HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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Pesquisas clínicas

PESQUISAS CLÍNICAS - 17° SIMPÓSIO EDWALDO CAMARGO E 1° CONGRESSO CANCERTHERA

USO DE UM MODELO PREDITIVO NA IDENTIFICAÇÃO DE DOENÇA METASTÁTICA EM PACIENTES COM CARCINOMA DIFERENCIADO DE TIREOIDE SOB ESTÍMULO DE TSH RECOMBINANTE

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Introdução/Justificativa: O câncer de tireoide é a neoplasia endócrina mais comum, sendo o câncer diferenciado de tireoide (CDT) o subtipo mais prevalente. O tratamento padrão envolve tireoidectomia total (TT) seguida de terapia com Iodo-131 (I131). Marcadores bioquímicos como a tireoglobulina sérica (Tg) e o TSH são frequentemente utilizados para prognóstico e detecção de doença metastática. Variáveis demográficas, como idade e sexo, também afetam o prognóstico, assim como o estadiamento patológico inicial. O sistema de estratificação de risco proposto pelas diretrizes da Associação Americana de Tireoide (ATA) de 2015 auxilia na prescrição de I131 pós-TT e basea-se principalmente em relatórios patológicos. Entretanto, pode apresentar falhas, como a deficiência em detectar doença persistente que requer uma intervenção terapêutica mais agressiva com I131. Em vista disso, a elaboração de um modelo preditivo pode prover uma estratificação de risco mais acurada e personalizada para pacientes com CDT submetidos a TT e terapia ablativa com I131. Em 2023, Giovanella e colaboradores elaboraram um modelo preditivo baseado em árvore de decisão para este cenário. Entretanto, todos os pacientes foram submetidos a suspensão de levotiroxina. **Objetivos:** Testar o modelo preditivo baseado em árvore de decisão descrito por Giovanella e colaboradores em pacientes submetidos a TT e terapia com I131 estimulados com TSH recombinante (rhTSH). **Materiais e Métodos:** Análise retrospectiva de 451 pacientes submetidos a tratamento com radioiodo entre 2016 e 2020. Foram incluídos pacientes adultos e com CDT comprovado histologicamente após TT, com níveis de anticorpo anti-tireoglobulina normais, uso de rhTSH pré-radioiodoterapia, além do resultado da PCI pós-tratamento. Foi aplicado o modelo de árvore de decisão descrito por Giovanella e colaboradores em pacientes com CDT estimulados por rhTSH. De forma simplicicada, o modelo proposto por Giovanella e colaboradores dividiu os pacientes em com e sem acometimento linfonodal. Aqueles com acometimento linfonodal e Tg estimulada acima de 35,0 ng/ml tinham alta probabilidade de doença metastática/persistente. O mesmo ocorrendo em pacientes sem acometimento linfonodal e com Tg estimulada acima de 23,3 ng/ml. Resultados: Dos 451 pacientes incluidos, 362 (80,3%) foram do sexo feminino, com uma mediana de idade de 41,41 anos (IQR 33,76 a 53,00) e de Tg estimulada sérica de 2,9 ng/mL (IQR 0,68 a 7,9). Aplicando o modelo de árvore de decisão descrito por Giovanella e colaboradores, foi obtido um valor preditivo positivo de 25,0% (IC 10,01 – 49,9%), um valor preditivo negativo de 87,3% (IC 86,6 – 88,1%) e uma acurácia de 85,1% (IC 81,4 – 88,3%). Gênero masculino e valor de Tg foram associados com PCI positiva ($p < 0,05$). Os resultados encontrados foram inferiores aos descritos por Giovanella e colaboradores (porém, semelhantes a um dos centros participantes). Isto pode ser explicado pela menor prevalência de PCI positiva e pela diferença dos valores de Tg com suspensão da levotiroxina e com TSH recombinante. **Conclusão:** Evidenciamos que o modelo de árvore de decisão descrito pode ser aplicado a pacientes com CDT estimulados por rhTSH com bons resultados, embora um modelo especificamente adaptado para essa população seja preferível. A Tg estimulada e o gênero apresentaram o melhor desempenho na previsão de doença persistente ou metastática na PCI após a cirurgia.

Palavras-chave: Carcinoma diferenciado de tireoide, Cintilografia, I-131, Modelo de decisão. rhTSH.

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COST SIMULATION OF GSTP1 C.313 A>G GENOTYPING FOR OTOTOXICITY RISK ASSESSMENT IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS UNDERGOING CISPLATIN-BASED CHEMORADIOTHERAPY

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Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is a prevalent malignancy worldwide, with substantial morbidity and mortality. Cisplatin-based chemoradiotherapy is a standard treatment modality for most HNSCC patients, but it is associated with significant adverse effects, including ototoxicity. Glutathione S-transferase pi 1 (GSTP1) is a gene involved in the detoxification of cisplatin, and single nucleotide variants as GSTP1 c.313 A>G have been linked to differential susceptibility to ototoxicity in HNSCC patients under therapy. It is unknown, however, if genotyping selection could improve patient outcomes and reduce treatment costs. **Objectives:** This study aims to investigate the potential cost reduction of GSTP1 c.313 A>G genotyping in identifying HNSCC patients at risk of cisplatin-induced ototoxicity, with the goal of optimizing therapeutic decision-making and reducing the economic burden associated with audiological support interventions (ASIs). **Materials and Methods:** A decision analytic model was designed, where patients with low-risk genotypes (GSTP1 c.313 AA) would receive cisplatin, while those with high-risk (GSTP1 c.313 AG/GG) would hypothetically receive docetaxel. Transitional probabilities were then calculated using Metropolis-Hastings algorithm. Costs included genotyping, therapy, and ASIs provision. A probabilistic Markov model was developed to simulate the clinical and economic outcomes associated with GSTP1 genotyping in HNSCC patients receiving cisplatin-based chemoradiotherapy. Transition probabilities, treatment costs, and the probabilities of adverse events were incorporated into the model over a ten-year time horizon. Sensitivity analyses were conducted to assess the robustness of the results. **Results:** The median total cost per patient in the conventional arm was R$ 2,025.05 (credibility interval R$ 1,975.58 to R$ 2,047.75). Simulation results indicated that implementing genotyping could result in significant cost reductions in the first year, with savings ranging from R$ 92.53 to R$140.06 per patient, depending on the number of simultaneous genotyping tests performed (in this case, 3 and 5 samples, respectively). Over a ten-year period, cumulative cost savings of R$75,689.10 were projected for 250 patients, primarily attributed to decreased expenditures on ASIs and audiological support services. **Conclusion:** The analysis demonstrated that GSTP1 c.313 A>G genotyping has the potential to yield cost savings in the management of cisplatin-induced ototoxicity in HNSCC patients. Genotyping for GSTP1 polymorphisms represents a promising approach to identify HNSCC patients at increased risk of cisplatin-induced ototoxicity, allowing for personalized treatment strategies. These findings highlight the importance of integrating pharmacogenetic testing into clinical practice to enhance patient outcomes and healthcare resource utilization. Further research and implementation efforts are warranted to validate this strategy in routine HNSCC management.

Keywords: Cisplatin, Cost simulation, GTSP1, Head and neck squamous cell carcinoma, Ototoxicity.

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68GA-NOTA-UBI AND 68GA-DOTA-UBI AS RADIOPHARMACEUTICALS FOR THE DIAGNOSIS OF INFECTIOUS PROCESSES: PRECLINICAL STUDIES AND TRANSLATION TO CLINICAL APPLICATION

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Introduction/Justification: Infectious diseases are the second leading cause of mortality worldwide. In this context, considerable efforts are being made to develop radiopharmaceuticals that enable the accurate diagnosis of bacterial infections. A new field of research is focusing on antimicrobial peptides, such as Ubiquicidin. The 29-41 fragment (Thr-Gly-Arg-Ala-Lys-Arg-Arg-Met-Gln-Tyr-Asn-Arg-Arg) UBI(29-41) labeled with radionuclides has proved to be an important tool for the specific diagnosis of infectious processes. **Objectives:** To present the radiochemical and "in vitro" studies of UBI(29-41) with the chelating agents 1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA) and 1,4,7,10- tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) for labeling with gallium-68 (68Ga) and to validate with a clinical application. **Materials and Methods:** After 68GaCl3 elution, the NOTA-UBI and DOTA-UBI reactions were performed at 85oC for 5 min and 95oC for 15 min, respectively. In both cases, the purification was carried out using a Sep-Pak C18 filter and radiochemical control by Thin-Layer Chromatography (TLC) and High-Performance Liquid

Chromatography (HPLC). The partition coefficient (Log P) and serum protein binding were determined, as well as the stability in saline and serum up to 90 min. After these studies, assays were carried out to determine the binding of the radiopharmaceuticals to "Staphylococcus aureus" bacteria. For the clinical study, the patient selected had a diagnosis of chronic osteomyelitis in the distal tibia, a positive blood culture for "Staphylococcus aureus" and a possible infectious/inflammatory process at the site identified by magnetic resonance imaging. The patient was injected intravenously with 281 MBq of 68Ga-DOTA-UBI to confirm the presence of an infectious process by PET-CT and the images were obtained 1 h post-administration. Resultados: The radiochemical purity (RP) of the radiopharmaceuticals after purification was 99.28±0.28% and 99.78±0.06% for 68Ga-NOTA-UBI and 68Ga-DOTA-UBI, respectively. Log P was -3.57±0.20 for 68Ga-NOTA-UBI and -3.63±0.17 for 68Ga-DOTA-UBI. Stability studies up to 90 min showed RP of 98.13±0.78% and 99.75±0.08% in saline; and 79.94±5.10% and 94.69±1.14% in serum, for 68Ga-NOTA-UBI and 68Ga-DOTA-UBI, respectively. The percentage of serum protein binding, evaluated at 30 and 60 min, was 59.90±1.21% and 53.45±2.16% for 68Ga-NOTA-UBI and 60.22±2.96% and 44.06±1.88% for 68Ga-DOTA-UBI, respectively. The binding of radiopharmaceuticals to "Staphylococcus aureus" revealed a direct relation to the amount of bacteria in the culture. Clinical images showed intense uptake of the radiopharmaceutical in the entire remnant of the talus and in the adjacent soft tissues of the left ankle. After scan, the secretion collected from the surgical site was cultured and the presence of "Staphylococcus aureus" was confirmed. **Conclusion:** The radiochemical and "in vitro" assays showed that the radiopharmaceuticals studied presented similar characteristics with the potential to be implemented in clinical practice. The clinical study showed that the UBI(29-41) fragment radiolabeled with 68Ga can be used as a potential biomarker for infectious processes, according to the availability of the chelating agent.

Keywords: 68Ga-DOTA-UBI, 68Ga-NOTA-UBI, Infectious processes imaging, PET-CT imaging, Ubiquicidin.

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DUAL TIME PSMA PET/CT WITH DIURETICS AND CONTRAST TO DETECT PROSTATE CANCER PELVIC METASTASES: IS THERE A BENEFIT?

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Introduction/Justification: The renal excretion of PSMA radiotracer may render PSMA PET/CT imaging interpretation difficult to identify local recurrence and lymph node metastases in prostate cancer patients. **Objectives:** To evaluate the best acquisition method to increase the detection rate of local recurrence and pelvic metastases on PSMA PET/CT by performing dual time-point imaging (delayed imaging) after hyperhydration, diuretics, and contrast enhancement. **Materials and Methods:** Patients with prior history of prostate adenocarcinoma underwent PSMA PET/CT for primary staging or due to biochemical recurrence. PSMA PET/CT acquisition consisted of delayed pelvic imaging after hyperhydration, diuretics, and excretory-phase contrast. SUV values obtained in local recurrence lesions, locoregional lymph node metastases, and bone metastases in the early and delayed PSMA PET/CT images were compared. **Results:** A total of 182 patients (medians: age = 66.5; Gleason score = 7.0; total PSA = 1.5) underwent PSMA PET/CT. Twenty-one patients (12%) were scanned due to primary staging, and 161 patients due to biochemical recurrence (88%). Delayed images (with only hyperhydration, without contrast or diuretics) increased diagnostic certainty in identifying local recurrence in 26.6% of patients and locoregional lymph nodes in 25%. There was a significant increase in SUV values in the delayed images compared to early images in the local recurrence ($p < 0.0001$), locoregional lymph node metastases ($p < 0.0001$), and bone metastases ($p < 0.0199$). Adding excretory-phase contrast to the delayed images increased diagnostic certainty in identifying local recurrence in 9.4% of patients and locoregional lymph nodes in 8.3%. The use of diuretics only in delayed images (without excretory-phase contrast) increased diagnostic certainty in identifying local recurrence in 14% of patients; while for identifying pelvic lymph nodes increase was only mild (2.8%). The association of diuretics with excretory-phase contrast increased the diagnostic certainty in identifying local recurrence in 15.6% of patients and locoregional lymph nodes in 5.6%. **Conclusion:** Delayed PSMA PET/CT images increase the diagnostic certainty of identifying local recurrence and locoregional metastases in prostate cancer patients. The addition of diuretics increases diagnostic certainty and may be useful in selected cases. However, the addition of excretory-phase contrast (regardless of the use of diuretics) only mildly impacted diagnostic certainty and may be omitted.

Keywords: Câncer de prostata, PET-CT imaging, PSMA.

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ARTIFICIAL INTELLIGENCE TO EVALUATE METABOLIC TUMOR BURDEN IN PRIMARY STAGING OF RECTAL CANCER WITH 18F-FDG PET/CT

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Introduction/Justification: The use of artificial intelligence using convolutional neural networks in clinical practice is

recent. Thus, a growing need exists to validate software performance in different tasks in different diseases. **Objectives:** To evaluate the performance of artificial intelligence software to determine metabolic tumor burden in the primary staging of rectal cancer. **Materials and Methods:** A cross-sectional retrospective analysis was conducted on 51 histology-proven rectal cancer patients (35% females; mean age = 61 years) who underwent a staging 18F-FDG PET/CT. Whole-body metabolic tumor burden parameters (wbMTV and wbTLG) were quantified semi-automatically and through AI algorithm (Syngovia VB60; Siemens Healthineers Medical Solutions). The AI software's ability to correctly identify and classify the primary lesion, regional lymph nodes, and distant metastases was evaluated. In addition, the intraclass correlation coefficient (ICC) was applied to evaluate concordance between the AI-based software and the semiautomatic software in determining wbMTV and wbTLG. Values above 0.7 were considered to indicate substantial agreement. Resultados: The AI and semiautomatic tumor burden metrics correlated strongly for both wbMTV (ICC = 1.00; 95% CI = 0.94 - 0.99; P < 0.0000) and wbTLG (ICC = 1.00; 95% CI = 0.80 – 0.90; P < 0.0000). Additionally, the AI software's ability to correctly identify lesions compared to the documented staging was better for the identification of distant metastasis (78,57% of patients), mildly adequate to identify regional lymph nodes (50,00%) and had poor performance for identification of the primary lesion (5,76%). On the other hand, the time spent calculating these metrics was less by AI than by the semiautomatic method, especially in patients with advanced disease. **Conclusion:** The determination of whole-body metabolic tumor burden on 18F-FDG PET/CT with artificial intelligence software is challenging because of the physiologic bowel activity. However, deep learning may have the ability to overcome these challenges and may therefore improve the primary staging of rectal cancer.

Keywords: 18F-FDG PET/CT, Artificial intelligence., Rectal cancer.

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SYNTHESIS, CHARACTERIZATION, AND RADIOLABELING OF MODIFIED PEPTIDE FRAGMENTS TARGETING AVB3 INTEGRIN ADHESION MOLECULE OVEREXPRESSED IN TUMORS

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Introduction/Justification: Peptides are biomolecules that have been associated with various physiological responses and have great potential for the diagnosis or treatment of diseases, including various types of tumors. Several studies have shown that biologically active peptides containing the RGD domain have a high affinity with the $\alpha v\beta 3$ integrin adhesion molecule overexpressed in tumor cells, assisting in molecular imaging or targeted radionuclide therapy (TRT) as an anti-tumor agent. **Objectives:** To obtain an anti-integrin peptide fragment modified by incorporating two spacers — hexa-aminocaproic acid (C6) or dodeca-aminocaproic acid (C12) — and by adding the chelating agent DOTA for subsequent radiolabeling with yttrium-86 (86Y). **Materials and Methods:** The modified peptides were synthesized by the solid-phase peptide synthesis method using the Fmoc/tBut strategy. In this strategy, the Fmoc group removal step was carried out with 20% 4-methylpiperidine / 80% DMF, and the amino acid coupling step is usually performed with the diisopropylcarbodiimide/1-hydroxybenzotriazole (DIC/HOBt) acylation mixture. In this step, an excess of Fmoc-amino acids and acylating agents of 2.5 times were used relative to the synthesis scale utilized in mmol/g. Peptide cleavage from the resin and removal of side chain protecting groups were carried out using a mixture containing a high concentration of TFA (reagent K). After synthesis and cleavage, the peptides underwent characterization and purification process through high-performance liquid chromatography (HPLC) and mass spectrometry. The radiolabeling process was conducted utilizing cyclotron-produced 86Y, employing a NaOAc buffer (pH = 5.5). The radiochemical reaction was performed at 95°C for 30 min, followed by filtration through a Sep-Pak C18 cartridge for purification and determination of the radiolabeling yield. **Results:** The DOTA-C6-anti-integrin and DOTA-C12-anti-integrin peptides were efficiently synthesized, and the yields obtained were approximately 12.7% and 26.4%, respectively. Chromatographic analyses obtained by HPLC, as well as mass spectrometry, showed that the entire synthesis, cleavage, and characterization process were carried out properly with visualization of profiles and molecular masses of 1165.3 g/mol and 1249.1 g/mol for the DOTA-C6-anti-integrin and DOTA-C12-anti-integrin peptides, respectively. After the purification process, 14.6 mg and 66.2 mg of pure peptides were obtained. The preliminary 86Y-labeling data indicated a radiochemical yield of approximately 97% for both peptides. **Conclusion:** The proposed modified anti-integrin peptides were efficiently synthesized, characterized, and purified. Preliminary radiolabeling studies with 86Y demonstrated a high radiochemical yield, paving the way for further exploration in radiochemical studies and assays of affinity to tumor cells.

Keywords: Anti-integrin peptides, Tumor cells, Yttrium-86, $\alpha v\beta 3$ integrin.

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AVALIAÇÃO DA BIODISTRIBUIÇÃO DO RADIOFÁRMACO 177LU-PSMA I&T EM ANIMAIS COM MODELO TUMORAL.

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Introdução/Justificativa: O antígeno de membrana específico da próstata (PSMA) é uma glicoproteína de transmembrana do tipo II que se mostra baixa ou não é expressa na próstata normal, mas é altamente expressa no câncer e apresenta-se ainda mais aumentada em pacientes metastáticos resistentes à castração, existindo um consenso no qual seu nível de expressão está ligado à malignidade da doença (MALIK, N. et al., 2015.; RUANGMA et al., 2019). Com isso, novos radiofármacos para o diagnóstico e terapia do câncer de próstata estão sendo descritos com base na descoberta de inibidores de PSMA, que se ligam especificamente ao grupo farmacofórico Glutamato-Ureia-Lisina (Di lorio, 2022). O radiofármaco baseado em PSMA-I&T, radiomarcado com lutécio-177 tem sido bastante estudado no mundo para essa terapia. **Objetivos:** O objetivo foi avaliar a captação do 177Lu-PSMA-I&T em camundongos com modelo tumoral por meio de estudos de biodistribuição invasiva (aprovado pelo CEUA-IPEN). Os estudos pré-clínicos representam importante passo para desenvolvimento e registro do produto, contribuindo para avaliação de segurança e eficácia. **Materiais e Métodos:** O radiomarcado 177Lu-PSMA-I&T (7,4 MBq/0,1 mL) foi inoculado em 20 camundongos com desenvolvimento de modelo pré-clínico de câncer de próstata utilizando células LNCaP, inoculadas no flanco superior esquerdo dos camundongos SCID. O estudo contemplou os tempos de 30, 60 min com e sem bloqueio e 2h após a administração do 177Lu-PSMA-I&T. Os animais foram eutanasiados para retirada do coração, pulmão, pâncreas, baço, estômago, fígado, rins, intestinos, cérebro, músculo, osso (fêmur) e cauda. Os órgãos foram pesados e contados em contador gama tipo poço (Cobra, Packard) para determinar a porcentagem da atividade administrada por grama (%AI/g). Os resultados foram analisados estatisticamente utilizando o programa GraphPad Prism. **Resultados:** O estudo de biodistribuição em camundongos SCID com tumor mostrou um rápido clareamento sanguíneo e excreção renal do 177Lu-PSMA-I&T. A maior captação do 177Lu-PSMA-I&T no tumor foi em 30 minutos, assim como na maioria dos órgãos que expressam PSMA, como os pulmões. Verificou-se uma correlação crescente na razão tumor:sangue em função do tempo, demonstrando a afinidade de ligação do radiofármaco. Analisando-se os grupos de 60 min, o bloqueio apresentou uma boa resposta, com diminuição da captação do 177Lu-PSMA-I&T nos órgãos que expressam PSMA e no tumor, sendo de 2,18 ± 0,27 %AI/g após 60 min sem bloqueio e 0,62 ± 0,17 %AI/g após 60 min com bloqueio. A captação nos rins também diminuiu drasticamente nos animais com bloqueio. **Conclusão:** Este estudo preliminar demonstra a especificidade do radiofármaco 177Lu-PSMA-I&T em modelo animal e representa importante pré-requisito para avaliação clínica, produção e o registro do produto no Brasil para uso disseminado na terapia de pacientes com câncer de próstata resistentes à castração. 1 - Malik, N. et al., Radiofluorination of PSMA-HBED via AI(18)F(2+) Chelation and Biological Evaluations In Vitro. Molecular Imaging and Biology, (2015). 2 - Ruangma A., et al., PSMA for Pet imaging of prostate cancer. The Bangkok medical Journal, (2019) 3 - Di lorio et al., Production and Quality Control of [177Lu]Lu-PSMA-I&T: Development of an Investigational Medicinal Product Dossier for Clinical Trials. (2022)

Palavras-chave: Biodistribuição, LNCaP, Pré-clínico, PSMA I&T.

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BODY COMPOSITION AND INSULIN SENSITIVITY IN PATIENTS WITH RECTAL CANCER

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Introduction/Justification: Glucose intolerance is a metabolic abnormality recognized in patients with cancer cachexia and has been implicated in the development of low muscularity (LM). LM is an important feature associated with the poor prognosis of cancer patients, leading to a reduction in functional capacity, poor quality of life, increased treatment intolerance, and reduced overall survival. LM have been shown to correlate with insulin sensitivity. However, clinical studies evaluating the association between body composition features and insulin resistance are scarce, and the results are contradictory. **Objectives:** The purpose of this study was to evaluate the association between insulin sensitivity and the body composition features of patients recently diagnosed with rectal cancer. **Materials and Methods:** This is a cross-sectional study involving patients diagnosed with rectal cancer. Body composition was analyzed using computed tomography (CT) images processed with the SliceOmatic software based on the difference in tissue measurements by Hounsfield Units (HU). Muscularity was categorized according to Martin's criteria. Cachexia was categorized according to Fearon's criteria. Insulin sensitivity was evaluated using euglycemic hyperinsulinemic clamp. Personal information, tumor characteristics, and biochemical exams were collected from medical records. Statistical analyses were conducted using Stata Corp LP® version 17.0 software. This study was approved by the Institutional Review Board (CAAE: 91217418.2.0000.5404). **Results:** A total of 33 patients were included in the analysis. Low muscularity and cachexia diagnosis were identified in 27% of the sample (n = 9). The low muscularity (LM) group consisted mostly of females aged 55–70 years. There was no

difference in BMI, weight loss, tumor stage, or ECOG score between muscularity groups. The LM group had a lower skeletal muscle area ($p < 0.001$), lower visceral adipose tissue area ($p = 0.01$), and there is no difference in skeletal muscle radiodensity ($p = 0.85$), subcutaneous adipose tissue area ($p = 0.76$), and intramuscular adipose tissue area ($p = 0.46$) when compared to normal muscularity group. A lower handgrip strength was also observed in the LM group ($p < 0.01$). Regarding insulin sensitivity, the LM group had a higher M-value adjusted for Free Fat Mass (FFM) ($p = 0.01$) and M-value adjusted for Total Body Weight (TBW) ($p = 0.0347$). Additionally, a significant negative correlation was found between muscularity and M-value-FFM (rho = -0.5047, $p = 0.004$) and M-value-TBW (rho = -0.4742, $p = 0.0076$). There was no difference in M-value between cachexia and non-cachexia patients. No statistical difference was observed in inflammatory markers (C-reactive protein, Glasgow prognostic score (mGPS), and neutrophil-to-lymphocyte ratio (NLR)) according to muscularity groups. **Conclusion:** There is no insulin resistance associated with LM or cachexia. It is possible that the main determinant of insulin sensitivity is the amount of visceral adipose tissue and systemic inflammation. The LM group exhibits a lower area of visceral adipose tissue, with no discernible difference in inflammatory markers. This study highlights the importance of expanding investigations into the determinants of metabolic changes and body composition in cancer cachexia.

Keywords: Cachexia, Insulin resistance, Metabolism, Muscularity, Rectal neoplasia.

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DEEP LEARNING FOR CT IMAGES SEGMENTATION

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Introduction/Justification: Computed tomography (CT) scans are integral to cancer patient diagnosis, revealing changes in body composition linked to survival progression. The conventional approach to body composition analysis using CT scans is labor-intensive and expensive, demanding skilled professionals and licensed software for manual segmentation of Regions of Interest (ROIs). To address these challenges, we introduce a Deep Learning algorithm designed for automated CT image segmentation, presenting an efficient alternative that overcomes the limitations of the current methodology. Beyond the advantages of speed, automation enhances result uniformity and enables uncertainty estimation. In this presentation, we will show preliminary results from our algorithm, highlighting its potential contributions to survival analysis in cancer patients. **Objectives:** The primary goal of this study was to develop an automated segmentation algorithm for CT scans using Deep Learning models. **Materials and Methods:** In developing segmentation algorithms, a dataset of 453 CT slices at the L3 lumbar vertebral level from gastric cancer patients was utilized, with an 80% training and 20% testing partition. Employing the UNET+ResNet18 deep learning architecture, supervised training utilized manually generated segmentation masks as references. Four dedicated UNET+ResNet18 algorithms were trained for distinct ROIs: Skeletal Muscle (SM), Intramuscular Adipose Tissue (IMAT), Visceral Adipose Tissue (VAT), and Subcutaneous Adipose Tissue (SAT). Segmentation performance on the test set was evaluated using the Dice Coefficient, underestimation and overestimation percentages, Bland-Altman analyses, and qualitative visual inspection of segmented images. **Results:** The UNet+ResNet18 models demonstrated superior segmentation performance for SM, VAT, and SAT, achieving mean Dice scores exceeding 0.95. In comparison to manual segmentation, the Deep Learning algorithm exhibited minor average underestimations and overestimations, both below 5% for these tissues. However, IMAT segmentation exhibited relatively lower performance, with a mean Dice score of approximately 0.86 and underestimation and overestimation percentages around 15% and 13%, respectively. The Bland-Altman analysis revealed mean bias and limits of agreement for mean radiodensities of SM, VAT, SAT, and IMAT as follows: 0.14 [-0.82, 1.10] HU, -0.53 [-2.03, 0.98] HU, -0.18 [-1.70, 1.33] HU, and 0.48 [-3.86, 4.82] HU, respectively. **Conclusion:** The Deep Learning approach provides a standard and fast solution for CT image segmentation, demonstrating good results for SM, VAT and SAT. For these tissues, derived radiomics features could provide valuable insights into the analysis of cancer patient outcomes. Further studies are necessary for enhancing IMAT segmentation, given its challenging small area. Additionally, future investigations should focus on uncertainty estimation in CT images, exploring its impact on segmentation procedures and radiomic feature extraction.

Keywords: Automated body composition analysis, Computed tomography, Deep learning.

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AUTOMATED SYNTHESIS AND IN VITRO STUDIES OF [68GA]GA-FAPI-46 IN HOSPITAL RADIOPHARMACY

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Introduction/Justification: Early evidence appointed fibroblast activation protein (FAP), a type II transmembrane serine protease, as highly expressed in the stroma of various tumor entities, designating FAP as the next target for cancer studies in nuclear medicine. Several radiolabeled fibroblast activation protein inhibitors (FAPI) are currently in development and investigation as potential PET imaging agents for different neoplasms, with the potential for future theranostic applications. **Objectives:** The aim of this study was to implement the efficient and convenient automated synthesis of [68Ga]Ga-FAPI-46 from ABX, using Modular Lab Pharm Tracer and the generator Gallia Pharm® from Eckert & Ziegler, for clinical applications in nuclear medicine services, as well as to evaluate routine quality control parameters such as radiochemical yield and purity, radiochemical stability, and sterility tests in accordance with the GMP rules. **Materials and Methods:** The synthesis was conducted in automated module, employing disposable cassettes in an adapted synthesis template with high purity raw materials and reagents. [68Ga]GaCl3 was percolated through resin and eluted with 0.5 mL of 5.5 M HCl in saline into a reaction vial containing 50 μg of FAPI-46 in 1.5 mL of 0.1 M acetate buffer (pH = 4.5) and 100 μL of ethanol. The solution was heated at 95°C for 10 min. The resulting product was purified through a Sep-Pak C18 cartridge, which was preconditioned with ethanol and 0.9% saline, and eluted with 0.4 mL of 70% ethanol. The final product was diluted with 0.9% saline and filtered through a Millipore 0.22 μm filter. Radiochemical yield (RCY) was assessed by determining the activity retained in the module in relation to the final product. Radiochemical purity (RCP) of [68Ga]Ga-FAPI-46 was analyzed by ascending chromatography using either ITLC-SG strip and 0.1 M ammonium acetate and methanol (1:1) solution or TLC and 1 M sodium citrate (pH = 5.5), and Sep-Pak C18 cartridge. Radiochemical stability was assessed through UHPLC analysis. Microbiological, pyrogenic, and filter tests were conducted on all batches. Additionally, in-vitro studies were carried out to assess Log P and serum protein binding for [68Ga]Ga-FAPI-46. **Results:** The automated synthesis produced [68Ga]Ga-FAPI-46 with an activity of 684 ± 67 MBq, a RCY of 88.4 ± 2.6%, and pH = 4.5 (n = 8). The RCP was determined as 97.32 ± 1.92% by ascending chromatography and 97.74 ± 2.12% by Sep-Pak C18 cartridge. The RCP remained above 97% for more than 120 min as analyzed by UHPLC, showing high radiochemical stability. Microbiological assays demonstrated that the final product was obtained as a sterile and pyrogen free solution. The filter test passed for all batches. The Log P was determined as -3.57 ± 0.15 (n = 10), showing the hydrophilic characteristics of [68Ga]Ga-FAPI-46 with a serum protein binding of 52.11 ± 1.49% (n = 6). **Conclusion:** The [68Ga]Ga-FAPI-46 was synthesized with consistently high RCY and RCP, exhibiting reproducibility, yielding a sterile and pyrogen free final solution, that means an efficient way for routine syntheses in nuclear medicine services confirmed by clinical application in six patients.

Keywords: Automated syntheses, PET-CT, Quality control., [68Ga]Ga-FAPI-46.

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CONTINUING EDUCATION IN RADIOPHARMACY IN LATIN AMERICA

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Introduction/Justification: Radiopharmacy is an area with increasing development and technological complexity. According to WHOs official documents (WHO Annex 2,3) the production of radiopharmaceuticals requires the supervision of qualified personnel with postgraduate training and appropriate experience in their function. Although most countries in Latin America have adopted these documents in their legislation the real situation is highly heterogeneous and specific qualification in Radiopharmacy is not clearly specified in the national regulations. Furthermore, the adequate educational offer is very restricted and heterogeneous in all Latin American countries. **Objectives:** With the objective to prepare the future generations of Radiopharmacists according to international and national regulations we have developed a series of options for postgraduate and continuing education in the field. **Materials and Methods:** N/A. **Results:** The Diploma of Specialization in Radiopharmacy offers a postgraduate program for specialization in Radiopharmacy. This diploma integrates comprehensive theoretical knowledge with the necessary practical experience to prepare professionals for specialized roles in this field. Admission to the program requires candidates to hold a university degree, with a minimum duration of four years, in Pharmacy, Chemistry, or Biochemistry, obtained from institutions in Uruguay or other countries. Applications from candidates with alternative qualifications are reviewed by a dedicated admission committee, and additional courses may be prescribed to supplement their foundational knowledge. The curriculum comprises both theoretical and practical components, totaling approximately 300 hours of instruction. The courses can be partially performed virtually, thus facilitating the participation of foreign students. However, practical laboratory sessions and supervised practice are required to be completed in Uruguay, typically spanning a duration of 3-4 months. Additionally, partial validation of prior studies may be considered, allowing eligible students to receive credit for relevant coursework completed elsewhere. Besides the postgraduate program we also offer the possibility of taking continuous education courses both with basic (physics of radiation, chemistry of radiopharmaceuticals, etc) and applied topics (legislation, clinical applications, et). We also offer customized courses for institutions or private radiopharmaceutical firms. Up to the moment we have more than 10 graduates, 40% coming from Colombia, Costa Rica or Bolivia and 7 students, 6 of which are from different countries in Latinamerica. Our continuing education courses have been taken by around 100 professionals from Chile, Costa Rica, México, Bolivia, Ecuador, Perú, Costa

Rica, Panamá, República Dominicana, etc. Conclusão: Radiopharmacy is a flourishing specialty of increasing complexity that requires solid theoretical knowledge and specialized practical skills. The Radiochemistry Area in the public University of Uruguay is fostering the development and generational replacement in our continent with the objective to improve the quality of the Radiopharmaceuticals received by our population. **Acknowledgments:** Centro Uruguayo de Imagenología molecular, CUDIM and Centro de Medicina Nuclear e Imagenología Molecular del Hospital de Clínicas.

Keywords: Education, Online courses, Posgraduate, Radiopharmacy.

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EVALUATION OF POTENTIAL PEPTIDE INHIBITORS THAT INTERACT WITH THE EGF RECEPTOR. RELEVANCE TO GLIOBLASTOMA

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Introduction/Justification: Peptides are implicated to various physiological responses and exhibit considerable potential for disease treatment, encompassing diverse types of tumors. The significant therapeutic promise of peptides is related from their characteristics, including the ability to inhibit angiogenesis, induce tumor apoptosis and block of epidermal growth factor receptor (EGFr) signaling. Their relevance is underscored by overexpression in a range of human cancers, notably glioblastoma, which represents the most prevalent and aggressive form of malignant brain tumors. **Objectives:** This study aims to assess the growth inhibition of rat (C6 cells) and human (U-87 MG cells) glioblastoma tumor cells using peptides that interact with the EGFr. **Materials and Methods:** The anti-EGFr peptides were synthesized through the solid-phase peptide synthesis using the Fmoc/tBut strategy. Peptide cleavage from the resin was performed using a mixture containing a high concentration of trifluoroacetic acid (reagent K). Subsequently, the peptides underwent a characterization and purification process employing high performance liquid chromatography (HPLC) and mass spectrometry. C6 and U-87 MG cell lines were cultured in supplemented DMEM F-12 medium at 37°C and 5% CO2 until reaching 90% confluence. To assess the effect of peptides on cell proliferation, cells were seeded at a concentration of 5×103 in 6-well plates, with the presence of 80 μM of each proposed peptide. Growth curves were performed in sextuplicate over a 7-day period, with cell counts conducted on days 1, 3, 5, and 7. Cell viability in the presence of peptides was determined using the MTT test. For this analysis, cells were plated at a concentration of 5×103 in 96-well plates, with peptide concentrations of 80, 120, and 160 μM. Spectrophotometric analyses were performed after 24 h and 7 days of incubation at 595 nm. **Results:** Anti-EGFr-LP and anti-EGFr-LG peptides were synthesized efficiently with yields of approximately 45 and 98%, respectively. Chromatographic analyzes obtained by HPLC confirmed that the entire synthesis, cleavage, and characterization process of peptides were performed efficiently, as evidenced by the presence of only a single peak corresponding to the synthesized peptides. Following the determination of growth curve profiles of C6 and U-87 MG cell lines, without the presence of peptides, the interaction of the peptides with both tumor cell types was assessed. The results demonstrated that both anti-EGFr-LP and anti-EGFr-LG peptides significantly interacted with and inhibited the growth of C6 and U-87 MG strains ($p < 0.0001$). Studies conducted with C6 cells showed inhibition percentages of approximately 55.3% and 99.1% for the Anti-EGFr-LP and anti-EGFr-LG peptides, respectively. On the other hand, an inhibition percentage of growth of U-87 MG cells was 44.4% for the Anti-EGFr-LP and 46.4% for the anti-EGFr-LG. Finally, based on the MTT test, the peptides exhibited no toxicity at any of the three concentrations tested. **Conclusion:** The findings indicate that both proposed peptides, at a minimum concentration (80 μM) effectively reduced the proliferation of tumor cells without inducing toxicity. While further experiments are warranted, the peptides have demonstrated the capability to inhibit tumor cell growth associated with glioblastoma, suggesting a potential therapeutic alternative.

Keywords: C6 cells, EGFr-targeting peptides, glioblastoma, U-87 MG cells.

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INVESTIGATION OF THE IN VITRO ASSESSMENT OF 99MTC-LABELED LAMININ-111 PEPTIDES AS PROSPECTIVE BIOMARKERS FOR BREAST CANCER

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Introduction/Justification: Breast cancer constitutes a significant public health issue as the second most prevalent type of tumor among women. In the past decade, radiolabeled peptides have been employed in both therapeutic interventions and tumor imaging, representing a substantial promise in the specific targeting of tumorigenic cells. Several studies demonstrate that biologically active peptides derived from laminin-111 regulate gene expression in breast cancer-derived cells, including the YIGSR and IKVAV peptides. **Objectives:** To synthesize the HYIGSR and HIKVAV fragments, derived from laminin-111, standardize and optimize their radiolabeling process with technetium-99m (99mTc), as well as, to assess the in vitro biological characteristics of these radiolabeled peptides as potential biomarkers for breast cancer. **Materials and Methods:** The HYIGSR and HIKVAV peptides were

synthesized employing the solid-phase peptide synthesis through the Fmoc/tBut strategy, characterized, and purified utilizing high-performance liquid chromatography (HPLC). By using the tricarbonyl method, it was possible to label the histidine residue of the peptide fragments with the organometallic aqua-ion [99mTc(H2O)3(CO)3]+, abbreviated as [99mTc]TcCO3, directly from reaction of [99mTc]TcO4- under 1 atm of CO for 30 min at 70°C. Subsequently, both peptides were labeled with approximately 148 MBq and incubated for 30 min at 85°C. The stability of the radiolabeled peptides in saline and serum was assessed at 1, 2, 3, and 4 h and evaluated using HPLC. The partition coefficient was determined for both radiopeptides. Studies to assess the percentage of binding to serum proteins were conducted at 60 min. The binding and internalization of radiolabeled peptides with tumorigenic cells derived from breast cancer (MCF-7) were assessed at 1, 2, and 4 h. **Results:** The HYIGSR and HIKVAV peptides were efficiently synthesized and characterized. The radiolabeling process with [99mTc]TcCO3 was optimized and the [99mTc]TcCO3-HYIGSR and [99mTc]TcCO3- HYIKVAV were successful obtained with radiochemical yields of 95.53% ± 1.19 and 95.13% ± 1.96 (n = 6), respectively. Notably, stability studies revealed that both radiopeptides exhibited stability within a four-hour timeframe when stored in either saline or serum. The [99mTc]TcCO3-peptides demonstrated hydrophilic properties, as indicated by Log P values of -2.12 ± 0.16 and -1.39 ± 0.19 (n = 3) for [99mTc]TcCO3-HYIGSR and [99mTc]TcCO3-HYIKVAV, respectively. Additionally, the binding percentage to serum proteins for [99mTc]TcCO3-HYIGSR and [99mTc]TcCO3-HYIKVAV was found to be 46.08% ± 3.75 and 24.87% ± 6.24 (n = 3) within 60 min, respectively. Furthermore, binding and internalization studies conducted with MCF-7 cells (n = 4) demonstrated a higher percentage of binding and internalization for [99mTc]TcCO3-HYIKVAV, with values of 9.20% ± 2.87 and 51.74% ± 8.00, respectively. In contrast, [99mTc]TcCO3-HYIGSR exhibited percentages of 2.96% ± 0.60 and 25.85% ± 3.33 for binding and internalization within a 1-hour period. **Conclusion:** Both peptides exhibited good radiochemical yields and demonstrated sustained stability over the course of the study. Both peptides showed hydrophilic characteristics and our findings specifically underscored the higher affinity of [99mTc]TcCO3-HYIKVAV towards human breast cancer cells. Nevertheless, it is imperative to note that further in vivo investigations are necessary.

Keywords: Breast cancer, Laminin-111, MCF-7 cells., Tricarbonyl-labeled peptides.

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ASSESSMENT OF IN VITRO STUDIES OF [131I]I-LABELED DEDEYFELV PEPTIDE AS PROSPECTIVE BIOMARKER FOR GLIOBLASTOMA

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Introduction/Justification: Glioblastomas (GBM) constitute the most prevalent malignant primary tumor in adults and rank as the third most frequent tumors in the central nervous system. The predominant alteration observed in GBM is associated with the tyrosine-kinase pathway, facilitating the connection of growth factors to receptors. Notably, in GBM the overexpression of the epidermal growth factor receptor (EGFr) has opened new treatment perspectives, including molecular targeted therapies, with peptides taking center stage. Recently, radiolabeled peptides with high affinity for EGFr have been employed as potential agents for molecular imaging or targeted radionuclide therapy as anti-tumor agents. **Objectives:** The aim of the study was to assess the interaction between [131I]I-DEDEYFELV peptide and human glioblastoma cells (U-87 MG), as well as with GBM tissue. Materiais e Métodos: The DEDEYFELV peptide was synthesized through solid-phase peptide synthesis using the Fmoc/tBut strategy. Peptide cleavage from the resin was performed using a mixture containing a high concentration of trifluoroacetic acid (reagent K). Subsequently, the peptides underwent a characterization and purification process employing high performance liquid chromatography (HPLC) and mass spectrometry. The U-87 MG cell line was cultured in supplemented DMEM F-12 medium at 37°C and 5% CO2 until reaching 90% confluence. The neoplastic tissue was surgically removed, histopathologically analyzed, and preserved at -80°C, with its homogenate prepared using PBS buffer (pH 7.4) at 10 mg of tissue/mL. The DEDEYFELV (20 nmol) was radiolabeled with the [131I]NaI radionuclide (18.5 MBq), using the chloramine-T method. The radiochemical yield of the [131I]I-DEDEYFELV was carried out by on Whatmann 3MM strips using 95% MeOH / 5% H2O as eluent. Binding and internalization studies of the [131I]I-DEDEYFELV with tumorigenic cells (U-87 MG) and neoplastic tissue homogenate were evaluated at 1 and 3 h of incubation and measured in an automatic gamma counter. **Results:** The DEDEYFELV peptide was efficiently synthesized and characterized, with yield of approximately 92%. Chromatographic analyzes obtained by HPLC confirmed that the entire synthesis, cleavage, and characterization process of peptides were performed efficiently, as evidenced by the presence of only a single peak corresponding to the synthesized peptide with molecular mass of 1158.18 g/mol. The radiolabeling process was successful obtained with radiochemical yield > 95%. Binding and internalization studies of the [131I]I-DEDEYFELV conducted with U-87 MG cells showed values of 15.90% ± 1.67 and 54.57% ± 0.90 (n = 5), respectively. On the other hand, the binding percentage of 12.45% ± 0.90 and internalization of 28.41% ± 3.15 (n = 5) were achieved with neoplastic tissue homogenate within a 3-hour period. **Conclusion:** The proposed peptide was efficiently synthesized, and radiolabeling studies with [131I]NaI exhibited a high radiochemical yield. Binding and internalization studies revealed that the [131I]I-DEDEYFELV peptide has a good

affinity for both U-87 MG and neoplastic tissue homogenate, demonstrating higher internalization of [131I]I-DEDEYFELV in human glioblastoma cells. Nevertheless, it is crucial to emphasize that additional in vivo investigations are necessary.

Keywords: EGFr-targeting peptide, Glioblastoma, U-87 MG cells, [131I]I-labeled-peptide.

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SYNTHESIS AND EVALUATION OF BIOACTIVE PEPTIDES FROM LAMININ-111 IN TRIPLE-NEGATIVE BREAST CANCER CELLS

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Introduction/Justification: Breast cancer stands as the neoplasm group with the highest incidence rate among women worldwide. Laminin-111 a constituent of the tissue basement membrane, is implicated in the development of breast tumors. Biologically active peptides of laminin-111 such as YIGSR and IKVAV, play crucial roles in tumor growth, metastasis, protease secretion, and angiogenesis. These peptides exert significant influence on various aspects of cancer progression, emphasizing their potential as key targets for therapeutic intervention. **Objectives:** The aim of the study was to synthesize the bioactive peptides of laminin-111 (YIKVAV and YIGSR) and assess their interactions in triple-negative breast cancer cells. **Materials and Methods:** The YIKVAV and YIGSR peptides were synthesized through solid-phase peptide synthesis using the Fmoc/tBut strategy. Subsequently, the peptides underwent a characterization and purification process employing high performance liquid chromatography (HPLC) and mass spectrometry. The MDA-MB-231 breast tumor cell line was cultured in supplemented RPMI-1640 medium at 37°C and 5% CO2 until reaching 90% confluence. The growth curve of the MDA-MB-231 cell line was conducted in sextuplicate over a 7-day period, with cell counts performed on days 1, 3, 5, and 7. To assess the effect of peptides on cell proliferation, cells were seeded at a concentration of 2×104 in 6-well plates, with the inclusion of both YIKVAV and YIGSR peptides at 50 μM (n = 6). Cell viability in the presence of YIKVAV and YIGSR was determined using the MTT assay. For this analysis, cells were plated at a concentration of 2×104, with peptide concentration of 50 μM. Spectrophotometric analyses were realized after 24 h and 7 days of incubation at 595 nm. **Results:** The YIKVAV and YIGSR peptides were efficiently synthesized, yielding approximately 80% for both. Chromatographic analyzes conducted by HPLC and mass spectrometry confirmed the efficiency of the entire synthesis, cleavage, and characterization process of the peptides by the presence of only a single peak corresponding to the synthesized peptides. The growth curve profile determination of MDA-MB-231 cell line revealed exponential growth between days 5 and 7 of cell culture. The results indicate that the YIGSR peptide significantly inhibited cell growth by approximately 45%, whereas the YIKVAV fragment promoted cell growth by approximately 38% and ($p < 0.0001$) on the seventh day of cell culture. Regarding the MTT analysis after 24 h, no significant differences were observed between the control and treated groups for both fragments, suggesting that the peptides exhibited no toxicity at concentration of 50 μM. Additionally, on the 6th day, a reduction in tumor cell viability was observed for the YIGSR fragment, while an increase in viability was noted for YIKVAV ($p < 0.0001$). **Conclusion:** The YIKVAV and YIGSR peptides were effectively synthesized, characterized, and purified. The YIKVAV peptide, at a concentration of 50μM, promoted cell growth, while the YIGSR peptide significantly hindered the growth of the MDA-MB-231 cell line. This observation is consistent with the findings of cell viability assays conducted using MTT. This study holds significance for enhancing our comprehension of peptide actions in their interaction with triple-negative breast cancer cells, with the ultimate aim of proposing more effective targets for treatment.

Keywords: Breast cancer, Laminin-111-peptides, MDA-MB-231 cells.

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ASSESSMENT OF IN VITRO INTERACTIONS BETWEEN RADIOLABELED EGFR-TARGETING PEPTIDE INHIBITORS AND GLIOBLASTOMA CELLS

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Introduction/Justification: Peptides are implicated in various physiological responses and hold significant potential as targeting molecules, especially in cancer diagnosis or treatment. Radiolabeled peptides have been investigated for their potential as theranostic agents, holding considerable promise for precisely targeting tumorigenic cells. Previous studies indicate that biologically active peptides exhibit a high affinity for the Epidermal Growth Factor receptor (EGFr), which is overexpressed in various tumor cells, including glioblastoma, the most prevalent and aggressive malignant brain tumor. **Objectives:** To evaluate the in vitro interactions involving two radiolabeled peptide inhibitors targeting the EGFr overexpressed in glioblastoma cells. **Materials and Methods:** Two EGFr-targeting peptide inhibitors, anti-EGFr-LP and anti-EGFr-LG, were radiolabeled with [131I]NaI (11.1–14.8 MBq) using

the chloramine T method (room temperature; reaction time = 120 s). The radiochemical yield (RCY) (n = 8) and stability (n = 3) were evaluated using ascending chromatography on TLC-SG strips and acetonitrile/water (95:5) as eluent. C6 and U-87 MG glioblastoma cell lines were cultured in supplemented DMEM medium (5% CO2 atmosphere; 37°C) until reaching ~85% confluence. Subsequently, aliquots of 2 x 10^6 C6 or U-87 MG cells were incubated with each radiopeptide (37°C) under agitation (500 rpm). In vitro binding and internalization percentages were assessed at 1 and 3 h post-incubation (n = 6). Data were expressed as 'mean ± standard deviation' and the statistical analysis was performed using GraphPad Prism software. **Results:** The RCY of [131I]I-anti-EGFr-LP and [131I]I-anti-EGFr-LG were 92.92 ± 3.42 and 97.80 ± 1.08, respectively. Both 131I-labeled peptides were radiochemically stable over 24 h. The in vitro interaction between C6 cells and [131I]I-anti-EGFr-LP showed binding percentages of 4.80 ± 0.37% (1 h) and 5.87±1.21% (3 h), with no statistically significant difference ($p = 0.1519$). The internalization percentages, within the bound fractions, increased from 64.45 ± 4.19% (1 h) to 75.15±1.60% (3 h) ($p < 0.0001$). For the [131I]I-anti-EGFr-LG, the data were of the same order of magnitude. The binding percentages increased from 3.95±0.33% (1 h) to 6.03 ± 0.66 (3 h) ($p < 0.0001$) and the internalization percentages, among the bound fractions, were 62.57±5.53% (1 h) and 64.04±3.21% (3 h), with no statistically significant difference ($p = 0.5959$). The in vitro interaction between U-87 MG cells and [131I]I-anti-EGFr-LP showed an increment of the binding percentages from 6.50 ± 0.93% (1 h) to 8.03 ± 0.29% (3 h) ($p < 0.0001$), but the internalization percentages, within the bound fractions, showed no statistically significant difference ($p = 0.2791$), 68.98 ± 2.23% (1 h) and 73.02±6.57% (3 h). For the [131I]I-anti-EGFr-LG, the binding percentages were 10.97±1.48 (1 h) and 11.28 ± 0.84 (3 h), with no statistically significant difference ($p > 0.6724$). The internalization percentages, among the bound fractions, were also statistically similar ($p > 0.3596$), 68.21 ± 0.16% (1 h) and 65.36 ± 3.56 (3 h). **Conclusion:** The in vitro interaction data revealed high affinity of [131I]I-anti-EGFr-LP and [131I]I-anti-EGFr-LG for the C6 and U-87 MG glioblastoma cell lines, which are known to overexpress EGFr. These preliminary findings support the potential use of these peptide inhibitors as specific peptide-based targeting molecules for EGFr, with potential applications as theranostic agents.

Keywords: EGFr-targeting peptide inhibitors, Glioblastoma cells, In vitro interactions, Radiolabeled peptides.

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SKELETAL MUSCLE RADIODENSITY AND INSULIN SENSITIVITY IN PATIENTS WITH RECTAL CANCER

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Introduction/Justification: The assessment of skeletal muscle attenuation via computed tomography plays a crucial role in identifying myosteatosis among cancer patients. Myosteatosis, characterized by ectopic adipose tissue infiltration in skeletal muscles, has been linked to poor prognosis in various cancers. However, its implications specifically in rectal cancer remain uncertain. Studies have shown that myosteatosis correlates with increased insulin resistance, highlighting the need for further investigation in clinical settings. **Objectives:** This study aimed to investigate the relationship between insulin sensitivity and skeletal muscle radiodensity in patients recently diagnosed with rectal cancer. **Materials and Methods:** A cross-sectional study design was employed, inviting patients diagnosed with rectal cancer to participate. Insulin sensitivity was assessed using the M-value obtained from euglycemic hyperinsulinemic clamp tests. Skeletal muscle analysis was conducted using computed tomography (CT) images of the third lumbar vertebra processed with SliceOmatic software. Skeletal muscle was defined within the attenuation range of -29 to +150 Hounsfield Units (HU), while intermuscular adipose tissue was defined within -190 to -30 HU. The mean skeletal muscle radiodensity (SMR) was reported. Demographic and clinical data were collected from medical records. Statistical analyses were performed using Stata Corp LP® version 17.0 software. The study protocol received approval from the Institutional Review Board (CAAE: 91217418.2.0000.5404). **Results:** The analysis included a total of 33 patients, predominantly male (67%) with ages ranging from 55 to 70 years (58%). Patients across stages I to IV were represented, with 48% in stage III, 11% in stage I, 11% in stage II, and 30% in stage IV. Overweight and obesity were diagnosed in 37.5% and 30% of the sample, respectively. Common comorbidities included diabetes (21%), hypertension (60%), and dyslipidemia (21%). The M-value adjusted for Total Body Weight (TBW) demonstrated a significant association with Skeletal Muscle Radiodensity ($rho = 0.3926$, $p = 0.0269$), whereas no statistical difference was observed when adjusting for Free Fat Mass (FFM) ($p = 0.1769$). **Conclusion:** In conclusion, our findings suggest a moderate positive association between insulin sensitivity and skeletal muscle radiodensity in rectal cancer patients.

Keywords: Insulin sensitivity, Rectal cancer, Skeletal muscle radiodensit.

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PROGNOSTIC EVALUATION OF THE NUTRITIONAL PROGNOSTIC INDEX IN PATIENTS WITH NON-METASTATIC RECTAL CANCER

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Introduction/Justification: Rectal cancer (RC) is one of the leading causes of cancer mortality worldwide. Recent studies indicate that systemic inflammation and nutritional status are associated with the prognosis of cancer patients. The prognostic nutritional index (PNI) has been increasingly studied as a predictor of survival outcome. However, despite these advances, there are few studies evaluating the prognostic capacity of this index in patients with RC. **Objectives:** To analyze the impact of PNI on the survival of patients with non-metastatic RC undergoing oncological treatment. **Materials and Methods:** This is a retrospective, cross-sectional and analytical study. It included patients diagnosed with stage I, II and III rectal carcinoma who had been treated surgically, with or without neoadjuvant and adjuvant chemotherapy, and who were attended to at the Clinical Oncology outpatient clinic of the Hospital das Clínicas of the University of Campinas between January 2000 and December 2016. Patients were categorized into low and high PNI, according to the median of the sample. PNI was calculated using the formula: PNI = (10xserum albumin [g/dl]) + 0.005xlymphocytes/μL). Clinical variables, body composition and systemic inflammatory indices were also analyzed. Body composition was analyzed using computed tomography, and skeletal muscle compartments and subcutaneous and visceral adipose tissue were assessed using SliceOmatic software (Tomovision, Canada). Statistical analyses were carried out using Stata software version 12.0 (Stata Corp LP®). This research was approved by the UNICAMP Research Ethics Committee (CAAE: 22438319.9.0000.5404). **Results:** The sample consisted of 298 patients, 118 of whom had low PNI. The group with low PNI had a lower muscle mass index (p = 0.025) and subcutaneous adipose tissue index (p = 0.044), and higher subcutaneous (p =0.049) and visceral (p = 0.012) adipose tissue radiodensity. Median disease-free survival was 24.5 months for patients with low PNI (HR 1.85; CI 1.30-2.62; p = 0.001). Patients with low PNI had a lower median disease-free survival (mDS) of 24.5 months compared to 107.4 months for the high PNI group [HR 1.85; IC 1.30-2.62; p = 0.001]. Median overall survival (mOS) was 75.3 months for the low NPI group and 140.4 months for the high NPI group (HR 1.67; CI 1.13-2.48; p = 0.011). **Conclusion:** The PNI performed at diagnosis is a prognostic tool for assessing the clinical outcome of patients with non-metastatic RC. Nutritional status and systemic inflammation are associated with survival in cancer patients. The PNI is a marker that combines both conditions and has been shown to be an important prognostic tool for desease-free survival (DFS) and overall survival (OS) in RC. The PNI is a simple, practical tool that uses low-cost clinical evaluation parameters and can therefore be easily implemented in clinical practice.

Keywords: Inflammation, Mortality, Nutritional status.

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EPIDEMIOLOGICAL ANALYSIS OF HOSPITAL ADMISSIONS FOR HODGKIN'S DISEASE IN BRAZIL: 2013-2023

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Introduction/Justification: Lymphomas are neoplasms originating from lymphoid tissue, with Hodgkin's Disease (HD) being noteworthy. HD manifests in two primary types: classical Hodgkin's lymphoma and Nodular lymphocyte-rich lymphoma. The classical types are identified by Reed-Sternberg multinucleated cells, subdivided as nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depletion. The development of HD is linked to various factors, including genetic predisposition, immunosuppression, autoimmune diseases, and exposure to carcinogens. Clinical symptoms commonly observed include pruritus, intermittent fever, nocturnal hyperhidrosis, and lymphadenopathy. Differential diagnosis plays a crucial role in HD identification since clinical symptoms may resemble various other medical conditions, including other lymphoma forms, viral or bacterial infections, and autoimmune diseases, emphasizing the importance of biopsy and thorough investigation. Epidemiological analysis of HD plays a pivotal role in early diagnosis and the implementation of appropriate therapies aiming for eventual patient remission. **Objectives:** To analyze hospitalization data within the Brazilian Unified Health System (SUS), estimating disease incidence across different regions, demographic disparities, treatment costs, and mortality, aiming to provide insights for public health policies to improve management and access to healthcare services for HD patients within the SUS context. **Materials and Methods:** A retrospective study using data from the Department of Health Informatics of SUS (DATASUS) from 2013 to 2023. Data included total hospitalizations, region, age, gender, race, deaths, mortality rate, and average hospitalization cost. **Results:** Brazil recorded 53,297 HD-related hospitalizations from 2013 to 2023. Geographical distribution revealed the Southeast region accounted for the majority of cases (47.64%), followed by the Northeast (24.74%) and South (17.29%). Males comprised the majority of hospitalizations (55.56%), with females representing 44.43%. Regarding race, whites accounted for 43.84% of hospitalizations, followed by mixed race individuals (37.52%). Hospitalizations were most common among individuals aged 20-29 (24.90%), followed by age groups 15-19 (14.85%) and 30-39 (14.34%). There were 2,149 deaths during this period, corresponding to a mortality rate of 4.03%. Based on the average value per hospitalization in SUS, a total of R$135,694,694.97 was spent. **Conclusion:** The epidemiological study reveals a higher incidence of Hodgkin's Disease in the Southeast region, predominantly among males in the age group between 20-29, along with a mortality rate of 4.03% among the hospitalized. These findings emphasize the public health challenge of HD and the need for comprehensive strategies, including awareness campaigns, screening programs, and

improved diagnostic and treatment capabilities. Understanding HD epidemiology is crucial for effective resource allocation and improved clinical outcomes.

Keywords: Epidemiology, Hodgkin's disease, Hodgkin's lymphoma, Oncohematology.

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ASSOCIATION BETWEEN BODY COMPOSITION AND SURVIVAL IN LOCALLY ADVANCED HEAD AND NECK CANCER TREATED WITH RADIOTHERAPY

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Introduction/Justification: Malnutrition is a frequent condition in patients with head and neck cancer (HNC) due to the location of the tumor, treatment, and difficulty in food intake. Body composition is recognized as a prognostic factor in cancer patients, independently of nutritional status. Low muscularity (LM) is related to decreased survival in patients with HNC, however, the adipose tissue (AT) impacts in prognosis is unclear. **Objectives:** This study evaluates the association between body composition parameters and survival in patients with locally advanced HNC. **Materials and Methods:** A retrospective study was conducted on patients diagnosed with locally advanced HNC who received radiotherapy as the first-line treatment at the University of Campinas Hospital between January 2010 and December 2018. The total adipose tissue (TAT) area and the skeletal muscle area were measured by analyzing computed tomography (CT) images at the level of the third cervical vertebra (C3) using the SliceOMatic V. 5.0 software. The muscle cross-sectional area (CSA) at C3 was used to estimate the CSA muscle area at L3, using a specific formula.Cox proportional hazard models were used for survival analysis. Model A was adjusted for age, while model B was adjusted for age, ECOG score, diabetes, hypertension, concomitant chemotherapy, and tumor stage. Model C maintained the variables of model B plus muscularity. The statistical analysis was performed using Stata software version 17.0, and a significance level of 5% was established. The study was approved by the Research Ethics Committee of UNICAMP (CAAE: 42743120.5.0000.5404). **Results:** Our sample included 132 patients that comprised mostly males (87.9%) aged between 55 and 70 years (60.6%) and considered eutrophic by the Body Mass Index (BMI) (52.3%). Patients in the highest tertile of TAT had a lower risk of death than those in the lowest tertile in model A [HR: 0.49 (CI 95%: 0.30–0.79); ptrend = 0.007], model B [HR: 0.56 (CI 95%: 0.32–0.96); ptrend = 0.039], and model C [HR: 0.51 (CI 95%: 0.29–0.89); ptrend = 0.017]. The highest tertile of TAT presented higher caloric intake (p = 0.030) and energy expenditure (p = 0.004). Low muscularity was associated with lower overall survival [HR = 1.77, 95%CI (1.01 - 3.07), p = 0.044)], but not with progression free survival. There was no statistical difference for NLR values between groups (p = 0.47). **Conclusion:** Higher adiposity was a protective factor for overall survival in locally advanced HNC treated with radiotherapy. Low muscularity was associated with reduced overall survival. The assessment of body composition, added to an early nutritional intervention, and the preservation of muscle mass and adipose tissue may play a role in improving the outcomes of locally advanced HNC patients undergoing radiotherapy.

Keywords: Adipose tissue, Computed tomography, Malnutrition, Mortality, Muscularity.

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LOW MUSCULARITY IMPACTS SURVIVAL IN PATIENTS WITH METASTATIC OR RECURRENT HEAD AND NECK CANCER

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Introduction/Justification: The prognosis of patients with head and neck cancer (HNC) is determined by factors extrinsic and intrinsic to the patient and the disease, such as age, smoking, alcoholism, HPV infection, tumor staging, and performance status and facts involving low muscularity, which is an independent adverse prognostic factor in some types of cancer, such as HNC. However, the impact of muscularity in the scenario of metastatic or recurrent HNC (mHNC) patients has still been little explored, especially when evaluated at the level of the third

cervical vertebra (C3). **Objectives:** To evaluate the impact of muscularity on the overall survival (OS) of patients with mHNC. **Materials and Methods:** Retrospective and analytical study carried out at the Hospital de Clínicas of the University of Campinas (HC-UNICAMP). Patients diagnosed with mHNC during the period from January 2010 to December 2018 were included. Demographic and clinical data were collected from information in the medical record. The computed tomography images were used to evaluate the area of muscle tissue at the C3 level (cm^2), calculated with Software SliceOMatic V.5.0. Muscularity was calculated after converting the muscular cross-sectional area (CSA) at C3 to the CSA at L3. Fisher's exact test was applied to investigate the difference between groups, the Kaplan-Meier method was used to construct survival curves. The Cox Proportional Hazard Model was used to investigate the association of muscularity with OS. Model was adjusted for age (categorical) and ECOG (categorical). This study was approved by the Institutional Review Board (CAAE: 42743120.5.0000.5404). **Results:** The study population consisted of 101 adult and elderly patients of both sexes diagnosed with mHNC, 79 of which were classified as having normal muscularity (NM) and 22 with low muscularity (LM). The LM group had a higher proportion of individuals aged over 70 years and with a body mass index less than 18.5. They also had lower total adipose tissue area (mean; NM = 22,4 cm^2; LM = 10,3 cm^2; p = 0,019) and total adipose tissue index (mean; NM = 8,3 cm^2/m^2; LM = 3,7 cm^2/m^2; p = 0,018). The LM group had a significantly worse survival rate (HR = 1.73; 95% CI 1.02-2.92) when compared to the NM group. The median survival was 4.4 months for the LM group and 8.4 months for the NM group. The LM group also had lower adiposity (p = 0.018). **Conclusion:** Low muscularity impacts the mortality of patients with HNCm independent of age and ECOG.

Keywords: Body composition, Oncology, Prognosis.

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177LU-PSMA IN METASTATIC CASTRATION RESISTANT PROSTATE CANCER: PRELIMINARY ANALYSIS OF A BRAZILIAN MULTICENTRIC STUDY

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Introduction/Justification: 177Lu-PSMA can be a promissor therapy in patients with metastatic castration resistant prostate cancer. **Objectives:** Investigate 177Lu-PSMA therapy in Brazilian patients with metastatic castration resistant prostate cancer (mCRPC). **Materials and Methods:** Data for this retrospective multicentric study was collected from 9 Brazilian centers from 6 federative units (SP, PE, CE, RJ, SC and DF) that performed at least two cycles of 177Lu-PSMA therapy in mCRPC. Data with skewed distribution were reported as median (min-max). Primary outcome was overall survival. Secondary outcomes was the maximal PSA response and hematological adverse events (HAE). **Results:** A total of 100 males were included, median age = 74 years old (min-max: 54 - 96 years old). 177Lu-PSMA was the fifth (median) line of therapy (min-max 2-10). A total of 333 cycles were performed with a median of 4 cycles (min-max 1-10). The mean overall survival was 12.8 months. Among the 72 patients with data available for the maximal PSA response at any time, 65% presented any PSA decline. 42% presented PSA decline ≥ 50% from baseline. 89% of patients did not present HAE or presented grades 1 or 2 HAE. Only 11% of patients presented grade 3 HAE. 0% of patients presented grade 4 HAE. **Conclusion:** 177Lu-PSMA therapy was effective and safe in the Brazilian population even with a median of 5th line of therapy (maximum 10th line). Overall survival and PSA decline ≥ 50% from baseline were similar to the literature data. Only 11% of patients presented grades 3 or 4 hematological adverse events.

Keywords: 177Lu-PSMA, Prostate cancer, therapy;.

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CONTRIBUIÇÕES DO PET/CT FDG-18F NA DETECÇÃO DE DOENÇA AVANÇADA NO CÂNCER DE MAMA

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Introdução Justificativa: O câncer de mama representa importante causa de morbimortalidade em mulheres, com significativa mudança de prognóstico se diagnosticado de forma precoce e instituída a terapêutica adequada. Alguns estudos apontam que a PET/CT FDG-18F é mais acurada que o estadiamento convencional no pré-operatório, mudando o estadiamento clínico em até 36%. A sensibilidade e a especificidade do estudo em identificar envolvimento linfonodal axilar são de 57-100% e 66-100%, respectivamente, ressaltando-se que o envolvimento microscópico (≤ 10 mm) pode não apresentar expressão ao método. **Objetivos:** O objetivo deste trabalho é avaliar a contribuição da PET-CT FDG-18F na detecção de doença avançada em exames realizados para estadiamento pré-

operatório de câncer de mama em um serviço privado de medicina nuclear. **Materiais Métodos:** Foi utilizada uma ferramenta de busca conectada ao banco de dados do RIS, usando a palavra de busca câncer de mama nos laudos de PET/CT FDG-18F realizados no período de 09 de janeiro de 2019 a 31 de outubro de 2021. A partir dos estudos encontrados, foram selecionados aqueles que tiveram a indicação de estadiamento. Com base nesses critérios, retirando-se também os estudos duplicados, de um total de 377 exames, 218 foram selecionados como amostra inicial para análise de dados. A partir dessa amostra, constatou-se que 205 (94%) estudos de PET/CT FDG-18F foram realizados no pré-operatório e 13 (6%) no pós-operatório de mastectomia parcial ou total. **Resultados:** Sendo assim, com base na amostra de 205 PET/CT FDG-18F realizadas com a finalidade de estadiamento pré-cirúrgico, observou-se que 196 (95,6%) foram exames positivos, entre os quais 24 apresentaram doença multifocal e 4 não tiveram a lesão primária identificada ao método. Ainda assim, mesmo nesses últimos casos, a PET/CT foi capaz de detectar doença extramamária. Do ponto de vista da avaliação linfonodal axilar, 134 estudos (65,5%) foram positivos, 60 (29,2%) negativos e 11 (5,3%) indeterminados. Além disso, 5 exames apresentaram acometimento axilar bilateral. O envolvimento linfonodal extra-axilar foi encontrado em 41 (20%) dos estudos, com as seguintes distribuições por cadeias envolvidas em número absoluto: supraclavicular (9), infraclavicular (6), mamária interna (22), supra e infraclavicular simultaneamente (4), mediastinais (18) e abdominais (5). Na avaliação quanto à presença de metástases à distância, foram encontrados 43 (20,9%) exames positivos. Na amostra estudada, a distribuição dos sítios de metástases foi de 19 ósseo (44,18%), 17 pulmonar (39,5%), 7 fígado (16,27%) e 1 adrenal (2,32%). Considerando que uma das principais vantagens da PET/CT FDG-18F no estadiamento do câncer de mama é a análise da doença avançada, buscou-se classificar os estádios avançados usando a 8ª edição do TNM na amostra de pacientes. Encontrou-se que 63 (30,7%) da amostra possuía estadiamento superior ao TxN3aM0, sendo 14 (6,8%) TXN3bM0, 6 (2,9%) TxN3cM0 e 43 (20,9%) TxNxM1. **Conclusão:** Os resultados mostraram que a PET/CT FDG-18F contribui significativamente para o estadiamento do câncer de mama, corroborando com a literatura no que tange à detecção de estágios avançados da doença (notadamente do ponto de vista linfonodal e metastático à distância), o que é fundamental para escolha do tratamento mais adequado.

Palavras-chave: 18F-FDG PET/CT, Breast cancer, Câncer de Mama, Estadiamento, Oncology.

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PANORAMA DOS EXAMES DE PET-CT – FDG-18F NO CÂNCER DO COLO DO ÚTERO EM UMA INSTITUIÇÃO PRIVADA DO BRASIL

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Introdução/Justificativa: Existem mais de 200 tipos de HPV no mundo, sendo 14 deles cancerígenos. Destes, os tipos 16 e 18 são responsáveis por 70% dos cânceres de colo de útero e lesões pré-cancerosas. Também podem provocar câncer em vagina, ânus, vulva, pênis e orofaringe. Em 2020, foram diagnosticados 602 mil novos casos de câncer cervical em todo o mundo, com 342 mil mortes. No Brasil, a mortalidade pela doença ente 1980 e 2020 foi de 165.087.2 O exame de PET-CT com Fluorodesoxiglicose marcada com F-18 (PET-CT 18F-FDG) pode ser fundamental para elucidação diagnóstica, estadiamento e acompanhamento de pacientes nos diferentes estágios da doença, trazendo maior acurácia e a possibilidade de detecção e localização de metástases. **Objetivos:** No Brasil, os dados oficiais revelam que cerca de 35% dos casos de câncer de colo uterino ainda são diagnosticados nas fases III e IV, ou seja, em doença avançada, sendo que a partir da fase III existe disseminação linfonodal pélvica ou para-aórtica. Diante disso, o objetivo deste estudo foi a avaliação do panorama dos exames de PET-CT 18F-FDG realizados em uma instituição privada com a indicação de câncer de colo uterino e verificar se os dados coletados são condizentes com os dados encontrados na realidade brasileira. **Materiais e Métodos:** Este estudo foi realizado utilizando-se o banco de dados de uma instituição privada. Buscados exames de PET-CT 18F-FDG com a indicação de neoplasia de colo uterino no período de 01.01.2019 a 31.08.2023. Identificados 183 estudos, sendo 36 excluídos por duplicidade e/ou indicação incorreta, permanecendo, no final, 147 exames para análise. **Resultados:** Quando avaliados por indicação, a grande maioria dos exames incluídos neste estudo foram realizados para avaliação de resposta (56,5%), seguidos de estadiamento (18,4%), suspeita de recidiva (15,6%) e seguimento (9,5%). Avaliando apenas os exames de estadiamento, a grande maioria apresentava doença avançada e apenas 3,6% tiveram exame negativo. 10,7% das pacientes possuíam doença nos estágios iniciais (menor que IIIB), 10,7 no estágio IIIB, 17,9% no estágio IIIC1, 25% no IIIC2, sendo que 3,6% já apresentavam envolvimento de órgãos pélvicos (estágio IVA) e 28,6%, de órgãos a distância (estágio IVB). Quanto à suspeita de recidiva, este trabalho considerou 23 pacientes da amostra. Deste total, 78,3% dos exames foram positivos, 8,7% indeterminados e 13,0% negativos. **Conclusão:** Os dados encontrados no nosso serviço são semelhantes aos encontrados no Brasil. As regras vigentes no nosso país não propiciam o diagnóstico precoce do câncer de colo uterino, na contramão dos protocolos atualizados nos Estados Unidos e na Europa. Não há autorização prevista para estadiamento, nem acompanhamento pelo SUS ou pelo rol da ANS. Este cenário configura sério obstáculo à detecção da doença em um estágio mais inicial, o que possivelmente pouparia custos de tratamento na doença avançada, e aumentaria a

sobrevida das pacientes, consolidando imediato benefício à saúde pública.

Palavras-chave: 18F-FDG PET/CT, Cervical cancer, Diagnóstico, Disseminação, Estadiamento.

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CONTRIBUTION OF OCCUPATIONAL THERAPY TO THE QUALITY OF LIFE IN PATIENTS WITH COLORECTAL CANCER DURING CHEMOTHERAPY

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Introduction/Justification: Occupational therapy (OT) has been recommended for hospitalized and outpatient patients, but its effects on occupational roles and quality of life in patients with cancer are uncertain. **Objectives:** This study aimed to evaluate the roles of OT as a therapeutic resource during chemotherapy for patients with colorectal cancer (CRC). **Materials and Methods:** This was a prospective, longitudinal, and quantitative study, carried out in the chemotherapy room of the Clinical Oncology Service of the General Hospital of University of Campinas from February to November 2018. Socio-demographic profile of patients was obtained from medical records, and Occupational Role Identification List, SF-36 Quality of Life Questionnaire and the FACT-F Fatigue Questionnaire were applied to patients before and after the OT intervention by the researcher responsible for the study. Four to six OT sessions were performed, depending on the number of chemotherapy cycles, and each session lasted one hour. The therapeutic interventions were making mandalas, reflecting on songs, playing bingo, playing dominoes and painting boxes. **Results:** Thirty-eight patients with CRC were enrolled in the study and 35 (92%) completed all procedures. The average age of the patients was 59 years, 58% of whom were male, undergoing neoadjuvant, adjuvant, and palliative chemotherapy. After OT intervention, there was a change in the occupational roles reported by patients. There was also a significant improvement in quality of life in the pain and functional capacity domain. Women had changes in social/family well-being and social aspects and the older they were, the lower their functional well-being. **Conclusion:** OT provided a new meaning in the performance of occupational roles and contributed to improving the quality of life of patients with CRC during chemotherapy. Acknowledgements: The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Colorectal cancer, Occupational therapy, Quality of life.

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PRELIMINARY ANTI-PROLIFERATIVE ACTIVITIES OF A PALLADIUM(II) COMPLEX OVER SQUAMOUS CELL CARCINOMA OF TONGUE

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Introduction/Justification: Oral squamous cell carcinoma is considered one of the most prevalent subtypes of head and neck cancers. Treatments include surgical resection, radiotherapy, and chemotherapy in the cases of patients with advanced squamous cell carcinoma (SCC). Cisplatin, or cis-diamminedichloridoplatinum(II), has been used for treatment of several types of cancer worldwide since 1978 including advanced head and neck SCC. The successful use of cisplatin led to the development of second-generation platinum-based drugs, with emphasis on carboplatin and oxaliplatin, which have been used for cancer treatment worldwide. Nevertheless, patients treated with platinum drugs as cisplatin are subjected to adverse effects as nephrotoxicity, and the search for new chemotherapeutic agents with reduced side effects is crucial. After the discovery of the platinum anticancer drugs, new metal-based compounds of copper, silver, gold, ruthenium, palladium and iridium were synthesized and evaluated as potential anticancer agents. Padeliporfin (Tookad®Soluble) was the first palladium(II) complex used in vascular targeted photochemotherapy for low-risk prostate cancer treatment, which also confirms the potential of use of this metal in the synthesis of new chemotherapeutic agents. In this context, our research group has dedicated efforts in the search of novel gold, silver, platinum and palladium complexes for treatment of cancer, with emphasis on SCC. One of the silver complexes with the anti-inflammatory drug nimesulide recently prepared in our group demonstrated in vitro and in vivo activity over SCC cells. **Objectives:** This study aimed to present the in vitro anti-proliferative activities over SCC of a water-soluble palladium(II) complex containing a cysteine derivative as a chelating ligand. **Materials and Methods:** SCC of tongue (SCC4 and SCC15) and a non-tumoral cell line (HaCat, immortalized keratinocyte) were used in this study. The cells were cultivated following methodology previously described in the literature. **Results:** The palladium(II) complex inhibited proliferation of SCC15 cells with a GI50 (concentration of a drug that reduces cell growth by 50%) of 40.28 μg mL 1 but low selectivity was observed when compared to HaCat cells (GI50: 28.33 μg mL 1). On the other hand, the complex did not inhibit SCC4 cell proliferation (GI50 > 250 μg mL 1). **Conclusion:** The palladium(II) complex seems to be indicated for

treatment of SCC of tongue, but further studies are envisaged to understand the selectivity of the complex over the considered SCC lines and propose its possible mechanism of action. **Acknowledgements:** This study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #309800/2021-8; #429463/2018-9), Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for the Cancer Theranostics Innovation Center (CancerThera), CEPID FAPESP #2021/10265-8), and International Atomic Energy Agency (IAEA) technical cooperation projects for development of Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Anti-proliferative activity, Oral squamous cell carcinoma, Palladium(II) complex.

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IMPAIRMENT OF THE FUNCTIONAL CAPACITY OF PATIENTS WITH ADVANCED LUNG CANCER: A PROPOSAL FOR PRACTICING PHYSICAL EXERCISES AT HOME

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Introduction/Justification: Lung cancer (LC) is a disease with high incidence, morbidity, and mortality in Brazil and around the world. Smoking plays a relevant role in the pathogenesis of CP. LC and tobacco limit lung mechanics and, consequently, gas exchange, leading to dyspnea and fatigue. The association of these symptoms with loss of weight and muscle mass secondary to protein catabolism, comorbidities and the effects of treatment limit the functional capacity of patients with LC. In turn, the reduction in patients' functional capacity favors the adoption of a sedentary lifestyle, resulting in a reduction in quality of life. Outpatient and home physical exercise protocols based on functional capacity have been successfully applied to LC patients from developed countries, but not to patients from developing countries. **Objectives:** The present study aimed to evaluate the functional capacity of patients with advanced stage LC at the Pneumology outpatient clinic of the General Hospital of the University of Campinas and propose a program of comfort measures and home physical exercises. **Materials and Methods:** The study was a cross-sectional clinical trial, approved by the Local Ethics Committee. Patients with stage III or IV non-small cell lung cancer (NSCLC), with ECOG less or equal to 2, without significant morbidities, and seen at diagnosis at the General Hospital of University of Campinas were invited to participate in the study. Patients previously treated by surgical tumor resection, chemo and/or radiotherapy or who did not want to participate in the study were excluded. Data relating to the clinical aspects of patients and pathological aspects of the tumor were obtained from medical records by the researcher responsible for the study. The functional capacity of the patients was assessed using of the six-minute walk test (6MWT) and lung function by spirometry. Comparison between groups was performed using the Mann-Whitney or Kruskal-Wallis's test. The association between categorical variables was assessed using Fisher's exact test. The linear regression test was used for multivariate analyses. **Results:** Sixty-three patients with a mean age of 65 years and a mean body mass index (BMI) of 24.4 kg/m^2 were enrolled in the study. Most patients were smokers or ex-smokers. Systemic arterial hypertension and chronic obstructive pulmonary disease were the most common comorbidities, identified in near half and a quarter of the sample, respectively. Almost 60% of the patients reported pain before the test and were medicated with analgesics before the start of the 6MWT. The patients had an average distance covered of 362.9 meters, 30% lower than the distance predicted ($p < 0.0001$). Forced vital capacity, forced expiratory volume in the first second and peak expiratory flow were also lower than predicted values ($p < 0.05$) and were indicative of ventilatory disorders. Habits, clinical and pathological aspects, such as smoking, patient's clinical condition, pain intensity, pre-existing comorbidities and tumor stage influenced the patients' functional capacity. **Conclusion:** Our patients with advanced NSCLC had a less satisfactory functional capacity than patients from developed countries. Therefore, we have created a booklet with comfort measures and recommendations for practicing physical exercises at home adapted to them. Acknowledgements: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Comfort measures, Home physical exercises, Lung cancer.

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THYROID DYSFUNCTION IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS AFTER EXTERNAL RADIOTHERAPY

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Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is the seventh leading cause of cancer in the world, and substantial morbidity and mortality have been attributed to the tumor effects. Radiotherapy (RT) alone or with chemotherapy (CHEMO) and/or surgery is a commonly used treatment but, despite its beneficial effects on tumor control, it can cause early and late adverse effects. RT can cause thyroid dysfunction (TD) in patients with HNSCC, but not all patients treated similarly develop TD. **Objectives:** The study aimed to identify TD among HNSCC patients submitted to external RT, and to identify risk factors for TD in these patients. **Materials and Methods:** This is a retrospective study focusing on early and long-term thyroid function in 285 HNSCC patients treated with RT alone or alone or combined with CHEMO and/or surgery. The patients were seen at diagnosis and follow up at the Clinical Oncology Service of the University Hospital between July 2001 and March 2016. The analysis of the thyroid function data of each patient included in study was done serially after the end of treatment, using free thyroxine (FT4) and thyroid-stimulating hormone (TSH) levels. The study was approved by the Institutional Human Research Ethics Committee (number: 2312237). **Results:** One-hundred fifty-six (54.7%) patients presented TD during follow-up, 153 (53.7%) in long-term. Subclinical hypothyroidism (SCH, 43.5%) was most common, of which 68.5% persisted SCH, 21% overt hypothyroidism, 0.8% central hypothyroidism, and 9.7% returned to euthyroidism at the study end. Mean time after RT for first TD detection was 7.2 months; 3.85 for subclinical thyrotoxicosis; 17.77 for SCH, 42.0 for long-term follow-up TD. Type 2 diabetes mellitus, tumor infiltration of lymph nodes, and no tumor resection were TD risk factors. About: One-hundred fifty-six (54.7%) patients presented TD during follow-up, 153 (53.7%) in long-term. Subclinical hypothyroidism (SCH, 43.5%) was most common, of which 68.5% persisted SCH, 21% overt hypothyroidism, 0.8% central hypothyroidism, and 9.7% returned to euthyroidism at the study end. Mean time after RT for first TD detection was 7.2 months; 3.85 for subclinical thyrotoxicosis; 17.77 for SCH, 42.0 for long-term follow-up TD. Type 2 diabetes mellitus, tumor infiltration of lymph nodes, and no tumor resection were TD risk factors. About SCH progression risk, a direct association with TSH was observed, all patients with TSH $\geq$ 7.5mIU/mL had primary hypothyroidism/SCH, whereas 19.5% with TSH $<$ 7.5mIU/mL persisted euthyroid in long-term follow-up. Oral cavity tumors were associated with euthyroidism/SCH; pharynx/larynx with overt hypothyroidism. **Conclusion:** The data indicate the need for frequent monitoring of thyroid function in HNSCC patients treated with RT, particularly in those with type 2 diabetes mellitus, lymph nodes infiltrated by the tumor, and not submitted to surgical tumor resection. Acknowledgements: This study was supported by grants from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Head and neck squamous cell carcinoma, Radiotherapy, Thyroid dysfunction.

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DOES PET/CT WITH 18F-FLUOROESTRADIOL (18F-FES) CONTRIBUTE TO THE ASSESSMENT OF BREAST CANCER COMPARED TO FLUORINE-2-D-DEOXYGLUCOSE (18F-FDG)?

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Introduction/Justification: While fluorine-2-D-deoxyglucose (18F-FDG) PET/CT is commonly used in the assessment of breast cancer, it has limitations, such as its inability to distinguish it from inflammatory and infectious conditions. In this context, another molecular imaging tool, PET/CT with 18F-fluoroestradiol (18F-FES), is emerging as a promising alternative. Preliminary data from the literature already shows comparable sensitivity between these exams in breast cancer with estrogen receptors. In addition, the latter seems relevant because it correlates with the concentration of these receptors, shows their expression non-invasively and suggests a theoretical gain in specificity. **Objectives:** To evaluate whether 18F-FES PET/CT provides supplementary information to clinical reasoning when compared to 18F-FDG PET/CT in the assessment of breast cancer. **Materials and Methods:** A retrospective, observational, and comparative analysis was performed using information stored in the databases of a private institution regarding 18F-FES PET/CT scans performed in the context of breast cancer. The selection criteria required a complementary scan using 18F-FDG, which was met by thirteen out of the 14 tests found, however, one study was excluded from the analysis because its indication could not be precisely classified with the available data. **Results:** The twelve selected tests were carried out between August 2022 and March 2024, on females with a mean age of 62.16 years. The time interval between studies using positron-emitting radioisotopes (18F-FES and 18F-FDG) ranged from 1 to 29 days. The administered activity of 18F-FES varied from 4.0 to 10.0 mCi, and the interval between administration and image acquisition ranged from 45 to 130 minutes. Among the findings showing 18F-fluoroestradiol uptake, breast lesions and thoracic lymph nodes were the most common, present in six and five reports, respectively. The indications for the scans varied, with ten intended for staging/restaging and two

to address clinical uncertainty about the presence of estrogen receptors. In 40% of the staging/restaging subgroup, 18F-fluoroestradiol contributed to the clinical reasoning. 18F-FES showed uptake in lymph nodes without hypermetabolism and was able to provide diagnostic specificity, either by raising suspicion in a finding initially taken as benign or by predicting false-positive metabolic findings due to the absence of estrogen receptors. Regarding the evaluation of hormone receptor expression status, 18F-fluoroestradiol has supported a proposed change in the tumoral immunohistochemistry of a lesion non-invasively. **Conclusion:** 18F-FES PET/CT appears to provide additional relevant information in breast cancer, but future studies should evaluate the method's impact on clinical management.

Keywords: 18F-FDG PET/CT, breast cancer, FES.

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COMPARISON OF 18F-FDG AND 18F-PSMA PET/CT IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Introduction/Justification: Lung cancer remains a major global cause of mortality. While 18F-FDG PET/CT is widely utilized for detection, staging, and monitoring, detecting increased glucose metabolism in tumor cells, it lacks theranostic potential. The prostate-specific membrane antigen (PSMA) tracer, initially linked to prostate cancer, is also recognized as a marker of neoangiogenesis, accumulating in various neoplasms and showing promising theranostic capabilities. **Objectives:** This study aims to compare the uptake patterns of 18F-FDG and 18F-PSMA in primary and metastatic lesions of non-small cell lung cancer. **Materials and Methods:** Four male patients diagnosed with non-small cell lung cancer (including two adenocarcinomas, one squamous cell carcinoma, and one unspecified type), aged between 58 and 71 years, underwent PET/CT imaging. 18F-FDG PET/CT scans were performed 60 minutes after intravenous administration of 0.1 mCi/kg of 18F-FDG, while 18F-PSMA PET/CT scans were obtained 90 minutes after intravenous injection of 0.1 mCi/kg of 18F-PSMA. Imaging data were analyzed by two nuclear medicine physicians and one radiologist. The maximum standardized uptake value (SUVmax) of each lesion was measured for both radiotracers in the primary tumor, lymph nodes, and metastatic sites identified through visual analysis, considering values obtained above the cardiac blood pool measured in the left atrium. **Results:** A total of 100 lesions were detected, with 82 identified using 18F-FDG and 92 using 18F-PSMA. Eight lesions were exclusively detected by 18F-FDG, while 14 were only identified by 18F-PSMA. The median SUVmax of lesions in 18F-FDG and 18F-PSMA images was 5.3 (1.7 – 25.0) and 3.7 (0.7 - 12.4), respectively. Brain lesions were more readily identified on 18F-PSMA images, whereas liver lesions were more notable on 18F-FDG images due to the intense physiological uptake of 18F-FDG and 18F-PSMA in the brain and liver, respectively. **Conclusion:** Both 18F-FDG-PET/CT and 18F-PSMA-PET/CT have the ability to identify most lesions of non-small cell lung cancer. Although 18F-PSMA images detected a greater number of lesions, the uptake intensity is generally higher with 18F-FDG. These findings suggest that the two radiopharmaceuticals may have complementary roles in lung cancer by independently detecting lesions with higher glycolytic activity or greater neoangiogenesis, or both simultaneously, which could contribute to a more personalized approach in managing these patients. The results also suggest a possible theranostic approach in selected patients with high uptake of PSMA. Further investigations involving a larger patient cohort are essential to validate these findings.

Keywords: Lung cancer, PET/CT, PSMA-18F, PSMA-68Ga, Theranostic.

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COMPARISON OF 68GA-PSMA AND 18F-FDG-PET/CT IN THE ASSESSMENT OF DESMOID TUMORS

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Introduction/Justification: Recently, the tracer Prostate Specific Membrane Antigen (PSMA), which can be labeled with the radioisotopes 68Ga or 18F, has been commercially

introduced. Theoretically, as the name suggests, it is a substance specific to the membrane of prostate cells and prostate cancer. However, several studies have shown that it is also a marker of neoangiogenesis, leading to its uptake in various other neoplasms and benign diseases. **Objectives:** This study aims to evaluate the utility of radiolabeled PSMA in detecting desmoid tumors, comparing it to 18F-luorodeoxyglucose (FDG). **Materials and Methods:** Three participants with a confirmed diagnosis of desmoid tumor underwent PET/CT examinations with 18F-PSMA and 18F-FDG, with a maximum interval of 3 days between examinations. Images were visually compared lesion by lesion and the maximum standardized uptake value (SUV) was calculated for each lesion and each radiopharmaceutical. **Results:** All lesions presented uptake of both 68Ga-PSMA and 18F-FDG. In the first patient, 3 lesions were identified: a mass adjacent to the pancreas measuring 5.4 cm (FDG: SUV = 2.0) (PSMA: SUV = 8.2), a mass in the right iliac fossa measuring 7.7 cm (FDG: SUV = 3.8) (PSMA: SUV = 5.7), and another involving the duodenojejunal transition measuring 4.1 cm (FDG: SUV = 1.9) (PSMA: SUV = 3.7). In the second patient, a mass was identified adjacent to the head and uncinate process of the pancreas measuring 9.2 cm (FDG: SUV = 9.8) (PSMA: SUV = 6.1). In the third patient, an irregular retroperitoneal mass was identified at the level of the aortic bifurcation (FDG: SUV = 2.3) (PSMA: SUV = 2.4). **Conclusion:** Desmoid tumors can demonstrate uptake of both 68Ga-PSMA and 18F-FDG. The intensity of tracer uptake in the lesions is variable, with some showing greater uptake of FDG, others of PSMA, suggesting a potential complementary role for these radiotracers in desmoid tumors.

Keywords: Cancer, Desmoid tumor, PET/CT, PSMA-18F, PSMA-68Ga.

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INFLUENCE OF A CONVENTIONAL CHELATOR-MODIFIED ANTI-INTEGRIN PEPTIDE ON PROLIFERATION AND MIGRATION OF HEAD AND NECK CANCER CELLS

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Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) represents a serious health problem worldwide. Approximately 75% of patients with HNSCC have locally advanced disease at diagnosis, and the therapy for those cases involves chemoradiation or induction chemotherapy, in which cisplatin is included despite of its substantial side effects. 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 HNSCC. Overexpressed in HNC, integrins are transmembrane proteins that play essential roles in cell proliferation and migration. Therefore, integrin inhibition may be a potential targeted therapy for HNC patients. **Objectives:** The study aimed to evaluate the effects of the DOTA-C6-anti-integrin peptide on HNSCC cell lines proliferation and migration, as an initial step for HNSCC theranostic development. **Materials and Methods:** The anti-proliferative activity of the DOTA-C6-anti-integrin peptide (0.01nM - 100μM) was assessed against FaDu and SCC-25 cells by considering the cell amounts at baseline and 48h after exposure (two untreated control groups). All 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 FaDu cells and FaDu cells treated with the DOTA-C6-anti-integrin peptide (1, 10, and 100μM) using the wound-healing assay. Wound cells were photographed immediately (0h) and after 16h, 24h, and 40h. 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). **Results:** At the tested concentration range, the DOTA-C6-anti-integrin peptide did not affect proliferation of FaDu or SCC-25 cells. In FaDu cells, the DOTA-C6-anti-integrin peptide significantly ($p < 0.05$) inhibited migration in comparison to untreated cells, independent on sample concentration (1, 10, and 100μM) or time exposure (16, 24, or 40 h). **Conclusion:** Despite the lack of anti-proliferative effect, the DOTA-C6-anti-integrin peptide inhibited migration in FaDu cells. As cell migration is an important process in HNSCC progression, our data present preliminary evidence that the DOTA-C6-anti-integrin may be used in development of theranostic agents for HNSCC. **Acknowledgements:** The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNP #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 Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Cell migration, Head and neck cancer, Theranostic.

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COMPARISON OF PET/CT IMAGES WITH 18 F-FDG AND 18 F-PSMA-1007 IN RELAPSED ADENOID CYSTIC CARCINOMA

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Introduction/Justification: Adenoid cystic carcinoma (ACC) is a tumor of the salivary glands, characterized by insidious growth, recurrences, and distant metastases. **Objectives:** This study aimed to describe the findings of PET/CT images performed with 18 F-FDG (FDG PET/CT) and 18 F-PSMA-1007 (PSMA PET/CT) in patients with relapsed ACC to verify whether any of these studies are more suitable for identifying local recurrence and distant metastases. **Materials and Methods:** Patients were submitted to restaging PET/CT studies with 18 F-FDG and 18 F- PSMA-1007 with a 24-hour interval between exams before treatment. Two nuclear medicine physicians compared imaging findings. **Results:** Patient 1. P.A.C., a 29-year-old female, was diagnosed with ACC of the parotid in 2016. She underwent total parotidectomy and RT. In 2021, a chest computed tomography (CT) identified lung nodules, and the patient underwent resection of the largest lesions. In 2024, the patient was submitted to restaging images with FDG PET/CT that were negative for metastases, but PSMA PET/CT images identified mild PSMA uptake in two pulmonary nodules (0.8 cm, SUV = 2.2; 0.9 cm, SUV = 3.4) suspicious for ACC metastases. The patient remains asymptomatic under supervised follow-up. Patient 2. L.C.O., a 49-year-old male with newly diagnosed ACC in the salivary gland, underwent tumor resection and RT in 2010. The patient recurred in lungs and skull and was submitted to resection of the lung nodules and total skull radiotherapy (RT). In 2022, the patient underwent RT to a metastasis in the 5th lumbar vertebrae. In 2023, FDG PET/CT revealed hypermetabolism in multiple pulmonary nodules (the largest measuring 1.8 cm, SUV = 13.4) and in the L5 vertebrae (SUV = 8.5), consistent with metastases. The PSMA PET/CT showed only mild PSMA uptake in the pulmonary nodules (the largest nodule had a SUV = 4.7) and similar PSMA uptake (as FDG) in L5 vertebrae (SUV = 8.7). The patient is currently asymptomatic. Patient 3. P.C.S., a 46- year-old male, was diagnosed with ACC in the parapharyngeal space and underwent surgical resection followed by RT in 2008. In 2022, a chest CT identified lung metastases, the largest nodule with 3.8 cm. In 2023, a FDG PET/CT demonstrated hypermetabolic lung nodule metastases (the largest measuring 3.0 and 3.8 cm; SUV = 12.3 and SUV = 6.1, respectively). The FDG PET/CT also demonstrated multiple liver nodules (the largest measuring 2.7 cm) without FDG uptake, suspicious for metastases. A PSMA PET/CT showed PSMA uptake in the same lung nodules, however incongruent when compared to FDG uptake: the two nodules measuring 3.0 and 3.8 cm had SUVs of 5.2 and 8.8, respectively). The patient currently reports dyspnea during moderate-intensity physical activity. **Conclusion:** The data show heterogeneity in FDG PET/CT and PSMA PET/CT findings in relapsed ACC. Combining both PET/CT radiotracers can provide additional information for monitoring patients. PSMA PET/CT has the advantage of the possibility of a theranostic approach. **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 (Cancer Theranostics Innovation Center, CEPID FAPESP #2021/10265-8), and International Atomic Energy Agency (IAEA) technical cooperation projects for development of Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Adenoid cystic carcinoma, FDG PET/CT scan, PSMA PET/CT scan.

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EVALUATION IN VITRO OF THE GOLD(I) COMPLEX WITH TRIPHENYLPHOSPHINE AND 4-DIMETHYLAAMINEPYRIDINE AS LIGANDS IN SKIN CANCER

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Introduction/Justification: Closely related to high UV exposure and comprising basal cell carcinoma, squamous cell carcinoma (SCC), and melanoma, skin cancer is the most prevalent tumor in the world. Cisplatin has been used for treatment of patients with skin squamous cell carcinoma (SSCC) with low response rate and pronounced adverse effects. Thus, the search for new chemotherapeutic agents for patients with SSCC or melanoma is required, and gold complexes have been explored as potential anticancer drugs. Targeting thioredoxin reductase or thiol-rich proteins, many gold complexes can induce cell death by reactive oxygen species. **Objectives:** Our study aimed to evaluate the in vitro anti-proliferative effects of a gold(I) complex with triphenylphosphine and 4-dimethylaminopyridine as ligand. **Materials and Methods:** The gold (I) complex was synthesized at the Department of Inorganic Chemistry, Institute of Chemistry, University of Campinas. Melanoma (UACC-62), squamous cell carcinoma of tongue (SCC4 and SCC15), and a non-tumoral cell line (HaCat, immortalized keratinocyte) were grown in complete medium

[RPMI-1640 (Gilco®) supplemented with 5% fetal bovine serum (Gilco®) and 1% penicillin:streptomycin mixture (1000 U/mL:1000 μg/mL, Vitrocell, Brasil)] at 37 °C and 5% CO2. Each cell line (100 μL/well, in 96-well plates, 4 - 6 x10^4 cel/ml) was exposed to the gold (I) complex (100 μL/well, 0.25 to 250 μg/mL, in triplicate) and incubated for 48 h. Doxorubicin (100 μL/well, 0.025 to 25 μg/mL, in triplicate) was used as a positive control. Before (T0) and after (T1) sample addition, cells were fixed with 50% trichloroacetic acid (TCA, 50 μL/well), and cell viability was determined using the sulforhodamine B protocol at 540 nm with a microplate reader spectrophotometer (VersaMax, Molecular Devices). The difference between T0 and T1 absorbance values represented 100% of cell growth, and the proliferation (%) of each cell line in the presence of each sample concentration was calculated accordingly. Effective concentration representing the sample concentration required to promote 50% growth inhibition (GI50) for each cell line was calculated by sigmoidal regression using Origin 8.0 software. **Results:** The gold(I) complex showed potent anti-proliferative effect against UACC-62 cells (GI50 < 0.25 μg mL-1) being less active against SCC15 (GI50 ≈ 2.5 μg mL-1) and SCC4 (GI50: 10.2 μg mL-1) cells. Moreover, the anti-proliferative effect of gold(I) complex showed a good selectivity being almost 10x less active against HaCaT cells (GI50 ≈ 2.5 μg mL-1) in comparison to melanoma cells. **Conclusion:** This data indicated gold(I) complex with triphenylphosphine and 4-dimethylaminopyridine as ligands as a promisor candidate for treatment of patients with melanoma. Further in vitro and in vivo evaluations is required to evaluate the mechanism of action and toxicity of the complex. **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 #2016/07729-4; #2023/09738-4; Cancer Theranostics Innovation Center, (CancerThera), CEPID FAPESP #2021/10265-8), and International Atomic Energy Agency (IAEA) technical cooperation projects for development of Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Antiproliferative effect, Gold(I) complex, Melanoma, SSCC.

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COMPARISON OF 18 F-FDG AND 18 F-PSMA-1007 PET/CT IN ADVANCED LOCOREGIONAL SQUAMOUS CELL CARCINOMA OF HEAD AND NECK: PRELIMINARY RESULTS

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Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is a health problem worldwide. Most patients with HNSCC have locally advanced disease, and progression or relapse of the tumor after treatment are common events. Imaging exams to assess the existence and/or extent of the tumor play a crucial role in managing these patients. 18 F-FDG and 18 F-PSMA-1007 are markers of glycolytic activity and neo angiogenesis, respectively. The PET/CT images performed with 18 F-FDG (FDG PET/CT) have unequivocal contribution in HNSCC, but the importance of the images with 18 F-PSMA- 1007 (PSMA PET/CT) in tumor is still unclear. **Objectives:** The aim of this study was to describe the findings of FDG PET/CT and PSMA PET/CT in patients with advanced locoregional HNSCC at diagnosis or relapse with the purpose of verifying whether any of these exams is more suitable for detecting the tumor. **Materials and Methods:** Patients with advanced locoregional HNSCC at diagnosis or relapse of HNSCC were enrolled in study. Patients who underwent surgical resection of the tumor or treatment with radio chemotherapy in the last six months were excluded from the study. All patients were submitted to FDG PET/CT and PSMA PET/CT with a 24-hour interval between exams. Two nuclear medicine physicians and one radiologist analyzed the images. Comparisons between groups were analyzed by t-test, and differences were significant when p-values were < 0.05. **Results:** Five patients (three patients at diagnosis and one relapsed patient) were analyzed by both PET/CT images. The median age of patients was 60 years old (variation: 52-75), four were males and 1 was female. Most patients were smokers/ex- smokers and/or drinkers/ex-drinkers, had good performance status (ECOG 0), and presented tumors at stage IV. The primary tumor was localized in oropharynx/larynx (with lymph node isease), and relapses were seen mainly in lungs, liver, and bone. The HNSCC lesions were typically characterized by FDG uptake, but most lesions also exhibited varying degrees of PSMA uptake. In primary tumors and lymph node disease, mean ± SD and median (min-max) values of SUV found with FDG PET/CT scan at 1 hour were 21.1 ± 7.6 and 21.0 (14.0-33.1) and 9.0 ± 6.1 and 7.2 (2.7-18.8), respectively. For PSMA PET/CT scan, mean ± SD and median (min-max) values of SUV at 1 hour in primary tumors and lymph nodal disease were 4.0 ± 1.0 and 3.7 (2.9-5.3) and 9.0 ± 6.1 and 7.2 (2.7-18.8), respectively. The values of FDG uptake were higher than values of PSMA uptake in both primary tumors ($p = 0.001$) and lymph nodes ($p = 0.02$). **Conclusion:** HNSCC lesions were better detected by PET/CT images with 18F-FDG than with 18 F-PSMA-1007. The uptake of both markers in most tumors indicates that glycolytic activity and neoangiogenesis occur in HNSCC, enabling a more personalized approach in patient management. Nevertheless, the current study's sample size was small to draw conclusive results. **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 (Cancer Theranostics Innovation Center, CancerThera, CEPID FAPESP #2021/10265-8), nd International Atomic

Energy Agency (IAEA) technical cooperation projects for development of Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Head and neck cancer, PET/CT scan, PSMA PET/CT scan;.

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TNFRSF1B GENE VARIANTS IN RISK AND CLINICOPATHOLOGICAL ASPECTS OF PATIENTS WITH CUTANEOUS MELANOMA

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Introduction/Justification: Cutaneous melanoma (CM) is a low incidence tumor worldwide but is associated with high mortality. Skin exposure to ultraviolet radiation from sunlight and genetic factors are related to carcinogenesis of CM. CM is also one of the most immunogenic types of solid tumors, eliciting an active antitumor response. Regulatory T lymphocytes (Tregs) modulate the destruction of abnormal cells by binding tumor necrosis factor (TNF) to /tumor necrosis factor receptor 2 (TNFR2) on their surfaces. Treg depletion reduced the number of metastases in TNFR2-deficient animals. Basal levels of TNFR2 altered relapse-free survival in CM patients, and antibodies targeting TNFR2 on Tregs are seen as promising agents to promote tumor immune-mediated control. TNFR2 is encoded by the polymorphic gene TNFRSF1B. Therefore, the ability to destroy abnormal cells varies among individuals, and may lead to distinct risk for melanoma and distinct clinicopathological aspects in CM patients. **Objectives:** This study aimed to analyze the roles of TNFRSF1B c.587T>G, c.*188A>G, c.*215C>T, and c.*922C>T single nucleotide variants (SNVs) in risk of CM and in clinicopathological aspects of CM patients. **Materials and Methods:** All consecutive patients with CM diagnosed at the General Hospital of the University of Campinas and the Cancer Hospital of Barretos from November 2018 to July 2000 were enrolled in study. Blood donors from the Hematology and Hemotherapy Center served as controls of the study. Clinicopathological characteristics of patients and controls were obtained from the medical records. Genotyping was performed by real-time polymerase chain reaction (RT-PCR) in DNA extracted from peripheral blood leukocytes of patients and controls. Differences between groups of patients were analyzed using Fisher's or chi-square test, and multiple comparisons were adjusted by the Bonferroni method. **Results:** A total of 433 patients and 502 controls were enrolled in the study. The TNFRSF1B c.587TT genotype was more common in patients than in controls (63.5 versus 61.6%, $p = 0.04$); individuals with c.587TT genotype were under 1.41 (CI95%: 1.01-1.98)-fold increased risk for CM than those with the remaining genotypes. An excess of the c.587TT genotype was seen in patients aged $\leq$ 54 years compared to older patients (69.5 versus 57.0%, $p = 0.007$). No associations of genotypes with pathological aspects of tumors were found in the study. **Conclusion:** Our findings show, for the first time, that TNFRSF1B c.587T>G can affect the risk and age of onset of CM. Acknowledgements: The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES #88887.337514/2019-00), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2019/09168-8).

Keywords: Clinicopathological aspects, Melanoma, Risk.

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COMPARISON BETWEEN PET/CT WITH 18F-PSMA-1007 AND WITH 18F-FDG IN MUSCLE-INVASIVE BLADDER UROTHELIAL CARCINOMA

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Introduction/Justification: Muscle-invasive bladder cancer (MIBC) presents high rates of metastasis and recurrence, making its monitoring challenging. PET/CT with 18F-FDG is relevant in evaluating this disease, although its urinary excretion makes the analysis of some cases difficult, even when diuretics are used. Prostate-specific membrane antigen (PSMA) is also expressed in neoangiogenesis of MIBC, making it a potential disease marker. In particular, the radiotracer 18F-PSMA-1007, unlike other analogs of this molecule, is predominantly excreted through the biliary tract, thereby facilitating the evaluation of the urinary tract. **Objectives:** The aim of this study was to compare PET/CT with 18F-FDG and with 18F-PSMA-1007 in evaluating MIBC. **Materials and Methods:** Four male patients (ages 57-73 years) were prospectively studied, undergoing PET/CT 60 minutes after intravenous administration of 0.11 mCi/kg 18F-FDG and 5 and 90 minutes after intravenous injection of 18F-PSMA-1007. Additional late (2h) pelvic images were obtained with both tracers after intravenous furosemide injection. Images were analyzed by 2 experienced nuclear physicians and 1 radiologist. The maximum standardized uptake value (SUVmax) of each lesion was measured

for both radiotracers. **Results:** 18F-PSMA-1007 uptake in bladder lesions and regional lymph nodes progressively increased between 5, 90 minutes and 2 hours. A total of 11 lesions were identified in the 4 patients using 18F-PSMA-1007 and 9 using 18F-FDG. Two patients had undergone transurethral resection and had no active macroscopic lesions in the bladder. 18F-PSMA-1007 detected bladder lesions in the other 2 patients (SUVmax = 9.8 and 23.4), while FDG detected only 1 (SUVmax = 30.0), with the other lesion indistinguishable from radioactive urine, even after diuretic administration. Both tracers detected lymph node metastases in 3 patients (SUVmax = 4.1 to 15.8, and 9.5 to 18.3, respectively, for 18F-PSMA-1007 and 18F-FDG), and bone metastasis in 1 patient (SUVmax = 11.1 and 10.1 for 18F-PSMA-1007 and 18F-FDG, respectively). Two patients had pulmonary inflammatory/infectious processes that were FDG-avid but not 18F-PSMA-1007-avid. **Conclusion:** PET/CTs with 18F-FDG and 18F-PSMA-1007 appear to have similar sensitivities for MIBC lesions. Due to lower uptake in inflammatory processes, 18F-PSMA-1007 appears to have higher specificity and, due to significantly lower urinary excretion than 18F-FDG, may be more favorable for evaluating the primary bladder lesion. The significant uptake of 18F-PSMA-1007 in MIBC lesions raises the possibility of theranostic approach in selected patients.

Keywords: 18F-FDG PET/CT, bladder cancer, PSMA PET;.

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COMPARISON OF IBI AND PBI CALCULATED FOR 68GA-PSMA AND 18F-FDG IN MULTIPLE MYELOMA PATIENTS

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Introduction/Justification: The benefits of using 18F-FDG PET/CT for staging and managing treatment in patients with multiple myeloma (MM) are extensively documented. Recent studies indicate that 68Ga-PSMA PET/CT is also an excellent marker for MM lesions and may complement 18F-FDG due to the significant genetic heterogeneity observed in these patients' lesions. The involvement of bone tissue stands out as one of the most critical aspects of MM. To quantify this involvement, two quantitative parameters have recently been proposed: Percentage of Bone Involvement (PBI) and Intensity of Bone Involvement (IBI). **Objectives:** This study aims to compare PBI and IBI in 68Ga-PSMA and 18F-FDG PET/CT images for multiple myeloma patients. **Materials and Methods:** Fifteen patients were included in the study, 8 men (53.3%), with a mean age of 66.7 ± 10.7 years. The patients underwent 68Ga-PSMA and 18F-FDG PET/CT scans with a maximum interval of 8 days between images (median 4 days). The bone tissue was segmented in the images based on the Hounsfield scale of the CT image, followed by processing for closing of the volume of interest (VOI). Both PBI and IBI were calculated for the two radiotracers, with the liver SUV used as a reference for 18F-FDG and the left atrium as a reference for 68Ga-PSMA. Spearman's rank-order correlation assessed the relationship between PBI and IBI data. **Results:** On average, PBI values were higher for 68Ga-PSMA than for FDG, at 3.07% ± 2.5% and 1.96% ± 3.8%, respectively. The mean IBI values were similar for both radiotracers: 0.08 ± 0.13 for 18F-FDG and 0.08 ± 0.09 for 68Ga-PSMA. The median IBI calculated for 68Ga-PSMA was 0.05, higher than the 0.01 found for 18F-FDG. Despite the similarity in average values between 68Ga-PSMA and 18F-FDG, the maximum PBI and IBI values were found in different patients for both radiotracers. Additionally, the Spearman test did not indicate correlation between the variables: ($r = 0.39$; $p = 0.16$) for PBI and ($r = 0.41$; $p = 0.13$) for IBI. **Conclusion:** The average and maximum values of PBI and IBI for 68Ga-PSMA and 18F-FDG are close. However, no correlation was found between them, highlighting that the heterogeneous genetic profile of the disease results in different uptake patterns for both radiotracers.

Keywords: FDG, IBI, multiple myeloma, PSMA.

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18F-FLUORIDE PET/CT vs 18F-PSMA-1007 TO DETECT BONE METASTASES IN PROSTATE CANCER – A HEAD-TO-HEAD PROSPECTIVE COMPARISON

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Introduction/Justification: There have been no head-to-head prospective studies comparing the ability of 18F-Fluoride PET/CT and 18F-PSMA-1007 PET/CT to detect bone metastases due to prostate cancer. So, this study aims to investigate the capacity of 18F-PSMA-1007 to detect bone metastases compared to the reference standard (18F-Fluoride PET/CT) in PCa patients, considering mainly the presence or absence, number and biodistribution of lesions. **Objectives:** This prospective study aimed to compare the ability of 18F-PSMA-1007 PET/CT and 18F-Fluoride PET/CT to detect bone metastases. **Materials and Methods:** Twenty-eight patients with prostate cancer biochemical recurrence were submitted to both 18F-PSMA-1007 PET/CT and 18F-fluoride PET/CT studies. These two radiotracers evaluated the presence or absence, number of lesions, body and bone localization, lesion pattern, and probability of malignancy. **Results:** Twenty-eight patients with prostate cancer biochemical recurrence, mean age of 70.8 ± 8.7 years; Gleason score = 7.72 ± 1.23 and the mean total PSA = 50.2 ± 183.9 ng/mL were included. On a per-patient basis, considering that 18F-Fluoride PET/CT is the gold standard, the 18F-PSMA-1007 PET/CT presented a concordance rate of 96.43%, sensitivity (S) of 92.3%, specificity (E) of 100%, predictive positive value (PPV) of 100% and predictive negative value (PNV) of 93.80% on lesion detection. Evaluating the number of lesions, 18F-PSMA-1007 PET/CT determined a PPV of 91.8% and sensitivity of 86.5%. Bone localization in 18F-Fluoride and 18F-PSMA-1007 were predominant in the dorsal spine (34.62%/62.65%), ribs (32.69%/32.65%)and pelvis (9.62%/12.24%), respectively. Both studies had a concordant rate of 80.76% on rib evaluation, the most conflicting site of uptake between the methods in actual literature. **Conclusion:** 18F-PSMA-1007 has the same ability as 18F-Fluoride to detect PCa bone metastasis in biochemical recurrence, with concordance of 96,43% and 80,00% on a per-patient and per-lesion evaluation, respectively. Both studies demonstrated predominancy of sclerotic and medullar lesions, located preferentially on dorsal spine and ribs, being the last one concordant in 80,76% of studies.

Keywords: Bone metastasis, Fluoride PET/CT, Prostate cancer, PSMA PET/CT, 18F-PSMA-1007.

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COMPARISON OF PET/CT IMAGES WITH 18F-FDG AND 18F-PSMA-1007 IN MUSCULOSKELETAL TUMORS TO EVALUATE THE POTENTIAL OF THERANOSTICS APPROACH

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Introduction/Justification: Sarcomas are malignant tumors in the bone, cartilage, fat, muscles, and vessels. Sar- comas are highly heterogeneous due to the wide variety of histological subtypes and various ana- tomical locations, and thus, the diagnosis and management of these tumors are challenging. Beyond sarcomas, the musculoskeletal system is a frequent site of metastatic tumors and multiple myeloma with lesions that present difficult local control. Imaging exams such as MRI and 18F-FDG (FDG PET/CT) to assess the extent of these tumors play a crucial role in managing these patients. However, PET/CT imaging with 18F-PSMA-1007 (PSMA PET/CT) may be a more interesting diagnostic marker due to the potential Theranostics implications. **Objectives:** This study aimed to compare the performance of FDG PET/CT and PSMA PET/CT images in patients with advanced-stage unresectable recurrent and metastatic musculoskeletal tumors. **Materials and Methods:** Patients underwent FDG PET/CT and PSMA PET/CT imaging with a 24-hour interval be- tween studies. Two nuclear medicine physicians compared imaging findings. **Results:** Eight patients underwent FDG PET/CT and PSMA PET/CT images. In five patients, PSMA uptake was higher than FDG uptake. The highest PSMA uptake occurred in a giant cell recurrent sacral tumor of a 27-year-old male patient; the SUVs for PSMA and FDG were 100 and 16, respectively. A 58-year-old male patient with osteolytic metastasis from renal cell carcinoma in the right scapula presented PSMA uptake higher than FDG (SUVs = 40 and 11, respectively). A recurrent spin- dle cell neural tumor in the upper limb of a 69-year-old male presented PSMA uptake also higher than FDG (SUVs = 27 and 8, respectively). A myxofibrosarcoma mass in the distal right leg of a 61- year-old female presented higher PSMA uptake slightly higher than FDG uptake (SUVs = 18 and 10, respectively). Interestingly, two patients with chordomas had heterogeneous PSMA and FDG up- take. The PSMA PET/CT of a 65-year-old male patient presenting multiple metastases from chor- doma with soft tissue invasion showed uptake higher than FDG in all lesions; the highest SUV was a lesion in the right acetabulum: PSMA SUV = 32 and FDG SUV = 19. This patient presented PSMA-avid additional sites of metastases in mediastinal lymph nodes and the right hepatic lobe, while FDG uptake was minimal in these metastases. In contrast, an FDG PET/CT of a 54-year-old male with a large recurrent chordoma (30x24 cm mass) extending from the level of L4 to the proximal left thigh presented FDG uptake higher than PSMA uptake (SUVs = 31 and 9, respectively). Also, FDG uptake of two patients (52-year-old males) with desmoid tumors in the upper limb was higher than PSMA uptake, although uptake of both radiotracers was low: PSMA SUVs of 3 and 5, and FDG SUVs of 4 and 7. **Conclusion:** The study results show the potential advantage of using PSMA PET/CT and FDG PET/CT to provide additional

information for monitoring patients and combining therapies, especially as PSMA PET/CT demonstrated more extensive disease. PSMA PET/CT has the advantage of the possibility of a Theranostic approach.

Keywords: Musculoskeletal tumors, PET FDG, PET PSMA, Theranostic.

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EVALUATION OF METABOLIC QUANTITATIVE VARIABLES AND QUALITATIVE/VISUAL PET/CT IN PATIENTS WITH RECTAL CANCER WHO ACHIEVED COMPLETE AND INCOMPLETE RESPONSE AFTER NEOADJUVANT RADIOCHEMOTHERAPY

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Introduction/Justification: Patients diagnosed with advanced rectal cancer (RC) are often submitted to neoadjuvant chemoradiotherapy (NACRT) treatment. There is no ideal imaging tool to measure the response of tumor after treatment. **Objectives:** The aim of this study was to evaluate the metabolic parameters obtained by FDG PET/CT, before and after NACRT. **Materials and Methods:** This retrospective study analyzed 518 patients with advanced RC. We divided patients in 2 groups: the ones who achieved a complete clinical response after treatment (good responder group) and the ones who did not achieved complete response (poor responder group). All patients underwent pre-treatment and post-treatment FDG PET/CT, with the post-treatment scan performed on average 19 weeks after treatment completion. Among the exclusion criteria were patients who began therapy before pre-treatment PET/CT and patients who did not have both studies, pre and post treatment. We included 37 patients in the good responder group who met all inclusion criteria and were selected for analysis, and 36 patients in the poor responder group. FDG PET/CT was analyzed by two nuclear medicine physician, and qualitative and quantitative analysis were performed. We used a visual response score (VRS) in qualitative analysis: grade 0 – (not reduce/progress) grade 1 (≤ 33% reduction), grade 2 (> 33% to 66% reduction), grade 3 (> 66% reduction), and grade 4 (no uptake after treatment). The following quantitative parameters were analyzed: SUV, MTV, and TLG, with ROIs drawn with a fixed threshold of 41% and a variable threshold which determined the best delimitation of the tumoral area (best fit value). **Results:** In visual analysis of good responders group the majority of patients had a VRS of grade 4 (62%) and grade 3 (33%). For poor responders group, 45.9% patients had a VRS grade 3 , 32.4% grade 2, 16.2%grades 0 and 1 and only 5.4% in grade 4. The average reductions in the analyzed variables were calculated: For good responders there was a reduction of 83% (SUV-mean with 41%); 68% (SUV-mean - BVF); 84% (TLG -41%); 94% (TLG- BVF); 7.29% (MTV-41%); 78% (MTV- BVF). For poor responders had a lower response rate: 51% (SUV-mean with 41%); 41% (SUV-mean - BVF); 63% (TLG -41%); 75% (TLG- BVF); 37 (MTV-41%); 6,5 (MTV- BVF.) **Conclusion:** FDG PET/CT can provide qualitative and quantitative variables in monitoring neoadjuvant radiochemotherapy response and possibly identify patients who will benefit from earlier monitoring and low-risk patients. Further analyses/studies are still needed to establish a cutoff/value for quantitative measures to aid clinicians.

Keywords: 18F-FDG PET/CT, Neoadjuvant response, Rectal cancer.

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THE NECESSITY OF 24-HOUR DELAYED IMAGING IN PATIENTS WITH PYELOCALICEAL DILATION FOR RELATIVE RENAL FUNCTION CALCULATION: A RETROSPECTIVE ANALYSIS

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Introduction/Justification: Static renal scintigraphy using 99mTc-DMSA is an accurate method for diagnosing and monitoring renal scars and allows for semi-quantification of relative tubular function (RTF). However, in cases of hydronephrosis, radiopharmaceutical accumulation in the pyelocaliceal system may interfere with RTF quantification. Although 24-hour images are typically requested to address this issue, they can inconvenience patients and disrupt the nuclear medicine service routine. **Objectives:** This study aimed to assess the impact of additional 24-hour imaging on RTF quantification in patients with hydronephrosis compared to standard 3-hour images. **Materials and Methods:** A retrospective analysis was conducted on patients who underwent renal scintigraphy with 99mTc-DMSA, focusing on those who received additional 24-hour imaging. Patients were divided into two groups: those aged up to 12 years (Group 1) and those over 12 years old (Group 2). Planar images were acquired 3 hours post-injection of 175 mBq of 99mTc-DMSA for adults and 1.5 MBq/kg for patients weighing up to 40 kg. Additional

delayed images were obtained after 24 hours if pyelocaliceal dilation was present. RTF was calculated using both 3-hour and 24-hour images, preferably using semi-automatic regions of interest. The T-Student test was utilized for statistical analysis, considering a difference of ≤ 3% between the two values as not significantly justifying the additional 24-hour image. **Results:** A total of 1,205 consecutive 99mTc-DMSA scans from February 2019 to December 2023 were evaluated. Group 1 comprised 662 patients, with 62 undergoing additional 24-hour imaging, while Group 2 consisted of 543 patients, with 43 undergoing 24-hour imaging. The mean value of the difference between the 3h and 24h images is 1.95% ± 1.83% and median 2 (0 - 6) for Group 1, and 2.40% ± 2.08% and median 2 (0 - 8) for Group 2. Statistical analysis demonstrated equivalence between RTF quantifications obtained at 3-hour and 24-hour imaging for Group 1 $p < 0.0001$, 95% confidence interval (1.45 - 2.42). However, for Group 2, quantifications at 3-hour and 24-hour imaging were not necessarily equivalent $p = 0.0714$, 95% confidence interval (1.76 - 3.05). **Conclusion:** Additional 24-hour imaging with 99mTc-DMSA in patients under 12 years of age with pyelocaliceal dilation does not appear to impact RTF compared to 3-hour images. However, for older patients, 24-hour imaging is necessary for greater accuracy in RTF determination. Further investigations are warranted to better understand factors influencing RTF calculation, guiding the indication for additional 24-hour imaging.

Keywords: DMSA, Hydronephrosis, Nuclear medicine, RTF.

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ACCESSING THE PHARMACOKINETICS OF MAGNETIC NANOPARTICLES IN CIRRHOSIS-ASSOCIATED HEPATOCARCINOGENESIS BY ORDINARY DIFFERENTIAL EQUATION MODELING AND AC BIOSUSCEPTOMETRY

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Introduction/Justification: Magnetic nanoparticles (MNPs) have been explored as a new potential theranostic agent, and several studies have devoted significant efforts to employ MNPs in biomedicine, including their applications as imaging contrast agents in alternating current biosusceptometry (ACB). In this field, the novelty of multichannel alternating current biosusceptometry (MC-ACB) devices allow the generation of real-time magnetic images of processes of biodistribution of MNPs in essays with animal models, including experiments focused on liver diseases. **Objectives:** This study refers to the in vivo biodistribution of MNPs detected by the multichannel ACB system, aimed at how the pharmacokinetics of MNPs is affected in the case of hepatocellular carcinoma. This evaluation has already been presented in a previous paper in terms of experimental results, but not in terms of pharmacokinetic modeling. **Materials and Methods:** In order to quantitatively describe how this disease may alter the biodistribution of MNPs, two different groups of animals are addressed here: a control group of healthy animals (SAL) and a group of animals with hepatocellular carcinoma (DEN/TAA). The MC-ACB system was used to simultaneously record the transit of MNPs in the heart and their accumulation in the liver. Pharmacokinetic rates of change of MNPs are reported here by proceeding with population parameter estimation for two groups of animals: cancer (DEN/TAA) and control (SAL). They refer to the change of MNPs from heart to liver (k1), from liver to heart (k2), and as the irreversible uptake of MNPs by Kupffer cells within a liver subcompartment (k3). All animal experiments were previously approved and performed according to the protocol 7571041120 by the Ethics Committee on Animal Use of the State University of São Paulo (IBB/UNESP). **Results:** Notably, both k2 and k3 were found to differ between groups, but not k1, consistent with the fact that MNP liver pharmacokinetics are expected to be affected by the chemically induced cirrhosis-associated hepatocarcinogenesis of the DEN/TAA group. The fact that k2 and k3 are higher for the DEN/TAA group is related to earlier MNP liver saturation in cirrhosis due to higher blood volume, and cirrhosis-associated hepatocarcinogenesis is revealed to affect the biodistribution of magnetic nanoparticles. **Conclusion:** The modeling approach proposed in the research provides a powerful tool to quantitatively describe the biodistribution of magnetic nanoparticles in healthy and cirrhotic rats, allowing the estimation of pharmacokinetic rate parameters related to the distribution of magnetic nanoparticles. The introduced modeling robustly describes the concentration of nanoparticles in compartments over time, which may assist in the development of targeted drug delivery strategies. Finally, this study highlights the relevance of mathematical modeling for understanding complex phenomena such as nanoparticle interactions with living systems, particularly in the development of effective theranostic applications.

Keywords: Cirrhosis-associated hepatocarcinogenesis, Magnetic nanoparticles, Ordinary differential equations, Parameter estimation, Pharmacokinetic modeling.

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