tificam a inclusão do exame FDG-PET na tabela de procedimentos do SUS para estadiamento do câncer de pulmão.

Radiofarmácia/Radioquímica

Abstract número: 7

COMPARATIVE BIODISTRIBUTION STUDIES WITH [99mTc]-EDDA-TRICINA-HYNIC-[Tyr3]-OCTREOTIDE IN SWISS AND NUDE MICE.

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Synthetic somatostatine (SST) analogues like Octreotide have been used in the preparation of receptor-specific radiopharmaceuticals for diagnostic and therapy of neuroendocrine (NE) tumors. 111In-DTPA-Octreotide (OctreoScan®) has found useful for imaging a range of tumors, including NE cancer, carcinoide and lymphoma. Unfortunately, 111In is a high-cost cyclotron produced radioisotope with gamma emission not so suitable for scintigraphic images and for dosimetry like 99mTc. This work studied the biological distribution in Swiss and Nude (this last one with AR4-2J rat pancreatic tumor cells) mice to evaluate the potential of the 99mTc-labeled peptide (99mTc-HYNIC-Tyr3-Octreotide) for tumor diagnostic application. 99mTc-HYNIC-Tyr3-Octreotide (99mTc-HYNIC-TOC) was produced by labeling conditions using tricine and EDDA as coligands, 20 μg of the respective peptide and 1110 MBq (30 mCi) of sodium pertechnetate eluted from 99Mo-99mTc IPEN-TEC generator. The reactions proceed for 10 minutes at boiling water bath. Radiochemical purity of labeled preparation was determined by appropriated ITLC-SG and TLC-SG systems. Biological distribution studies in Swiss and Nude mice were performed after injection in tail vein of 1.48 MBq (40 μCi) of radiopharmaceutical in animal groups that were sacrificed at 1.5 and 4 hours after the dose administration. The results were expressed as percentage injected dose/organ (%ID/organ) and percentage ID/gram. For scintigraphyc images of Nude mice, 20 MBq (0.54 mCi) of the radiopharmaceutical was injected in tail vein. After 3 hours of the dose administration, the images were obtained in gamma camera. Labeling procedures resulted on high radiochemical purity. Biological distribution studies showed fast blood clearance and elimination by urinary tract. The labeled peptide presented a relative low uptake on liver and intestines. The %ID of 99mTc-HYNIC-TOC in organs with high density of SST receptors like pancreas and adrenals and in tumor were significant probably due to the high affinity of this radiopharmaceutical for the specific receptors. The scintigraphyc images showed good uptake of the labeled compound in tumor when compared with the uptake in normal muscle (B.G.). These results suggest that 99mTc-HYNIC-TOC could be applied in diagnostic studies for localization and staging of neuroendocrine tumors.

Abstract número: 9

USE OF INSTRUMENTAL NEUTRON ACTIVATION ANALYSIS TO STUDY ANTIMONIAL AGENT IN LIPOSOMES.

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Visceral leishmaniasis is caused by hemoflagellate protozoa which is obligatory parasite of the mononuclear phagocyte system (MPS). Leishmaniasis causes high morbidity and mortality worldwide. The treatment of choice remains pentavalent antimonials, but high toxicity and failures have been reported. An alternative to conventional treatment is to deliver antileishmanial agents using carrier systems, as liposomes, which improve drug activity by decreasing the required dose and increasing the efficacy of entrapped drug at the intracellular disease involving the mononuclear phagocyte system. Instrumental neutron activation analysis (INAA) has very good sensitivity and selectivity for measuring antimony in very low levels, and it has the advantage of being independent from the sample matrix and from the efficiency of the digestion or extraction procedure. Moreover, if a nuclear reactor is available, this analysis is easier, faster and less expensive than a conventional analytical method. The aim of this present study was to evaluate the concentration of the antimonial agent encapsulated in liposomes using INAA. Liposomes formulations were prepared from phosphatidylserine, cholesterol and phosphatidylcholine in the molar ratio 1:4:5. Meglumine antimoniate was encapsulated in liposomes by two different methods: freezed-dried empty liposomes (FDEL) or in multilamellar vesicles by filter extrusion (FEL). Aliquots of liposome in clean polypropylene tubes were irradiated together with the antimony standards. Irradiations were carried out at the IEA-RI nuclear reactor of IPEN-CNEN/SP at a thermal neutron flux of 1x10E12 n.cmE-2.sE-1 for 15 minutes. Radioactive concentration was determined by gama-spectrometry, using an HPGe detector coupled to the GeniePC program. Encapsulation efficiency of FEL and FDEL loaded with meglumine antimoniate was about 12% of initial amount of the drug. In conclusion, INAA showed to be a very interesting and important method to determine the antimony concentration in delivery drug system, as liposome, which may be useful as carriers of drugs to treat infectious diseases involving MPS. Encapsulation of antimonial agents and reduction of the dose required for effective therapy should minimize such systemic toxicities. Another potential use of this methodology could be the combined chemotherapy and radionuclide therapy.

Abstract número: 10

DEVELOPMENT OF METHODOLOGIES FOR Y-90 PRODUCTION AT IPEN/CNEN-SP FOR THERAPEUTIC APPLICATIONS.

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In recent years, investigators have developed site-specific delivery of radionuclides for various applications involving the treatment of cancer. Radiosynovectomy is a well-accepted therapeutic procedure in inflammatory joint diseases. There are several radionuclides available for this treatment such as, Y-90, Sm-153, Dy-165, Ho-166, Re-186,188, etc. However, Yttrium-90 (Y-90) is often believed to be among the most useful of the radionuclides that have been considered for therapeutic applications. Y-90 has a half-life of 64.1 hours and emits beta rays of high energy (Ebetamax = 2.3 MeV), with no accompanying gamma-rays, and decays to a stable daughter (Zr-90). It is generally obtained from Sr-90/Y-90 generator systems. Although several methods for the separation of Y-90 from high yield fission product Sr-90 have been published, the most frequently used procedures are ion exchange and solvent extraction. High specific activity, no-carrier added Y-90 is obtained by these methods for radioimmunotherapy. Using these methods for the preparation of Y-90 has many advantages, such as the fact that the final product is carrier free, is less costly, and has long-term reuse capability. However, Sr-90 (T1/2 = 28 years) is a bone seeker which produces bone marrow depression and the maximum permissible dosage is only 74 kBq (2 μCi). Actually, the Radiopharmacy Center at IPEN imports Y-90 at a high cost and label several molecules for clinical use. Because of the significative results in radiosynovectomy treatment and other therapeutic applications, the Center is performing studies for Y-90 production through a Sr-90/Y-90 generator. In this work, the Sr-90/Y-90 generator was developed using a cation exchange resin method. Sr-90 is strongly adsorbed in the resin and Y-90 is eluted in 0.003M EDTA. The generator efficiency and radionuclide control results will be shown using also Sr-85 (γ-ray emitter) as a tracer. Weekly elutions were performed for this generator. The efficiency yield was 95% in the last elution, after about 40 days. The breakthrough of 90Sr was less than 0.04%. The quality control showed that Y-90 had no Sr-85 impurities, inside the detection limits of the detector. The results presented here are very promising, showing that the methodology is able

to separate the two nuclides, with low quantities of Sr-90 impurity and satisfactory elution yields. The results show that is possible to obtain Y-90 for several therapeutic applications nationally. The research was supported by IAEA and CNPq granted a fellowship.

Abstract número: 35

99mTc-DMSA(V): PREPARATION AND QUALITY CONTROL.

Bernardes DML; Castanheira CE; Muramoto E; Fukumori NTO; Matsuda MMN; Barboza MF; Mengatti J.
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Pentavalent dimercaptosuccinic acid (DMSA) labeled with 99mTc concentrates on primary and metastatic head and neck tumors, medullary thyroid carcinoma, breast cancer metastases and multiple myeloma. It is considered an excellent imaging agent in patients with medullary carcinoma of the thyroid. This report describes the preparation and quality control of 99mTc-DMSA(V) using DMSA(III) (vial a) and 4.2% sodium bicarbonate (vial b). The DMSA(III) lyophilized kit contains: 1.0 mg of DMSA; 0.44 mg SnCl2.H2O; 0.7 mg ascorbic acid and 50.0 mg inositol, pH = 2.5. Labeling was performed by adding into the vial a, 1.0 mL of 4.2% NaHCO3 (vial b) and 2-3 mL of pertechnetate with the desired activity of 37 up to 3,700 MBq, final pH = 9.0. The formulation was validated for routine production during 9 months at 2-8°C, using three batches of 99mTc-DMSA(V) labeled with 370 MBq/3 mL. The radiochemical purity was determined by three chromatographic systems: Whatman 3MM paper (1.5 x 12.5 cm) as adsorbent and acetone and 0.9% NaCl as solvents, respectively, and TLC-SG Al (1.5 x 9.5 cm) as adsorbent and butanol:acetic acid:H2O (3:2:3) as solvent. The radiochemical purity was evaluated 30; 60; 120 and 240 minutes after labeling at room temperature and the product stability was studied for 9 months. 99mTc-DMSA(V) presented a radiochemical purity > 90% with neither significant free pertechnetate nor other 99mTc derivative. Biological distribution in Wistar rats was evaluated one hour after intravenous dose of 7.4–11.1 MBq/0.1 mL 99mTc-DMSA(V) showing renal uptake ≤ 20% I.D; liver retention ≤ 3% I.D., spleen ≤ 1% I.D., femur ≤ 1.5% I.D. and skeleton ≤ 70% I.D. Sterility tests were performed by the microbiology procedures outlined in the pharmacopoeias and apyrogenicity by the "in-vitro" Limulus test. The preparation and quality control procedures, under cGMP condition, have been developed and validated at Radiopharmacy Directory of IPEN-CNEN/SP and the first clinical application was successfully performed.

Abstract número: 16

RESIN-BASED MICROSPHERES LABELED WITH HOLMIUM-166 FOR LIVER CANCER THERAPY: A BRAZILIAN ALTERNATIVE.

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The nuclear medicine is based on the use of radionuclides for diagnosis and therapy. In the last decades, the use of radiopharmaceuticals for therapy has increased, especially in cancer treatment. The reason is the development of researches in this area. In this context, the aim of this work is the development of resin-based microspheres labeled with Ho-166, in order to obtain selective delivery of radioisotopes to liver tumor, thus maximizing the irradiation effect while sparing toxicity to the surrounding healthy liver. Liver metastases cause the majority of deaths from colorectal cancer, and response to chemotherapy and external radiotheraphy is poor. An alternative is an internal radionuclide therapy using microspheres labeled with Ho-166, a beta minus emitter (Emax = 1.84 MeV), with maximum tissue range of 8.4 mm, that also emits photons (81 keV, 6.2%) suitable for imaging. The production of Ho-166 is feasible in the IEA-R1 Reactor at IPEN-CNEN/SP. The nuclear reaction has a cross section of 64 barns and Ho-165 has a natural abundance of 100%. It is possible to produce 344 mCi (~12 GBq) (IEA-R1 Reactor, 60 hours, 4.0x10E13n.sE-1.cmE-2) a sufficient therapeutic dose, depending on the demand of doses. The cation exchange resin Sepharose is labeled with Ho-166 under optimized conditions and it has essential characteristics for treatment liver therapy, such as high labeling yield, stability and particle size range. The results showed that it is possible to offer this radiopharmaceutical for the Brazilian nuclear medicine community at a fair value, excluding the necessity of importation of the radiopharmaceuticals available in another countries, such as SIR-Spheres® (SIRtex, Australia) and Therapheres® (MDS Nordion, Canada). However, further in vivo studies should be performed to prove its effectiveness.

Abstract número: 24

A PORTABLE TEST SYSTEM (PTS) FOR DETERMINATION OF BACTERIAL ENDOTOXINS IN 18F-FDG RADIOPHARMACEUTICAL.

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Radiopharmacy Directory – IPEN-CNEN/SP.

Introduction: Pyrogens include any substance capable of eliciting a febrile response upon injection or infection. Endotoxin is a type of pyrogen that is strictly of gram-negative origin, a natural complex of lipopolysaccharide ocurring in the outer layer of the bilayered gram-negative bacterial cell. An automated portable test system (PTS) has been developed for determination of bacterial endotoxins in water, in-process and end-products using the Limulus amebocyte lysate (LAL) kinetic chromogenic test. The aim of this work was to validate this method for 18F-FDG radiopharmaceutical. **Materials and methods:** Experiments were performed in three batches of 18F-FDG produced at IPEN-CNEN/SP in a portable test system (PTS) from Endosafe, Inc.TM, Charleston, SC. Single polystyrene cartridges containing dry LAL-reagents, control standard endotoxin (CSE) and synthetic color substrate were used. The LAL sensitivity was 0.05 EU mL-1. 25 μL samples of the product in serial dilutions were pipetted into the cartridge wells and the temperature of the reaction was 37 ± 1 °C. Results were obtained for the endotoxin concentration in samples by interpolation of an archived standard curve (5.0; 0.5 and 0.05 EU mL-1) at OD (optical density) 405 nm, after 20 minutes. **Results:** The maximum valid dilution was calculated to establish the extent of dilution to avoid interfering test conditions (MVD = 500). The endotoxin concentration was lower than the lowest concentration of the standard curve in all samples, and the parameters of coefficient correlation (R) ≤ 0.980, recovery of positive product control (RPPC) 50-200% and coefficient variation (CV) of the samples < 25% were satisfied from 1:5 until 1:50 dilution factor. **Discussion/conclusion:** The PTS is a new kinetic chromogenic technique for bacterial endotoxin determination. Especially for short-lived radiopharmaceuticals, it trends to be the method of choice. The technique showed to be simple, easy, fast and accurate and the validation was successfully performed.

Abstract número: 34

PRODUCTION AND QUALITY CONTROL OF 99mTc-GLA (GLUCARIC ACID).

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Radiopharmacy Directory – IPEN-CNEN/SP.

Previous studies have showed that 99mTc labeled glucaric acid (GLA) is emerging as a promising metabolic marker of myocardial viability as it shows high affinity for necrotic myocardial tissue, acute cerebral injury and tumors. GLA is a 6-carbon dicarboxilic acid that has been proposed as a potentially useful SPECT imaging agent for myocardial infarction. This paper describes the production and quality control process of GLA in lyophilized form, under GMP condition, for labeling with Tc-99m. The process was performed under vacuum and low temperature in the Super Modulyo–"Edwards" lyophilizator and each lyophilized vial contained:

12.0 mg of GLA; 0.5 mg of gentisic acid and 0.5 mg of SnCl2.H2O, pH = 5.0. The radiochemical purity was determined by two paper chromatography systems in Whatman 3MM paper (1 x 8 cm), using acetone and saline (0.9% NaCl) as solvents. Sterility tests were performed by the microbiology procedures outlined in the pharmacopoeias and pyrogen test by the "in-vitro" Limulus test. Biological distribution in Wistar rats was evaluated 30 minutes after intravenous dose of 7.4–11.1 MBq/0.1 mL of 99mTc-GLA in different organs (% injected dose/organ). The radiochemical purity was > 95%. Sterility and pyrogen tests were negative in all the delivered lyophilized vials. The biological distribution of 99mTc-GLA in rats showed low uptake in lung and heart (< 1%) and low activities in liver and muscle (< 5%). Scintigraphic images of 99mTc-GLA were performed in 4 patients (Campinas University) with symptoms highly suggestive of acute myocardial infarction. The patients were injected with 740 MBq of 99mTc-GLA, 3 to 9 hours after the onset of chest pain and images were obtained 2 hours later. At rest, images from 99mTc-MIBI were also obtained for comparison. Acute infarction was confirmed in 2 patients with focal 99mTc-GLA uptake. In one patient without 99mTc-GLA uptake, myocardial infarction was finally excluded. The fourth patient injected 9 hours after the onset of chest pain had a final acute infarction diagnosis and a negative 99mTc-GLA scan. We concluded that 99mTc-GLA is a promising radiopharmaceutical for the diagnosis and localization of acute myocardial infarction and should be injected in less than 9 hours of the onset of chest pain. More studies are necessary to determine the accuracy of the method. The lyophilized form and quality control procedures of GLA labeled with Tc-99m have been developed and validated at Radiopharmacy Directory of IPEN-CNEN/SP.

Abstract número: 38

177Lu-LABELING, STABILITY AND PRECLINICAL EVALUATION OF BBNp4: A NOVEL BOMBESIN ANALOGUE FOR PROSTATE TUMOR IMAGING AND THERAPY.

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Prostate cancer is the second deadly form of cancer in men in Brazil and also one of the most frequently diagnosed cancer in men in the world. Treatment options have varied, but once the tumor has metastasized, treatment become less effective and the cancer can progresses to a hormone refractory state characterized by high morbidity and mortality. Bombesin (BBN) receptors – in particular, the gastrin-releasing peptide (GRP) receptor peptide – have been shown to be massively overexpressed in several human tumors types, including prostate cancer, and could be an alternative as target for its treatment by radionuclide therapy (RT). A large number of BBN analogs had already been synthesized for this purpose and have shown to reduce tumor growth in mice. Nevertheless, most of the studied analogs exhibit high abdominal accumulation, especially in pancreas. This abdominal accumulation may represent a problem in clinical use of radiolabeled bombesin analogs probably due to serious side effects to patients. This work describes the radiolabeling with lutetium-177 (177Lu), a b-emitter with optimal physical characteristics for RT of small tumors and metastases, and the in vivo properties of the novel bombesin analog BBNp4 – DOTA-X-BBN(6-14), where X is a spacer of four aminoacids. Preliminary studies were done to establish the ideal labeling conditions for obtaining the highest yield of labeled BBNp4. ITLC and HPLC chromatography were applied to determine free lutetium and the stability of the preparations was evaluated either after storing at 4 °C or incubation in human plasma at 37 °C. In vivo experiments involved biodistribution, pharmacokinetics and single photon emission tomography images and were performed after intravenous administration in both Balb-C and Nude mice bearing PC3 xenografts. BBNp4 was successfully labeled with high yield (> 99%) at optimized conditions and kept stable for more than 96 hours at 4 °C and 4 hours in human plasma. In vivo studies showed that BBNp4 exhibited fast clearance and became almost undetectable in blood at 60 min p.i., indicating rapid peptide excretion, which is performed mainly by renal pathway. In addition, biodistribution in Nude mice showed 0.37, 0.17 and 0.04% ID/g of PC3 tumor uptake after 1, 4 and 24 hours p.i., respectively. Although tumor uptake was not as high as other bombesin analogs described by the literature, this peptide exhibits low abdominal accumulation with tumor:organs uptake ratios of 21.28 (blood), 0.05 (kidneys), 0.27 (intestine) and 3.26 (pancreas) after 24 p.i. Further experiments are in development to verify BBNp4 effects in PC3 cells in vitro. Modifications at BBNp4 spacer will be also investigated to produce different analogs with higher specific receptor affinity.

Abstract número: 39

ESTUDO COMPARATIVO DE CONTROLE RADIOQUÍMICO DE DTPA E Sn COLOIDAL.

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Os métodos analíticos mais usados para determinar impurezas radioquímicas de um radiofármaco são cromatografia em papel, em camada delgada e em gel, cromatografia líquida de alta eficiência, eletroforese em papel e em gel e extração por solvente e em fase sólida. As impurezas radioquímicas podem ser causadas pela decomposição do radiofármaco por ação do solvente, luz, radiólise ou marcação de uma impureza com o mesmo radionuclídeo, como por exemplo, 99mTc reduzido hidrolisado em complexos marcados com 99mTc. O objetivo deste trabalho é comparar as metodologias de controle radioquímico dos reagentes liofilizados para radiodiagnóstico (RL) DTPA e Sn coloidal (SnCol), marcados com 99mTc descritas na Farmacopéia Européia, Americana e a utilizada na Diretoria de Radiofarmácia do IPEN-CNEN/SP. DTPA (ácido dietilenotriaminopentacético), SnCol e o gerador 99Mo/99mTc utilizados foram produzidos no IPEN-CNEN/SP. Três lotes consecutivos de cada produto e 2 frascos de cada lote foram marcados com 74 MBq Na99mTcO4 e analisados após 15 minutos e 4 horas. Para o DTPA, utilizou-se a metodologia da Farmacopéia Européia para a quantificação de TcO2 e TcO4- empregando como fase estacionária ITLC-SG de 10 segmentos (1,5 x 12,5 cm) e solventes NaCl 0,9% e metiletilcetona, respectivamente. Segundo a metodologia do IPEN, para quantificar TcO2 e TcO4-, usou-se fita de papel Whatman 3MM de 2 segmentos (1,0 x 8,5cm) e como solventes NaCl 0,9% e acetona, respectivamente. Para SnCol, a quantificação de TcO4- segundo a Farmacopéia Européia foi feita utilizando como solvente NaCl 0,9% e fase estacionária ITLC-SG de 10 segmentos (1,5 x 12,5 cm). Na metodologia do IPEN, usou-se como solvente acetona e papel Whatman 3MM de 2 segmentos (1,0 x 8,5 cm). Os resultados para o DTPA e SnCol, tanto pela metodologia da Farmacopéia Européia quanto pela metodologia utilizada no IPEN, estiveram acima de 95% de pureza radioquímica e variação de cerca de 2% entre as metodologias, demonstrando que a natureza da fase estacionária e o solvente não interferiram significativamente na separação das espécies. Este estudo contribuiu para o atendimento aos requisitos de boas práticas de fabricação, dentro do plano de validação de metodologias analíticas utilizadas no controle de qualidade.

Abstract número: 41

PRELIMINARY EVALUATION OF AN AUTOMATION SYSTEM FOR THE CONCENTRATION OF Tc-99m FROM MOZR GEL GENERATOR.

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There are two ways of producing the Mo-99/Tc-99m generators at the Radiopharmacy Center (RC) of IPEN-CNEN/SP: using Mo-99 produced by the fission of uranium and imported from Canada and through the reaction Mo-98(n,γ)Mo-99 that occurs in IEA-R1 Nuclear Reactor (IPEN-

CNEN/SP). The latter employs the technique of the gel type chromatographic generator of MoZr. Despite all efforts in the study of the optimization conditions for the preparation of MoZr gel, the radioactive concentration is lower and the volume of elution is also higher (12 mL) when compared to the fission generator (6 mL). One way to increase the radioactive concentration is to use concentration systems. The objective of this study is to evaluate the automation of the concentration systems developed for the MoZr gel generator. For this study two systems were employed: the single one and tandem one and they could be operated in both manual and automated ways. The MoZr gel generator was prepared using the pre-formed technique developed by IPEN and further irradiated in the IEA-R1 Reactor at IPEN-CNEN/SP. Two grams of gel were placed in a glass column (conditioned with 50 mL of the same eluent used for the elution of the generator) and the concentration system was connected to the generator. Daily eluitons were performed and the activity of Tc-99m was measured. The single concentration system consisted of an anionic cartridge (AcellTM Plus QMA - Waters) with the elution of the gel generator with deionized water and the concentration system eluted with saline. The tandem system consisted of two cartridges connected in series, the cation column (IC-Ag-Alltech or On Guard II-Ag-Dionex) and an anion column (AcellTM Plus QMA-Waters) and both the generator as well as the concentration system were eluted with saline. The parameters of evaluation and comparison were the efficiency of the generator and the elution time. Preliminary results show the good similarity between the two systems (automatic and manual).

Abstract número: 48

SODIUM FLORIDE-18F: PREPARATION AND QUALITY CONTROL.

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The use of 18F-fluoride for bone scintigraphy dates back to the early days in the 1950s and 1960s. Several decades before the introduction of modern PET system, 18F-NaF was recognized as an excellent radiopharmaceutical for skeletal imaging. Sodium fluoride-18F (18F-NaF) has the desirable characteristics of high and fast bone uptake accompanied by very rapid blood clearance, which results in a high bone-to-background ratio in a short time. The purpose of this work was to describe the development and validation of 18F-NaF production and quality control at the Radiopharmacy Directory. For clinical application 18F- is easily produced in a cyclotron utilizing a one step reaction 180(p,n)18F, with enriched water H2180 (> 95%) as target: with short irradiation time (15–30 minutes). After bombardment, the target water was passed through an ion-exchange column (QMA-light, Waters) to trap the 18F-fluoride while the enriched water was eluted and collected for discarding or reusing. The 18F-fluoride was eluted off with 0.5 M sodium bicarbonate solution / 0.3mL. The final product (18F-NaF) was diluted with 15 mL of 0.9% saline solution and sterilized m Millipore filter to a sterile pyrogen-free?by passing into a 0.22 vial and final pH 5.0–8.0. The doses were fractioned according to demand. A thin layer chromatography system was carried out for radiochemical purity determination in ITLC-SG (Al) (1 x 12 cm), using acetonitrile:water (95:5) as solvent. Stability of 18F-NaF was determined immediately and 4 hours after the end of process. Radionuclides purity was determined by the radioactivity decay curve during 125 minutes. Sterility tests were performed by the microbiology procedures outlined in the pharmacopoeias in different culture media 2.5 °C. The apirogenicity was ??2 °C and at 32.5 ??incubated at 22.5 evaluated using the “in-vitro” Limulus (LAL) test. The radiochemical purity of 18F-NaF was (99.85 ± 0.08)% in 10 batches, with t1/2 = 110 minutes and the sterility and pyrogen tests negative in all delivered vials. The labeling and quality control procedures under cGMP condition have been developed and validated at Radiopharmacy Directory of IPEN-CNEN/SP and the first clinical application was successfully performed.

Abstract número: 50

IMPROVEMENT IN 67Ga-CITRATE PRODUCTION AT IPEN-CNEN/SP.

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For many years, 67Gallium-citrate has been used for the detection of both acute and chronic abscesses and immflamatory processes. Ga-67 is a cyclotron–produced radionuclide by the irradiation of Zn with protons: 67Zn(p,n)67Ga, yielding no beta rays, with 78,1 hours physical half-life. Ga-67 emits four main gamma rays but the moderate gamma energies of 0.1846 and 0.3002 MeV are suitable for imaging with gamma cameras or SPECT. The aim of this work was to present the improvement in the production and quality control of 67Ga-citrate, prepared from imported 67GaCl3 (Nordion®) and delivered to nuclear medicine clinics in Brazil. Approximately 166.500 GBq at the time of process, were transferred in the hot-cell, diluted with 1 mL of 3,5 N HCl and dried at 100º C under vacuum. The residue was diluted with 2 mL 30% H2O2 and dried to eliminate organic materials. The activity was diluted 2 times with 4 mL of sterile water and dried. The volume was completed with 140 mL of 3.8% pyrogen-free sodium citrate solution. The process of transference of initial activity (Vo) up to the final 67Ga-citrate activity (Vf) was evaluated under peristaltic and vacuum (current) pump. The hot-cell was designed and assembled by IPEN technical staff as well as the glassware and inner devices. The doses were fractioned according to demand and autoclaving 20 minutes at 121 °C. The radiochemical purity was determined in Whatmann 3MM paper (1 x 10 cm), using pyridine:ethanol:water(1:2:4) as solvent. The Rf = 0.8 (67Ga-citrate) and Rf = 0.0 (67GaCl3). The radionuclide purity was determined by g-ray spectroscopy using hipper-pure Ge-detector. Sterility tests were performed by the microbiological procedures outlined in the pharmacopoeias in different culture media incubated at room temperature and at (37.5 ± 2.5) °C. The apirogenicity was evaluated using the “in-vitro” Limulus test (LAL). The radiochemical purity of 67Ga-citrate was (95.52 ± 0.85)% in 15 batches and the sterility and pyrogen tests were negative in all the delivered vials. The labeling and quality control procedures for 67Ga-citrate have been developed, validated and simplified to large-scale productions at Radiopharmacy Directory of IPEN-CNEN/SP. At present the 67Ga-citrate is manufactured, in hot cell using vacuum pump, on Thursdays and delivered on Fridays with calibration for next Mondays. The improvement and performance in the cell were corroborated by the yield and short time of process. Since 2002 up to 2007, 55.72 GBq / 3,548 batches and 91.50 GBq / 4,690 batches were distributed, respectively, to Hospitals and Nuclear Medicine Centers in Brazil.

Abstract número: 57

LABELLING OF HYNIC-[Tyr3]-OCTREOTATE WITH 99m-TECHNETIUM: PREPARATION OF LIOPHYLIZED KIT FOR CLINICAL APPLICATION.

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The development of labeled molecules with high specificity for tumors has been improved in the last years and contributed to the introduction of tumor target molecules applied in specific diagnostic and therapy in nuclear medicine. The most important example of labeled peptide applied in oncology is the use of somatostatin derivatives labeled with different radionuclides in the diagnostic and therapy of neuroendocrine tumors. Nowadays, 111-indium-DTPA-octreotide is the radiopharmaceutical of choice to visualize tumors that express receptors for somatostatin. However, 111-indium has sub optimal physical characteristics (physical half life of 67 h and gamma fotons of 173 keV and 247 keV), that contributes to low resolution images in SPECT (single photon emission computed tomography) and high dosimetry to the patients. The favourable

physical properties of the 99m-technetium (half life of 6.02 h and 140 keV monoenergetic gamma ray) have been estimulated the development of a somatostatin derivative labeled with this radionuclide. This work studied the labeling conditions of HYNIC-Octreotate with 99m-technetium, using EDDA (etilendiaminediacetic acid) and tricine as coligands. A lyophilized formulation was proposed and the labeling conditions were evaluated as well the stability of the preparation. A high stable lyophilized formulation was obtained that can be applied in routinely evaluation of patients with neuroendocrine tumors in nuclear medicine. Preliminar scintigraphic studies in rabit suggests favourable biodistribution pattern of the labeled compound. Biodistribution studies in xenographed mice (AR42J-pancreatic tumor cells) showed high tumor uptake and suggests that the 99m-technetium -labeled somatostatin derivative can be a potential substitute for 111-indium-DTPA-octreotide in the diagnostic and staging of patients with neuroendocrine tumors.

Abstract número: 55

ANALYSIS OF THE RADIOCHEMICAL PURITY OF 99mTc-LABELED HUMAN SERUM ALBUMIN BY SIZE-EXCLUSION CHROMATOGRAPHY AND THIN LAYER CHROMATOGRAPHY.

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Albumin is a water-soluble polypeptide with a molecular mass of about 68,000 daltons. Human serum albumin (HSA) is the major component of plasma protein in healthy adults at concentration 35-50 mg L-1. The function of the albumin is to keep colloid osmotic pressure to the capillary membrane, which prevents plasma loss and maintains the plasma volume. 99mTc-HSA is an important radiopharmaceutical clinically applied for cardiac function tests or assessment of protein-losing gastroenteropathies. Serum albumin reacts with 99mTc (in +5 oxidation state) to form 99mTc-HSA. It is recommended at least 90% radiochemical purity (RCP) of 99mTc-HSA for clinical use. The present study reports the comparison between two chromatography methods for purity determination of 99mTc-HSA: size-exclusion chromatography (SEC) and thin layer chromatography (TLC), 30 minutes and 4 hours after reconstitution of the HSA lyophilized reagent with sodium pertechnetate (Na99mTcO4). HSA lyophilized kit and 99Mo/99mTc generator were from IPEN-CNEN/SP, reagents were from Merck and water was purified in a Milli-RX system from Millipore. A vial containing HSA was reconstituted by the addition of 3 mL eluate containing 166.5 MBq Na99mTcO4. TLC analysis using a silica gel coated glass-fiber sheet L sample and methanol:μ(5 x 20 cm) as adsorbent was performed using 5 water (85:15; v/v) as solvent. The plate was cut in 1 cm strips and the radioactivity measured by a gamma counter with NaI detector. Free pertechnetate has Rf 1.0 and 99mTc-HSA and TcO2 remain at the origin. SEC analysis was performed in a HPLC system (LC 20AT Prominence) (Shimadzu) composed by two pumps, auto sampler (SIL 20A), system controller (CBM 20A), a Protein-Pack 300 SW column (300 mm x 7.5 mm m particle size), diode array (SPD M20A) and a gamma μi.d., 10 L sample volume (99mTc-HSA and μradiation detector (Bioscan). A 200 concentrated mobile phase, 1:1, v/v) was injected and the mobile phase disodium hydrogen phosphate, potassium dihydrogen phosphate, sodium chloride and sodium azide, 4:1:1:0.1, m/m) was isocratically eluted, at 0.6 mL min-1 flow rate, continuously monitored by the radiation detector. The samples were analyzed in duplicate in the two methods. SEC analyses showed a labeling average efficiency of (97,28 ± 0.09)% and peaks were eluted with retention times 8.71 min, 9.25 min, 11.44 min, 12.58 min, 14.48 min, 20.63 min, corresponding to high molecular mass compound, poly III-albumin, poly II-albumin, poly I-albumin, 99mTc-HSA and pertecnetate, respectively. Each method gave similar results for radiochemical purity. The difference between TLC and SEC was 2.39%. The identity of some radiochemical impurities of the 99m Tc-HSA was confirmed by 2 different methods. TLC and SEC are important techniques for quality control of 99mTc-HSA radiopharmaceutical.

Abstract número: 66

PREPARATION OF DMSA (V) KIT FOR LABELLING WITH Tc-99m.

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Technetium-99m is the most useful radionuclide in diagnostic imaging procedures in nuclear medicine, more than 80 percent of radiopharmaceuticals are Tc-99m-labeled compounds. The reason for such a position of Tc-99m in clinical use is its favorable physical characteristics of decay, like short half life of 6.02 h, gamma emission of low energy (140 keV) and absence of particulated emission. Another advantage of the Tc-99m is that it can efficiently label many kits by one step method. One of the many kits labeled with Tc-99m is the DMSA (V) (pentavalent dimercaptosuccinic acid), that is used for the detection of medullary thyroid cancer and other soft tissue tumors. Other studies carried out by this agent include head and neck tumors, brain, liver and skeletal metastases from breast carcinoma. Recently it has been studied for imaging of small cell and non small cell lung cancer, imaging patients with bone metastases, hepatocellular carcinoma and bone tumors. Tc-99m-DMSA (V) can be prepared by two methods, one of them, here called two steps method, uses a commercial kit of Tc-99m-DMSA (III) and a certain amount of NaHCO3 to elevate the pH to 8.0–8.5. This one is already commercialized by IPEN. The other method, here called one step method, is a lyophilized formulation of the DMSA(V), where the product will be ready to be labeled with Tc-99m. The Brazilian nuclear medicine community has great interest in this radiopharmaceutical and the final result of this project is to make possible its routine production with the adequate quality requirements. The aim of this work is the development of a lyophilized DMSA (V) kit for the one step labeling with Tc-99m. The study started with the evaluation of the labeling yields of the 99mTc-DMSA (V) in a liquid kit, and then the preliminary results from the lyophilized DMSA (V) kit. 99mTc-DMSA (V) was prepared in a liquid kit that contained 1.8 mg of DMSA and different amount of SnCl2.2H2O (1.12, 0.56, 0.28 and 0.14 mg) in a total volume of 1 mL. The pH was adjusted to about 9.5 with NaOH and then 740 MBq of Na99mTcO4 in 1 mL of 0.9% NaCl was added to the liquid kit. The solution was stirred and incubated for 30 minutes at room temperature. The radiochemical purity was evaluated by thin layer chromatography (TLC) on silica gel (TLC-SG) to determine the labeling efficiency and impurity formation. TLC-SG strips (1.5 x 12 cm) were developed in two different solvent systems. A solvent system containing: n-butanol/acetic acid/H2O (3:2:3 by volume) was used in order to separate 99mTc-DMSA (V) (Rf 0.6-0.7) from 99mTcO4– (Rf 1) and 99mTc-DMSA (III) (Rf 0). The second system used water as solvent in order to determine 99mTcO2, that stayed at the origin and the other species migrated with the solvent front. The first formulation chosen to be lyophilized was the one containing 1.8 mg DMSA and 0.56 mg SnCl2.2H2O and it showed a good labeling yield of 92%.

Abstract número: 114

VALIDAÇÃO DE MÉTODOS DE ANÁLISE E INCERTEZA DE MEDIÇÃO NO CONTROLE DE QUALIDADE DE RADIOFÁRMACOS: UMA ANÁLISE CRÍTICA.

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O controle de qualidade de um radiofármaco depende, fundamentalmente, do tipo de radiofármaco a ser ministrado. Um radiofármaco pode conter substâncias que não sejam aquelas que se deseja no produto final obtido, ou que estejam acima dos limites permissíveis para o uso do mesmo. A presença destas substâncias indesejáveis, que podem ser tóxicas ou se localizarem em áreas que não sejam aquelas preten-

didas, pode resultar na degradação da qualidade da imagem ou no aumento da dose de radiação absorvida pelo paciente. Dados não confiáveis sobre a quantificação destas substâncias podem resultar na necessidade de repetição do exame, expondo novamente o paciente, além de onerar o Estado quanto aos custos de produção. A qualidade destas medições é então essencial para assegurar a confiabilidade nos dados obtidos, além de minimizar todos estes problemas. O modo de se comprovar o desempenho de um método de análise é através da validação. Validar um método de análise significa comprovar, através do fornecimento de evidência objetiva, que os requisitos para uma aplicação ou uso específicos pretendidos pelo método foram atendidos. Um processo de validação bem definido e documentado oferece às agências reguladoras evidências objetivas de que os métodos analíticos adotados são adequados ao uso desejado. Um método de análise validado pode respaldar um laboratório através do provimento da confiabilidade dos resultados nos laudos emitidos aos seus clientes. A informação sobre a confiabilidade pode ser mais completa com a associação de uma incerteza ao resultado de medição. A qualidade de uma medição é avaliada através da incerteza de medição. A incerteza expressa a dúvida acerca de quão corretamente o resultado da medição representa o valor da grandeza que está sendo medida. As medições estão presentes, direta ou indiretamente, em praticamente todos os processos de tomada de decisão. É estimado que cerca de 4 a 6% do produto interno bruto, PIB, de países industrializados sejam dedicados ao processo de medição. A crescente consciência da cidadania e o reconhecimento dos direitos do consumidor e do cidadão amparados por leis, regulamentos, usos e costumes consagrados, garantem o acesso a informações mais detalhadas e transparentes, tornando imprescindível a confiabilidade nas medições. Sob este contexto, a garantia da confiabilidade nos resultados obtidos no controle de qualidade de radiofármacos deve ser vista como uma melhoria do processo de produção dos mesmos. Esta melhoria irá reafirmar e evidenciar a competência nacional e internacional dos atuais e futuros institutos e centros da CNEN produtores de radiofármacos.

Abstract número: 127

MULTIELEMENTAR DETERMINATION OF TRACE METALS IN RADIOIODINE COMPOUNDS BY INDUCTIVELY COUPLED PLASMA OPTICAL EMISSION SPECTROMETRY.

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Aim: The major use of radioiodinated compound is in nuclear medical imaging. The two most important isotopes of iodine radiopharmaceuticals are iodine-123 (123I) and iodine-131 (131I). The quality control specifications for labeling molecules with 131/123I injection involve sterility, bacterial endotoxins, pH and radiochemical purity tests. However, little attention has been given to the analysis of chemical impurities. The presence of impurities before radiolabeling can result in undesirable labeled molecules that may affect the diagnostic. Chemical impurities with potential toxic, physiologic or pharmacological effects must be evaluated and quantified. The aim of this work was to perform multielementar determination of 24 trace metals in 131/123I labeling molecules used in nuclear medicine by inductively coupled plasma optical emission spectrometry (ICP-OES). **Materials and methods:** The measurements were carried out in a Vista MPX simultaneous ICP-OES (Varian Inc., Australia) equipped with axially viewed plasma and concentric glass nebulizer. Argon was used as plasma and auxiliary gas. The sample was introduced directly into the hot g mL–1 μplasma where metals were atomized and determined. The 100 multielementar standard (Merck) contained aluminum, boron, barium, beryllium, bismuth, cadmium, calcium, chromium, cobalt, copper, iron, gallium, lithium, magnesium, manganese, nickel, lead, potassium, selenium, sodium, strontium, tellurium, thallium and zinc was used for g mL–1 range. The μobtaining calibration curves in the 0.0-1.0 calibration and blank solutions were prepared with purified water and stabilized in 3% v/v concentrated HN03. Some batches of MIBG-131/123I, Hippuran-131I and HSA-131I samples were diluted to 1:25 with purified water and analyzed. Three injections of each standard and samples were made to obtain the results. The correlation coefficients of the calibration curves were higher than 0.995. **Results and discussion:** It was observed that 5 ppm standard in the analytical curve decreases correlation coefficient increasing standard deviation mainly for Ca, Ba, Mg, K and Na, which had emission lines of lower sensitivity established. Al, Cu, Mg and Pb were the impurities observed in the samples and the concentration was lower than 2 ppm. **Conclusion:** ICP is an important tool for simultaneous metal analysis using minimum volume sample of radiopharmaceuticals and being a fast and accurate method for determination of impurities.

Abstract número: 131

QUEBRANDO MITOS: IMPLANTANDO O CONTROLE DE QUALIDADE DOS RADIOFÁRMACOS MARCADOS COM 99mTc NA ROTINA DIÁRIA DE UM SERVIÇO DE MEDICINA NUCLEAR.

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Introdução: O artigo 6.16 da RDC-ANVISA nº 38 para a medicina nuclear estabelece: "O serviço de medicina nuclear deve realizar controle de qualidade do eluato dos geradores e radiofármacos conforme recomendações dos fabricantes, evidências científicas ou compêndios oficiais aceitos pela ANVISA". Devido às características físicas do radionuclideo e pela praticidade dos "kits diagnósticos" poderem ser preparados no próprio local de uso, os radiofármacos marcados com tecnécio-99m são os principais agentes para diagnósticos utilizados nas clínicas de medicina nuclear. No entanto,durante a marcação podem ser geradas algumas impurezas que proporcionam a formação de produtos com baixa qualidade ou com características diferentes das desejadas e que podem interferir na qualidade final da imagem cintilografica obtida. A qualidade do eluato e dos componentes dos "kits" e os procedimentos utilizados na marcação são possíveis causas destas eventuais ineficiências. **Objetivo:** Demonstrar um programa de controle radioquímico dos kits conforme a exigência da RDC nº 38 da ANVISA; com baixo impacto financeiro no custo operacional dos exames; sem "tumultuar" a rotina do laboratório de manipulação do serviço de medicina nuclear (SMN) e agregando benefícios práticos no dia a dia. **Métodos:** A metodologia especifica para cada "kit" é descrita na bula de cada fabricante sendo que a principal técnica utilizada no controle de qualidade dos radiofármacos marcados com tecnécio é a cromatografia ascendente, em que uma pequena amostra (uma gota apenas) do "kit" a ser analisado é aplicada sobre uma fase estacionária (placas), que é arrastada por uma fase móvel (solvente) em uma cuba cromatográfica. As fases estacionárias mais utilizadas são a placa Whatman e a placa de sílica gel, que podem ter tamanho de 6,5 x 1,0 cm. Geralmente são utilizadas duas placas uma com solvente hidrofílico (soro fisiológico) e outra com solvente orgânico (acetona PA ou butanona PA ou metanol PA). Com estes conjuntos de reagentes é possível se obter a eficiência de marcação de quase todos os "kits" utilizados no dia a dia do SMN. A cuba cromatográfica pode ser improvisada com a utilização de vidros tipo penicilina e uma vez ocorrida a migração dos solventes e a devida separação das fases, utiliza-se o curiômetro para efetuar a leitura dos dados que serão utilizados para realizar os cálculos do controle de qualidade. **Conclusão:** A implantação deste programa é simples, conforme será demonstrado durante a apresentação oral e pode ser facilmente incorporada na rotina de trabalho do laboratório de manipulação de qualquer SMN, não impactando de forma importante no custo do exame. A garantia final dos radiofármacos é fundamental num SMN, uma vez que os artefatos gerados por uma má marcação do "kit" poderá prejudicar o diagnóstico

final do paciente e também pode gerar impacto financeiro, pois a remarcação de um único exame tem um custo operacional muito superior ao da realização de centenas de controles de qualidade.

Abstract número: 132

IMPLANTAÇÃO DA ISO 17025 NA PRODUÇÃO DE RADIOFÁRMACOS DO IEN.

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O IEN orgulha-se de ter uma contribuição histórica e significativa para o atual estágio da medicina nuclear no Brasil. Os últimos 10 anos foram marcados pelo sucesso do fornecimento pioneiro do radioisótopo I-123 ultra-puro, que vem beneficiando milhares de pacientes/ano com diagnósticos mais precisos e uma menor dose de radiação ionizante a que estão sujeitos. O sistema de produção de 123I ultra-puro (Kipros – Karlsruhe Iodine Production System) do Instituto de Engenharia Nuclear (IEN) completou 10 anos de funcionamento ininterrupto com mais de 1500 operações com um índice de 98% de confiabilidade. São incomensuráveis os benefícios gerados por diagnóstico com o iodo-123 e suas moléculas marcadas. Essa foi uma grande conquista não somente do IEN, mas da sociedade em geral. Em 1999 o IEN adquiriu um segundo cíclotron, RDS/Eclipse para produção de radiofármacos pósitron emissores e duplicou seus laboratórios de radiofarmácia com o apoio da Agência Internacional de Energia Atômica. Em 2002, dois novos radiofármacos foram disponibilizados para os serviços de medicina nuclear pelo IEN, 123I marcado com MIBG (meta-iodo benzilguanidina) e o 18F-FDG (flúor dezoxi glicose). Devido ao impacto positivo da utilização da tecnologia PET para diagnósticos mais precisos a produção do pósitron emissor, 18F-FDG, vem registrando forte crescimento. O IEN tem produzido e distribuído 18F-FDG cinco vezes na semana, para Rio de Janeiro, Brasília, Vitória, Salvador e Belo Horizonte. Na linha de produção de radiofármacos o controle de qualidade, ocupa um papel de destaque. Embora, os radiofármacos não tenham ação farmacológica, porém, sua administração em seres humanos torna imperativo que se cumpram os requisitos exigidos aos fármacos convencionais, além dos específicos, por tratar-se de substâncias radioativas. Após a preparação e antes de seu uso em pacientes, é necessário verificar a qualidade dos mesmos. Deve-se, portanto, submetê-los a uma série de controles e procedimentos padronizados internacionalmente. Dentro deste contexto, o IEN está implementando em seus ensaios do controle de qualidade a ISO 17025 visando a acreditação ou certificação de seus laboratórios. Esta norma tem a preocupação clara de estabelecer orientações gerais e modernas para que os laboratórios desenvolvam um sólido gerenciamento segundo padrões de qualidade internacionalmente reconhecidos. A ISO 17025 tem total convergência e compatibilidade com a ISO 9001/9002, entretanto existe uma nítida separação entre os requisitos gerenciais e os requisitos técnicos: a seção 4 contém os requisitos para a administração e a seção 5 especifica os requisitos para a competência técnica dos ensaios e ou calibrações que o laboratório realiza. Esta norma estabelece os critérios técnicos para que os laboratórios demonstrem sua competência técnica, com um sistema de qualidade efetivo e capaz de produzir resultados tecnicamente válidos, o que não está presente na 9001 nem na 9002.

Abstract número: 142

PRELIMINARY STUDY OF THE CYTOGENETIC EFFECTS OF NEUTRONS PRODUCED IN REACTOR ON HUMAN BLOOD LYMPHOCYTES.

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Studies on the effects of different types of ionizing radiation on cells are of great value not only from a radiobiological viewpoint but also for dosimetric and therapeutic purposes. In general, the high-LET radiation (linear energy transfer), including alpha particles and neutrons, produce more damage that low-LET radiation, as gamma radiation, X-ray and beta particle. This is because all the energy is deposited within a short distance, causing dense ionizing and therefore the damage is more complex and located and it is less efficiently repaired by the cell. Despite the considerable quantity of published data on cytogenetic effects of gamma radiation and X-rays, there is little information on the effect of the neutrons in human cells, also of great importance since it is involved in several nuclear accidents. The purpose of this study is to evaluate the cytogenetic effect of neutrons on peripheral blood lymphocytes through the technique of chromosome aberrations. For that, blood samples from two, 22 and 25 years old, healthy donors, of the both sexes, were irradiated in the reactor research IEA-R1 of IPEN/CNEN-SP with thermal and epithermal neutrons, at doses of 0.5, 1, 2 and 4 Gy. The cytogenetic analysis showed an increase in the frequency of cells containing aberrations as function of radiation dose (7.5, 12.4, 24 and 45%) with 0.8% in the control sample. The number of aberrations/cell ranged from 0.008 to 0.729 in the control and 4 Gy samples, respectively. The hypomodal chromosome number increased at a dose of 0.5 Gy (9.8%), reaching value of 14.3% in the dose of 4 Gy in relation to the control (7.2%). These observations suggest a possible aneugenic effect of the neutrons when compared to data obtained from low-LET radiation, showing a potentially higher damage of neutrons, both clastogenically and aneugenically.

Abstract número: 145

COMPARATIVE LABELLING STUDIES OF 177Lu-HA FOR RADIOSYNOVECTOMY.

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Radyosinovectomy (RSV) is a local intraarticular injection of radionuclides in colloidal form for radiotherapy. The technique has been applied for more than 50 years for treatment of resistant synovitis of individual joints. RSV relieves pain and inflammation from rheumatoid arthritis (RA), osteoarthritis and hemophiliac arthropathy. Lutettium-177 is considered to be a promising radionuclide for use in RSV of small-sized joints owing to its favourable characteristics [t1/2 = 6.73d, Eβ(max) = 0.49 MeV, Eγ = 113 KeV (6.4%), 208 KeV (11%)] and feasible and cost-effective production route. Hydroxyapatite particles are regarded as one of the most suitable carriers for applications in RSV for being a bone constituent. The aim of this work was to compare the methodology of labeling first described by Chakraborty et al. (2006) with the method described by Couto et al. (2006) in the labeling of 90Y-HA. In both of the methodologies the radiochemical purity of 177Lu-HA were further confirmed by carrying out paper chromatography using aqueous solution of DTPA. For the determination of the radiolabeling yield the reaction were centrifuged at 2000 rpm for 5 minutes after the completion of the reaction. Aliquots of 177Lu-HA were passed through membranes of different pore m, followed by μsizes (Millipore®) in sequence: 12; 10; 8; and 3 flushing air. The percentages of activity retained on the filter and in the eluent were determined by counting in a dose calibrator to determine the size of particles. It was observed a radiolabeling yield higher than 95% after 1 hour of preparation, with a radiochemical purity > 98% in all labeling procedures. The "in vitro" stability studies showed that the 177Lu-HA preparations in saline, were highly stable at room temperature during 7 days, with radiochemical purity higher than 98% in this period of time. The particles size distribution of the compounds indicated that more than 99% of the particles presented a size > 12 μm in the labelling process described by Chakraborty et al., and 100% when labeled using the methodology by Couto et al. The products described in the work present ideal characteristics for use in radiosynovectomy, for a determined intra-articular cavity. The method of labeled and quality control described by Couto et al. is simples and

easily, with high labeling yields as well as excellent radiochemical purity. The final products present stability up to 7 days at room temperature. All products offer potential as suitable agents in the management of RSV, but the process of labelling can be simplified.

Seção de Tecnólogos

Abstract número: 162

ALTERAÇÃO DA BIODISTRIBUIÇÃO DO 18F-FDG CAUSADA POR UMA DIETA HIPERCALÓRICA, INGERIDA 2 HORAS APÓS A ADMINISTRAÇÃO DO RADIOTRAÇADOR: RELATO DE CASO.

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O 18F-FDG, molécula análoga à glicose, é utilizado em exames de PET/CT para avaliar o metabolismo dos tumores. Esta substância entra nas células seguindo o mesmo mecanismo de transporte da glicose, porém, após sofrer a fosforilação, ele se transforma em 18F-FDG-6-fosfato e a partir daí deixa de ser reconhecido pelas enzimas que dão continuidade ao metabolismo da glicose, e com isso ocorre o seu acúmulo no interior das células. O tempo para que a concentração do 18F-FDG atinja o seu platô no interior da célula varia com o metabolismo da própria célula, e esse mecanismo também é influenciado pelo nível de glicose no plasma. Estudos demonstram que o acúmulo do 18F-FDG em tumores benignos encontra uma estabilidade após 30 minutos da infusão do material, porém em determinados tumores malignos é possível observar que a concentração do radiotraçador continua crescendo, mesmo após quatro horas da sua administração. Esse é um dado importante para diferenciação dos tumores. **Relato de caso:** Paciente do sexo masculino, portador de linfoma foi convidado a participar de um protocolo de pesquisa que compara a aquisição em 2D com a 3D, realizada com um intervalo de duas horas entre as duas. Nesse intervalo ofereceu-se uma dieta leve para auxiliar o cliente a suportar o longo jejum. Após o lanche, o paciente optou por sair do departamento e aproveitou o período para ingerir uma dieta hipercalórica enquanto aguardava o horário da próxima etapa. Ao adquirir as imagens em 3D, observamos uma mudança acentuada da biodistribuição do 18F-FDG circulante. Além do esperado clareamento da radiação de fundo, as imagens evidenciavam um acúmulo da molécula no músculo esquelético e no coração, provavelmente causado pelo aumento da oferta de glicose circulante. Essa mudança da distribuição do 18F-FDG nos alertou para a necessidade de orientar os pacientes, com indicação para realização de imagens tardias (dual-time-point), quanto à obrigatoriedade de manter a dieta pobre em carboidratos, mesmo após um período superior à uma hora da administração do radiotraçador.

TEMAS LIVRES

Abstract número: 22
Área: Cardiologia

TERAPIA DE RESSINCRONIZAÇÃO CARDÍACA AVALIADA PELA CINTILOGRAFIA COM MIBI-99mTc: MUDANÇAS NA CAPTAÇÃO MIOCÁRDICA, DISSINCRONIA E FUNÇÃO VENTRICULAR ESQUERDA.

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Introdução: A cintilografia cardíaca com MIBI-99mTc sincronizada ao eletrocardiograma (GS) avalia integridade celular e perfusão miocárdica, dissincronia e função ventricular esquerda. A terapia de ressincronização cardíaca (TRC) pode melhorar os sintomas de insuficiência cardíaca, mas seus benefícios sobre a função do ventrículo esquerdo (VE) são menos pronunciados. **Objetivos:** Os objetivos deste estudo foram avaliar se as mudanças na captação miocárdica do MIBI-99mTc após a TRC estão associadas à melhora clínica, na sincronia e no desempenho do VE e se a GS adiciona informação na seleção de pacientes para a TRC. **Método:** Trinta pacientes (idade média 59 ± 11 anos, 47% masculinos) com miocardiopatia dilatada não isquêmica, bloqueio de ramo esquerdo e insuficiência cardíaca classe funcional III ou IV foram prospectivamente avaliados pré e 3 meses pós TRC. As variáveis analisadas foram: classe functional de insuficiência cardíaca pela New York Heart Association (NYHA), duração do QRS ao eletrocardiograma, fração de ejeção do VE (FEVE) pela ecocardiografia, captação miocárdica do MIBI-99mTc, volumes diastólico (VDF) e sistólico finais (VSF) do VE, índices de dissincronia pela análise de fase e movimentação regional do VE pela GS. Pós-TRC, os pacientes foram divididos em dois grupos de acordo com a melhora na FEVE: grupo 1 (G1 = 12 pacientes) com aumento ≥ 5 pontos absolutos na FEVE e grupo 2 (G2 = 18 pacientes) sem aumento significante na FEVE. **Resultados:** Pós-TRC, ambos os grupos melhoraram significantemente a classe functional de insuficiência cardíaca, reduziram QRS e aumentaram a captação miocárdica do MIBI-99mTc na parede septal. Apenas G1 apresentou mudanças favoráveis no VDF, VSF, índices de dissincronia e movimentação regional do VE. Pré-TRC, o VDF e o VSF foram menores no G1 comparados ao G2 e a captação do MIBI-99mTc nas paredes anterior e inferior foram mais altas no G1 em relação ao G2, $p < 0,05$. O VDF foi o único preditor independente de aumento na FEVE após terapia, $p = 0,01$. O ótimo ponto de corte foi 315 mL com sensibilidade de 89% e especificidadede 94% pela curva ROC na predição de melhora da FEVE após TRC. **Conclusões:** A TRC aumentou a captação miocárdica de MIBI-99mTc e melhorou a classe funcional de insuficiência cardíaca independentemente da melhora do desempenho cardíaco. Pós-TRC, o aumento da FEVE ocorreu em corações menos dilatados e com uma melhor captação miocárdica do MIBI-99mTc.

Abstract número: 62
Área: Cardiologia

CINTILOGRAFIA DE PERFUSÃO MIOCÁRDICA NA INVESTIGAÇÃO DA ISQUEMIA SILENCIOSA EM PACIENTES DIABÉTICOS.

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Introdução: A doença arterial coronariana (DAC) é freqüente em diabéticos e geralmente silenciosa, o que torna indispensáveis exames não-invasivos que promovam sua detecção precoce, a fim de diminuir a morbi-mortalidade desses pacientes. **Objetivo:** Estudar a perfusão e a função miocárdicas de pacientes diabéticos tipos 1 (DM1) e 2 (DM2)