyzed by an expert neuroradiologist using T2/FLAIR signal intensity with perfusion, without knowledge of patient group allocation. MRIs are part of routine treatment, performed every 3-4 months in the first year, and response will be assessed using MacDonald and RANO criteria for high-grade gliomas. Toxicity assessment of standard treatment with POH will follow the NCI Common Terminology Criteria, version 5.0. Progression-free survival will be compared between patients receiving only RT and CT and those also undergoing POH inhalation, with survival curves calculated using the Kaplan-Meier method. **Results:** *Perspectives:* Patients in the intervention group are expected to have higher survival rates, indicating a benefit of intranasal POH with standard treatment. **Conclusion:** *Acknowledgement:* The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Glioblastoma, Perillyl alcohol, Protocol.

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ANTIPROLIFERATIVE ACTIVITIES IN VITRO OVER SQUAMOUS CELL CARCINOMAS OF A PALLADIUM(II) COMPLEX WITH AMANTADINE

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A B S T R A C T

Introduction/Justification: Metal-based drugs have been used in diagnosis and treatment of different types of cancer since the discovery of cisplatin's antineoplastic properties in the 1960's. Second-generation drugs based on the platinum(II) complex cisplatin, such as carboplatin and oxaliplatin, were developed and used for cancer treatment worldwide. However, platinum(II) drugs typically cause side effects, such as nephrotoxicity, neurotoxicity and myelosuppression, which motivates the search for new drug candidates. Since the platinum(II) and palladium(II) ions have similar characteristics and form analogous compounds, palladium(II) complexes have been also studied as potential anticancer agents. Recently, a new palladium(II) drug named padeliporfin (Tookad® Soluble) has entered the clinic for the treatment of low-risk prostate cancer, which further motivates the investigation of palladium(II) complexes as potential antineoplastic drugs. Adamantanes are a class of organic compounds that consist of a single diamond-like carbon cage. The functionalization of adamantane with an amine group lead to amantadine, which has been used in the clinic as an antiviral and

anti-Parkinson drug and has also been evaluated for its anticancer activity. **Objectives:** In this study, we report for the first time the antiproliferative studies of a palladium(II) complex with amantadine (Pd-atd) over squamous cell carcinomas **Materials and Methods:** The Pd-atd complex was prepared following the literature protocol. Briefly, the complex was prepared by the reaction of Li2PdCl4 with amantadine hydrochloride in methanol under stirring and at room temperature. The yellowish solid obtained was collected by filtration, washed with methanol and dried. Yield 72%. The [PdCl2(C10H17N)2] composition was confirmed by chemical and spectroscopic analyses. Squamous cell carcinoma of tongue (SCC-4 and SCC-25) and of hypopharynx (Fadu), and a non-tumoral cell line (HaCat, immortalized keratinocyte) were used in this study. Cells were cultivated following the methodology previously described in the literature. Cell viability was determined by dose-response curves obtained from an MTT assay measuring the absorbance after 48h. **Results:** The Pd-atd complex inhibited proliferation of SCC-4 cells with an IC50 of 1.87 μM and it was non-toxic to HaCat cells. Cisplatin, a standard drug, presented an IC50 of 7.02 μM and it was less selective toward HaCat cells in the same experimental conditions. **Conclusion:** The promising results of the antiproliferative activities of the Pd-atd complex over SCC-4 cells warrant for additional studies about the potential of application of the complex as an antiproliferative agent for the treatment of squamous cell carcinomas. **Acknowledgements:** This study was supported by grants from the Brazilian Agencies FAPESP (2022/08320-3 and 2021/10265-8 Cancer Theranostics Innovation Center - CEPID), CNPq (309800/2021-8) and Program PPPD at the University of Campinas-UNICAMP (ID number 325141).

Keywords: Aminoadamantane, Antiproliferative agent, Palladium(II), Squamous cell carcinoma.

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EFEITO DA ATIVAÇÃO NEUTRÔNICA NO COPOLÍMERO PLA-PEG ASSOCIADO À NANOPARTÍCULAS DE OURO

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R E S U M O

Introdução/Justificativa: Nos últimos anos, vários estudos têm sido dedicados à compreensão dos efeitos da radiação ionizante sobre moléculas orgânicas, especialmente aquelas com potencial para aplicações médicas e farmacológicas. Devido à sua variedade, versatilidade e propriedades, os materiais poliméricos são a classe de materiais mais investigada no desenvolvimento de sistemas para aplicação na medicina. O polietilenoglicol (PEG) é um polímero quimicamente estável, regularmente utilizado em cosméticos e como carga em produtos farmacêuticos, pois o organismo o elimina sem metabolizá-lo. Além disso, as partículas de PEG escapam do reconhecimento e captura por células fagocíticas após a administração in vivo, permanecendo por um período prolongado na circulação sistêmica. Já o ácido polilático (PLA) é um poliéster alifático biocompatível e biodegradável, sintetizado a partir de recursos renováveis, como amido de milho ou cana-de-açúcar. Devido às sua taxa de degradação lenta e baixa toxicidade, o PLA tem sido amplamente utilizado em sistemas de liberação de fármacos. A combinação de PEG e PLA como copolímero (PLA-PEG) oferece um efeito sinérgico ao combinar a hidrofilicidade do PEG com a biodegradabilidade do PLA. O uso deste copolímero na área médica tem ocorrido de diversas formas, sendo de interesse principal estudar sua associação com nanopartículas de ouro (AuNPs) e a aplicação desses nanossistemas tanto para exames de imagem quanto para terapia. A utilização do copolímero PLA-PEG para a funcionalização superficial das AuNPs pode otimizar ainda mais o desempenho deste nanossistema, melhorando a estabilidade e permitindo um encapsulamento e liberação mais eficiente dos fármacos de interesse. A alta energia emitida por fontes radioativas causa a formação de radicais livres que podem se recombinar, levando a um rearranjo das cadeias poliméricas. Esse processo pode resultar em reticulação ou degradação do material irradiado. **Objetivos:** O objetivo deste estudo é avaliar os efeitos da ativação neutrônica do complexo formado por AuNPs-SH-PEG-PLA, observando se ocorre radiólise desses polímeros ou alguma degradação nesse sistema. Este estudo também nos fornecerá informações sobre a dose mínima necessária para a ativação desse complexo, o que é de extrema importância não apenas para os pacientes, mas também para a proteção radiológica de todos os profissionais envolvidos no processo. **Materiais e Métodos:** A obtenção do nanossistema AuNPs-SH-PEG-PLA foi baseada na metodologia de Reena et al. (2017). O nanosistema foi irradiado no canal J9 com um fluxo de nêutrons de 10^8 n. $cm^{-2}.s^{-1}$ no reator Argonauta, com um tempo de irradiação de 2h para cada amostra. Foram obtidas 2 amostras, cada uma contendo uma alíquota de 3 ml do nanosistema. As amostras foram divididas de acordo com a dose aplicada, sendo que a primeira amostra não recebeu nenhum tipo de irradiação e as outras receberam 2,10 Gy. **Resultados:** Em função do estágio inicial da pesquisa, os resultados e suas respectivas análises estão em andamento, conforme o planejado. **Conclusão:** Mesmo com os estudos ainda em andamento, o revestimento de AuNPs com PEG-PLA desenvolvido neste estudo tem potencial para ser uma ferramenta útil para a obtenção de nanomateriais funcionalizados adequados para posterior ligação a fármacos com atividade antitumoral ou para uso como agentes de contraste em diagnóstico.

Palavras-chave: Ácido polilático, Argonauta, Nanopartículas de ouro, Polietilenoglicol, Polímeros.

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QUANTIFYING INTERSPECIFIC COMPETITION BETWEEN CANCER AND NORMAL CELLS USING USING NONLINEAR MIXED EFFECTS AND ORDINARY DIFFERENTIAL EQUATION MODELING

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A B S T R A C T

Introduction/Justification: Tumor growth has been widely studied through various methodologies. In mathematical oncology, researchers use ordinary differential equations (ODEs) to analyze tumor dynamics. These models present meaningful parameters to link mathematical theory with experimental data. For in vitro cocultures, parameters quantifying cellular competition clarify interactions between tumor and normal cells. **Objectives:** This research investigates the interaction between cancer and normal cells during competition, focusing on the in vitro growth of SK-MEL-147 (metastatic melanoma) and HaCaT (immortalized epithelial cells) cell lines. Using an ODE model with cell numbers as dependent variables, we quantify interspecific competition through the parameters α_{12} (impact of SK-MEL-147 on HaCaT) and α_{21} (impact of HaCaT on SK-MEL-147). **Materials and Methods:** The in vitro cell growth experiments from Morais \textit{et al}., (2017), https://doi.org/10.1038/s41598-017-07553-6, allowed us to estimate parameters for Gatenby's 1996 ODE model. We used a nonlinear mixed effects model from NLME-Modeling (https://doi.org/10.48550/arXiv.2011.06879) to account for observation errors and biological variability. **Results:** The curve fitting matched the experimental data for both cell types. Parameter estimates showed that SK-MEL-147 cells experienced stronger inhibition from HaCaT cells than the reverse, suggesting normal cells hinder cancer cell growth upon contact. **Conclusion:** Nonlinear mixed effects modeling successfully fit Gatenby's mathematical model to the experimental data, providing competition parameters that clarified interspecific interactions in tumor dynamics. Such models can predict cell growth behavior, supporting experimental design and reducing the need for preliminary \textit{in vitro} tests.

Keywords: HaCaT Cell Lineage, SK-MEL-147 Cell Lineage, Skin cancer.

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EFEITO DO SILENCIAMENTO DA CHAPERONA ERP29 NA EXPRESSÃO DE GENES DA VIA PI3K/AKT EM CÉLULAS DE CÂNCER DE FARINGE SENSÍVEIS E RESISTENTES À CISPLATINA

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R E S U M O

Introdução/Justificativa: As proteínas chaperonas, como a ERp29, são essenciais para o enovelamento e para a secreção de proteínas do retículo endoplasmático para o complexo de Golgi. Alterações nesse processo podem comprometer a funcionalidade proteica e influenciar o comportamento celular, incluindo a progressão tumoral. O silenciamento do gene ERP29 foi associado ao aumento da progressão de células tumorais da faringe, sugerindo que a ERp29 pode atuar na inibição de fenótipos tumorais agressivos. No entanto, os mecanismos envolvidos nessa regulação ainda não estão esclarecidos. A via PI3K/AKT desempenha um papel importante na progressão tumoral, regulando processos como sobrevivência celular e resposta inflamatória no microambiente tumoral. No entanto, a relação entre ERP29 e a modulação dessa via ainda não foi elucidada. **Objetivos:** O objetivo deste trabalho foi avaliar os padrões de expressão de genes da via PI3K/AKT na linhagem de células tumorais de faringe FaDu, com supressão do gene ERP29, em três condições experimentais: FaDu, FaDu tratada com cisplatina (CDDP) (FaDu-CDDP) e FaDu resistente à CDDP (FaDu-R). **Materiais e Métodos:** A linhagem celular FaDu (HTB-43, ATCC) é sensível à CDDP e foi cultivada seguindo protocolo padrão. A resistência celular foi induzida com 0,5 μM de CDDP, conforme protocolo previamente estabelecido. O gene ERP29 foi silenciado utilizando RNA de interferência (s21576, Invitrogen). Para identificar genes da via PI3K/AKT modulados pelo ERP29, o cDNA de cada amostra foi amplificado utilizando a placa TaqMan Array Human Molecular Mechanisms of Cancer (4418806, Applied Biosystems). Os resultados foram validados por qPCR. O teste t foi utilizado para comparação entre os grupos e os resultados foram expressos como fold change (FC). O valor de $p < 0,05$ foi considerado significativo. **Resultados:** A expressão do gene SRC foi maior nas células FaDu-CDDP em comparação com FaDu (FC: 3,4, $p = 0,02$) e FaDu-R (FC: 4,6, $p < 0,001$). No entanto, após o silenciamento de ERP29, os níveis de SRC tornaram-se semelhantes entre as linhagens celulares. O gene AKT1 apresentou maior expressão nas células FaDu (FC: 4,2, $p = 0,03$) e FaDu-CDDP (FC: 3,9, $p = 0,04$) em comparação com FaDu-R. No entanto, nas células com ERP29 silenciado, a expressão de AKT1 foi maior em FaDu do que em FaDu-CDDP (FC: 1,7, $p = 0,04$). Não foram observadas diferenças significativas na expressão de ITGAV entre as linhagens celulares. Entretanto, após o silenciamento do ERP29, ITGAV apresentou maior expressão em FaDu (FC: 3,3, $p = 0,02$) e FaDu-R (FC: 2,3, $p = 0,01$) em comparação com FaDu-CDDP. A expressão de JUN foi maior em FaDu-CDDP em relação a FaDu-R (FC: 2,6, $p = 0,04$). Entretanto, após o silenciamento do

ERP29, a expressão de JUN foi maior em FaDu em comparação com as outras linhagens celulares (FC: 4,5, p= 0,03 e FC: 3,0, p= 0,03). A expressão de MDM2 foi menor em FaDu do que nas demais linhagens celulares (FC: 0,3, p= 0,002 e FC: 0,2, p = 0,01). No entanto, nas células com ERP29 silenciado, a expressão de MDM2 foi maior em FaDu do que em FaDu-CDDP (FC: 2,0, p = 0,02). **Conclusão:** Nossos resultados sugerem que o gene ERP29 modula a expressão de genes-chave da via PI3K/AKT, influenciando potencialmente o comportamento das células tumorais no carcinoma de faringe. Estudos adicionais, incluindo experimentos com diferentes linhagens celulares e modelos in vivo, são necessários para confirmar esses achados.

Palavras-chave: Câncer de cabeça e pescoço, ERP29, PI3K/AKT.

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PDCD1 VARIANTS ARE INDEPENDENT PROGNOSTIC FACTORS IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA

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A B S T R A C T

Introduction/Justification: Laryngeal squamous cell carcinoma (LSCC) is a common malignancy in the upper aerodigestive tract, strongly associated with smoking and alcohol consumption. It is already well known that tumors development and progression depend on immune evasion. PD-1/PD-L1 pathway is a primary mechanisms of immune evasion. The PDCD1 gene encodes PD-1 and is a polymorphic gene. **Objectives:** His study aims to evaluate the influences of the PD1.1 (c. -606G>A), PD1 (c.627+252C>T), PD1.5 (c.804C>T) and PD1.9 (c.644C>T) single variants (SNVs) in PDCD1 gene influence the risk, clinicopathological aspects and survival of LSCC patients. **Materials and Methods:** This is a retrospective observational study including 284 patients with LSCC and 296 healthy controls (blood donors) seen at the General Hospital of University of Campinas. Clinical and pathological data were collected from the medical records by the main researcher. Genotypes of PDCD1 variants were identified using real-time PCR with TaqMan® probes. Statistical analyses included chi-square tests and logistic regression for LSCC risk assessment. Bonferroni analysis was used in comparison of multiple variables. Kaplan-Meier curves, log-rank test and univariate and multiple Cox regression were used to evaluate the impact of clinicopathological aspects and genotypes of SNVs on overall survival (OS) and event-free survival (EFS). **Results:** Similar frequencies of isolated and combined SNV genotypes were seen patients and controls. The frequencies of combined genotypes of SNVs, GA or AA + CT or TT of PD1.1 + PD1.5 and CT or TT + CT or TT of PD1.5 and PD1.9, were more common in patients with glottic tumor than in patients with tumors in other locations. The CC genotype of PD1 SNV and the CC + CC combined genotype of PD1.5+PD1 SNVs were more common in patients with tumors at stage III or IV than in patients with tumors at stage I or II. In multivariate Cox analysis, patients with BMI≤ 24.9 kg/m^2, ECOG ≥ 1, tumors at stage III/IV, and not submitted to surgical tumor resection had 1.81 (95%CI: 1,25-2,62%), 1.60 (95%CI: 1,14-2,24), 1.93 (1,24-3,00), and 1.80 (1,20-2,71) more chances of evolving to death than the remaining patients. In addition, patients with TT genotype of PD1.5 SNV and TT + CC combined genotype of PD1.5 and PD1 SNVs had a 1.59 (95% CI: 1.06-2.41) and a 2.97 (95% CI:1.43-6.18) more chances of evolving to death than others. **Conclusion:** Our data indicates: 1) The analyzed SNVs in the PDCD1 gene do not influence LSCC risk, 2) PD1, PD1.5, and PD1.9 affect LSCC location, 3) PD1 and PD1.5 influence LSCC aggressiveness, 4) BMI, ECOG, tumor stage, lack of surgical tumor resection, PD1 and PD1.5 SNVs are independent prognostic factors for OS of LSCC patients. These findings reinforce the importance of studying inherited biomarkers in oncology, which may contribute to risk stratification and personalized therapeutic approaches. **Acknowledgements:** The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2019/09168-8; #2023/09738-4, and Cancer Theranostics Innovation Center, CancerThera, CEPID FAPESP #2021/10265-8).

Keywords: Genetic polymorphisms, Laryngeal squamous cell carcinoma, PDCD1, Prognosis, Survival.

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PLATINUM-BASED CHEMORADIOTHERAPY AS DEFINITIVE TREATMENT IN ADVANCED SQUAMOUS CELL CARCINOMA OF HEAD AND NECK IN REAL-WORLD SETTING

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A B S T R A C T

Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is one of the most prevalent malignant tumor globally, and over 60% of patients present

locoregionally advanced tumors. Platinum-based chemoradiotherapy is a widely adopted treatment for patients with unresectable locoregionally advanced HNSCC, those ineligible for surgery and those refusing surgery due to potential sequelae. While this approach has yielded favorable results in developed countries, its effectiveness in real-world settings in developing countries remains underexplored. Investigating treatment outcomes in this context is essential for optimizing oncologic care. **Objectives:** To assess the toxicity profile, tumor response, event-free survival (EFS), and overall survival (OS) in patients with locoregionally advanced HNSCC treated with definitive platinum-based chemoradiotherapy. **Materials and Methods:** This retrospective study included 233 patients treated at the Oncology Service of the General Hospital of University of Campinas (UNICAMP). Inclusion criteria encompassed patients aged 18 or older, with an Eastern Cooperative Oncology Group (ECOG) of 2 or lower, who underwent radiotherapy (RT) combined with either weekly or every-three-weeks administration of cisplatin (CDDP) or carboplatin (Carbo) as definitive treatment. Grade 3 or 4 adverse events were documented according to the National Cancer Institute, Common Terminology Criteria for Adverse Events (NCI CTCAE v5.0) standards. Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Survival outcomes were estimated with the Kaplan-Meier method, and statistical comparisons were performed using the log-rank test and Cox proportional hazards regression for univariate and multivariate analyses. **Results:** The median age of patients enrolled in study was 60 years. Most enrolled subjects were males, active or former smokers and drinkers, had good performance status and comorbidities, and presented moderately differentiated and advanced tumors. Tumors were equally distributed in oral cavity, pharynx and larynx. Half of the patients developed grade 3 or 4 toxicities, with nausea/vomiting and nephrotoxicity being more frequently observed in the RT + CDDP group, while anemia and neutropenia were predominant in the RT + Carbo group. A total of 75% of patients achieved either complete or partial tumor response, with no significant impact from the treatment regimen. The two-year EFS and OS rates were 43.3% and 66.0%, respectively. Poor prognosis was associated with active smoking, ECOG performance status ≥ 2, stage IV disease, and treatment with RT + Carbo. Patients with these characteristics had an approximately twofold higher risk of presenting relapse and disease progression leading to death. **Conclusion:** This study highlights RT and CDDP as the most effective definitive treatment for patients with locoregionally advanced HNSCC from a Brazilian public hospital. Nevertheless, further prospective and randomized phase III study conducted with those patients is essential to define the optimal treatment strategy for these patients Acknowledgements: The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Definitive therapy, Head and neck squamous cell carcinoma, Outcome.

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BIODISTRIBUTION OF A TECHNETIUM-99M RADIOLABELED PEPTIDE DERIVED FROM LAMININ-111 IN A BREAST CANCER MODEL

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A B S T R A C T

Introduction/Justification: Breast cancer is a significant public health concern, ranking as the second most common tumor type among women. According to the World Health Organization (WHO), more than 14 million people develop breast cancer annually, with this number projected to rise to over 21 million by 2030. Studies have shown that biologically active peptides derived from laminin-111 can regulate gene expression in breast cancer-derived cells, among which the YIGSR peptide is of particular interest. Peptides designed to inhibit intracellular signaling pathways fall within the realm of molecular targeted therapies, which commonly focus on receptors overexpressed in tumors. **Objectives:** This study aimed to evaluate the biological behavior of the HYIGSR peptide, a laminin-111 derivative, radiolabeled with technetium-99m ([99mTc]Tc(CO)3), in a biodistribution assay using both control and breast cancer model mice. **Materials and Methods:** The HYIGSR peptide was radiolabeled using the tricarbonyl method, which enabled labeling at the histidine residue with the organometallic aqua-ion [99mTc(H2O)3(CO)3]+, abbreviated as [99mTc]Tc(CO)3. The reaction was carried out by reducing [99mTc]TcO4- under 1 atm of CO for 30 min at 70° C, followed by incubation with approximately 148 MBq of [99mTc]Tc(CO)3 for 30 min at 85°C. The radiochemical purity of [99mTc]Tc(CO)3-HYIGSR was assessed using TLC-SG strips with 0.9% NaCl as the eluent. A breast cancer animal model was established by inoculating female Balb/c nude mice with 1×10^7 MDA-MB-231 breast cancer cells. After 30 days, in vivo (molecular imaging) and ex vivo biodistribution studies were performed. The radiolabeled peptide was intravenously administered to both healthy and tumor-bearing female Balb/c nude mice, and ex vivo biodistribution analysis was conducted at 1 and 3 h post-injection. Molecular imaging of healthy mice was acquired via planar scintigraphy using a single-hole collimator on a Discovery VH clinical gamma camera, with an acquisition time of 5 min and a geometric magnification of 9 × . All animal experiments adhered to local ethical guidelines for animal research (Protocol number: CEUA – HIAE 6015-24). **Results:** The radiolabeling process using [99mTc]Tc(CO)3 was successfully standardized, yielding [99mTc]Tc(CO)3-HYIGSR with a radiochemical purity of 95.53 ± 1.19% (n = 5). Ex vivo biodistribution analysis in female Balb/c nude mice (n = 4) demonstrated rapid blood clearance

over time, with increased uptake in the kidneys. Minimal accumulation of the radiolabeled peptide was observed in the heart, spleen, lungs, and muscle, with the percentage of the injected dose per gram (%ID/g) remaining below 5%. However, high uptake was observed in the liver, stomach, intestine, and thyroid. In tumor-bearing mice, tumor uptake was measured at 0.58 ± 0.25 %ID/g, with a tumor-to-muscle ratio of 1.54 ± 0.14. Preliminary molecular imaging in the healthy group confirmed in vivo biodistribution findings consistent with ex vivo data. **Conclusion:** These findings suggest that while the [99mTc]Tc(CO)3-HYIGSR complex demonstrated efficient radiolabeling, further modifications may be necessary to enhance its tumor-targeting capabilities and improve its overall diagnostic potential.

Keywords: Biodistribution, Breast, Laminin-111, Radiolabeled, Technetium-99m.

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THE ROLE OF PSMA PET/CT IN THE CHARACTERIZATION OF HEAD AND NECK SQUAMOUS CELL CARCINOMA

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A B S T R A C T

Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is an aggressive malignancy, often diagnosed at advanced stages. The 18-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) reflects glycolytic activity in tissues and has been widely used for staging and monitoring HNSCC. However, its specificity is limited by false positives in inflammatory processes. PET/CT with prostate-specific membrane antigen (PSMA) has been investigated as an alternative to 18F-FDG due to its expression in tumor neovasculature, but its role in HNSCC remains unclear. **Objectives:** To evaluate the uptake patterns of 18F-PSMA-1007 PET/CT in HNSCC, in comparison with 18F-FDG PET/CT, aiming to explore its potential in tumor characterization, staging, and monitoring. **Materials and Methods:** Patients with advanced locoregional HNSCC, either at initial diagnosis or with tumor relapses, were enrolled in the study. Individuals who had undergone surgical tumor resection or received chemotherapy and/or radiotherapy within the last six months were excluded. All enrolled patients underwent 18F-FDG PET/CT and 18F-PSMA-1007 PET/CT imaging, with a 24-hour interval between the exams. The images were analyzed independently by two nuclear medicine physicians and one radiologist. Statistical comparisons between groups were performed using the t-test, with significance set at $P < 0.05$. **Results:** Fourteen patients (nine at initial diagnosis, five with recurrent disease) were analyzed using both PET/CT imaging modalities. The median age was 61 years (range: 49-81), with eleven males and three females. Most patients were current or former smokers and alcohol consumers, had good performance status (ECOG 0), and presented with stage IV tumors. The primary tumors were located in the oropharynx, larynx, and oral cavity, with one sinonasal tumor. Recurrences, were observed in locoregional lymph nodes, lungs, and bones. HNSCC lesions were typically characterized by FDG uptake, although most lesions also exhibited varying degrees of PSMA uptake. In primary tumors and nodal disease, the mean ± SD and median (range) SUV values obtained with FDG PET/CT at 1 hour were 25.6 ± 16.4 and 21.0 (10.7–59.8), and 11.7 ± 7.7 and 8.6 (2.7-26.4), respectively. For PSMA PET/CT, the mean ± SD and median (range) SUV values at 1 hour in primary tumors and nodal disease were 4.5 ± 1.3 and 4.3 (2.9-6.3), and 4.9 ± 2.6 and 3.9 (2.8-10.2), respectively. FDG uptake values were higher than PSMA uptake values in primary tumors ($P < 0.001$) and lymph nodes ($P = 0.01$). **Conclusion:** HNSCC lesions were more effectively detected by FDG PET/CT, highlighting its superior sensitivity for assessing tumor activity. However, PSMA uptake in most tumors suggests the coexistence of glycolytic activity and neoangiogenesis, reinforcing the value of integrating FDG and PSMA PET for tumor characterization, staging, and monitoring. The pronounced PSMA expression in certain cases supports the feasibility of theranostic PSMA-targeted therapies or anti-angiogenic treatments. Further research is needed to elucidate the relationship between PSMA expression, tumor angiogenesis, and HNSCC biology. Acknowledgements: The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (Cancer Theranostics Innovation Center, CancerThera, FAPESP #2021/10265-8).

Keywords: Head and neck squamous cell carcinoma, PET CT PSMA, PETCT FDG.

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EGFR-TARGETING PEPTIDE INHIBITS HELA CELL PROLIFERATION: A NOVEL STRATEGY FOR CERVICAL CANCER THERAPY?

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A B S T R A C T

Introduction/Justification: Cervical cancer remains one of the leading causes of cancer-related mortality in women worldwide, with EGFR overexpression contributing to uncontrolled proliferation, resistance to apoptosis, and tumor progression. Despite advances in radiotherapy and chemotherapy, many patients develop resistance, highlighting the urgent need for

targeted therapies that can disrupt these oncogenic pathways. Peptide-based drugs represent a promising avenue for precision oncology, offering high specificity, low toxicity, and potential to inhibit key molecular drivers of cancer. This study investigates the YHWYGYTPQNVT peptide, designed to interact with EGFR, and evaluates its effect on proliferation and migration of HeLa cells, a widely used model of cervical cancer. **Objectives:** This research aims to determine whether the YHWYGYTPQNVT peptide can effectively suppress EGFR-mediated growth signaling in HeLa cells, by analyzing cell proliferation, metabolic activity, and migration, aiming at establishing its potential as a therapeutic alternative to traditional cancer treatments. **Materials and Methods:** The YHWYGYTPQNVT peptide was synthesized using solid-phase peptide synthesis, purified via HPLC, and confirmed by mass spectrometry. HeLa cells were cultured in DMEM + 10% fetal bovine serum and incubated at 37°C with 5% CO_2. To establish a baseline proliferation rate, HeLa cells were plated at 5×104 cells in 6-well plates, and the growth curve was performed in sextuplicate over a 5-days period, with cell counts conducted on days 1, 3 and 5. For the experimental group, cells were treated with YHWYGYTPQNVT (80 μmol/mL). Statistical analysis was conducted using GraphPad Prism, with significance set at $p \leq 0.05$. **Results:** The YHWYGYTPQNVT peptide was synthesized efficiently with yield of approximately 45%. Chromatographic analyzes obtained by HPLC and mass spectrometry confirmed that the entire synthesis, cleavage, and purification process of peptides were performed efficiently. Control group displayed an aggressive proliferation rate with an exponential growth, reaching $\sim 96.8 \times 10^4$ cells, consistent with the known oncogenic potential of HeLa cells. In contrast, the peptide-treated group showed a significant reduction in proliferation, with final cell counts averaging 61.5×10^4 cells - corresponding to a 25.5% decrease compared to untreated cells. **Conclusion:** Our findings highlight YHWYGYTPQNVT as a promising EGFR-targeting agent capable of reducing cervical cancer cell proliferation. By directly interfering with EGFR-driven oncogenic pathways, this approach could lay the groundwork for a new class of peptide-based therapeutics in oncology. Further in vivo validation and molecular pathway analysis are necessary to determine its potential clinical application in patients with EGFR-overexpressing cervical tumors.

Keywords: Anti-EGFr-peptide, Cell proliferation, Cervical cancer, HeLa cells.

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COMPARISON BETWEEN 18F-PSMA AND 18F-FDG RADIOTRACERS FOR PET/CT IN THE EVALUATION OF PATIENTS WITH METASTATIC MELANOMA

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A B S T R A C T

Introduction/Justification: PET/CT has emerged in the last two decades as a dominant imaging modality used for staging, monitoring response and surveillance of melanoma using 18F-FDG as radiotracer. Recent publications have demonstrated the possibility of use of 18F-PSMA PET/CT as an additional resource to the evaluation of melanoma, due to the expression of Prostate-Specific Membrane Antigen protein (PSMA) in these cancer cells and because anti-PSMA antibodies react with malignant melanoma neo vasculature. **Objectives:** Would 18F-PSMA PET/CT have the potential role of a novel diagnostic imaging technique in melanoma cases? **Materials and Methods:** Eleven participants with diagnoses of metastatic melanoma underwent 18F-FDG PET/CT and 18F-PSMA PET/CT (24-hours interval), and the lesions uptakes were evaluated with both radiotracers. The results were grouped in three categories: A - greater expression of 18F-PSMA compared to 18F-FDG; B – equivalent uptake between the radiotracers; and C - greater expression of 18F-FDG compared to 18F-PSMA. **Results:** 18,1% of participants were in category A, 54,5% in category B and 27,2% in category C. The lesions with greater 18F-PSMA uptake compared to 18F-FDG were mainly in the brain, lungs, adrenals, and scattered throughout the chest. Furthermore, one subjects presented only 18F-PSMA uptake in brain metastasis, showing the importance of this method to the clinical follow-up of these patients. Our findings align with the Chang et al.'s, who demonstrated in vitro expression of PSMA in the neovasculature of melanoma lesion and with Snow et al.'s who observed PSMA positivity in endothelial cells of capillaries within stage III/IV melanoma metastases. **Conclusion:** Therefore, apart from the use of 18F-PSMA PET/CT in staging prostate cancer patients, this method shows a great potential in the evaluating of metastatic melanoma, still needing further and longer studies to confirm these advantages.

Keywords: 18F-FDG PET/CT, 18F-PSMA PET/CT, Melanoma.

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EVALUATION OF THE AFFINITY OF RADIOLABELED PEPTIDE [^{131}I]I-DEDEYFELV FOR EGFR-OVEREXPRESSING RECEPTORS IN ADULT-TYPE DIFFUSE GLIOMAS

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A B S T R A C T

Introduction/Justification: Cancer remains one of the leading causes of death worldwide. Among the various tumor sites, the central nervous system is particularly significant, with gliomas accounting for the majority of primary brain tumors. In gliomas, alterations in the tyrosine kinase pathway lead to the overexpression of the Epidermal Growth Factor receptor (EGFr). Over the past decades, radiolabeled peptides with high affinity for EGFr have emerged as promising molecular targets with potential applications in both diagnosis and therapy. **Objectives:** This study aimed to evaluate the affinity of the peptide DEDEYFELV, radiolabeled with iodine-131 (^{131}I), for EGFr-overexpressing receptors in adult-type diffuse gliomas using tumor tissue samples. **Materials and Methods:** The peptide was synthesized using solid-phase peptide synthesis following the Fmoc/tBu strategy. Upon completion of the synthesis, the peptide was characterized and purified via high-performance liquid chromatography (HPLC). DEDEYFELV (20 nmol) was radiolabeled with [^{131}I]NaI (18.5 MBq) using the chloramine-T method. The radiochemical yield of [^{131}I]I-DEDEYFELV was determined via chromatography on Whatman 3MM strips using a 95% MeOH / 5% H_2O eluent. Binding studies of [^{131}I]I-DEDEYFELV with neoplastic tissue homogenates were conducted at 1 and 4 h of incubation and quantified using an automatic gamma counter. Tumor tissue homogenates were obtained from surgical resections performed by a designated neurosurgeon, following informed consent. Gliomas were confirmed through pathological analysis, and tumor samples were preserved at -80°C. All human protocols adhered to local ethical guidelines (Protocol number CEP – FCMSCSP: CAAE 79336124.7.0000.5479). Statistical analysis was conducted using ANOVA or Student's t-test. **Results:** The peptide DEDEYFELV was successfully synthesized with a yield of approximately 92%. Mass spectrometry and HPLC analyses confirmed efficient synthesis, cleavage, and purification, as evidenced by a single peak and a molecular mass corresponding to the expected peptide. Radiolabeling was achieved with a radiochemical yield exceeding 95%. Binding studies of [^{131}I]I-DEDEYFELV with neoplastic tissue homogenates showed values of 3.25 ± 0.31% for high-grade tumors, 2.62 ± 0.34% for low-grade tumors, and 1.61 ± 0.25% for tumors of unknown grade at 1 h of incubation (n = 5). At 4 h, the binding values increased to 6.45 ± 0.66% for high-grade tumors, 10.27 ± 1.58% for low-grade tumors, and 7.74 ± 1.21% for tumors of unknown grade (n = 5). **Conclusion:** These findings demonstrate that the radiolabeled peptide [^{131}I]I-DEDEYFELV exhibits specific binding to EGFr-overexpressing tumor tissues, with an increasing affinity over time. The higher binding observed at 4 h suggests favorable interaction dynamics, particularly in low-grade gliomas. These results highlight the potential of [^{131}I]I-DEDEYFELV as a theranostic agent for EGFr-targeted imaging and therapy, warranting further investigations into its in vivo stability and clinical applicability.

Keywords: EFFr-targeting peptide, Glioma, Tumor tissue, [^{131}I] I-labeled peptide.

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EXPRESSÃO DE GENES ASSOCIADOS COM RESISTÊNCIA À CISPLATINA EM LINHAGEM DE CÉLULAS DE CÂNCER DE CAVIDADE ORAL: PASSOS INICIAIS PARA O DESENVOLVIMENTO DE UM PAINEL MOLECULAR

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R E S U M O

Introdução/Justificativa: A cisplatina (CDDP) é um dos principais agentes quimioterápicos utilizados no tratamento do carcinoma de células escamosas de cavidade oral (CCECO). No entanto, a resistência ao tratamento representa um desafio clínico, reduzindo a eficácia terapêutica e impactando negativamente o prognóstico dos pacientes. A quimiorresistência à CDDP envolve mecanismos moleculares complexos, incluindo alterações na expressão de genes relacionados ao reparo do DNA e ao metabolismo do fármaco. Nesse contexto, genes como AKR1C1, CCND1, CCND3, ERCC1 e SLC31A1 têm sido implicados em processos biológicos associados à resistência, como detoxificação de drogas, regulação do ciclo celular e transporte de íons. **Objetivos:** O objetivo deste estudo foi avaliar a expressão desses genes em células do CCECO sensíveis e resistentes à CDDP, buscando identificar potenciais biomarcadores de resistência e novas abordagens para otimizar a terapia em pacientes com o CCECO. **Materiais e Métodos:** A linhagem celular SCC-25 (câncer de língua, CRL-1628, ATCC) sensível à CDDP foi cultivada seguindo protocolo padrão. A resistência celular foi induzida com 10,64 μM de CDDP, conforme protocolo previamente estabelecido. Os modelos experimentais utilizados foram: SCC-25 e SCC-25 resistente à CDDP (SCC-25-R). O cDNA de cada amostra foi amplificado por qPCR para avaliar a expressão dos genes AKR1C1, CCND1, CCND3, ERCC1 e SLC31A1 utilizando iniciadores específicos e reagentes do kit com o corante SYBR green no equipamento QuantStudio 3, seguindo as recomendações do fabricante. O gene GAPDH foi utilizado como controle endógeno. A comparação entre os grupos foi realizada por meio do teste t e os resultados foram expressos como fold change (FC). Valores de $p < 0,05$ foram considerados significativos. **Resultados:** A expressão dos genes AKR1C1 (FC: 74,19, $p = 0,001$), CCND1 (FC: 1,91, $p = 0,003$), CCND3 (FC: 1016,29, $p = 0,009$) e ERCC1 (FC: 14,90, $p = 0,004$) foi maior nas células SCC-25-R em comparação com as células sensíveis à CDDP. Em contraste, o gene SLC31A1 apresentou uma expressão reduzida na linhagem SCC-25-R (FC: 0,56, $p = 0,005$) em relação às células sensíveis ao tratamento. **Conclusão:** Nossos

resultados indicam que a resistência à CDDP na linhagem SCC-25 pode estar associada ao aumento da expressão dos genes AKR1C1, CCND1, CCND3 e ERCC1, bem como à redução da expressão do gene SLC31A1, o que sugere que esses genes desempenham um papel na quimiorresistência. Esses achados reforçam o potencial desses genes como biomarcadores para um futuro painel de predição de resistência à cisplatina no CCECO. No entanto, novos estudos devem ser realizados em outras linhagens de tumores, assim como em modelos animais, para validar esses resultados.

Palavras-chave: Biomarcadores, Câncer de cabeça e pescoço, Cisplatin, Quimiorresistência.

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A BORON COMPLEX DESIGNED FOR FLUORINE-18 LABELING AIMING FOR PET IMAGING APPLICATION

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A B S T R A C T

Introduction/Justification: Positron emission tomography (PET) is a rapidly expanding clinical modality worldwide due to the availability of compact medical cyclotrons and automated chemistry for the production of radiopharmaceuticals. Despite the availability of various positron-emitting radionuclides such as carbon-11 [11C], fluorine-18 [18F], and gallium-68 [68Ga], 18F has gained more importance and preeminence in research and diagnostic nuclear medicine due to its appropriate half-life of 110 min. Currently, 18F-fluorodeoxyglucose [18F]FDG is the most used radiopharmaceutical for the detection of various neurological disorders and cancer diseases. Since standard 18F-fluorination methods to form carbon-fluorine bonds have some limitations, such as low yield and the requirement for harsh reaction conditions, inorganic approaches, including the formation of boron-fluorine-18 bonds, have the potential to give high specific activities at room temperature, forming a bond that is stable in vivo. The boron complex is planned to be used in fluorine-18 labeling, aiming to develop a potential radiopharmaceutical for PET. **Objectives:** This work aims to produce a new boron compound with a trivalent and tetradentate chelating agent, relatively stable in air and in solution, but reactive in the presence of fluoride ions, to form an inert fluorinated species, aiming for its use in fluor-18 labeling and application in PET imaging. **Materials and Methods:** A tetradentate trivalent chelator, named 3-((bis-(2-hydroxyethyl)amino)methyl)-2-hydroxy-5-methylbenzaldehyde (abbreviated as H3L), was synthesized as previously described and used to prepare a neutral tetracoordinated boron complex, named [BL], by its equimolar quantitative reaction with boric acid in acetonitrile under reflux conditions overnight, as a white solid, which was filtered, dried, and characterized. By spectroscopic monitoring, the formation of a new species was observed in methanol solution from [BL] and NaF, supposedly forming Na[BFL]. The structures of the [BL] molecule and of the [BFL]1- anion were theoretically calculated by DFT methods. **Results:** The H3L free ligand and the boron complex were satisfactorily characterized by diverse techniques, including mass spectrometry, FT-IR, UV-Vis, and NMR spectroscopies (1H, 13C, and 11B) and single crystal X-ray diffraction. The complex [BL] was formed upon deprotonation of three hydroxyl groups in the free ligand, whose oxygens formed the coordination sphere together with the nitrogen atom. The coordination compound has a distorted tetrahedral coordination geometry, which might favor the formation of the bond between the boron atom and the fluoride ion, which is a strong nucleophile, by weakening the boron-nitrogen bond but keeping the oxygen donor atoms strongly coordinated to the boron center. **Conclusion:** Both, the free ligand and the boron complex have been successfully synthesized and characterized. The complex forms a new species in the presence of fluoride. X-ray diffraction on a single crystal of [BL] confirms its structure. The boron center is tetracoordinate with the ligand L3-, which coordinates trianionically and tetradentate through one nitrogen and three oxygen donor atoms. The obtained boron complex exhibited reactivity upon fluoride in solution, resulting in the formation of a novel species, confirming its potential application in [18F]fluoride labeling.

Keywords: Boron, Fluorine-18, Polyvalent chelator, Radiopharmaceutical.

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PREPARATION OF PHOSPHATIDYLSERINE LIPOSOMES FOR 99MTC RADIOPHARMACEUTICALS ENCAPSULATION

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A B S T R A C T

Introduction/Justification: Liposomes are microscopic vesicles containing an aqueous core surrounded by a lipid bilayer, enabling lipophilic and hydrophilic drugs to be encapsulated. Due to this characteristic, they have been used as transporters of substances to treat or diagnose diseases, including radiopharmaceuticals. **Objectives:** This work aims to prepare liposome from phosphatidylserine, encapsulate 99mTc- MDP inside it, and compare murine 4T1 breast cell tumor uptake for 99mTc-MDP and 99mTc-MDP-liposome. **Materials and Methods:** Liposome was prepared by adding 90 mg of phosphatidylserine in a chloroform/methanol solution at a concentration of (9:1). The solvents were evaporated in a desiccator until the lipids formed a film at the bottom of the vial. The radiopharmaceutical 99mTc-MDP was obtained from the reconstitution of a lyophilized kit with a 99mTcO4- solution, according to radiolabeling instructions. The liposome was reconstituted with saline and 99mTc-MDP was added; the solution was sonicated for 10 min. The purification and encapsulation of percentage were done by size exclusion filtration in an Amicon® 10 kD filter, including two water washes. Murine 4T1 breast cancer cells were grown in RPMI-1640 culture medium supplemented with 10% fetal bovine serum, under 37°C in a humidified atmosphere with 5% CO2 and seed at 5 × 104 cell/well and stood overnight in culture conditions. 99mTc-MDP and 99mTc-MDP-liposome were added to wells, in triplicate, and stood in culture conditions for 15, 30, 60 and 120 min. Culture medium was removed, cells were washed twice with PBS, the cells were detached from the wells, and radioactivity was measured in a gamma counter. The cell internalization percentage was determined by dividing cells counts by a standard sample. **Results:** The 99mTc-MDP encapsulation in the liposome reached an average of 68 ± 26% (n = 3), determined by size exclusion filtration. In vitro tumor cells uptake for 99mTc-MDP fluctuated between 0.2% during interval time. On the other hand, 99mTc-MDP-liposome tumor cells uptake had 0.7% ± 0.1% (15 min), 0.8 ± 0.2% (30 min) 0.9 ± 0.2% (60 min) and 1.2 ± 0,4 (120 min). **Conclusion:** The experiments demonstrated the feasibility of liposome production and their use for encapsulate 99mTc-MDP radiopharmaceutical. Loaded 99mTc-MDP-liposome had significantly high tumor uptake compared to 99mTc-MDP alone, demonstrating the effectivity of the phosphatidylserine liposome in delivering radiopharmaceuticals in tumor cells.

Keywords: 99mTc, Liposome, Phosphatidylserine, Radiopharmaceuticals.

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AUTOIMMUNE ENCEPHALITIS AND PARANEOPLASTIC SYNDROMES: A CLINICAL AND FDG-PET/CT STUDY

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A B S T R A C T

Introduction/Justification: Autoimmune encephalitis (AE) is a debilitating neurological disorder characterized by inflammation of brain tissue. Frequently, it is associated with the detection of highly specific antibodies, as such as NMDA, Yo, GAD, Hu, among others. Oftentimes, this condition is expressed as a paraneoplastic syndrome (PNS), for which the neurological manifestation precedes the tumor diagnosis up to 4 years in about two-thirds of the patients. **Objectives:** This work applied the review of clinical findings and FDG-PET/CT images analysis to characterize and explore the outcomes of patients diagnosed with AE, both clinically and by antibodies test. **Materials and Methods:** The study includes 37 patients, aged from 13 to 75 (47.08 ± 20,00 years), 65% female, who had been presented neurological manifestations of encephalitis and PNS. The group of patients was divided according to the antibodies detected (NMDA, Yo, Hu, LGI1, GAD, Amphiphysin, Aquaporin-4), being also studied a group of patients with negative antibodies and untested. Retrospectively, the clinical records were analyzed by the neurology staff, being the clinical manifestations and the results of antibodies tests correlated with FDG-PET/CT brain images, analyzed by an expert in nuclear medicine. **Results:** Among the groups studied, 24.3% had suspicion or confirmed neoplasia (most of them breast or thyroid lesions), being 49% of the patients positive for antibodies related autoimmune encephalitis (AE). In the pretreatment phase, patients with Yo antibodies, manifested epilepsy and cerebellar ataxia, with FDG-PET/CT revealing hypermetabolism in the basal ganglia, cingulate gyri, thalamus, and midbrain, with hypometabolism in the cerebellar hemispheres. Hu antibodies has been associated with epilepsy, sensitive and behavior alterations, being the hypermetabolism in the cingulate gyrus and hypometabolism in the cerebellar hemispheres identified in the PET/CT images; on the other side, GAD antibodies resulted in higher FDG uptake in the thalamus and midbrain, with hypometabolism in the

frontal lobes. In this case, the neurological manifestations include epilepsy, ataxia with aspects of stiff-person syndrome, behavior and sensitive alterations. Most of the clinical manifestations mentioned has also been observed in patients with NMDA antibodies, who expressed cingulate gyri, precuneus, parietal lobes and basal ganglia hypermetabolism, and cingulate hypermetabolism, with cerebellar hemispheres hypometabolism, characterizing an anteroposterior gradient of FDG uptake. LGI1 antibodies resulted in hypermetabolism in the basal ganglia and temporal mesial lobe, with frontal hypometabolism. For most of the groups of patients, epilepsy was a common manifestation, followed by behavior and sensitive alterations. The exception is the aquaporin-4 antibody for which muscular disorders are the main symptom, also highlighted in GAD patients. **Conclusion:** PET/CT FDG is able to detect metabolic alterations in brain images with a high sensitivity. Different anti-bodies can show different patterns of hypermetabolism and hypometabolism. More studies with higher casuistic are necessary to better identify each pattern. Moreover, PET/CT FDG with whole body studies is able to detect neoplasm or suspicious neoplasm lesions.

Keywords: Autoimmune encephalitis, FDG-PET/CT images, Paraneoplastic syndromes.

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DIRECT COMPARISON BETWEEN 18F-FDG PET/CT AND 18F-PSMA PET/CT IN RADIOIODINE-REFRACTORY DIFFERENTIATED THYROID CARCINOMA PATIENTS

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A B S T R A C T

Introduction/Justification: Differentiated thyroid carcinoma (DTC) is the most common endocrine malignancy and generally has a good prognosis when properly treated. However, approximately 5-15% of cases become refractory to radioiodine therapy (rRIT), limiting diagnostic and therapeutic options and significantly impacting patient survival. Recent studies have demonstrated prostate-specific membrane antigen (PSMA) uptake in positron emission tomography/computed tomography (PET/CT) scans of advanced DTC, suggesting its potential as a diagnostic imaging target and possibly opening new avenues for theranostic approaches. **Objectives:** To compare 18F-PSMA and 18F-fluorodeoxyglucose (18F-FDG) PET/CT scans of patients with rRIT DTC. **Materials and Methods:** This cross-sectional study included 21 patients with rRIT DTC and locoregional or distant metastases. All patients underwent both 18F-FDG PET/CT and 18F-PSMA PET/CT scans. Uptake intensity was assessed using the maximum standardized uptake value (SUVmax), and lesion location was categorized as thyroid bed, cervical, thoracic, and abdominal lymph nodes, lungs, liver, and bones. The median SUVmax (range) was calculated for both radiotracers. **Results:** Both radiotracers detected lesions in all patients. The number of patients with active disease identified by 18F-FDG PET/CT and 18F-PSMA PET/CT, respectively, in each region was: thyroid bed (6 vs. 5), cervical lymph nodes (15 vs. 15), thoracic lymph nodes (11 vs. 11), abdominal lymph nodes (3 vs. 0), lungs (16 vs. 15), bones (4 vs. 6), and liver (1 vs. 1). In five patients, 18F-FDG identified more affected regions than 18F-PSMA, while in three patients, the opposite was observed. The median SUVmax was 24.2 (5.6–80.9) for 18F-FDG and 17.3 (4.1–73.3) for 18F-PSMA. In 12 patients (57.14%), the SUVmax of 18F-PSMA was higher than that of 18F-FDG. **Conclusion:** Both radiotracers demonstrated uptake in at least some lesions in all rRIT DTC patients. Uptake intensity varied among lesions, with some showing higher 18F-FDG uptake and others higher 18F-PSMA uptake, suggesting a potential complementary role for these tracers in this disease. 18F-PSMA demonstrated a higher SUVmax than 18F-FDG in more than half of the patients, indicating that, in selected cases, PSMA-labeled theranostic approaches may be a viable option.

Keywords: 18F-FDG PET/CT, 18F-PSMA PET/CT, Differentiated thyroid carcinoma, Radioiodine-refractory.

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BRAIN-TO-LIVER RATIO FROM 18F-FDG-PET/CT AS A PROGNOSTIC MARKER IN MULTIPLE MYELOMA

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A B S T R A C T

Introduction/Justification: 18F-FDG PET/CT imaging is widely used in oncology for staging and monitoring treatment response in multiple myeloma (MM). Studies have shown reduced 18F-FDG uptake in the brains of patients with disseminated malignancies, such as malignant lymphoma and other aggressive cancers. This phenomenon is likely associated with the Warburg effect and hyperlactatemia. **Objectives:** This study aimed to evaluate whether the brain-to-liver ratio (BLR) of 18F-FDG uptake in MM patients serves as a prognostic marker. **Materials and Methods:** A total of 82 MM patients diagnosed between March 2011 and May 2019 were included, with a median follow-up of 25 months (range: 0.1 −113). All patients underwent whole-body 18F-FDG PET/CT at diagnosis after fasting for at least six hours and with peripheral blood glucose levels below 180 mg/dL. A dose of 0.1 mCi/kg of 18F-FDG was intravenously administered 60 minutes before image acquisition. Brain and liver standardized uptake values (SUVmean) were determined using automated whole-brain segmentation and a spherical volume of interest (VOI) in the liver. The BLR was calculated by dividing the brain SUVmean by the liver SUVmean for each patient. Descriptive and bivariate analyses were performed. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method and compared with the log-rank test (IBM-SPSS v.24). The follow-up data were updated in January 2025. **Results:** The cohort included 55% male patients, with a median age of 64 years (range: 39−87). At diagnosis, 67% had ISS stage III disease, 16% had an ECOG performance status ≥ 2, and 88% presented with bone lesions. Chemotherapy was administered to 94% of patients, with 27% receiving bortezomib. A complete response (CR), very good partial response (VGPR), or partial response (PR) was achieved by 71% of patients. Disease progression occurred in 47% of cases, and the overall mortality rate was 69%. The 60-month OS and PFS rates were 35% and 10%, respectively. The BLR was significantly correlated with sex (R= 32%, P= 0.006), overweight status (R = 32%, P =0.007), ISS stage (R = 23%, P = 0.04), and beta-2 microglobulin levels (R = 42%, P < 0.0001). Patients with a median BLR >2.7 had significantly better OS (50% vs. 13%, P= 0.006) and PFS (3% vs. 0%, P = 0.006). **Conclusion:** BLR derived from 18F-FDG-PET/CT at diagnosis appears to be a strong prognostic indicator of OS and PFS in MM patients, with a cut-off value of 2.7. BLR also correlates with beta-2 microglobulin, a well-established serum marker of tumor burden, and ISS stage III disease. The lower 18F-FDG uptake in more aggressive MM cases may be associated with neoplastic lactate production. Given that brain cells can utilize lactate as an alternative energy source when blood lactate levels rise, this may result in reduced brain FDG uptake. Consequently, BLR may serve as a marker of high glycolytic MM burden and provide an estimate of disease severity.

Keywords: 18F-FDG PET/CT, Brain-to-Liver Ratio (BLR), Multiple Myeloma, Prognostic Marker, Tumor Glycolysis.

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SYNTHESIS, CHARACTERIZATION, AND RADIOLABELING OF MODIFIED EGFR-TARGETING PEPTIDES: POTENTIAL THERANOSTIC AGENTS?

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A B S T R A C T

Introduction/Justification: Cancer remains one of the leading causes of mortality worldwide. Consequently, efforts to overcome the limitations of conventional therapies have increasingly focused on molecularly targeted treatments, with particular emphasis on peptides due to their anti-tumorigenic properties and high affinity for receptors overexpressed in tumors. Peptides designed to inhibit intracellular signaling pathways play a key role in molecularly targeted therapies, often focusing on receptors such as the Epidermal Growth Factor receptor (EGFr), which is overexpressed in many solid tumors. As targeting biomolecules, these peptides can also serve as carriers for radionuclides, enabling both molecular imaging and targeted radionuclide therapy. **Objectives:** This study aimed to develop modified peptides with high affinity for EGFr, thereby enabling their potential application as theranostic molecules. **Materials and Methods:** Anti-EGFr peptides were modified by incorporating two different spacers—hexa-aminocaproic acid (C6) or dodeca-aminocaproic acid (C12)—and by adding the chelating agent DOTA. These peptides were synthesized using the Fmoc/tBu strategy for peptide synthesis. Cleavage from the resin was performed using a reagent mixture with a high concentration of trifluoroacetic acid (reagent K). Subsequently, the peptides underwent characterization and purification through high-performance liquid chromatography (HPLC) and mass spectrometry. A preliminary radiolabeling assay of DOTA-C6-anti-EGFR was conducted using cyclotron-produced yttrium-86 (^{86}Y) in a NaOAc buffer (pH 5.5). The radiochemical reaction was carried out at 95°C for 30 min, followed by purification through a Sep-Pak C18 cartridge to determine the radiolabeling yield. **Results:** The peptides DOTA-C6-anti-EGFr and DOTA-C12-anti-EGFr were successfully synthesized, with yields of 33.8% and 3.3%. HPLC and mass spectrometry analyses confirmed the efficiency of the synthesis, cleavage, and purification processes, as evidenced by the molecular masses corresponding to the expected peptides. Preliminary radiolabeling data for DOTA-C6-anti-EGFr with ^{86}Y demonstrated a radiochemical yield of approximately 96.5%. **Conclusion:** The modified peptides targeting EGFr were successfully synthesized, characterized, and purified. The significantly lower yield obtained for the C12 spacer suggests that peptides incorporating the C6 spacer are more viable for further development. Moreover, the high radiochemical yield of DOTA-C6-anti-EGFR highlights its potential for future radiochemical and theranostic applications, warranting further investigation.

Keywords: Anti-EGFr peptides, Cancer, Radiolabeled peptides.

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COMPARATIVE STABILITY OF CT-BASED BONE VOLUME QUANTIFICATION USING 18F-FDG AND 68GA-PSMA PET/CT IN MULTIPLE MYELOMA

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A B S T R A C T

Introduction/Justification: Computed Tomography (CT) images obtained from hybrid nuclear medicine equipment have shown great potential for PET image segmentation. Previous studies in patients with Multiple Myeloma (MM) have demonstrated the feasibility of calculating bone volume (BV) from CT data in 18F-FDG PET/CT images. This segmentation technique allows for the extraction of variables such as mean Standardized Uptake Value (SUVmean), Percentage of Bone Involvement (PBI), and Intensity of Bone Involvement (IBI) across the entire skeleton. The aim of this study is to determine whether BV quantification based on CT Hounsfield units (HU) is stable across different radiotracers. **Objectives:** To compare BV calculations from PET/CT scans using 18F-FDG and 68Ga-PSMA in patients with MM. **Materials and Methods:** This study included 18F-FDG and 68Ga-PSMA PET/CT scans performed within a 1 to 8-day interval in 15 patients (53% male, mean age 66.7 ± 10.7 years) with biopsy- confirmed symptomatic MM. The study was approved by the local Ethics Committee (CAAE 91231918.0.0000.5404). BV was calculated using the Beth Israel plugin for PET image pre-segmentation, applying a threshold of HU > 100. The cropped PET images were converted to binary format using FIJI, followed by the application of a morphological closing image processing tool to include areas such as bone marrow within the binary contour. For 18F-FDG PET, the skull was excluded during pre-segmentation due to overlapping artifacts caused by cerebral uptake. Descriptive statistics were used to compare FDG and PSMA BV calculations for each patient, with individual percentage deviation assessed relative to the FDG-derived BV. The correlation between BV values was evaluated using Spearman's rank correlation coefficient (r_s), with a significance level of $p < 0.05$. **Results:** The average individual percentage deviation in BV between 18F-FDG PET/CT and 68Ga-PSMA PET/CT was 13 ± 3%, with a range of 7% to 20%. A strong positive correlation was observed between BV values ($p = 3 \times 10^{-10}$), with a very strong Spearman correlation coefficient ($r_s = 0.98$). **Conclusion:** Despite the exclusion of the skull in BV calculations for 18F-FDG, the results indicate a minimal decrease in BV compared to whole-skeleton BV derived from PSMA PET/CT. The very strong correlation between BV values for the two radiotracers suggests that the segmentation approach remains consistent across different PET tracers. Additionally, the proportional exclusion of the skull across patients supports the reliability of the method for BV quantification.

Keywords: 18F-FDG, 68Ga-PSMA, Bone Volume Quantification, Multiple Myeloma, PET/CT imaging.

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SERUM METABOLOMIC ANALYSES IN RECTAL CANCER PATIENTS: AN EXPLORATORY STUDY FROM A TIME-COURSE PERSPECTIVE

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A B S T R A C T

Introduction/Justification: Patients with colorectal cancer frequently develop cachexia, leading to severe depletion of skeletal muscle. Metabolomics, through the analysis of

metabolite profiles using nuclear magnetic resonance (NMR), shows promise in identifying biomarkers for diagnosis and treatment, providing crucial insights into tumours and metabolic changes, allowing for an enhanced understanding of the mechanisms related to the cancer-cachexia process. **Objectives:** In the present study, we analysed the most impacted metabolic pathways affected after a glycaemic clamp in the serum of patients with rectal cancer diagnosed with sarcopenia (S) or not (NS). **Materials and Methods:** In this preliminary study, serum samples collected from rectal cancer patients were prepared through filtration to remove proteins and lipids, followed by the addition of deuterium buffer for magnetic field calibration. The spectra were obtained using NMR (500 MHz), allowing precise identification and quantification of metabolites in biological samples. The obtained spectra were processed by CHENOMX software for phase adjustment, baseline correction, and spectral alignment, and then analysed for metabolic pathways using MetaboAnalyst software. Finally, metabolic profiles were correlated with clinical data from patients ((S) or (NS)) and the time course of the glycaemic clamp (initial time (T0) and final time (after 120 minutes, T1)). Institutional Review Board approval (CAAE: 91217418.2.0000.5404). **Results:** A total of 7 patients were analysed, 3 S and 4 NS. All S were female, and NS group had 3 males and 1 female. The median age was 64 (43-66) years for S and 69 (58-74) years for the NS group. The M-value-TBW and M-value-FFM median (P25-P75) were 4,2 (3,40-5,55) and 4,4 (3,75-5,25), for the S group, and 7,20 (5,65-8,95) and 6,10 (5,63-6,63) for the NS group, respectively. Sarcopenic patients – S –, compared to NS patients, at T0, exhibited increased levels of glycerol (indicating mobilisation of body fat), glycine and threonine (suggesting lean body mass depletion), as well as methylhistidine (corresponding to skeletal muscle degradation), with maintained levels of alanine and urea. After 120 minutes (T1), S patients showed an increase in serum alanine, glycine, and urea, still with a high serum concentration of glycerol, though similar to NS patients, and a reduction in threonine and methylhistidine levels compared to NS patients. These metabolite alterations directly impacted metabolic pathway vias related to lipoic acid metabolism, glutathione metabolism, tryptophan metabolism, branched-chain amino acid degradation (leucine, isoleucine, and valine), glycolytic and gluconeogenic pathways, and pyruvate and pyrimidine metabolism in S patients compared to NS patients. **Conclusion:** The study reveals that S patients present a distinct metabolic profile, impacting metabolic pathways, mainly related to cachexia syndrome effects, compared to NS individuals, thereby enhancing our understanding of the metabolic disturbances in this condition. Mendes, MCS and Madeira, BSM are sharing the first authorship. Gomes-Marcondes, MCC and Carvalheira, JBC were co-advisors in these studies.

Keywords: Cachexia, Metabolism, Metabolomic analysis, Rectal cancer, Sarcopenia.

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PREPARATION OF 1-[18F]FLUORO-2-IODOETHANE AS A PROSTHETIC GROUP FOR [18F]FLUOROETILATION

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A B S T R A C T

Introduction/Justification: [18F]Fluorine is of considerable importance in radiochemistry for positron emission tomography (PET) due to its decay characteristics (18F; beta+ 96.7%, T1 = 2. 109:8 min). Numerous methods for introducing 18F into organic molecules have been developed, with alkylation being one of the methods. Thus, developing the radiochemistry process for the fluorination of dihaloalkyl compounds is a crucial step for the development of new radiotracers. **Objectives:** This work aims to prepare the 1-[18F]fluoro-2-iodo-ethane as a prosthetic group for radiolabeling amine or alcohol functionalized molecules, focusing on developing the radiotracers for molecular imaging. **Materials and Methods:** [18F] Fluoride was produced by the 18O(p,n)18F reaction on [18O] water using cyclotron (GE 16.5 MeV). Radiolabeling method 1: [18F]Fluoride was trapped in a QMA cartridge and released by eluting tetraethylammonium bicarbonate (TEAHCO3 (7.5 mg, 2.47 μmol) in methanol into a vial. The methanol solution was heated at 100oC with a gentle stream of N2 until methanol was evaporated. Acetonitrile (AcN) was added (0.5 mL $\times$ 2) and evaporated to complete drying the system. A solution containing 9 mg (3.19 μmol) of 1,2-diiodoethane in 0.5 mL AcN was added and heated at 100oC for 10 or 15 min. Radiolabeling method 2: Water solution containing [18F]fluoride was added to a vial and dried by azeotropic evaporation with acetonitrile (0.5 mL $\times$ 2) at 100 oC with a gentle stream of N2 over 10 min. An acetonitrile solution containing TEAHCO3 (7.5 mg, 2.47 μmol) or TBAHSO4 (8.3 mg, 2.47 μmol) was added and evaporated; finally, 9 mg (3.19 μmol) of 1,2-diiodoethane in 0.5 mL of AcN was added and heated at 100oC for 10 min. At the end of the reactions, vials were allowed to reach room temperature; a sample was removed and analyzed in TLC-SG and TLC-RPc18 using ethyl acetate or ethanol as the mobile phase. [18F]fluoride ion and [18F]fluoride/ammonium quaternary ion pair were also analyzed by TLC chromatography. Stripes were cut in segments of 1 cm and read in a well

counter. **Results:** All the chromatographic systems evaluated presented [18F]fluoride and [18F]fluoride/ammonium quaternary retained in the origin of the systems. Samples of the reaction showed a radioactive product moving to the front of the TLC-RPc18 using ethanol, and this TLC system was used to analyze the reaction efficiency. Radiochemical yield was calculated considering the Rf 0.5-1.0 radioactive counts in the TLC-RPc18/EtOH. Reaction under condition 1: heating time: 10 min = 24.5%, 15 min = 10.6%. Reaction under condition 2: TEAHCO3 - 10 min = 47.6%, TBAHSO4 - 10 min = 24.8%. **Conclusion:** The results demonstrated the feasibility to produce 1-[18F]fluoro-2-iodo-ethane by both techniques, and heating time and kind of ammonium salt can influence the reaction yield. Directly adding [18F]fluoride to the vial, without using a QMA cartridge, seems to be a good alternative to optimize multiple reaction parameters in the radiolabeling process. This route will be used to optimize parameters for the proposed reaction and for other dihaloalkyl molecules.

Keywords: 1-[18F]fluoro-2-iodo-ethane, Ammonium quaternary, Radiolabeling, [18]fluor.

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EVALUATION OF 18F-PSMA PET/CT UPTAKE IN PATIENTS WITH GASTRIC ADENOCARCINOMA: AN EXPLORATORY ANALYSIS

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A B S T R A C T

Introduction/Justification: Gastric cancer is the fifth most common cancer and the third leading cause of cancer-related death worldwide. The diagnosis of gastric tumors involves a multimodal approach, including upper gastrointestinal endoscopy with biopsy, computed tomography (CT), and endoscopic ultrasound. Positron emission tomography combined with computed tomography scanners (PET/CT) is widely used in cancer diagnosis and staging as it reflects the tumor's molecular activity. However, its indication in gastric cancer is limited, being reserved for specific clinical scenarios. In this context, evaluating new imaging methods for gastric tumors becomes crucial. In recent years, PET/CT targeting PSMA (Prostate-Specific Membrane Antigen) has been explored beyond prostate cancer. PSMA expression in the endothelium of newly formed vasculature (neoangiogenesis) has already been described in other cancer types, such as colorectal, gastric, and pancreatic; however, its role in gastric cancer evaluation remains poorly understood. **Objectives:** This study aims to investigate 18F-PSMA PET/CT uptake in different clinical scenarios of patients with gastric cancer and compare it with 18F-FDG PET/CT uptake (glucose metabolism). **Materials and Methods:** This study was approved by the Institutional Review Board (CAAE 76237023.0.0000.5404). It was conducted in patients diagnosed with gastric adenocarcinoma treated at the Clinic Hospital of Unicamp (HC-UNICAMP) who underwent both Fludeoxyglucose F-18 (FDG) and prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) to evaluate radiotracer uptake in the primary lesion and metastases. **Results:** A total of 24 patients with a confirmed diagnosis of gastric adenocarcinoma through upper gastrointestinal endoscopy and biopsy underwent 18F-PSMA PET/CT and 18F-FDG PET/CT. Among them, 5 had metastatic disease, and 19 had localized tumors. Among the 5 metastatic patients, 3 demonstrated PSMA uptake, of whom 2 had undergone chemotherapy before imaging, while 1 had not received chemotherapy prior to imaging. Among the 19 patients with localized tumors, 5 showed PSMA uptake, all of whom had not received neoadjuvant therapy. The remaining 14 patients showed no PSMA uptake, with 2 having undergone neoadjuvant therapy before the scan. Among these 14 patients without PSMA uptake, 6 also showed no FDG uptake, and only 1 had previously undergone neoadjuvant therapy. **Conclusion:** Our results demonstrated that PSMA uptake in gastric cancer is heterogeneous. It is well known that gastric cancer has high molecular, histological, and phenotypic heterogeneity, making its classification and treatment challenging. Accordingly, the findings of this descriptive analysis suggest that PET-PSMA uptake in gastric cancer may be associated with tumor biology, as well as the molecular profile of the tumor and its metastases, supporting the hypothesis that tumor heterogeneity contributes to the uptake or lack thereof of the radiotracer. Differential gene expression analysis may provide valuable insights into tumor heterogeneity and help identify potential biomarkers for patient stratification and the development of novel therapeutic approaches.

Keywords: 18F-FDG PET/CT, 18F-PSMA PET/CT, Gastric Cancer, Tumor Heterogeneity.

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PET/CT WITH ^{18}F-FDG AND ^{18}F-PSMA IN LUNG CANCER: DIFFERENCES BETWEEN ADENOCARCINOMA AND SQUAMOUS CELL CARCINOMA

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A B S T R A C T

Introduction/Justification: Lung cancer remains a leading cause of mortality worldwide. PET/CT with ^{18}F-FDG is widely used for detecting, staging, and monitoring lung cancer by assessing increased glycolytic metabolism in tumor cells. Prostate-specific membrane antigen (PSMA), although primarily a marker for prostate cancer, is also associated with tumor neoangiogenesis and has shown uptake in various malignancies, including lung cancer, suggesting potential theranostic applications. **Objectives:** This study aims to compare the uptake of ^{18}F-FDG and ^{18}F-PSMA in primary and metastatic lung cancer lesions, analyzing differences between adenocarcinoma and squamous cell carcinoma (SCC) subtypes. **Materials and Methods:** Fourteen patients (9 men and 5 women), aged 55–82 years and diagnosed with lung cancer (10 adenocarcinoma, 4 SCC), underwent PET/CT scans on two separate days: 60 minutes after intravenous administration of 0.1 mCi/kg of ^{18}F-FDG and 90 minutes after intravenous administration of 0.1 mCi/kg of ^{18}F-PSMA. Images were assessed by two nuclear medicine physicians and one radiologist. The maximum standardized uptake value (SUVmax) was measured for both tracers in primary tumors, regional lymph nodes, and distant metastatic lesions. The lesions were defined in both tracers by an SUVmax uptake above the background and visual analysis. **Results:** A total of 288 lesions were analyzed (247 adenocarcinoma, 41 SCC). In adenocarcinoma, ^{18}F-PSMA identified 215 lesions, compared to 237 detected by ^{18}F-FDG. Nine lesions were exclusive to ^{18}F-PSMA, while 32 were detected only by ^{18}F-FDG. Forty-five lesions showed higher ^{18}F-PSMA uptake, while 174 exhibited predominant ^{18}F-FDG uptake. The median SUVmax for ^{18}F-FDG was 6.5 (range: 1.8–24.5), compared to 4.0 (range: 0.7–24.8) for ^{18}F-PSMA. In SCC, ^{18}F-PSMA identified 36 lesions, while ^{18}F-FDG detected 41. No lesions showed predominant ^{18}F-PSMA uptake, and SUVmax values were higher for ^{18}F-FDG (median: 8.8; range: 1.3–36.6) compared to ^{18}F-PSMA (median: 2.5; range: 0.9–10.4).We found that SUV values for ^{18}F-PSMA are statistically different between SCC and adenocarcinoma subtypes in the lesions that showed uptake of both radiotracers (Mann-Whitney U test, p-value < 0.0001). Also, a positive correlation was observed for ^{18}F-FDG and ^{18}F-PSMA SUVs in both histological subtypes, being strong for SCC (r = 0.0,8140, p-value < 0.0001) and moderate for adenocarcinoma (r = 0.4278, p-value < 0.0001). **Conclusion:** These findings highlight distinct uptake patterns between adenocarcinoma and SCC using ^{18}F-FDG and ^{18}F-PSMA PET/CT. SCC demonstrated markedly higher ^{18}F-FDG uptake with minimal ^{18}F-PSMA uptake, indicating limited utility of ^{18}F-PSMA in this subtype. In contrast, adenocarcinoma showed higher ^{18}F-FDG uptake in most lesions, but a subset exhibited significant ^{18}F-PSMA uptake, suggesting a potential link between neoangiogenesis and glycolytic metabolism. These results support a complementary role for ^{18}F-PSMA in adenocarcinoma evaluation, particularly in cases with high PSMA expression. Further studies are needed to determine its clinical impact on personalized treatment strategies and theranostic applications.

Keywords: Lung cancer, PET/CT, Tumor Metabolism, ^{18}F-FDG, ^{18}F-PSMA.

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ADIPOSE TISSUE METABOLISM IN RECTAL CANCER PATIENTS WITH CACHEXIA

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A B S T R A C T

Introduction/Justification: Adipose tissue (AT) glucose uptake, assessed by Fludeoxyglucose F-18 (FDG) positron emission tomography/computed tomography (PET/CT), reflects tissue metabolic activity and may be linked to both glucose metabolism by adipocytes and inflammatory cell activity. Additionally, adipose tissue radiodensity, measured by computed tomography (CT), has emerged as a promising metabolic biomarker. Increased AT radiodensity may indicate inflammation or the presence of brown adipose tissue (BAT), providing insights into pathophysiological processes underlying cancer cachexia. **Objectives:** The purpose of this study was to evaluate adipose tissue metabolism, assessed by the visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) glucose uptake through ^{18}F-FDG PET/CT analysis and VAT and SAT radiodensity assessed by CT in cachexia (C) and non-cachexia (NC) rectal cancer patients. **Materials and Methods:** This is a cross-sectional study involving patients diagnosed with rectal cancer. Cachexia was categorized according to

Fearon's criteria, being defined as weight loss greater than 5%, or weight loss greater than 2% in individuals already showing depletion according to current bodyweight and height (body-mass index [BMI] < 20 kg/m^2) or low skeletal muscle mass (defined according to Martin's criteria). Body composition and tissue radiodensity was analyzed using computed tomography (CT) images processed with the SliceOmatic software based on the difference in tissue measurements by Hounsfield Units (HU). The segmentation and data collection of PET/CT images are performed in FIJI and the Beth Israel Plugin for FIJI. In the segmented areas (VAT and SAT), glucose uptake values (^{18}F-FDG) are collected, represented by the Standard Uptake Value (SUV) variable. M-value was determined using euglycemic hyperinsulinemic clamp. Demographics characteristics, disease-related data, and biochemical test results were collected from medical records. Statistical analyses were performed using Jamovi® version 2.3. This study protocol was approved by the Institutional Review Board (CAAE: 91217418.2.0000.5404). **Results:** A total of 36 patients were included in the analysis. Cachexia was diagnosed in 25 patients (69.4%). The median age was 64 years (range: 43-74) in the C group and 62 years (range: 47-72) in the NC group. Weight loss greater than 5% occurred in all C patients, and low muscularity in 36.4% of this group. Cachexia patients had a higher VAT SUV mean (0.815 ± 0.184) compared to NC (0.644 ± 0.148), p = 0.005. VAT glucose uptake was correlated with VAT radiodensity (rho = 0.678, p < 0.001) and weight loss (rho = 0.434, p = 0.015) while it was negatively correlated with VAT area (rho = -0.412, p = 0.021). Additionally, VAT radiodensity showed a negative correlation with VAT area (rho = -0.452, p = 0.008), SAT area (rho = -0.465, p = 0.006), and BMI (rho = -0.695, p = 0.015). Positive correlations were observed between VAT radiodensity and SAT radiodensity (rho = 0.633, p < 0.001) and SAT SUV mean (rho = 0.532, p = 0.002). No significant correlation was found between VAT SUV mean and M-value; however, M-value-TBW correlated with VAT radiodensity (rho = 0.369, p = 0.03). **Conclusion:** These findings suggest that VAT metabolism may serve as a potential biomarker in cachexia and underscore the need to expand investigations into the metabolic alterations that influence the pathophysiology of cachexia.

Keywords: Adipose tissue radiodensity, Cancer cachexia, Fludeoxyglucose F-18 (^{18}F-FDG) PET/CT, Weight loss.

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FATORES ASSOCIADOS À PIOR QUALIDADE DE VIDA DE PACIENTES COM CÂNCER DE CABEÇA E PESCOÇO TRATADOS COM RADIOTERAPIA E QUIMIOTERAPIA NA UNICAMP

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R E S U M O

Introdução/Justificativa: A radioterapia (RT) e a quimioterapia (QT) são essenciais no tratamento do câncer de cabeça e pescoço (CCP), mas seus efeitos adversos comprometem a qualidade de vida (QdV) dos pacientes. Sintomas como xerostomia, mucosite e disfagia afetam a funcionalidade, enquanto alterações na aparência e dificuldades na comunicação impactam o bem-estar emocional e social. Embora esses efeitos sejam reconhecidos, ainda há uma necessidade de melhor compreensão dos fatores sociodemográficos e clínicos associados à QdV desses pacientes. **Objetivos:** Este estudo teve como objetivo avaliar se as características sociodemográficas, os aspectos clínicos e as características do tumor influenciam a percepção da QdV de pacientes com CCP tratados com RT e QT. **Materiais e Métodos:** Foram avaliados 32 pacientes com CCP atendidos no Hospital de Clínicas da UNICAMP durante o tratamento com RT e/ou QT exclusiva. As informações sociodemográficas (idade, sexo, cor da pele, grau de instrução, tabagismo e etilismo), aspectos clínicos (dor, escala de performance ECOG, marcadores hematológicos, índice de inflamação imune sistêmica e de resposta à inflamação sistêmica) e as características do tumor (localização, grau de diferenciação e estágio TNM) foram coletadas dos prontuários dos pacientes e por questionário específico. A QdV dos pacientes foi avaliada pelo instrumento FACT-H&N que possui 39 questões distribuídas nos domínios de bem-estar físico, social, emocional, funcional e preocupações adicionais específicas para CCP. A análise dos dados foi realizada por meio do cálculo das médias dos escores de cada domínio e do escore total, sendo que menores escores indicam pior QdV. A análise estatística foi realizada utilizando o teste t para comparação entre grupos, o valor de p < 0,05 foi considerado significativo. **Resultados:** Observamos que pacientes negros apresentaram menor bem-estar emocional (19,0 vs. 23,5; p = 0,002), enquanto tabagistas apresentaram escores mais baixos de bem-estar físico (20,0 vs. 25,5; p = 0,03) e bem-estar específico (19,0 vs. 29,0; p = 0,02). Dor moderada ou intensa foi associada a pior bem-estar físico (20,5 vs. 26,5; p = 0,002), emocional (18,0 vs. 22,0; p = 0,01) e global (101,0 vs. 122,0; p = 0,02). Pacientes com status funcional ECOG ≥ 1 apresentaram piores escores de bem-estar funcional (19,0 vs. 23,0; p = 0,001) e total (101,5 vs. 123,5; p = 0,04). A presença de anemia foi associada a menor bem-estar específico (21,5 vs. 30,0; p= 0,002) e total (99,0 vs. 120,5; p= 0,009). Pacientes com índice de resposta à inflamação sistêmica elevado apresentaram menor bem-estar físico (20,5 vs. 25,0; p = 0,04), funcional (16,5 vs. 22,0; p = 0,01), específico (21,0 vs. 28,0; p = 0,03) e total (99,0 vs. 116,0; p = 0,03). Além disso, pacientes com tumores na faringe relataram pior bem-estar físico (20,0 vs. 26,5; p = 0,01), enquanto aqueles com tumores pouco diferenciados apresentaram menor bem-estar

funcional (10,0 vs. 22,0; p = 0,03). **Conclusão:** Os resultados deste estudo sugerem que a QdV de pacientes com CCECP tratados na UNICAMP pode ser influenciada por fatores sociodemográficos e clínicos. Esses achados destacam perfis de maior vulnerabilidade e reforçam a necessidade de estratégias individualizadas para minimizar os impactos do tratamento na QdV desses pacientes.

Palavras-chave: Aspectos clínicos, Aspectos sociodemográficos, Câncer de cabeça e pescoço, Qualidade de vida.

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DUAL-TRACER PET/CT IMAGING IN HEPATOCELLULAR CARCINOMA: COMPARING THE PERFORMANCE OF 18F-FDG AND 18F-PSMA

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A B S T R A C T

Introduction/Justification: Hepatocellular carcinoma (HCC) is a prevalent malignancy with rising incidence in Western countries, often diagnosed at advanced stages. Early detection and accurate assessment of tumor extent are crucial for optimal treatment planning. 18F-FDG PET/CT has limited diagnostic value in HCC. While prostate-specific membrane antigen (PSMA) is primarily a marker for prostate cancer, its association with tumor neoangiogenesis and demonstrated uptake in various malignancies, including HCC, suggests potential diagnostic applications. **Objectives:** This study compared 18F-FDG and 18F-PSMA uptake in PET/CT for evaluating hepatic lesions in HCC. **Materials and Methods:** Eleven patients with HCC were included, six with Barcelona Clinic Liver Cancer (BCLC) staging system stage C (advanced) and five with BCLC stage B (intermediate), with a median age of 74 years (range: 59–86). All patients underwent 18F-FDG and 18F-PSMA PET/CT scans with a one-day interval between them. 18F-FDG images were acquired at 60 and 120 minutes post-injection, while 18F-PSMA images were obtained at 90 and 150 minutes. The maximum standardized uptake value (SUVmax) was measured for all hepatic lesions, and the change between early and delayed images (ΔSUVmax) was calculated. Spearman's rank correlation coefficient (ρ) was used to assess the correlation between SUVmax values for the two radiotracers, with statistical significance set at $\rho <$ 0.05. **Results:** Nine of the 11 patients had multiple hepatic lesions. A median of 3 lesions per patient (1–15) was detected with 18F-FDG, and 2 lesions per patient (1–11) with 18F-PSMA, totaling 75 lesions. Fifty-six lesions were positive for both radiotracers, 16 were only for 18F-FDG, and 3 only for 18F-PSMA. In the BCLC-B group (n = 5), 11 lesions were detected with 18F-FDG, 15 with 18F-PSMA, and 32 with both. The median SUVmax (early images) was 6.3 (3.5–8.5) for 18F-FDG and 17.2 (15.0–25.6) for 18F-PSMA. In the BCLC-C group (n = 6), 34 lesions were detected with 18F-FDG, 14 with 18F-PSMA, and 24 with both. The median SUVmax (early images) was 8.1 (4.7–17.2) for 18F-FDG and 23.3 (17.1–50.2) for 18F-PSMA. For BCLC-B patients, the median ΔSUVmax was 17.65% (-6.35% to 28.57%) for 18F-FDG and -30.17% (-9.74% to -50.67%) for 18F-PSMA. For BCLC-C patients, the median ΔSUVmax was 0.00% (-66.67% to 10.47%) for 18F-FDG and -0.47% (-67.26% to 16.37%) for 18F-PSMA. Spearman's correlation between 18F-FDG and 18F-PSMA SUVmax was ρ = -0.5357 (ρ = 0.2357). **Conclusion:** The 18F-FDG and 18F-PSMA PET/CT provide complementary information for evaluating hepatic lesions in BCLC stage B and C HCC. 18F-FDG detected more lesions, particularly in advanced disease, while 18F-PSMA showed higher uptake, especially in BCLC-C patients. The lack of significant correlation between 18F-FDG and 18F-PSMA SUVmax values suggests they reflect distinct biological processes. This independent uptake pattern may inform treatment strategies. Further research is needed to investigate whether antiangiogenic therapy might be more effective in patients with high 18F-PSMA uptake. The more pronounced 18F-PSMA washout phenomenon observed may have implications for its theranostic potential.

Keywords: 18F-FDG PET/CT, 18F-PSMA PET/CT, Comparative Analysis, Hepatic Lesions, Hepatocellular Carcinoma (HCC).

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CT-SEGMENTED BONE SUV IN MULTIPLE MYELOMA: A COMPARATIVE STUDY OF ^{18}F-FDG AND ^{68}GA-PSMA PET/CT

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A B S T R A C T

Introduction/Justification: ^{18}F-FDG PET/CT is widely used in the management of multiple myeloma (MM), a disease that often presents with extensive bone involvement. Radiolabeled prostate-specific membrane antigen (PSMA), primarily a marker for prostate cancer, is also associated with tumor neoangiogenesis, and studies have demonstrated its uptake in MM lesions. Hybrid PET/CT imaging with both FDG and PSMA tracers allows for several quantitative metrics, enabling objective comparisons beyond visual analysis. **Objectives:** This study aims to compare ^{18}F-FDG and ^{68}Ga-PSMA PET/CT quantitative metrics in the skeletal system of patients with MM. **Materials and Methods:** The study included ^{18}F-FDG and ^{68}Ga-PSMA PET/CT images acquired within a 1- to 8-day interval from 15 patients (53% male, mean age 66.7 ± 10.7 years) with symptomatic, biopsy-proven MM. CT was used to segment the entire skeleton in PET images, with the skull excluded in ^{18}F-FDG images due to artifacts from brain uptake coregistration. SUV quantification was performed using in-house software developed in MATLAB. Descriptive statistics and individual percentage deviations between the radiotracers were used to evaluate bone mean and maximum Standardized Uptake Values (SUVmean and SUVmax). Correlation analysis between the radiotracers was conducted using Spearman's rank correlation coefficient (r) with a significance level of $p < 0.05$. **Results:** For bone SUVmean, values were higher for ^{18}F-FDG compared to ^{68}Ga-PSMA, with an average of 0.9 ± 0.1 vs. 0.5 ± 0.1, corresponding to a -40% ± 9% difference (range: -25% to -57%). Conversely, for bone SUVmax, values were lower for ^{18}F-FDG compared to ^{68}Ga-PSMA, with an average of 8 ± 3 vs. 19 ± 14, corresponding to a 154% ± 2% difference (range: -21% to 762%). A moderate correlation was found for bone SUVmean between ^{18}F-FDG and ^{68}Ga-PSMA ($r = 0.55$, $p = 0.03$), while no significant correlation was observed for bone SUVmax ($r = 0.17$, $p = 0.55$). **Conclusion:** This study reveals distinct quantitative uptake patterns between ^{18}F-FDG and ^{68}Ga-PSMA PET/CT in the skeletal system of MM patients. ^{18}F-FDG exhibited significantly higher SUVmean than ^{68}Ga-PSMA, likely due to physiological ^{18}F-FDG uptake in bone marrow. A moderate correlation was observed for SUVmean between the two tracers. The higher SUVmax values for ^{68}Ga-PSMA, with no correlation with ^{18}F-FDG SUVmax, may reflect the different biological targeting mechanisms of each tracer. This suggests that some regions of increased PSMA uptake (possibly indicating neoangiogenesis) may not correspond to areas of increased glycolysis, highlighting the potential complementary role of these radiotracers in MM evaluation.

Keywords: Multiple Myeloma, PET/CT, SUV Quantification, ^{18}F-FDG, ^{68}Ga-PSMA.

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MIR-4421 AS A POSSIBLE MODULATOR OF MAPK/AKT PATHWAY THROUGH ERP29 IN PHARYNGEAL CANCER

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A B S T R A C T

Introduction/Justification: ERP29 gene encodes a chaperone protein essential for protein folding and secretion. Our previous study linked ERP29 inhibition to an increased risk of pharyngeal cancer (PC) and reduced patient survival, possibly due to the binding affinity between microRNA miR-4421 and ERP29 messenger RNA (mRNA). This interaction leads to ERP29 silencing, which may influence PC progression especially by decreasing necrosis and increasing cell migration. However, the precise mechanism underlying this process remains unknown, particularly its impact on well-established signaling pathways such as MAPK/Akt, which are frequently dysregulated in PC and play a critical role in tumor progression, cell survival, and metastasis. **Objectives:** This study aims to explore the role of miR-4421 and ERP29 in PC survival and progression. **Materials and Methods:** We first evaluated ERP29 and miR-4421 prognostic value in head and neck cancer patients assessing the Kaplan–Meier Plotter (kmplot.com/analysis/). We used PC FaDu cell line (ATCC) in two different scenarios: FaDu cisplatin (CDDP)-sensitive and FaDu CDDP-resistant (FaDu-R). ERP29 expression was silenced using a specific siRNA. We identified and validated genes modulated by ERP29 in FaDu and FaDu-R cells by TaqMan plate array and quantitative PCR (qPCR), respectively. We tested if miR-4421 inhibitor could reverse ERP29 silencing effect, with gene expression analyzed by qPCR in FaDu and FaDu-R cells. Statistical analysis was performed by t-test using SPSS 21.0 software (SPSS Incorporation, USA). **Results:** Lower ERP29 ($p = 0.03$) and higher miR-4421 ($p < 0.01$) expressions were associated with poor overall survival in head and neck cancer patients. In FaDu cells, ERP29 silencing increased MAPK1 (FC: 2.4, $p = 0.03$), AKT1 (FC: 17.5, $p < 0.01$), and JUN (FC: 29.0,

p = 0.01) expression when compared to cells expressing ERP29. In contrast, the transfection of miR-4421 inhibitor reverted those effects, decreasing the expression of MAPK1 (FC: 0.6, p = 0.03), AKT1 (FC: 0.1, p = 0.02), and JUN (FC: 0.1, p = 0.02) compared to the negative control. In FaDu-R cells, ERP29 silencing increased SOS1 (FC: 2.2, p < 0.01), MAPK1 (FC: 2.1, p < 0.01), and AKT1 (FC: 2.2, p = 0.04) expression when compared to cells expressing ERP29. Conversely, miR-4421 inhibitor decreased the expression of SOS1 (FC: 0.2, p = 0.03), MAPK1 (FC: 0.4, p = 0.01), and AKT1 (FC: 0.2, p = 0.04) compared to the negative control. **Conclusion:** Inhibition of ERP29 expression may impact MAPK/Akt pathway, contributing to PC patients' poor survival. However, these effects could be reversed by inhibiting the binding of miR-4421 to ERP29. Our study enhances the understanding of PC progression and CDDP resistance, and we hope that our findings will aid in the development of targeted therapy for PC patients by ensuring ERP29 expression. **Acknowledgements:** The study was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq grant numbers 140019/2020-0, 307944/2022-0, and 408177/2023-3) and Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP grant number 2023/12810-9) - Cancer Theranostics Innovation Center, (CancerThera) (CEPID FAPESP grant number 2021/10265-8).

Keywords: ERP29, MAPK/Akt pathway, miR-4421, Pharyngeal cancer.

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PAPEL DO PET/CT COM 18F- FDG NA AVALIAÇÃO DO COLANGIOCARCINOMA: UM ESTUDO RETROSPECTIVO

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R E S U M O

Introdução/Justificativa: O colangiocarcinoma é uma neoplasia maligna do trato biliar com prognóstico geralmente desfavorável. O diagnóstico precoce e o estadiamento preciso são cruciais para o manejo adequado desses pacientes. A tomografia por emissão de pósitrons/tomografia computadorizada (PET/CT) com 18F-fluordesoxiglicose (FDG) tem se mostrado uma ferramenta promissora na avaliação dessa doença, porém seu papel ainda não está completamente estabelecido. **Objetivos:** Este estudo visa avaliar o impacto do PET/CT com 18F- FDG no estadiamento do colangiocarcinoma, com foco na detecção de envolvimento linfonodal regional e doença metastática à distância. **Materiais e Métodos:** Realizamos um estudo retrospectivo utilizando um programa de busca de expressões no laudo RIS, com as palavras-chave "CID 10 C22" e "colangiocarcinoma", no período de 01/01/2019 a 01/01/2023. Inicialmente, 176 exames foram identificados, resultando em 71 exames após remoção de duplicidades. Excluímos ainda 5 exames que utilizaram outros traçadores, além de 2 pacientes por apresentarem colangiocarcinoma como tumor sincrônico durante avaliação de outro câncer primário, totalizando 64 exames elegíveis. Os exames foram classificados de acordo com suas indicações: • Estadiamento: 27 exames • Reavaliação: 31 exames • Diagnóstico diferencial de lesão hepática: 4 exames • Outros tumores hepáticos: 2 exames Focamos nossa análise nos 27 exames realizados para estadiamento, avaliando o impacto do PET/CT na detecção de envolvimento linfonodal e metastático. **Resultados:** Avaliação Linfonodal Regional: • Exames positivos: 11 pacientes (40,7%) • Exames negativos: 16 pacientes (59,3%) Os sítios de linfonodos regionais que apareceram nos estudos foram: ducto hilar, cístico, ducto biliar comum, artéria hepática, pancreaticoduodenal posterior e linfonodos da veia porta. Avaliação Metastática: • Exames positivos: 14 pacientes (51,9%) • Exames negativos: 13 pacientes (48,1%) Distribuição dos Sítios Metastáticos: 1. Pulmão: 5 pacientes (35,7%) 2. Osso: 5 pacientes (35,7%) 3. Linfonodos abdominais: 8 pacientes (57,1%) 4. Carcinomatose peritoneal: 2 pacientes (14,3%) 5. Linfonodos torácicos: 1 paciente (7,1%) 6. Adrenal: 1 paciente (7,1%). **Conclusão:** O PET/CT com 18F-FDG demonstrou ser uma ferramenta valiosa no estadiamento do colangiocarcinoma, detectando envolvimento linfonodal regional em 40,7% dos casos e doença metastática em 51,9% dos pacientes. A técnica foi particularmente útil na identificação de metástases em diversos sítios, com destaque para linfonodos abdominais, pulmão e ossos. Esses achados sugerem que o PET/CT com 18F-FDG pode ter um impacto significativo no manejo clínico desses pacientes, potencialmente alterando a estratégia terapêutica em casos onde a doença metastática não era previamente suspeitada.

Palavras-chave: 18F-FDG PET/CT, Colangiocarcinoma, MEDICINA NUCLEAR, Oncologia, PET/CT.

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COMPARATIVE RADIOLABELING OF THE CYCLIC PEPTIDE CTHRSSVVC WITH [68GA] GALLIUM AND [18F]FLUORINE. A POTENTIAL PROBE FOR MOLECULAR IMAGING OF CD163^{+} MACROPHAGES

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A B S T R A C T

Introduction/Justification: CD163⁺ macrophages play a critical role in chronic inflammation, cancer, and hematologic disorders, making them a promising target for molecular imaging. These cells contribute to tumor immunosuppression, disease progression, and poor prognosis in solid and hematologic tumors. Recent studies indicate that CD163 is a relevant biomarker in Hodgkin's lymphoma, multiple myeloma, and leukemias, which are directly associated with tumor resistance and immune evasion. The cyclic peptide CTHRSSVVC has been identified as a CD163 ligand, showing high reactivity with inflammatory and atherosclerotic lesions, suggesting its potential for targeting CD163⁺ macrophages. In vitro assays demonstrated that [111In]In-DOTA-CTHRSSVVC binds to atherosclerotic plaques, further supporting its applicability in molecular imaging of inflammation and cancer. Cyclic peptides are widely used in radiotracer development due to their high specificity, enzymatic stability, and resistance to degradation. Radiolabeling of these peptides with PET radioisotopes such as 68Ga3+ and [^{18}F]AlF2+ expands their potential applications in tracking inflammatory processes and hematologic malignancies. **Objectives:** To evaluate the radiolabeling efficiency and chemical stability of the NOTA-CTHRSSVVC cyclic peptide with 68Ga3+ and [18F]AlF2+, aiming to develop a novel radiopharmaceutical for molecular imaging of CD163⁺ macrophages. **Materials and Methods:** The NOTA-CTHRSSVVC conjugate was radiolabeled [68Ga]Ga(AcO)3 or [18F]AlF2+, which were prepared in 0.2 M sodium acetate buffer (pH 4.1); reactions carried out under different peptide amounts. When necessary, the final products were purified using solid phase columns. The radiochemical efficiency was assessed by HPLC coupled with a gamma radiation detector, while chemical stability was evaluated in the labeling solution for up to 4 hours. The partition coefficient (logP) was determined in n-octanol/water system, in triplicate. **Results:** The NOTA-CTHRSSVVC peptide was successfully radiolabeled and purified with the [68Ga]Ga-NOTA-CTHRSSVVC exhibited a radiochemical purity of 97.8% (n = 3), while [18F]AlF-NOTA-CTHRSSVVC reached 95.5% (n = 3). Both radiolabeled peptides demonstrated high chemical stability, maintaining their integrity for up to 4 hours in physiological solution. The logP analysis indicated a hydrophilic profile with the value of -3.08 ± 0.16. **Conclusion:** The radiolabeling of the NOTA-CTHRSSVVC peptide with 68Ga3+ and [18F]AlF2+ was efficient and stable, demonstrating chemical feasibility for the development of a novel radiopharmaceutical. Given the potential interaction of the peptide with CD163, future investigations may focus on assessing its biological affinity and molecular imaging applications for CD163⁺ macrophages in hematologic and inflammatory diseases.

Keywords: Macrophage, Peptide, Radiolabeling, [18F]fluorine, [68Ga]gallium.

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IN VITRO POPULATION GROWTH OF HUMAN GLIOBLASTOMAS: REAL PATIENTS AND CURVE FITTING

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A B S T R A C T

Introduction/Justification: For more than a century, a variety of ordinary differential equation growth models have been used to describe and predict the proliferation of human malignancies. Indeed, in the field of mathematical oncology, the growth of cell populations over time is typically represented by sigmoidal functions, such as logistic or Gompertz curves and their generalizations. These models are particularly focused on understanding and predicting the proliferation of cancer cells, including those from human glioblastomas, which can be very aggressive brain tumors with a survival rate of less than two years. **Objectives:** This research examines in vitro cell cultures of five lines of human glioblastoma using curve fitting and numerical parameter estimation of real datasets to separately describe the growth profile of all these cell populations lineages over time. **Materials and Methods:** Cell culture experiments were performed in the Advanced Therapeutics Laboratory at FCF-UNICAMP. These included a well-established human glioblastoma cell line (NG97) and four other glioblastoma cell lines derived from clinical patients designated N07, C03, L09 and J01. Twelve repeated time series of experiments were collected for each cell line. Cell counting was performed daily on days 1 to 6. The drda R package was used for curve fitting of the measured data aiming to determine the intrinsic growth rate and other parameters for each of the five cell lines. The 5-parameter generalized logistic curve was used, and all the resulting models were analyzed under statistical criteria such as the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC). **Results:** Curve fitting analysis revealed significant diversity in the population growth of different cell lines. The drda R package proved to be highly effective in capturing these different behaviors and the unique sigmoidal shapes associated with them. Notably, the population growth of NG97 cells showed the least variability over time, with the

narrowest confidence intervals for the fitted curves and their associated parameters. This consistency can be attributed to the fact that NG97 is a well-established cell lineage. In contrast, the new patient-derived cell lines showed a greater degree of uncertainty, particularly when their confidence intervals were extrapolated beyond the last day of measurement. This observation highlights the need for additional time points in in vitro experiments with newly derived human patient cells. **Conclusion:** According to the numerical and graphical results, to AIC and BIC metrics, and also to the respective levels of provided uncertainty, the fitted models present a reasonable growth description of all the studied lineages of glioblastoma, regardless of cell line being well-established (NG97) or newly originated from human patients (N07, C03, L09, and J01). Further correlations between those results and prognostics and clinics may be of value for translational oncology.

Keywords: Generalized Logistic Function, Glioblastomas, Mathematical Oncology.

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NANOPARTÍCULAS SUPERPARAMAGNÉTICAS DE ÓXIDO DE FERRO RECOBERTAS POR COPOLIÉSTER FUNCIONALIZADAS PARA APLICAÇÕES BIOMÉDICAS

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RESUMO

Introdução/Justificativa: O câncer engloba mais de 100 tipos de doenças malignas caracterizadas pelo crescimento descontrolado de células, que podem invadir tecidos adjacentes ou se espalhar para outras partes do corpo. Há décadas, as nanopartículas magnéticas (NPMs) de óxido de ferro vêm sendo estudadas por apresentarem grande potencial para aplicações biomédicas, especialmente na oncologia, no uso de agentes de contraste para imagem por ressonância magnética no realçamento de contraste negativo nos tecidos com a presença de tumores e não tumorais, em magneto hipertermia para destruição seletiva de células cancerosas e atuando no transporte vetorizado de fármacos quimioterápicos. Independente de suas aplicações biomédicas, para evitar a aglomeração das NPMs em células, tecidos e órgãos, que pode levar a embolismos, é essencial recobri-las com materiais biocompatíveis e não citotóxicos. Poliésteres derivados de lactonas e macrolactonas, como o copoliéster poli (globalide-co-ε-caprolactona) (PGlCL), têm sido explorados devido à sua biocompatibilidade, hidrofilicidade e biodegradabilidade. **Objetivos:** Este trabalho teve como objetivo a modificação e a funcionalização do copoliéster PGICL com cisteína, a fim de atingir três objetivos associados a funcionalização das NPMs, que garantirão sua aplicação em nanomedicina, tais como: a) melhorar sua hidrofilicidade (diminuindo sua cristalinidade) para que seja carreado com mais facilidade no meio intracelular; b) permitir que grupos amina e tiol sejam pontos de ancoragem para constituírem partes de ligantes com receptores de superfície celular, tais como o ácido fólico (AF) que só são expressos em células tumorais e c) possibilitar a ligação desses grupos químicos em sistemas de "drug-delivery" com o análogo do AF, o quimioterápico metotrexato (MTX) para o tratamento de câncer de mama. Neste estudo, o PGlCL foi modificado com cisteína (PGlCL-Cys) e utilizado para recobrir NPMs de óxido de ferro (Fe3O4 - magnetita), visando futuramente em um segundo passo, a funcionalização com AF e MTX em aplicações como vetorização ativas em sistemas como "drug-delivery" e a posteriori, em ensaios in vitro de radiosensibilização em células de câncer de mama. **Materiais e Métodos:** Soluções de Fe^{3+} e Fe^{2+} em HCl. Sob refluxo, adicionaram-se H_2O aquecida, NH_4OH (30mL, pH10, 90°C), PGICL em etanol. Agitou-se 45min, purificou-se com imã, lavou-se e armazenou as NPMs. **Resultados:** A caracterização físico-química das NPMs recobertas com PGlCL-Cys foi realizada por espectroscopia no infravermelho, confirmando a presença de bandas características da cisteína (ligações C-S-C em 715,21 cm^{-1} e C-N em 1573,1 cm^{-1}) e do recobrimento das NPMs (bandas de deformação angular da ligação Fe- O em 635,63 cm^{-1} e ~590 cm^{-1}, correspondentes aos sítios octaédricos e tetraédricos da magnetita, respectivamente). A Microscopia Eletrônica de Transmissão (MET) revelou que as NPMs de Fe3O4@PGlCL-Cys possuem um diâmetro médio de 11,44 nm e exibem comportamento superparamagnético. **Conclusão:** Conclui-se que o método de coprecipitação e a síntese do copoliéster modificado com cisteína (PGlCL-Cys) foi eficaz, produzindo NPMs estáveis e monodispersas de modo que serão realizados futuramente outras caracterizações físico-químcias para avançar os estudos em ensaios biológicos in vitro para citotoxicidade e biocompatibilidade a fim de serem aplicadas no diagnóstico e tratamento de câncer de mama.

Palavras-chave: Câncer de mama, Copoliéster, Nanopartículas magnéticas, Óxido de ferro.

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APPLICABILITY OF PSMA PET/CT IN THE EVALUATION OF ADENOID CYSTIC CARCINOMA

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A B S T R A C T

Introduction/Justification: Introduction: Adenoid Cystic Carcinoma (ACC) is a rare and aggressive tumor characterized by slow and indolent growth, high recurrence, high metastasis rates, and challenging early detection, and 18F-FDG PET/CT imaging has become essential for diagnosis, staging, and monitoring of it. In the last decade, the promising theranostic approach of 18F-PSMA PET/CT for prostate carcinoma has led to the evaluation of PSMA target with 18-Fluor (diagnostic) and 177-Lutetium (therapeutic) in ACC, whose cells overexpress this surface antigen. **Justification:** As it is a recent discovery, further studies are needed to evaluate the use of 18F-PSMA PET/CT to predict the prognosis and assess therapy response in ACC cases. **Research Question:** Could 18F-PSMA PET/CT, compared to 18F-FDG PET/CT, be used as a diagnostic technique for ACC and, as a consequence, labeled PSMA be potentially a therapeutic resource for this cancer? **Objective:** Evaluate the applicability of 18F-PSMA PET/CT compared to 18F-FDG PET/CT in the management of ACC. **Materials and Methods:** Five patients (A, B, C, D, and E) diagnosed with ACC underwent 18F-FDG PET/CT and 18F-PSMA PET/CT (24-hour intervals, except by two cases), and the lesions uptakes were evaluated with both radiotracers. **Preliminary Results:** Patient A showed hypermetabolism only for 18F-FDG PET/CT at cervical lymph nodes; B exhibited an uptake substantially higher on 18F-FDG PET/CT at the primary lesion site, cervical lymph nodes, and lung (46 days between the exams and after treatment with doxorubicin); C and D showed similar uptake on both tracers: C at L5 vertebra and lung, and D at lung; E exhibited uptake of both tracers, in cervical lymph nodes with 18F-FDG, suggesting inflammation, and in the lung with 18F-PSMA. **Discussion:** Preliminary data suggest similar uptake patterns for both tracers in ACC, with variations warranting further investigation. **Conclusion:** The study highlights the potential use of 18F-PSMA PET/CT in the diagnostic management of ACC, expanding its possible therapeutic application.

Keywords: 18F-FDG PET/CT, 18F-PSMA PET/CT, Adenoid Cystic Carcinoma, Theranostic.

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