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