eSRS Latin America 2021: Abstracts

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Radioisotope Production in Reactor or Cyclotron

CR-01, Production of ^{89}Zr and ^{64}Cu for Sse in molecular imaging studies

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Background: Positron emitting metal radionuclides, with medium and long physical half-lives, support molecular imaging using antibodies or other studies associated with long biological half-life. However, the production of these radiometals is limited to some cyclotron facilities, since external beam line usually is required, targets are expensive and commercial demands are low, with impact in productions costs.

Aims: This project aims to optimize the production process of ^{89}Zr and ^{64}Cu in a fully GMP cyclotron facility for molecular imaging studies.

Methods: The production was carried out in a GE cyclotron PETtrace 880, using a homemade target built in aluminium. ^{89}Zr was produced by $^{89}Y(p,n)^{89}Zr$ reaction using high purity (>99 %) ^{89}Y sheet (0.125 mm), which was bombarded with 12.4 MeV protons, at a current of 10 µA for 180 min. The activated ^{89}Y sheet was dissolved in 2 M HCl and ^{89}Zr was purified by filtration in a hydroxamate column eluted with oxalate solution (0.1 M). ^{64}Cu was produced by $^{64}Ni(p,n)^{64}Cu$ reaction of a target previously electroplated over a high purity (>99%) silver and bombarded with 12.4 MeV protons at a current of 15 µA for 90 min. Activated target material was dissolved in 2 M HCl and ^{64}Cu was purified by sequential ion exchange in a BioRad AG1-X8 column and eluted with 0.1 M HCl. Radionuclidic purity was assessed by half-life determination and by gamma spectrometry using a germanium detector.

Results: ^{89}Zr yield at EOB/acid digestion was 444±74 MBq (n=8), and activity was recovered in 80-85% from the hydroxamate column. Gamma spectrometry did not show the formation of undesired ^{88}Zr ($t_{1/2}$ 83 d; 393 keV gamma line). Preliminary results gave expected yields and proper purification through ion-exchange for ^{64}Cu. Gamma spectrometry showed all predicted energy lines for the compounds.

Conclusion: The production of ^{89}Zr on a PETtrace cyclotron using a homemade target is feasible and can be performed regularly. Initial results to produce ^{64}Cu showed production feasibility, while scaling up the activity is in progress.

Funding/Acknowledgements**:** to HCFMUSP and CINRAD for support

CR-02, Preliminary settings of a liquid ^{68}Ga-target and post purification system tunings

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Background: In the recent years, several ^{68}Ga-radiopharmaceuticals received approval for routine clinical practice. Moreover, its suitable half-life, high positron emission yield, low radiation exposure, the convenient chelator-based labeling and the straightforward possibility of forming theranostic pairs with alpha and beta emitters, makes this radionuclide one of the first choices for new drug design. Therefore, constant and affordable ways for ^{68}Ga-production are critical, especially in the developing countries.

Aims: The aim of this work is the evaluation of a new liquid target design for the ^{68}Zn(p,n)^{68}Ga reaction, and the tuning of a suitable post-purification system for the produced ^{68}Ga.

Methods: A set of seven irradiations were carried out with beam currents around 35 µA in an IBA 18/9 Cyclone cyclotron. Target irradiated had a tantalum window for 18 MeV beam degradation to 12.5 MeV, and a 4 mL niobium chamber. In the first irradiation cycle, a solution of 25 mg/mL of [^{68}Zn]$ZnNO_3$ was used as enriched material. The obtained ^{68}Ga was processed by two different purification systems: (A) a hydroxamate – trioctylphosphine oxide system using mild HCl concentrations, or (B) a quaternary ammonium system using HCl 6 M.

Results: After irradiations of 30 min, a mean activity of 1295 MBq of ^{68}Ga (EoB: end of bombardment) was obtained. During irradiation, target pressure never exceeded 8 bars and no leakage or cloggings were observed. With post-purification system (A), a mean value of 560 MBq reached the reactor after 12 min, whereas with post-purification system (B) an average of 1084 MBq of ^{68}Ga were transferred to the reactor after 7 min.

Conclusions: The low pressures observed during irradiations suggest the possibility to further increase incident target currents and [^{68}Zn]$ZnNO_3$ concentrations in order to obtain higher activities at EOB in a safe manner. On the other hand, even though post-purification system B enabled to transfer higher activities in a shorter time it must be carefully evaluated whether it is worth to work with high and corrosive hydrochloric acid concentrations.

CR-03, Hydrogen production by urea electrolysis and application in nuclear medicine: A sustainable and modern way of production

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Background: PET (Positron Emission Tomography) is a non-invasive diagnostic imaging technique using labeled radiopharmaceuticals administered to the test subject. Among the main radioisotopes used for this diagnosis are carbon (^{11}C), fluorine (^{18}F) and nitrogen (^{13}N). Generally, a gaseous target with approximately 99% nitrogen gas and 1% oxygen is used to produce ^{11}C within a cyclotron. Additionally 99.99% hydrogen gas is used in the ion source. This work develops the design and construction, as well as the theoretical analysis of the electrolysis of urea to produce hydrogen. The design was carried out using AUTOCAD software and its construction was done with 3D printing technology and polylactic acid (PLA). **Aims:** The aims of this work focused on (1) the electrolyzer design to meet the hydrogen generation criteria. (2) the construction of the hydrogen generator and (3) to measure of electrolysis gas, available to use in cyclotron.

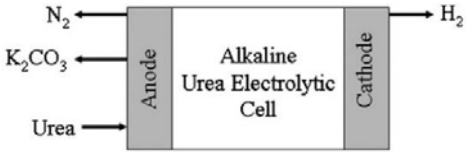

Figure 1. Urea electrolysis Process
Source: Boggs, 2009.

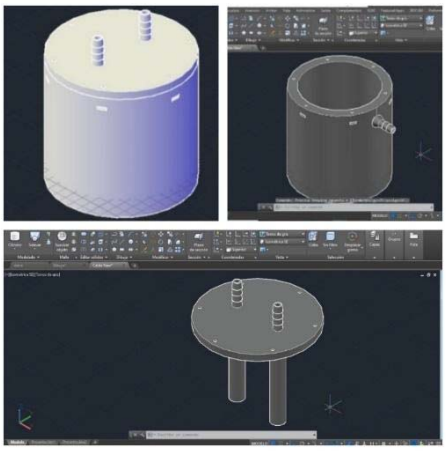

Figure 2. Electrolyzer design

Methods: The decomposition of urea into hydrogen at a concentration of 0.33 M can be electrochemically oxidized with a low-cost metal, nickel, according to Equation $CO(NH_2)_{2(aq)} + 6OH^- \rightarrow N_{2(g)} + 5H_2O_{(l)} + CO_{2(g)} + 6e^-$. The electrooxidation of urea is shown in Figure 1. An electrolytic cell is a device where electrolysis reactions take place. Such cell must meet certain requirements such as hermetically sealed large liquid volume area, large electrode area, and ease automation. To build our electrolytic cell, we used the AUTOCAD design tool to enable 3D technology printing. Figure 2 shows the design. **Results:** The results showed an average gas flow rate of the generator of 7mL/min. Hydrogen generation depends mainly on the volume of liquid capacity and the area of the electrodes. However, with 3D technology this can be easily scaled according to the flow needs. **Conclusion:** Previous results of others researches showed that the purity of the hydrogen gas reaches up to 99.99%, while at the anode; the gas was a mixture of nitrogen (96.1%) and oxygen (1.9%). With these additional data, it is concluded that the hydrogen produced by this technology can be minimally viable for use in the production of radioisotopes and it would proceed to perform a storage stage and then measure the gas yield in the cyclotron.

Funding/Acknowledgements: To the Polytechnic and the Department of Energy and Electronics at the University of Altamira for experiments support.

CR-04, Preliminary irradiation tests and calculations to obtain ^{32}P from a (n,γ) reaction at RA-6 for SIRT treatments

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Background: Hepatocellular carcinoma (HCC) is the most frequent type of liver cancer, with major incidence and mortality, causing annually more than half a million deaths worldwide. Selective internal radiation therapy (SIRT) using pure β^- emitting radioisotopes microspheres (MS) is used in palliative and curative treatment of patients, extending their life expectancy. Likewise, vitreous ^{32}P MS, are an alternative to ^{90}Y MS treatments, which are currently not produced in Argentina but imported, which means a high cost for the health system.

Aims: To evaluate (1) the suitability of the Argentinian nuclear reactor RA-6 to obtain ^{32}P with clinical nuclear purity from the stable isotope ^{31}P in a P, Al, Si and Mg (PASM) vitreous matrix, and (2) to evaluate the image quality parameters of the ^{32}P Bremsstrahlung signal in a clinical SPECT equipment.

Methods: Computation was carried out considering the neutron activation of ^{31}P in the irradiation box I of the RA-6, which has an integrated thermal flux of approximately $1.4x10^{13}$ $cm^{-2}s^{-1}$ and an epithermal flux of $8x10^{11}$ $cm^{-2}s^{-1}$. A 100 mg $AlPO_4$ sample was irradiated for 30 min. Sample was allowed to decay for 72 h prior to the SPECT measurement in an anthropomorphic liver phantom designed and 3D printed with PLA and PETG materials for this project. On the other hand, Monte Carlo simulations with the GATE platform were used to evaluate the image quality obtained from the Bremsstrahlung photons of ^{32}P and gamma photons of ^{99m}Tc using different acquisition parameters. The calculated images were compared with the measured ones.

Results: The study of the reaction rates for neutronic capture and subsequent decay indicates that an irradiation time of 24 h and a decay time of 72 h are enough to achieve an acceptable activity of ^{32}Pin RA-6. Comparison of simulated and acquired ^{99m}Tc images in a liver phantom established the suitability of the simulation to perform prediction of activity and distribution with a 10% uncertainty.

Conclusion: The activities and doses per MS applied to 1 kg of tissue, with 60 μm diameter MS of ^{32}P in PASM, irradiated at RA-6, would result in 73 Bq/MS and 14.4 μGy/MS. These values are in the order of the activities and doses of ^{90}Y MS commercially available at the moment. Although the ^{32}P image quality in a liver phantom is poor compared to the ^{99m}Tc, our simulations using the GATE platform suggest that it is possible to detect the ^{32}P signal in a clinical standard SPECT scanner. Further studies with higher activities are needed in order to adjust and quantify the image quality to determine the possibility of analyzing its bio-distribution with this scanning method.

Funding/Acknowledgements: PIP 1122 (CONICET), Dr M. Arribere and RA-6 team

^{99m}Tc and Other Gamma Radiometal Radiochemistry

GE-01, In vivo biodistribution comparison of [1,2,4,5]tetrazine systems bearing 6-hydrazinonicotinyl- or cyclam-ligand for technetium-99m coordination

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Background: Although monoclonal antibodies (mAbs) have been used to deliver radionuclides in targeted imaging, they have particular pharmacokinetic which results in a high dose to non-target tissues due to slow clearance. The use of the bioorthogonal inverse electron demand Diels–Alder reaction between *trans*-cyclooctene (TCO) and [1,2,4,5]tetrazines (TZ) can help to improve these weaknesses. In this kind of process, the conjugated mAb-TCO is administrated in first instance and after a period of clearance, the radiolabeled-TZ derivative is administered and the bioorthogonal reaction occurs in the targeted tissue.

Aims: Synthesis of TZ derivative bearing a 1,4,8,11-tetraazacyclotetradecanyl chelator (cyclam) for ^{99m}Tc radiolabeling and biological comparison with the previously described TZ-derivative bearing the 6-hydrazinonicotinyl (HYNIC) coordinator.

Methods: The new TZ-cyclam derivative was synthesized using adequate cyclam starting material. Afterwards, radiolabeling conditions, stability, log*P*, and *in vivo* biodistribution in C57BL/6J mice were studied.

Results: In previous studies, our research group has developed the HYNIC–tetrazine derivative showed in Figure 1 (right). According to biodistribution studies in mice, it has fast clearance from the blood and most of the organs, but in the liver and intestines, high radioactive uptakes occur from 1 h to 24 h.

In this work, the synthesized TZ-cyclam derivative (Figure 1, left) was able to coordinate ^{99m}Tc. Log*P* analysis revealed a higher hydrophilicity compared to the HYNIC-tetrazine. Furthermore, it exhibits higher stability, at different pH. Finally, biodistribution studies in normal mice showed lower uptake in liver and intestine compared to HYNIC-tetrazine.

Conclusions: Novel TZ-cyclam derivative was successfully synthesized and labeled with ^{99m}Tc. *In vivo* biodistribution revealed a main route of excretion through the bladder and urine after 1 h, showing at this time lower liver and intestines accumulation compared to the HYNIC-tetrazine.

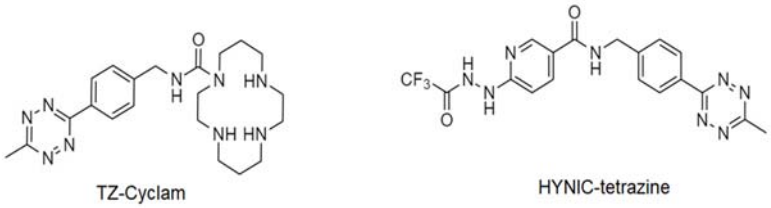

Figure 1 – Tetrazine ligands

GE-02, Design, synthesis and evaluation of a family of ^{99m}Tc-labeled estradiol derivatives for breast cancer imaging.

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Background: Estrogen receptors are overexpressed in 70% of breast cancer patients and their level of expression determines both the prognosis and the treatment to be followed.

Aims: With the objective to develop potential radiopharmaceuticals for estrogen receptors imaging, we present the design of a family of ^{99m}Tc-complexes derived from estradiol, using different oxidation states of the metal and chelating units and studying their influence on the overall properties of the resulting products.

Methods: Ligands were synthesized starting from ethinylestradiol and derivatizing the triple bond to incorporate different donor atoms to coordinate the ^{99m}Tc. The selected labeling strategies were the formation of a ^{99m}Tc(I)-tricarbonyl complex (C1) with an N,N,O donor atom set, a ^{99m}Tc(V)-nitride symmetric complex (C2) with two units of estradiol and dithiocarbamate as bidentade chelator and a ^{99m}Tc(III)-4+1 complex (C3) using a ligand bearing an isonitrile moiety and an NS_3 tetradentate coligand.

Results: Synthesis of the ligands was successful in all cases; structures were confirmed by spectroscopic techniques. The selected labeling strategies gave the desired ^{99m}Tc-complexes with high radiochemical purity. All complexes showed high stability in labeling milieu and in human serum for at least 3 hours. Lipophilicity expressed as logP (partition coefficient between octanol and phosphate buffer 0.1M, pH = 7.4) was 1.3±0.1 for C1, 0.8±0.1 for C2 and 0.48±0.06 for C3. A moderate protein binding in comparison to ethynilestradiol (98%) was observed in all the three cases with values of 33±11%, 41±9% and 46±6, respectively. Binding to MCF7 cells, expressing estrogen receptors was 2.0±0.2%, 6.8±0.9% and 3.3±0.1%, respectively, while tritiated estradiol (Estradiol [6,7-^{3}H (N)]) exhibited a binding of 6.6±1.4%. Biodistribution in normal rats for C1 and C2 showed low blood activity (0.70±0.26% and 5.13±2.49% at 2 h, respectively). However, liver uptake was very high for C1 (40.8±2.4%) and moderate for C2 (13.0±1.3%). Excretion occurred mainly through the hepatobiliary system with only a minor fraction excreted in the urine. Studies in nude mice bearing induced breast tumors showed that C2 has a better tumor/muscle ratio (3.59±0.63) compared to C1 (2.91±1.48). In vivo studies for C3 are being performed.

Conclusion: Influence of the chelating system in the physicochemical and biological properties of ^{99m}Tc-labelled in biomolecules is clearly demonstrated by our experimental results. Consequently, the design of the suitable chelator is crucial in obtaining the biological stability and pharmacokinetics desired for a radiopharmaceutical.

Funding/Acknowledgements: ANII (FCE_1_2017_1_136416), CAP, PEDECIBA-Química, Bayer Schering Pharma AG, Hans-Jürgen Pietzsch.

GE-04, New precursor for obtaining a naphthalene-derivative compound labeled with ^{99m}Tc.

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Background: Alzheimer's disease is the most frequent form of dementia, being the sixth cause of death in Cuba and all over the World. The possibility of having a precursor for ^{99m}Tc-labeling, would set the first bases for the development of a potential pharmaceutical for the study of Alzheimer's disease by using SPECT imaging in Cuba.

Aim: The aim of the present research was to develop a naphthalene-derivative compound, with a thioamidoalkyl chain, protected by an acetyl-group, as a precursor for a ^{99m}Tc-labeled radiopharmaceutical, with potential affinity for beta-amyloid plaques.

Materials and Methods: 1-Naphthylamine was used as a starting reagent. The synthesis had three steps, obtaining S-[2-({2-[(2-{[4-(1-naphthylamino)-4-oxobutanoyl] amino}ethyl)amino]ethyl}amino)-2-oxoethyl] ethanethioate (**4**), as final compound. All of the obtained compounds through the process of synthesis were characterized by infrared spectroscopy, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. The kit of pyrophosphate-Sn *(CENTIS, Cuba)* was used for the labeling of the compound **4** with ^{99m}Tc.

Results: The reaction yields obtained for each one of the three steps were 60%, 49% and 90 %, respectively. The labeling efficiency of *S*-[2-({2-[(2-{[4-(1-naphthylamino)-4-oxobutanoyl]amino}ethyl)amino]ethyl}amino)-2-oxoethyl]ethanethioate (Amylovis) with ^{99m}Tc was (89.0±0.9)%.

Conclusions: Acetylated amylovis was synthesized and labeled with ^{99m}Tc. Labeling procedure should be optimized in the future.

^{11}C, ^{18}F, ^{13}N or ^{15}O Radiochemistry

CFNO-03, ^{18}F-FDG production optimization through process management

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Background: Process management has become one of the most widely used methodologies in terms of analysis and optimization. In relation to [^{18}F]FDG production, it is important to systematically identify and manage the developed processes and their respective interactions to guarantee the quality of the final product.

Aims: The goal of this work is to show the methodology for analysis and optimization of the [^{18}F]FDG production process.

Methods: The following phases were considered: 1. Identification of strategic processes; 2. Identification of key processes for [^{18}F]FDG production; 3. Identification of synthesis and quality control stages related to [^{18}F]FDG production; 4. Identification of support processes that allow controlling and improving the laboratory's management system.

Results: Strategic processes were identified, as well as key processes in [^{18}F]FDG production; it allows the establishment of sequence of stages in the synthesis and quality control processes of [^{18}F]FDG, then, time of each stage is estimated, as well as waste generated for its subsequent disposal, as it is shown in Figure 1.

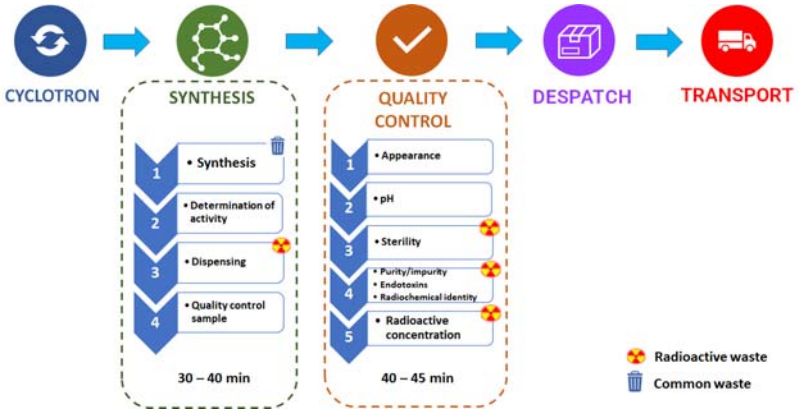

Figure 1. Diagram of the synthesis process and quality control of [^{18}F]FDG

Conclusion: The process management methodology proved to be appropriate for the identification of the interactions between the processes executed in the radiopharmacy during [^{18}F]FDG production. This contributed to the modeling through the interaction of the processes, facilitating the quality management of the laboratory.

CFNO-04, Title: Validation Plan for [^{18}F]FDG Quality Control Assessment in Costa Rica

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Background: Due to the installation of the first cyclotron in Costa Rica, a validation plan to ensure reliable results for the assessment of [^{18}F]FDG has been created. As part of the Good Manufacturing Practice (GMP), written quality control protocols for the assessment of radiopharmaceuticals are mandatory to ensure the use of the products into humans. This is the first step in the development of a PET-radiopharmacy in Costa Rica.

Aims: The goal of this work is to show the validation plan followed for the [^{18}F]FDG QC assessment.

Methods: Bibliography review was performed to develop the validation plans. United States Pharmacopeia (USP) was used for establishing identification, purity, impurities and specifics test for the quality control of [^{18}F]FDG, with extensive information of the number of samples and guidelines to validate each method.

Results: Based in the United Stated Pharmacopeia (USP), the parameter established for this validation are reported in Table 1.

Table 1. Validation parameters for [^{18}]FDG quality control.

Test	Validation Parameter	Test	Validation Parameter
Radioactive concentration	Accuracy, Repeatability, Specificity, Linearity	pH	Linearity, Accuracy
Radionuclide Identity	Repeatability, Specificity, Linearity	Limit of Acetonitrile and Ethanol	Specificity, Detection limit
Radiochemical purity/Impurities	Accuracy, Repeatability, Specificity, Quantification limit, Linearity, Intermediate precision, Robustness	Radionuclide purity/Impurity	Specificity, Accuracy, Detection limit
Limit of Fluorodeoxyglucose Related Compound B	Recovery, Accuracy, Repeatability, Specificity, Quantification limit, Linearity, Intermediate precision, Robustness	Limit of Fluorodeoxyglucose Related Compound A	Detection limit, Robustness, Specificity
Radiochemical identity	Specificity	Bacterial endotoxins test	Validation will be carried out through an interlaboratory test

Conclusion: This validation plan will be applied once the cyclotron accepting test are finished.

CFNO-05, ^{18}F-labeled kenpaulone, potential radioligand for Alzheimer's disease

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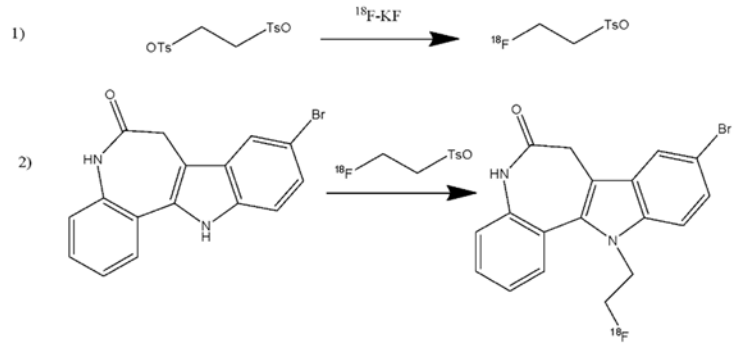
Background: Alzheimer's disease (AD) is the most common form of dementia. The phosphotransferase glycogen synthase kinase 3-beta (GSK-3beta) has gained attention due to its association with axonal dysfunction, neuronal death and as a mediator of pro-inflammatory responses. For this reason, GSK3 is an interesting target in Alzheimer's disease.

Aims: The objective of this study was the labeling of 9-Bromo-7,12-dihydroindolo[3,2-d][1]benzazepin-6(5H)-one (Kenpaullone) with fluorine-18 ([^{18}F]KEN). Kenpaullone is a GSK3 inhibitor with an IC_{50} of 23 nM.

Methods: [^{18}F]KEN was synthesized by a two-step procedure. The first step was the synthesis of 1-[^{18}F]fluoro-2-(tosyloxy)ethane. The labeling of ethyleneglycol-1,2-ditosylate was performed by nucleophilic substitution on an SYNTHRA RNplus Research platform located in a hot cell MIP-1 (Comecer). The ^{18}F-labeled intermediate 1-[^{18}F]fluoro-2-(tosyloxy)ethane was purified through a silica cartridge. ^{18}F-labeled intermediate was reactive manually the kenpaullone. 5-bromoindole was used to optimize the second synthesis step because of the high cost of kenpaullone. The optimized parameters were the base (NaOH, Li_2CO_3, K_2CO_3), solvent (DMSO, DMF, MeCN), temperature (120 °C, 135 °C, 145 °C), time (5, 10, 20, 30, 60 min), mass of 5-bromoindole (10 µmol, 20µmol).



Results: The yield of the [^{18}F]fluoroethylation reaction was highly dependent on the base and was also influenced by temperature. So the highest yield (30±1)% of the fluoroethylation reaction was achieved at 145 °C in 0.3 ml of dry DMSO for 10 min with 4mg Cs_2CO_3 and 20 µmol 5-bromoindole. These conditions were selected for the kenpaullone labeling, obtaining a yield of (30±1)% and a radiochemical purity greater than 90%.

Conclusion: Optimization of the synthesis of ^{18}F-labeled kenpaullone was performed. The product was obtained in an adequate yield, and resulted stable in the reaction medium for at least 3 hours. Ongoing physicochemical and biological evaluation will make it possible to evaluate the usefulness of [^{18}F]KEN for the determination of GSK3 activity.

Funding/Acknowledgements **:**ANII(POS_NAC_D_2020_1_164001) and PEDECIBA-Química.

GT-06, *In silico* evaluation of new ^{18}F-labeled PET radiodrugs, analogs of mangiferin

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Background: Positron Emission Tomography (PET) is one of the most important technologies that has been put at the service of diagnosis of oncoproliferative diseases. Although more than 95% of PET studies are performed with [^{18}F]FDG, it is not a specific agent. Mangiferin (MF), a C-glucosylxanthone, has several antitumoral properties, standing out its ability to inhibit selectively MMP-9. Therefore, the ^{18}F radiolabeling of MF might be very useful in the diagnosis of cancer through PET.

Aims: This work aims to assess the reactivity of MF based on DFT calculations and to propose strategies for the preparation of MF-based compound labeled with ^{18}F. Furthermore, characterizing the ligand/MMP-9 interactions of MF and its analogs through a molecular docking study.

Methods: A conformational search, based on Python 3, was performed in order to obtain the most stable structure of MF. DFT calculations were performed for assessing the reactivity of MF at M062X/6-311G(2df,2pd). Furthermore, a molecular docking study was performed to MF and its analogs against MMP-9 in Autodock4.2.6.

Results: The conformational search applied over the starting structure of MF let the achieving of the most stable structure at the theory level M062X/6-311G(d,p). The reactivity study shows that the most nucleophile site of MF belongs to the phenolic oxygen number 12 and the most electrophile region is the carbonyl group. Three MF-based compounds labeled with ^{18}F were obtained through click chemistry approach. The results of the re-docking study, 93.75% of similar contacts with a binding ΔG of -7,52 kcal/mol and the maintenance of the ligand/MMP-9 penta-coordinated complex within the active site, validate the molecular docking study which was also applied to the MF. This penta-coordinated complex, the most important feature of MMP-9 inhibitors, was also obtained in the MF/MMP-9 system. Furthermore, the binding ΔG of the complex is even better (-10.95 kcal/mol).

Conclusion: These theoretical results corroborate all experimental studies made to the MF/MMP-9 system and contribute on the knowledge of structural features of the MMP-9 inhibition by MF. The ^{18}F-analogs of MF will be tested against MMP-9 through the same molecular docking methodology to propose new PET compounds.

Funding/Acknowledgements**:** AGR would like to appreciate the support given by the scientists of the Wahoo cluster at University of Antilles, France for the calculations facilities.

GT-07, *In silico* evaluation of ^{18}F-fluorinated derivatives of Telmisartan as potential PET radiopharmaceuticals

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Background: Renin-Angiotensin-Aldosterone System (RAAS) is a hormonal cascade recognized for decades as the major determinant of blood pressure and the main target for treating cardiovascular diseases. Angiotensin II Type 1 Receptor (AT1R) is the primary effector of RAAS. AT1R is present in many tissues and its overexpression is correlated with manifestation of the hallmarks of cancer. Telmisartan is a highly selective, competitive nonpeptide AT1 receptor antagonist (ARB). It has the largest volume of distribution and the highest affinity for AT1R of all ARBs.

Aims: This work proposes a virtual screening methodology for evaluating the potentiality of ^{18}F-fluorinated derivatives of Telmisartan as PET radiopharmaceuticals for diagnosis of both cardiovascular diseases and cancer.

Methods: Density Functional Theory (DFT) calculations of all derivatives were performed with further analysis of electrostatic potential surfaces and intramolecular interactions. The screening was performed taking into account possible metabolites predicted by SyGMA, pharmacokinetic properties calculated using SwissADME and docking simulations in order to evaluate association to AT1R.

Results: Of nine proposed Telmisartan derivatives, the one obtained by using 5-[^{18}F]fluoro-1-pentyne as a prosthetic group *AlfFTel* (wt=625.30 Da, LogP=4.98, HBD=0, HBA=8, ΔG_{AT1R}=-12.42 kcal/mol) shows more interactions with AT1R and seems to have better pharmacokinetic properties than Telmisartan (wt=514.24 Da, LogP=3.88, HBD=1, HBA=6, ΔG_{AT1R}=-11.86 kcal/mol). Another interesting candidate was obtained using 2-[^{18}F]fluoroglucopyranosyl azide as a prosthetic group *GlucFTel* (wt=807.35 Da, LogP=6.07, HBD=0, HBA=12, ΔG_{AT1R}=-10.73 kcal/mol, ΔG_{GLUT1}=-9.63 kcal/mol). This molecule could have both AT1R and glucose transporter 1 (GLUT1) as targets.

Conclusions: The proposed screening methodology could assist radiopharmaceuticals design, specifically those targeted to AT1R. Further synthesis of the suggested molecules could be performed in an automated fashion via prosthetic groups for click chemistry.

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PET Radiometal Radiochemistry

PR-01, Radiolabeling of DOTA-Ubiquicidin peptide with ^{64}Cu

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Background: Antimicrobial peptides labeled with isotopes can be used as specific infection localizing agents since they bind specifically to bacterial cell membranes. The antimicrobial peptide Ubiquicidin labeled with ^{99m}Tc and ^{68}Ga has shown encouraging results as a molecular agent in recent publications (A. Bunschoten, 2013). This peptide can also be labeled with the positron emitter ^{64}Cu and be used in PET imaging for monitoring efficacy and duration of antibiotic treatment in patients, which are important issues from prophylactic, therapeutic, and socioeconomic point of view.

Aims: Radiolabeling of DOTA-Ubiquicidin peptide with ^{64}Cu separated from proton-irradiated ^{64}Ni.

Methods: The mass of DOTA-Ubiquicidin (29-41) (ABX, Product no. 9601.XXXX) required for the radiolabeling reaction was calculated based on the effective specific activity of ^{64}Cu obtained by titration with the chelator NOTA (Macrocyclics), resulting in a peptide ratio of 6.0 µg/mCi. ^{64}Cu was separated in 0.4 mL 2 M HCl after elution from a 0.5 cm diameter column packed with DGA resin (Eichrom), following the methods reported by Valdovinos et al. (HF Valdovinos, 2017). The radiosynthesis is carried out in the iQS radiolabelling module (ITG) used for ^{68}Ga-elution from a $^{68}Ge/^{68}Ga$-generator and radiolabeling. Reaction conditions: [^{64}Cu]CuCl in 2 M HCl, 3 mL H_2O, 3 M NaOH and 1 mL 0.25 M NaOAc to adjust pH to 4-5, total volume 4.6 mL, t= 30 min, T= 95 °C. The purification of the radio-peptide is carried out in a C18 Sep-Pak Light cartridge (Waters) eluted with 1 mL of 70% EtOH and diluting the final solution with 15mL of 0.9% NaCl solution, passing this through a Millex GV 0.22 µm membrane filter. Radiochemical purity is determined by TLC and HPLC. The TLC method uses silica gel as the stationary phase and 1:1 MeOH:10% NH_4Oac as the mobile phase. The HPLC method uses a column 150x3.9mm Nova-Pak C18 (Waters), a flow gradiente of (1.0 mL/min) 0-1.5 min=95-0% A, 1.5-2.0 min = 95-0% A, 2-3 min = 100% B, 3-4 min = 0-95% A, 4-5 min = 95% A (A = 0.1% TFA in H_2O, B = 100% MeCN).

Results: The radiolabeling efficiency is 94±3% (n = 3). The R_f of the analysis by TLC is 0.17 and the t_R by HPLC is 3.7 min.

Conclusion: DOTA-Ubiquicidin was efficiently labeled with ^{64}Cu and the product was successfuly characterized following the same analytical chemistry techniques that are used for ^{68}Ga-labeled peptides.

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Automation For Radiochemistry

GE-03, Unexpected problems during automated one-pot labeling of high specific activity [^{131}I]mIBG for therapy

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Background: High specific activity (h.s.a.) [^{131}I]mIBG (>92500 MBq/mg) demonstrated to administer effective anti-tumoral radiation doses while keeping the risk of adrenergic complications as low as possible in the treatment of pheochromocytomas and paragangliomas. 3-tributylstannylbencylguanidinium polymer supported has become a successful way for *I-radiolabeling of mIBG, due to its simple post-purification requirements. However, electrophilic iodine generated for stannyl-precursor substitution is a very reactive species that can produce unexpected radiochemical impurities causing serious complications during routine production.

Aims: The first aim of this work is the identification of the possible sources of radiochemical impurities observed during polymer supported [^{131}I]mIBG labeling in order to establish reliable production conditions. The second aim of this work is the design of an automated synthesis module for routine h.s.a. [^{131}I]mIBG production.

Methods: Different conditions for radiochemical impurities production were simulated, such as previous resin degradation by air oxygen and moisture, radiolysis of different [^{131}I]NaI, initial activities (from 3.7 to 37 GBq), and different oxidant concentrations. A first automated synthesis module prototype for routine production of this radiopharmaceutical was also tested. All the samples obtained were analyzed by HPLC.

Results: Stannyl precursor resin demonstrated to be robust enough to oxygen and moisture exposure and to radiolysis in the range of the activities tested. Oxidant concentrations had to be slightly adjusted. However, several plastic parts (syringes, tubes and connectors), also employed in many other commercial synthesizers, demonstrated to be a source of soluble organic compounds able to be radiolabeled under the reaction conditions.

Conclusions: Automated synthesizer materials employed for electrophilic substitution of 3-tributylstannylbencylguanidinium polymer supported must be carefully chosen in order to avoid radiochemical impurities formation.

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CFNO-01, Enhanced radiochemical yield of [^{18}F]SFB using a fully automated approach

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Background: N-Succinimidyl-4-[^{18}F]fluorobenzoate ([^{18}F]SFB) is a well-known potential prosthetic agent that been used to conjugate with biomolecules to from corresponding ^{18}F-fluorobenzoylated products for a variety of applications in nuclear medicine. [^{18}F]SFB can react with primary amines of biomolecules. It has been demonstrated to be a suitable and versatile ^{18}F-prosthetic group to radiolabel peptides, proteins, and antibodies in terms of in vivo stability and radiolabeling yield. However, the drawback of flourine-18 labeling with biomolecules (antibodies, proteins and peptides) is that the radiosynthesis of the intermediate labeling agent ([^{18}F]SFB) involved a long synthesis time applying manual methodology. Thus, the reaction of [^{18}F]SFB with biologically relevant resin-bound peptides will be studied and optimized. For comparison, each peptide will be ^{18}F-fluorobenzoylated in solution under different conditions and the product distribution will be analyzed proving the advantages of the solid-phase approach. The method's feasibility for selective radiolabeling either at the N-terminus or at the lysine side chain shall be demonstrated.

Aims: To fully automate the radiosynthesis of ([^{18}F]SFB) using a synthesizer module and to use the produced ([^{18}F]SFB) in labeling peptides and other molecules aiming to improve the radiochemical yield of the conjugate product in a shorter reaction time.

Methods: Ethyl 4-(trimethylammoniumtriflate) benzoate (1) (5mg, 20 µmol) in anhydrous DMSO (1 mL) was added to the dried K222/[^{18}F]KF complex. The mixture was heated at 110 °C for 15 min to produce ethy-4-[^{18}F]fluorobenzoate. The ethyl ester was hydrolyzed with 20 µL of tetramethylammonium hydroxide (1.0 M in water) and 1 mL MeCN at 120 °C for 4 min. A 2 mL of MeCN then added and the mixture azeotropically dried (two times step). A solution of *N*,*N*,*N*,*N*-tetramethyl-*O*-(*N*-succinimidyl) uranium tetrafluoroborate (TSTU) (15 mg, 50 µmol) in MeCN (1 ml) was added and the resulting solution was heated at 100 °C for 5 min. After cooling, 5% aqueous acetic acid (3 mL) and water were added. The reaction mixture was passed through a C18 Sep-Pak cartridge, where [^{18}F]SFB was trapped. The cartridge was washed with water (4 mL) and [^{18}F]SFB then eluted with MeCN (1 mL).

Results: Good to comparable radiochemical yields to both reported and the manual procedures are achieved with shorter time and higher radiochemical purity.

Conclusion: The presented automation process is the first using the mentioned synthesizer and improving steps are ongoing to increase the radiochemical yields of the [^{18}F]SFB.

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Preclinical Studies for Diagnostic and Therapy

GE-05, Interaction of furosemide – [^{99m}Tc]Tc-mercaptoacetiltriglicine (MAG3) in low dose using paper chromatography.

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Background: The diagnosis of some nephrological pathologies is a procedure that is performed routinely in nuclear medicine laboratories. In Cuba, the most widely used radiopharmaceutical for kidney morphology and function studies is [^{99m}Tc]Tc-MAG3 which can interact with other drugs that are incorporated into work protocols, such is the case of furosemide. The work protocols report that the interaction of [^{99m}Tc]Tc-MAG3 with furosemide is stable when working in the range of activities from 74 to 185 MBq. However, by reducing this activity for the administration of doses in pediatric use, an exhaustive analysis of how this interaction behaves has not been carried out: it is not reported how stable this interaction is, or for how long, and if this stability changes with varying doses, since the lower the activity administered, the risk that this interaction will lead to a significant loss of specific activity increases.

Aims: To study if it exists or not an interaction between furosemide and [^{99m}Tc]Tc-MAG3 applied at low doses.

Methods: To study the interaction of furosemide with [^{99m}Tc]Tc-MAG3, it was performed an experimental design using a factorial plan 2^3. Considering the independent variables to study the delivered activity dose of [^{99m}Tc]Tc-MAG3, the delivered dose of furosemide and the time.

Variables	**Values**		
	Mín. (-)	**0**	**Máx. (+)**
Radiation doses (MBq) **(X_1)**	56	94	132
Furosemide doses (mg) **(X_2)**	5	12.5	20
Time (h) **(X_3)**	0	2	4

The radiochemical purity determination of [^{99m}Tc]Tc-MAG3 interacting with furosemide was performed by ascending paper chromatography, using as solvents: acetone and sterile physiological saline solution.

Results: The preliminary results of the study show an increase of the radiochemical purity when administering furosemide, as well as the stability of mixture for 4 hours, which imply a modification of ^{99m}Tc-MAG3 by furosemide.

Conclusion: Considering the obtained results, we concluded that it exists an interaction between furosemide and [^{99m}Tc]Tc-MAG3, as well as this interaction, is stable until after 4 h.

GE-07, Development and evaluation of a series of ^{99m}Tc-complexes for androgen receptor imaging.

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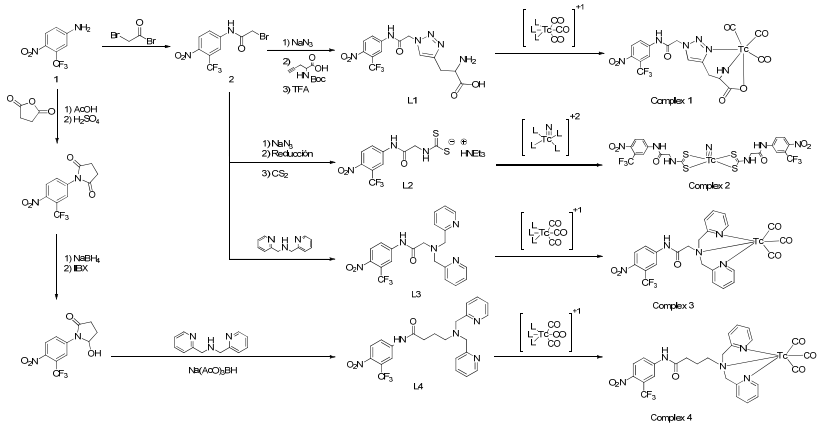
Background: Confirming the presence of androgen receptors in prostate cancer cells determines the treatment selection and response evaluation. Molecular imaging can contribute to both aspects by targeting this receptor.

Aims: The aim of this work was to design, develop, synthesize, and evaluate a series of four novel ^{99m}Tc-complexes for prostate cancer imaging.

Methods: Four ligands containing the same pharmacophore and different chelating units were synthesized as shown in the figure. All labeling procedures involved the preparation of an adequate ^{99m}Tc-precursor followed by the substitution with the ligands. Radiochemical purity (RP) was assessed by HPLC and physicochemical evaluation (lipophilicity, protein binding (PBB) and stability) was performed.



Results: All four complexes were obtained with high RP(>90%). The complexes were stable after 6 h post labeling and 4 h in human plasma. They all showed lipophilic behavior with optimal logP values for passive diffusion through cellular membranes (C1=1.2±0.1; C2=1.3±0.1; C3=1.5±0.2 C4=1.1±0.1). For all complexes, PBB was evaluated at 30 and 60 min, obtaining moderate PPB values. For C2, PPB values were: (28.8±1.0)%, (31.3±1.6)% and (36.3±2.6) (27.6±3.7) for C1. C4 presented the highest PBB values (41.9±2.1 and 45.1±2.4) and C3 the lowest values (17.0±1.8)% and (14.2±1.0)%.

Conclusion: All studied complexes were successfully labelled with ^{99m}Tc, obtaining a single product in each case with high RP and stability. Further biological *in vitro* studies will be carried out to select the complex with the best properties.

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GT-08, *In silico* characterization of the interaction of Thalassia testudinum derivates labeled with iodine-125

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Background: The chemical-pharmacological characterization of derivatives obtained from marine plants is of interest in Cuba, since they can synthesize bioactive molecules that are not equivalent to those found in terrestrial organisms. Thalasiolin B, a flavone isolated from the marine angiosperm Thalassia testudinum, and chrysoeriol, another flavonoid also found in this species, are molecules of interest for their antioxidant properties and their antineoplastic potential. Both molecules are attractive therapeutic agents against cancer due to their ability to induce apoptosis.

Aims: The objective of this research is to elucidate the possible labeling sites of thalassiolin B and chrysoeriol with the radioisotope iodine-125 using molecular modeling.

Methods: Calculations based on the Density Functional Theory (DFT) of these molecules and an analysis of the chemical properties based on the dual descriptor were performed. A study of the natural bond orbitals (NBO) was also carried out in order to determine the conjugative and hyperconjugative interactions of the molecules.

Results: The most reactive sites were obtained through the analysis of the dual descriptor. This allows us to propose the compounds labeled with iodine-125. The study of NBO showed the presence of conjugative and hyperconjugative interactions of the benzene rings present in the molecules.

Conclusion: The analysis of the chemical properties of these compounds made possible to propose, for the first time, the site of labeling with the radioisotope studied. The radiolabeled analogues of the compounds studied are proposed as candidates for radiopharmaceuticals for the diagnosis of oncogenic diseases.

PC-01, Brain metabolism in a middle age down syndrome animal model

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Background: Down Syndrome (DS) is the most common genetic cause of intellectual disability in the world. Positron emission tomography (PET) using the radiopharmaceutical [^{18}F]FDG is used in neurology to assess brain metabolism.

Aims: The aim of this study was to evaluate brain metabolism in an animal model with DS at middle age.

Methods: Down syndrome transgenic mice TS65Dn (n=11) and its littermate wild type (WT n=12), were evaluated at the age of 12-months with [^{18}F]FDG PET imaging. [^{18}F]FDG was injected intravenously (≈ 8 MBq) and 45 min after the injection, a static image was acquired for 15 min in a PET scanner for small animals (β-cube, Molecubes, Belgium). Images were quantified by PMOD™ v4.1 software (Switzerland) using T1 MRI as brain template and the data was analyzed by T-Test (GraphPad Prism) and the results are expressed in SUV (Standardized Uptake Value) mean ± standard deviation in different brain regions: striatum, cortex, hippocampus, thalamus, cerebellum, amygdala, brainstem, superior colliculi, midbrain, and inferior colliculi.

Results: Analyzed brain regions showed differences in [^{18}F]FDG uptake between the trisomic and euploid animals. The [^{18}F]FDG uptake (SUV) in the WT was 2.48±0.18 for the striatum, 2.34±0.20 for the cortex, 2.23±0.23 for the hippocampus, 2.41±0.23 for the thalamus, 2.33±0.36 for the cerebellum, 1.69±0.18 for the hypothalamus, 1.64±0.13 for the amygdala, 2.06±0.24 for the brainstem, 2.37±0.23 for the superior colliculus, 2.22±0.16 for the midbrain and 2.34±0.24 for the inferior colliculus. Comparing to the Ts65Dn animals the uptake was 2.27±0.26 (p= 0.03), 2.08±0.29 (p=0.01), 1.88±0.29 (p=0.004), 2.16±0.31 (p=0,04), 2.06±0.40 (p=0.09), 1.59±0.23 (p=0.25), 1.49±0.22 (p=0,04), 2.03±0.32 (p=0.79), 2.13±0.31 (p=0.04), 2.00±0.28 (p=0.03) and 2.11±0.36 (p=0.08) in the respective brain regions.

Conclusion: [^{18}F]FDG imaging showed lower brain uptake in the transgenic model of Down syndrome at middle age (12-month-old) compared to its littermate wild-type animals.

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PC-02, Development of theranostic agents based on the anti-HER2 monoclonal antibody: influence of chelating agents and radionuclides on biological properties

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Background: Breast cancer is the second leading cause of mortality worldwide. HER2 positive tumors occur in 20% to 30% of breast cancers and are characterized as the second worst prognosis compared to the other subtypes. It indicates a more aggressive clinical behavior, with the worst response to conventional therapies. In this context, the development of non-invasive imaging techniques using monoclonal antibodies (MAbs) is a fast-developing field. Due to the high affinity to HER2 receptors, the humanized MAb trastuzumab has been radiolabeled and studied, aiming radioimmunodiagnosis (RID) and radioimmunotherapy (RIT).

Aim: Taking into account the potential influence of bifunctional chelating agents and radionuclides in the physicochemical and biological properties of radioimmunoconjugate (RIC), this work aimed to develop and to compare the theranostic potential of [^{111}In]In-DTPA-trastuzumab and [^{177}Lu]Lu-DOTA-trastuzumab.

Methods: The trastuzumab was immunoconjugated with the chelators p-SCN-Bn-DTPA and DOTA-NHS-ester in 1:20 (antibody:chelator) and radiolabeled with [^{111}In]$InCl_3$ and [^{177}Lu]$LuCl_3$, respectively. The stability of the RICs was evaluated in serum, and the immunoreactive and internalization fractions were determined in SK-BR-3 breast cancer cells. The *in vivo* pharmacokinetics quantification and the *ex vivo* biodistribution were performed in normal and SK-BR-3 tumor-bearing mice.

Results: The results showed that the different chelating agents and radionuclides did not influence in the following properties: integrity and stability of the immunoconjugates; radiolabeling process and stability of RICs, internalization and immunoreactivity. On the other hand, there was an influence on the lipophilic feature of RICs, in serum stability, as well as the pharmacokinetics, biodistribution profile and tumor uptake.

Conclusion: Despite these differences, the data indicate that [^{111}In]In-DTPA-trastuzumab and [^{177}Lu]Lu-DOTA-trastuzumab is a theranostic pair with potential for future clinical studies in RID and RIT of cancers that overexpress HER2 receptors, especially breast cancer.
Funding: not applicable.

PC-04, A database of voxel-based small animal models for internal dosimetry: improving dose evaluation in preclinical trials.

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Background: Small animals have been widely used in experimental trials involving radiopharmaceuticals and their use is increasing due to Target Radionuclide Therapy (TRT) development, especially for cancer treatment. TRT main purpose is to deliver the highest possible absorbed dose to the tumor while sparing healthy tissues to achieve the highest therapeutic efficacy. Nevertheless, a risk of toxicity due to the radiation is always present. Therefore, internal dosimetry for absorbed dose estimates is essential to obtain absorbed dose response relationships. Dosimetric preclinical approaches are based on models capable of representing the animals used in the trials. Anatomical variations between models may generate significant differences in dosimetry. In this sense, development of computational phantoms, based in a realistic animal anatomy and representative for each strain is essential.

Aims: The aim of this study is to create and make available a database of voxelized computational phantoms for preclinical internal dosimetry estimates. Our intention is to build a database of voxelized mice, representative of different strains (nude, Swiss, C57BL, etc). Two models are already modeled and will be presented here. In addition, S-values for the main radioisotopes will be made available to allow dosimetric calculations by other research groups.

Methods: Two set of Micro CT images of mice (*Mus musculus*) were chosen for the manual 2D segmentation processes (coronal slices): (i) from DIGIMOUSE project (nude male, 28g) and (ii) from https://www.tcdm.fi/, (C57BL/6 female, 26g). An in house C^{++} program was used to convert the segmented images to MCNP voxel models. The tissue chemical compositions and densities were based on ICRP 110 or ICRU 44 human data. MCNP6 was used to calculate the energy deposition in targeted-organs due to emissions in source-organs. S-values were calculated for all tissues and organs of the models.

Results: DM_BRA and FM_BRA voxelized mice models were obtained. S-values (absorbed dose rate per unit activity) were determined for ^{18}F, ^{11}C, ^{99m}Tc and ^{64}Cu, considering gamma, electron, and/or positron emissions. The S-values tables are available for both male and female models.

Conclusion: This work demonstrated that the production of mouse phantoms representative of different strains can be carried out. The models will be available under demand, for Monte Carlo (MC) users. S-values will make the dosimetric calclulations for non-MC simulators.

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PC-05, Evaluation of MCP anticancer activity using molecular imaging

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Background: Modified citrus pectin (MCP) is a polysaccharide consisting of galacturonic acid with anti-cancer activity that can act synergistically with other treatments to reduce tumor growth, stimulate programmed cell death and reduce the number of metastases. In addition, MCP prevents acute and severe renal syndromes caused by radiation/chemotherapy. All of these effects were reported to be due to MCP ability to specifically inhibit Galectin-3 protein functions.

Aims: The aim of this work was to evaluate the anticancer effect of MCP in a Balb/c nude mice xenograft model of ovarian cancer.

Methods: The human ovary cancer cell line, SKOV-3, was subcutaneously injected in Balb/c nude mice and tumor growth was monitored daily with a caliper. When tumors reached 250-300 mm^3, 20 mg/kl of MCP was administered intravenously (i.v.) in a daily based for 21 days. Tumor growth and mice weight were monitored daily. Additionally, MCP was radiolabeled with ^{99m}Tc by incubating of MCP (2.5 mg) in saline with $SnCl_2$ (4 mg/ml), HCl (0.01 M), NaOH (0.01 M) and ^{99m}Tc (129.5 MBq) at pH 7 for 30 min. The radiochemical purity was determined by iTLC-SG with acetone and ethanol/NH3/H2O (1:2:5). [^{99m}Tc]Tc-MCP (37 MBq) was administrated i.v. in Balb/C nude mice bearing SKOV-3 tumors and after 1, 2 and 4 h, µSPECT/CT image was acquired (Albira SI Buker). *Ex-vivo* biodistribution studies were performed after the i.v. injection of 10 MBq of [^{99m}Tc]Tc-MCP for 1 h. The % of injected dose per gram (%ID/g) of tissues of interest, including the tumor, was calculated.

Results: The i.v. administration of MCP was able to significantly reduce SKOV-3 tumor growth (52% tumor volume reduction) in comparison with the non-treated group, after 21 days of treatment. Our biodistribution studies showed that [^{99m}Tc]Tc-MCP was mainly found in kidneys, bladder and liver of mice (%ID/g = 12.25, 38.57 and 5.71, respectively), and was able to reach the tumor (%ID/g = 0.765 ± 0.045) 1 hour after i.v. administration. [^{99m}Tc]Tc-MCP accumulation in the tumor site was visualized by µSPECT/CT imaging 1 h after i.v. administration. Because of MCP high accumulation in kidneys, renal toxicity was also evaluated. We were able to find that MCP does not induce renal toxicity when administered in a daily base at a concentration of 20 mg/Kg.

Conclusion: In this work, we demonstrated that a daily treatment of i.v. MCP was able to reduce the tumor growth of ovarian tumor xenografts (SKOV-3 cells). Although we found that MCP can reach the tumor site, we cannot rule out that other mechanisms may contribute to MCP anticancer activity. Moreover, since MCP is not toxic, it could be a useful agent for cancer treatment.

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PC-06,In vitro uptake evaluation of a 18F-Labeled Sulforhodamine 101 in CNS cells

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Background: We have previously reported the synthesis and biological evaluation of a sulfonamide derivative of Sulforhodamine 101 (SR101), namely SR101 *N*-(3-[^{18}F]-Fluoropropyl)sulfonamide ([^{18}F]2B-SRF101), designed as a new positron emission tomography (PET) agent for detecting astrocytosis in early stages of Alzheimer´s disease (AD). The fluorescent dye SR101 is an astroglial marker and has been used for the detection of astrocytes in the neocortex of rodents in numerous works. We have confirmed 2B-SRF101's ability to detect astrocytes in culture similarly than SR101, using fluorescence microscope images. *In vivo* biological assessment of [^{18}F]2B-SRF101 using micro-PET/CT revealed a higher uptake in cortex and hippocampus of 10-month-old triple-transgenic (3xTg) mice compared with the control group (1). However, the cellular specificity of this radiotracer in the CNS needs to be elucidated, especially considering that SR101 uptake was reported also in other CNS cells (2).

Aims: In this work, we aimed to elucidate the cellular specificity of 2B-SRF101 in neurons and astrocytes using isolated mice cortex/hippocampus cells.

Methods: Enriched astrocytes cultures were prepared from cortices of P0-P2 3xTg or C57 control mice. Neuronal primary cultures were obtained from C57 embryos. Fluorescence confocal images were acquired after 1 min SR101 or 2B-SRF101 (10 μM) incubation in live cells. Cell uptake was determined after 10, 20 and 40 min incubation of confluent cells with [^{18}F]2B-SRF101 (90 μCi) using a gamma counter.

Results: Enriched astrocytes cultures were prepared from cortices of P0-P2 3xTg or C57 control mice. Neuronal primary cultures were obtained from C57 embryos. Fluorescence confocal images were acquired after 1 min SR101 or 2B-SRF101 (10 μM) incubation in live cells. Cell uptake was determined after 10, 20 and 40 min incubation of confluent cells with [^{18}F]2B-SRF101 (90 μCi) using a gamma counter.

Conclusion: In this work, we brought evidence of astrocytic preference of both SR101 and 2B-SRF101, validating [^{18}F]2B-SRF101 as a promising candidate tracer for astrocytosis detection.

Funding/Acknowledgements: We thank ANII for financial support (FMV_3_2020_1_162870) and Unidad de Bioimagenología Avanzada de IPMon.

[1]Kreimerman I, et al. Front Neuroscience, 13: 734; 2019.

[2]Hill R, et al. Nat Methods, 11: 1081-1082;

PC-07, Development of ^{177}Lu-DN(C19)-CXCR4 Ligand Nanosystem for Combinatorial Therapy in Pancreatic Cancer.

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Background: Pancreatic cancer is highly lethal and has a poor prognosis. The most common alteration during the formation of pancreatic tumors is the activation of KRAS oncogene. As a new therapeutic strategy, the C19 molecule blocks the KRAS-membrane association in cancer cells. In addition, the chemokine receptor CXCR4 is overexpressed in pancreatic cancer.

Aims: In this research, a new dendrimer-based nanoradiopharmaceutical ([^{177}Lu]Lu-DN(C19)-CXCR4L) encapsulating C19 and functionalized to target CXCR4 receptors is proposed as both, a targeted radiotherapy system (lutetium-177) and an oncotherapeutic approach by the stabilization of KRAS4b-PDE complex to produce dual specific therapy in pancreatic cancer.

Methods: The [^{177}Lu]Lu-DN(C19)-CXCR4L was synthesized and characterized, C19 was encapsulated with 81% efficiency, the final nanosystem rendered a particle size of 67 nm and the specific uptake in pancreatic cell lines was demonstrated.

Results: The major cytotoxic effect was observed in the KRAS-dependent and radioresistant cell line Mia PaCa-2, which expresses a high density of CXCR4 receptors. The radiation dose of 3 Gy/Bq decreased viability to 7%, and this effect was attributed to the presence of C19. A synergistic effect (radio and chemotherapy) capable of reducing viability in pancreatic cancer cells through apoptotic mechanisms was demonstrated.

Conclusion Thus, [^{177}Lu]Lu-DN(C19)-CXCR4L nanoradiopharmaceutical is efficacious in pancreatic cancer cell lines overexpressing the CXCR4 receptor.

Funding/Acknowledgements**:** This study was supported by grant CONACyT-CB-A1S38087 and the International Atomic Energy Agency (CRP-F2264, Contract 18358). It was performed as part of the activities of the “Laboratorio Nacional de Investigación y Desarrollo de Radiofármacos, CONACyT.”

PC-08, Functionalized Auger Emitting Au-198 Doped Nanoparticles as a Therapeutic Strategy for the Treatment of Cancer Metastases

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Background: The use of Auger emitters for the therapy of cancer has been well studied. The concentration of Auger radioactive emission using intrinsically radioactive nanoparticles may provide a higher cytotoxic effect for cancer treatment. We established a method to produce radioactive ^{198}Au gold nanoparticles and functionalized them against specific DNA targets using the HIV-TAT cell-penetrating peptide (CPP).

Aims: The objective was to assess and characterize the cytotoxicity of functionalized [^{198}Au]Au-AuNPs-TAT CPP using the SKBr-3 breast cancer cell line as a model for micro-metastases.

Methods: The radionuclide ^{198}Au was produced at the TAMU NSC, and it was used to produced radioactive gold nanoparticles (^{198}Au-AuNPs) using the Turkevich method. Characterization was carried out using TEM and UV-VIS spectrometry. Functionalization with HIV-TAT CPP and DNA targeting agents were carried out as per labeling protocol. An acute dose of 2 Gy x-rays and doxorubicin (0.55, 1.10, 2.0 µM) were used for cytotoxicity comparison purposes. A real-time cell analyzer (RTCA) was used to assess cell growth of the cell cultures (10,000 tumor cells per well) with activity concentrations of 50, 100, 500, 1000, 1500 kBq per well. Cytotoxicity was estimated 200 hours post-administration.

Results: The average size of the AuNP was 32.9±12 nm. The measured activity per radioactive batch was 480 µCi, and the resulting average number of ^{198}Au-radioactive atoms per AuNP was 26. The Monte Carlo transport code GEANT4 was used to model the energy distribution of the Auger emitting particles per ^{198}Au-NP. The cytotoxic response of [^{198}Au]Au-NPs-TAT targeting SKBr-3 cells was found to be dose-dependent. When compared with controls, [^{198}Au]Au-NPs-TAT was found to be as cytotoxic as doxorubicin at concentrations of 50 kBq per well.

Conclusion: The development of nuclear nanotechnologies is becoming a potential strategy for the treatment of cancer. We provide preliminary results for using [^{198}Au]Au-NPs-TAT CPP as a strategy for the treatment of minimal residual disease. Our studies showed the potential of ^{198}Au-NPs as a treatment strategy. Further studies are warranted.

Funding/Acknowledgements : Nuclear Regulatory Commission (NRC) Grant No. NRC-38-10-923

PC-09, Physicochemical and biological evaluation of a radiolabeled antimicrobial peptide as potential agent for diagnostic fungal infections.

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Background: The development of new radiopharmaceuticals for the detection of fungal foci that are able to differentiate them from a sterile inflammation has great relevance for early detection and the selection of the appropriate treatment. Particularly radiolabeled antimicrobial peptides from native plants that specifically bind to pathogens causing the infection, could provide a suitable radiotracer to distinguish between both kinds of lesions.

Aim: To optimize the radiolabeling procedure with ^{99m}Tc, of the synthetic defensin EcgDf1 obtained from *Eritrina Crista Galli (Ceibo)* and determine the physicochemical and biological properties of the complex in order to be used as a radiotracer.

Methods: The defensine was labeled with ^{99m}Tc using HYNIC as a bifunctional chelating agent and tricine as co-ligand. Labeling conditions were optimized and the physicochemical characteristics of the complex were evaluated as well as its binding capacity to different pathogenic microorganisms.

Results The defenisin complex was obtained with a radiochemical purity (RCP) higher than 90%, it was stable up to 180 min in milieu and 120 min in presence of a competitive ligand (cysteine). It showed an intermediate plasma protein binding of 49.9±6.7% at 60 min and a hydrophilic behavior with Log P = -0.60 ± 0.01 . The complex presented in vitro uptake of 98.7% in *C. albicans* culture, 76.7% in *A.niger* culture and 88.6% in *S.aureus* culture.

Conclusion: The ^{99m}Tc-complex showed high RCP and stability in vitro. Concomitantly, it presented adequate physicochemical properties and high *in vitro* uptake in fungal culture. Further studies will be performed in order to complete the characterization of the radiolabeled peptide.

Funding/Acknowledgements: CSIC Project 2014, CMNIM Hospital de Clínicas.

PC-10, Evaluation of the renal protection of Pectin and Gal-3 after treatment with [^{177}Lu]Lu-DOTATATE

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Background: A big disadvantage during [^{177}Lu]Lu-DOTATATE treatment is its nephrotoxicity induced by long-term accumulation of radiopharmaceutical in rinses via reabsorption in the proximal tubules. The total clearance of the radiopharmaceutical is 14 days and thus it becomes a chronic problem for the kidneys and causing a limiting treatment

Aims: Reduction of [^{177}Lu]Lu-DOTATATE induced nephrotoxicity.

Methods: For this, 12 healthy animals C57/B16 approved by the ethics committee (282/21) at IPEN were used. The experiment consisted of four different groups (Control -Saline. Amino acids 208/kg, Pectin 20 mg/kg, Galectin-3–100 µg) committing 3 mice each group, in which the test solutions were intravenously administered in the groups, 5 min after application of the test solutions, 10 µCi of [^{177}Lu]Lu-DOTATATE were applied. At the end of 24 h, the animals were sacrificed and the kidneys were collected for autoradiography. The autoradiography process was performed according to the protocol, for which is necessary to leave the cryostat at -20 °C for 20 min before processing to acclimatize the equipment. The tissue sample was frozen with isopentane in dry ice for 5 – 10 min. Afterwards, the sample was placed at the support with Tissue-tek for sectioning in the cryostat. Subsequently, the slices with a thickness of 10 µm were positioned on the slides and placed in a development cassette, recording the order and positions of the slides, placing the phosphor film with the white part facing the slides and closing the cassette. After 24 h, the reading of the phosphor plate took place.

Results: The above autoradiography results demonstrated that kidney uptake after 24 h using (20 mg/kg Pectin) and (100 µg – 200 µL Galectin-3) were higher compared to the amino acid pool. We verified that, in comparison with the control group, the treatment containing arginine and lysine reduced the accumulation of activity in the kidneys after administration of [^{177}Lu]Lu-DOTATATE, indicating its effectiveness. We also show that Pectin partially inhibits [^{177}Lu]Lu-DOTATATE accumulation, however with less efficiency compared to the amino acid group. Treatment with injected galectin-3 did not inhibit [^{177}Lu]Lu-DOTATATE accumulation after 24 h. The results obtained from the autoradiography were corroborated by the quantification of the kidneys through biodistribution.

Conclusion: Pectin concentrations (20 mg/kg) were shown not to be toxic to mice and showed reduced uptake of [^{177}Lu]Lu-DOTATATE compared to galectin-3 after 24 h. Possibilities for further studies with pectin using different concentrations or co-administration with the set of amino acids, thus enabling promising new studies for a new innovative strategy to decrease acute kidney injury.

Funding/Acknowledgements **:** CNPq, FAPESP, CAPES, IPEN, USP.

PC-11, Comparative studies of the physical and biological properties of peptides labeled with ^{131}I and ^{99m}Tc. Relevance to glioblastoma

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Background: Radiolabeled peptides with high specificity for receptors overexpressed in tumor cells hold great promise for diagnostic and therapeutic applications. Most integrin targeted radiotracers are based on the Arginine-Glycine-Aspartate (RGD) peptide sequence, due to its high affinity and specificity for the $\alpha_v\beta_3$ integrin.

Aims: The goal of this work was to evaluate the physical and biological properties of the [^{131}I]I-GRGDYV and [^{99m}Tc]Tc(CO)$_3$-GRGDHV peptides, as well as to compare theirs *in vitro* and *ex vivo* interactions with tumorigenic cells related to glioblastoma.

Methods: Peptide fragments were synthesized by solid-phase using the Fmoc protocol. The fragments were radiolabeled with ^{131}I and ^{99m}Tc, using the chloramine T and the tricarbonyl methods, respectively. The radiochemical yields were carried out by ascending chromatography using thin layer chromatographic-silica gel (TLC-SG) strips and acetonitrile/water (95:5), as mobile phase. The stabilities of the radiopeptides were assessed at 1, 4, and 24 h after the radiolabeling procedure. Binding and internalization studies of the radiolabeled peptides with tumorigenic cells were evaluated using C6 culture cells and brain homogenate of glioblastoma-bearing rats, at 1, 4, and 24 h of incubation. *Ex vivo* biodistribution was evaluated at 15, 60, and 240 min after radiopeptides injection into normal and allograft C6 tumor-bearing rats.

Results: The [^{131}I]I-GRGDYV and [^{99m}Tc]Tc(CO)$_3$-GRGDHV were efficiently synthesized and radiolabeled. The radiochemical yields were 96.70±0.72% and 98.30±0.17%, respectively (n=5). Both radiopeptides were stable up to 24 h, with an average radiochemical purity >94% (n=3). Mean values of the logP were -3.11±0.49 and -1.13±0.14 (n=6) for [^{131}I]I-GRGDYV and [^{99m}Tc]Tc(CO)$_3$-GRGDHV, respectively. The binding and internalization studies into C6 cells and in brain homogenates of glioblastoma bearing rats showed high affinity of both radiopeptides. Biodistribution data showed high accumulation in the brain of glioblastoma allograft tumor-bearing rats was observed compared to normal rats ($p < 0.001$). #

Conclusion: Both radiopeptides presented high radiolabeling efficiency and stability. Furthermore, they showed high in vitro and in vivo affinity for glioblastoma cells. Although further imaging studies are necessary, our data suggest that these radiopeptides have interesting and consistent characteristics, with potential to be used as radiopharmaceuticals for glioblastoma imaging.

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Clinical Studies for Diagnostic and Therapy

GT-10, Advancing Nuclear Medicine Molecular Imaging and Therapy Using Nuclear Nanotechnologies

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Background: The use of nuclear nanotechnologies can enhance the potential utility of radionuclides for the diagnosis and therapy of cancer. Here, we provide a critical review of the utility of nuclear nanotechnologies for the development of new diagnostic, treatment, and theranostic strategies using PET, gamma, beta, and alpha-emitting radionuclides.

Aims: To assess the potential utility of nuclear nanotechnologies for developing new strategies for the diagnosis and therapy of cancer and cancer metastases.

Methods: We carried out a literature review of nuclear nanotechnologies used for the diagnostic and treatment of cancer where single or binary modalities are used for the diagnostic and therapy of cancer using PET/SPECT radionuclides in as single or in combination with beta, alpha-particle emitting radionuclides. We also provide an overview and dosimetry analysis of the potential clustering radiation dosimetry and effects in a single cell using histological images of tumor tissues.

Results: A search in clinicaltrials.gov resulted in a total of 560 clinical trials using nanoparticles for different diagnostic and therapeutic purposes. However, there were only three (3) clinical trials using radiolabeled nanoparticles. The low number of clinical trials indicates a regulatory bottleneck for their implementation. We thus present a framework for the development, preclinical and clinical study and assessment based on their permutation, using PET/SPECT and beta/alpha-particle emitting radionuclides. We investigated multiple nanoparticle construct that combine a PET emitting radionuclide (^{18}F, ^{68}Ga, ^{22}Na, ^{124}I, ^{64}Cu) with a beta-emitting radionuclide (^{90}Y, ^{131}I, ^{125}I, ^{168}Au, ^{177}Lu), or an alpha-emitting radionuclide (^{223}Ra, ^{225}Ac, ^{211}At, ^{212}Bi, ^{213}Bi, ^{212}Pb, ^{227}Th).

Conclusion: Radionuclide delivery systems using nuclear nanotechnologies have a significant potential for enhancing the field of nuclear medicine molecular imaging and molecular radiotherapy. However, a regulatory approach needs to be established that will allow these nuclear nanotechnology constructs to be introduced into clinical trials.

Funding/Acknowledgements**:** Nuclear Regulatory Commission (NRC) Grant No. NRC-38-10-923

Education in Radiopharmacy and Molecular Imaging

GT-09, Validation of bacterial endotoxin test for a variety of PET-radiopharmaceuticals using the LAL method with chromogenic assay

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Background: Radiopharmaceuticals (RPs) are mostly intravenous solutions and before their release for medical use, apyrogenicity should be confirmed by assessing the presence and concentration of bacterial endotoxins. Given the short half-life of PET-RPs the bacterial endotoxin test (BET) must be carried out as quickly and as accurately as possible. The Endosafe® Nexgen Portable Test System (PTS) reader is a device dedicated to performing the BET by the Limulus Amebocyte Lysate (LAL) method with chromogenic assay, using disposable cartridges. The PTS reader is capable to quantify the concentration of bacterial endotoxins in a solution or sample provided that it is used carefully and conforms to well-established procedures. Using this device with the correct cartridges the PTS provides quick results in reasonable times.

Aims: To validate the BET for a variety of routinely produced PET-RPs using the Endosafe® Nexgen-PTS reader.

Methods: The endotoxin limits were determined in accordance with USP (usual acceptance criterion is an endotoxin content less than 175 EU/ injection volume). Maximum valid dilutions (MVD) were determined for each evaluated RP in accordance with endotoxin limits calculated and the sensitivity of the used cartridges (0.5-0.005 EU/mL). BET conditions were verified in triplicated using inhibition and enhancement (I/E) cartridges (0.05 EU/ml) and four dilutions of RPs. Acceptance criteria for the dilution was the nearest spike to 100 % and coefficients of variation (CV) <20%. The repeatability and reproducibility were performed in triplicated in different days and batches by two analysts. Acceptance criteria for these parameters were CV<20% for repeatability and no statistically significant difference (SSD) between assays performed at different days and analyst.

Results: Table below summarizes the obtained results for the evaluated RPs.

		[^{11}C]ACE[1]	[^{11}C]MET[2]	[^{18}F]NaF	[^{18}F]FDOPA	[^{18}F]FPSMA[3]	[^{18}F]FDG	[^{18}F]FOC[4]	[^{68}Ga]Ga-GDN[5]
A)	pH	5.5	5.5	5.5	4.5	7.0	5.0	5.0	5.5
	% Ethanol	5	8	N.A.	0.05	0.05	0.05	5	7
B)	Spike recovery	95	110	101	121	95	97	93	99
	C.V. %	15.5	5.73	10.1	6.9	16	2.7	5.7	16
C)	Repeatability (CV)	3.18	2.85	2.93	6.48	3.8	2.4	7.9	9.25
	Reproducibility	There was no SSD between assays performed at different days and participating analysts							

[1]Acetate, [2]Methionine, [3]PSMA-1007, [4]AlF-NOTA-Octreotide, [5]Ga-DOTA-NOC. A) Sample characteristic, B) I/E tests, C) Repeatability/reproducibility

Conclusion: BET for routinely produced PET-RPs can be performed in a fast and reliable way using the Endosafe® Nexgen-PTS. Quantitative results on the concentration of bacterial endotoxins are obtained in less than 20 min, facilitating the decision-making for the release of RPs. Ethanol concentration in the final formulation of RPs was an important factor in defining the MVD.

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Acknowledgment: Zarate-Morales A; Flores-Moreno A

Other

CFNO-02, Optimization of analytical method for determining the [^{11}C]PK11195 compounds and metabolites

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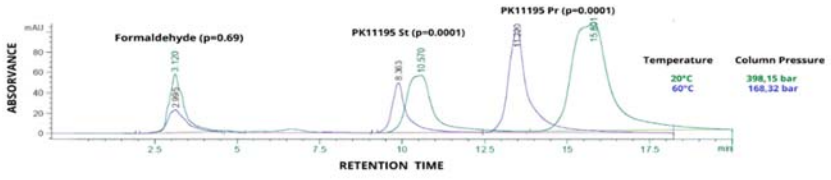
Background: [^{11}C]PK11195 is used for positron emission tomography imaging in studies of neuroinflammatory diseases. The compound is metabolized *in vivo*, generating two radioactive metabolites, and knowing the intact fraction of the tracer in the plasma is essential for the quantitative image analysis. Usually, the radio-HPLC is the choice method for the determination of metabolites and intact PK. However, this method is time-consuming and affects the detection of radioactive compounds during sequential analysis due to ^{11}C decay.

Aims: Evaluate the impact of the HPLC column temperature on the retention time of compounds to improve the methodology applied in the analysis of [^{11}C]PK11195 metabolites using non-radioactive compounds.

Methods: Analysis was performed in an HPLC 1260 Infinity II LC system equipped with a column oven, UV detector, and a quaternary mobile phase pump. The non-radioactive compounds: PK11195 standard (St) and precursor (Pr), and the metabolite formaldehyde (the second metabolite was not available), were eluted through a Luna® RPC18 column (250x10 mm x 5 µm - Phenomenex®), using ethanol/water (60:40) as mobile phase, at the isocratic flow of 4 mL/min. The column temperature was maintained at 20 °C and 60 °C, and the UV detector was set up to 254 nm. Data were analyzed by two-way ANOVA.

Results: At 60 °C, the retention time for the PK standard (St) and precursor (Pr) significantly decreased, as well as the pressure in the system, when compared to analysis at 20 °C. **Figure 1.** Graphic about the effect of the temperature on the retention time of the compounds and in the pressure of the chromatographic system



Conclusion: These preliminary results have demonstrated that column heating proved to be an efficient technique to reduce the retention time of the analyzed compounds, reducing the pressure of the chromatographic system, enabling a faster and efficient analysis. From this data, new improvements can be achieved.

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CS-01, Clinical Pharmaceutical Screening in Radioiodine Therapy: First Year Experience of a Novel Approach in Radiopharmacy

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Background: Radioiodine therapy (RIT) can be used in differentiated thyroid carcinoma (DTC) and requires extensive evaluation to ensure effectiveness and safety. Therefore, it is necessary to evaluate all health problems and medications pre-RIT and comprehensive medication management (CMM) services can serve as a screening tool in this context.

Aims: The present study describes initial assessments of a CMM service offered to DTC patients pre-RIT, and interventions performed.

Methods: Descriptive study regarding the first year of a CMM service carried out in a reference oncology hospital. Patients ≥ 18 years with DTC who received 1110 to 7400 MBq of I-131 activities were included. Patients referred for RIT underwent initial pharmaceutical consultation prior to therapy. Descriptive analysis was applied to critical clinical situations identified, as well as the correspondent drug therapy problems (DTP) and the type, acceptability and outcomes of the pharmaceutical interventions performed.

Results: Forty nine patients (n=49) were included, 59.2% < 55 years (46,9 years mean age); 85.7% female; 81.7% papillary DTC. Main comorbidities identified were Diabetes Mellitus; Hypertension (SAH); dyslipidemia; Central Nervous System disease (anxiety, depression, insomnia); Overweight and obesity (body mass index - BMI ≥ 25 Kg/m² in adults). Regarding drug use, all patients used at least one drug, and the maximum number was fourteen (14), with a mean of 4.7 medications. During pre-RIT CMM assessment, six critical clinical situations were identified for six patients (12.2%) that could potentially impair RIT effectiveness or safety: i) Physical signs and symptoms of an anxiety crisis in a patient without any previous anxiety diagnosis; ii) Dyspnea and chest pain in a patient without any previous diagnosis of lung or heart disease; iii) Hypertensive crisis in a patient with treated SAH; iv) Lesions on the tongue and mouth compatible with syphilis; v) Severe pain at the surgical intervention site previously performed for the management of lung metastasis (pain scale = 9); vi) Hypertensive crisis in a patient with treated SAH and breast cancer in use of cardiotoxic antineoplastic chemotherapy. These situations triggered pharmaceutical interventions, which were all fully accepted corresponding to DTP2 (needs additional drug therapy – n=5); and DTP4 (dosage too low – n=1). Other interventions: i) patient with constipation; ii) patient without a contraceptive method pós-RIT.

Conclusion: The CMM service to DTC patients during RIT is feasible and effective, representing an important pre-RIT screening strategy.

ED-01, “Post-graduate courses on radiation protection”: an opportunity to work more safety

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Background: The Applied Sciences and Technologies Institute of the University of Havana, in collaboration with other Cuban institutions, has been developing a solid work for 40 years, in order to establish and improve undergraduate and postgraduate programs of academic formation with high quality, which include courses of radiation protection.

Aims: The present work makes a comprehensive evaluation of the registered postgraduate programs in radiation protection in our institute.

Methods: The objective of this assessment was to analyze the programs correspondence with the necessities of the country, the national and international recommendations in the radiation protection qualification, the achievements and deficiencies found in its development and theirs potentialities for the future.

Results: The programs of the four Master degrees in Radiopharmacy, Nuclear Engineering, Nuclear Physicist and Medical Physicist have solid and sufficient content to satisfy the regulatory authority’s requirements and also the IAEA’s latest recommendations for basic radiation protection knowledge and also for the radiation protection qualify expert in the selected field. The university offers two Diploma postgraduate courses: Radiation Safety Diploma and Radiation Protection in Medicine, with high compliance with national and international safety standard recommendations. The last one, it is modular, with an open design and it can be developed “at distance” and all these modules can be developed individually like specialization in radiation protection in some radiation medicine area like nuclear medicine, conventional radiology, etc.

Conclusions: The institute has postgraduate academic figures that play a vital role in the personnel qualification of basic radiation protection issues and also to generated experts in radiation protection in the field.

GT-01, Good manufacturing practices applied to the Cyclotron-PET/CT Laboratory

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Background: The Atomic, Nuclear and Molecular Science Research Center (CICANUM) at the University of Costa Rica has installed a cyclotron. This building also has a radiopharmacy. The radiopharmacy products must fulfill good radiopharmaceutical practices to ensure their quality before being used by patients.

Aims: The goal of this work is to show the protocols considered in our team to achieve good radiopharmaceutical practices within the production area of the radiopharmacy at the Cyclotron - PET/CT Laboratory.

Methods: Protocols writing was based – on the CICANUM quality management system, which is according to the INTE-ISO/IEC 17025: 2017 standard. Protocols developed are related to using, maintenance, calibrations, verifications, and QC of the synthesis radiopharmaceuticals equipment. Protocols for radiological protection, handling/disposal radioactive/biological/chemical waste materials were also written. All protocols are in accordance with the Technical Regulation of Good Practices of Manufacturing for the Pharmaceutical Industry (Pharmaceutical Products and Medicines for Human Use N ° 35994-S).

Results: Figure 1 shows the different areas of the developed protocols.

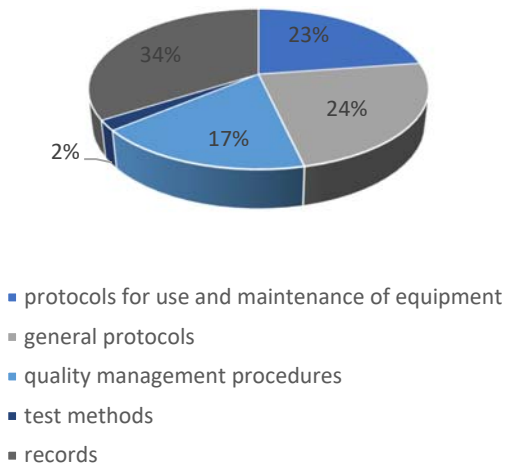

Figure 1. Number of protocols developed

Two different test methods were developed, one for the radiopharmaceutical synthesis of [^{18}F]FDG, based on the manuals of the equipment and training received. The second one for QC tests according to the Pharmacopoeia. 23 protocols detailing access/exit, clothing, cleaning, sanitation, use of personal protection equipment, among others. 22 protocols for using and maintenance of equipment were created. All equipment has been verified according to these protocols. 17 protocols are related to the CICANUM quality management system. Finally, 33 forms were developed to record the results and give traceability to those records.

Conclusion: Protocols were developed to comply with good radiopharmaceutical manufacturing practices. Initial status of the equipment has been verified using these protocols. After national authorities' approval these protocols are going to be used in the production area on the routine bases.

Acknowledgements: To María Herrera for reviewing the wording and format of the protocols.

GT-02, Radiation protection implementation through management processes in a cyclotron facility

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Background: Recently, management processes have created a growing interest due to its applicability and its achieved results in several organizations in which quality management is used as a reference. Considering radiation protection as a management process makes it possible to systematically identify and manage the processes developed in the organization and particularly the interaction between them (ISO 9000:2000).

Aims: The goal of this work is to use management process methods for radiation protection implementation in a cyclotron facility.

Methods: The following stages were carried out: 1. Strategic processes identification for the cyclotron laboratory; 2. Key processes identification directly related to the radiological protection in the facilities, 3. Support process identification which allows control and to improve the system management. Individual and group work sessions were carried out to discuss the processes and their interactions, focusing on processes flow, facility layouts, interaction between different areas, inputs supplies, and output product expected from each area of the laboratory.

Results: Strategic processes of the laboratory were identified. Relationships between each process and radiation protection internal guidelines, national standards and international recommendations were established for a cyclotron facility. Control tools were identified for the support processes, hence, continuous improvement of the radiological protection system management within the facilities will occur.

Conclusion: Management process methodology proved to be appropriate for the identification of different interactions between executed processes within the cyclotron laboratory facilities. Cause-effect links help to model processes relationships, allowing the development of each process in a coordinate path. Then, effectiveness and satisfaction of all stakeholders in terms of radiation protection will occur. Likewise, the methodology helped to create individual and collective awareness of the radiation protection culture within the cyclotron laboratory facilities.

GT-03, Geiger Müller Detectors Performance at the University of Costa Rica's Cyclotron Facility

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Background: The first cyclotron in Costa Rica was installed in 2020 at the Atomic, Nuclear and Molecular Science Research Center (CICANUM), at the University of Costa Rica. Among the equipment acquired four gaseous detectors were installed to survey the radiopharmaceutical production area. Under Costa Rican local authorities, calibration of these detectors must be carried-on once a year. CICANUM has an Ionizing Radiation Metrologic Laboratory (LMRI-SSDL) and base-on its experience a calibration procedure was developed.

Aims: The goal of this work is to develop a method to evaluate the performance of the Geiger Müller gaseous detectors installed at the cyclotron facility at CICANUM.

Methods: Using a calibrated ^{137}Cs-source (vial geometry) the response of the detector (µSv/h) was obtained, varying the source – detector distance according to figure 1. Data was extracted from the computer used to store all data. Data was plotted to verify the inverse – square law. R^2 correlation coefficient is obtained for each detector.

Results: For all detectors inverse – square law is obtained, mathematical expression of it can be seen in table 1, also in the same table R^2 results can be seen.

Table 1. Detector response (y(x)) and correlation coefficient for all Geiger Müller detectors.

Detector id	y(x) (µSv/h)	R^2
SA1	$764376\ x^{-1.981}$	0.9929
SA2	$326939\ x^{-1.834}$	0.9894
SA3	$677736\ x^{-1.971}$	0.9948
SA4	$906189\ x^{-2.011}$	0.9847

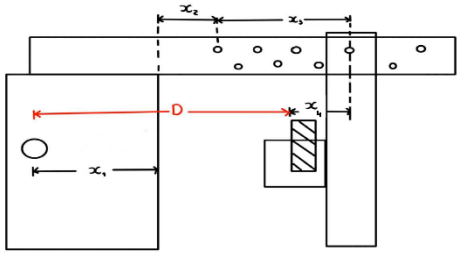

Figure 1. Experimental set-up used to evaluate the Geiger Müller performance, where x_1 is the distance from the detector to the outer wall of its case, x_2 is the distance from the outer wall to the first horizontal position available in the horizontal mast, x_3 is the variable distance, x_4 is the distance from the center of the vertical post to the edge of the source that is closed to the detector and D is the total distance source – detector (Own design).

Conclusion: The initial performance evaluation of the gaseous Geiger Müller detector was carried out. Inverse – square law behavior of the ionizing radiation was obtained for all detectors. Further

set – up will be conducted to establish methods to develop quality control tests for these detectors.

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GT-04, Ventilation air system issue at the University of Costa Rica's Cyclotron Facility

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Background: The first Cyclotron in Costa Rica was installed in 2020 at the Atomic, Nuclear and Molecular Science Research Center (CICANUM), at the University of Costa Rica. During the first acceptance tests of the Cyclotron, ^{18}F was produced, sent to the hot-cells in order to measure the amount of ^{18}F produced. However, an incident occurred during activity measurement because gas was detected in the ventilation exhaust pipe and detected by the environmental detectors into the production main floor.

Aims: The goal of this work was to show how to avoid recirculation radioactive gas through the building ventilation system.

Methods: Inlet and outlet configuration analysis of the HVAC system occurs. Air trajectory using HYSPLIT model by the NOAA Air resources laboratory was studied. An anemometer was placed between the main HVAC inlet and outlet of the building to evaluate wind direction. Along with that study, analysis of the hot-cell incident also occurred.

Results: One rotation of nearly 100° at the elbow of the exhaust pipe, along with a 20 meters extension of its length was performed, as it is shown in figure 1. The incident occurred when a gap in the plastic cap of the vial was presented.

Figure 1. A. Inlet and outlet pipe HVAC system initial arrangement installed in the building and radioactive gas trajectory entering production main floor. B. Final placement of the outlet pipe.

Conclusion: HVAC system configuration requires a meticulous analysis for these types of installations to prevent recirculation of radioactive gases. Our solution considered wind speed and direction using the HYSPLIT model. Incident analysis gave a solution to prevent this type of events within our hot cells.

GT-05, "IN SITU" ^{131}I INTAKE SURVEILLANCE OF NUCLEAR MEDICINE WORKERS USING A THYROID PROBE: TWO YEARS EXPERIENCE

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Background: ^{131}I-inhalation it is one of the critical risks in a nuclear medicine radiopharmacy lab, due to the ^{131}I-intake surveillance program requirements of the radiation protection program.

Aims: This research, propose to establish and verify a monitoring procedure of ^{131}I-intake of nuclear medicine workers using the thyroid probe of the Nuclear Medicine Department. The counter used is a gamma probe with NaI(Tl) scintillation detector of 30x30 cm.

Methods: The efficiency calibration was performed with a thyroid phantom, simulating the adult thyroid anatomical shape and volume, filled with radioactive solution of known activity of ^{131}I (uncertain activities < 2.24%). The intake and the effective dose estimation were made following the steps suggested in the IDEAS - General Guidelines for the Estimation of the Committed Effective Dose from Incorporation Monitoring Data.

Results: The efficiency (E) was 3.76x 10^{-3}± 1.15x 10^{-4} CPS/Bq, Minimum Detectable Amount (MDA) was 46 Bq. The probe system is capable to detect dose as low as 0.004mSv at 24 h and 0.02 mSv at 2h. A worker monitoring ^{131}I-intakes procedure was proposed and established, based on routine screening 2 h and 24 h after finishing daily activities in the "hot lab", "administration routine" of ^{131}I dose to patient, contaminated wastes manipulations, or in case of detected or suspected radionuclide intake. If the contamination was positive, confirmatory monitoring was developed using the "probe" and also a gamma camera if the preliminary intake was greater than 75KBq. The committed equivalent thyroid dose was evaluated considering the real worker thyroid mass and his/her own bio-kinetic behaviour. The measurement uncertain of 100 Bq thyroid uptake was ±15%. The effective doses were significant lower using specific worker contamination information than calculated doses for the previous monitoring methods (p=0.028). The previous surveillance methods lost the 15% of internal contamination incidents. The thyroid activity quantification uncertain were less than 15%.

Conclusions*:* The proposed procedure is easy to implement, is effective and it can contribute to improve the accuracy of internal dose estimation of workers, furthermore it can increase the low intake activities detection rate.

PC-03, Behavioural Characterization and Assessment of Cerebral Glucose Metabolism by using [^{18}F]FDG PET imaging in BALB/c Mice (*Mus musculus*) Infected with Genetically Different Strains of *Toxoplasma gondii*

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Background: Behavioral manipulation is one of the main theories used to explain alterations in the behavior of rodents infected by *Toxoplasma gondii*. However, some factors related to the behavioral manipulation are not yet well elucidated, highlighting a possible strain dependent effect on the changes in behavior.

Aims: This study aims to assess the effect of chronic infection with genetically different strains of *T. gondii* on the behavior and in the cerebral glucose metabolism of mice.

Methods: For that, BALB/c isogenic mice were infected with the archetypal ME-49 and VEG strains as well as with two non-archetypal strains (i.e. TgHumIMTBr2 and TgHumIMTBr3). Humoral immune response in mice was performed by ELISA and the behavioural alterations were analysed by inhibitory avoidance, Y-maze and open field tests. In addition, [^{18}F]FDG PET imaging was used to evaluate the glucose metabolism in different brain regions.

Results: Infection with VEG strain induced more humoral immune response, whereas no influence of the infection by different strains was observed regarding acquisition and learning of aversive memory. Infections with VEG and TgHum1MTBr3 strains caused locomotor impairments. Only animals infected with the TgHumIMTBr2 strain presented attraction to cat urine odor. Examination using [^{18}F]FDG PET imaging revealed unpublished data showing that infected animals with VEG, TgHumIMTBr2 and TgHumIMTBr3 strains presented greater variations in the uptake of the radiopharmaceutical in the forebrain, whereas there was a significant reduction of uptake in this cerebral region compared to the hindbrain.

Conclusion: our results indicate a strain-dependent effect on the behavior and metabolism of glucose in different cerebral regions of animals infected by *T. gondii*.

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