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RENAL FUNCTION EVALUATION BY Tc-99m-DTPA IN ATHLETIC HORSES.

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The aim of this study was to measure the glomerular filtration rate (GFR) in athletic horses of Three Days Events Competition – a sport model for horses seemed with Triathlon Competition for men –. The GFR was measured by the single injection method using Tc99m-DTPA. This method uses a two-compartment blood clearance curves to calculate GFR, at rest and after exercise. Mean GFR was $160,0 \pm 50,0$ mL/100kg/min, at rest, and $158,2 \pm 64,8$ mL/100kg/min, after exercise. Significant ($P = 0,29$) difference was not observed in the Wilcoxon Test ($W = 1,05$). This study show that the Tc99m-DTPA blood clearance method is a practical procedure to measure GFR in the horse, because it not require urine collection, a very difficult procedure in this animal specie. The results show that were no significant differences between the GFR at rest and after the exercise.

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99mTc-DIMERCAPTOSUCCINIC ACID (DMSA) ABSOLUTE RENAL UPTAKE WITH NEW KIT FORMULATION FROM CENTRO DE RADIOFARMÁCIA – INSTITUTO DE PESQUISAS ENERGÉTICAS E NUCLEARES (IPEN-CNEN).

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Introduction: 99mTc-dimercaptosuccinic acid (DMSA) is used for static renal imaging. Renal scintigraphy with 99mTc-DMSA is a well-known procedure for assessment of renal morphology and relative function. Absolute uptake measure is desirable to evaluate decreased individual renal function or to determine if there is kidney function deterioration resulting in low bilateral renal concentration when both kidney were affected. It has been shown that organ distribution of 99mTc-DMSA can be modified markedly by method of preparation, especially the original pH and lyophilized kit composition. The aim of this study was to evaluate de the normal ranges for absolute uptake of new DMSA kit formulation. **Material and methods:** A total of 23 voluntaries adult normal patients were evaluated with ages that ranges from 18 to 69 years median 42.60 and standard deviation 13.69, between April and June of 2006. A commercial IPEN kit for labeling DMSA with 99mTcO₄ was used and prepared according to the instructions of the manufacturer. A dose of 111 MBq was intravenously injected. Six hours later scintigraphy of the kidneys was performed using a gamma camera with a parallel-hole, low-energy, high-resolution collimator, on 128x128 matrix. One minute duration images were made for at posterior position to renal counts right and left. For determination of the absolute 99mTc-DMSA uptake, liquid dose injected was calculated measuring syringe activity before and after administration to the patient. Determination of renal depth was made by means of software that makes correction using Raynaud formula. **Results:** Values of right kidney 99mTc-DMSA uptake ranged from 19.16 to 31.58. A mean value of 25.84 and standard deviation of 3.47 were found. Left kidney values ranged from 21.3 to 33.4. The mean value and the standard deviation found were respectively 27.40 and 3.51. **Conclusion:** Our data suggest that the newly synthesized 99mTc-DMSA by IPEN have uptake values similar to those founded in national and international literature. Based on our initial results, further evaluation with a larger number of patients will be necessary to determinate more accurate means values.

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Oncologia

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APLICAÇÕES DA MEDICINA NUCLEAR NO DIAGNÓSTICO E TERAPIA DO HEPATOCARCINOMA: RELATO DE 2 CASOS E REVISÃO DA LITERATURA.

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Objetivo: Relatar dois casos em que a medicina nuclear (MN) contribuiu na conduta de pacientes com hepatocarcinoma (HC). Fazer breve revisão da literatura sobre o tema. **Métodos e resultados:** *Caso 1:* Paciente do sexo masculino, de 67 anos, apresentando nódulo hepático suspeito. Uma cintilografia com hemácias marcadas excluiu a presença de hemangioma. A TC abdominal evidenciou lesão extensa e mal definida no segmento IV, sugestiva de HC. Uma biópsia confirmou o diagnóstico. Decidiu-se pela embolização da lesão com lipiodol- I131. Uma cintilografia com MAA-99mTc foi indicada para excluir a presença de shunt hepato-pulmonar. Após a cateterização da artéria hepática, infundiu-se 60 mCi de lipiodol- I131. O paciente foi submetido a cintilografia e TC de controle. As imagens da TC foram fundidas às cintilográficas (SPECT) e revelaram presença focal do lipiodol - I131 na lesão hepática. O paciente evoluiu clinicamente bem no seguimento de três meses. *Caso 2:* Paciente do sexo feminino, de 72 anos, submetida a exérese de HC no lobo direito, há 10 anos. Evoluiu com redução dos marcadores tumorais e tomografias negativas. Há três meses uma TC evidenciou nódulos hepáticos sugestivos de recidiva. Foi encaminhada à MN, onde realizou SPECT hepático 48 horas após injeção de 7 mCi de gálio-67 e 15 minutos após administração de 10 mCi de fitato-99mTc. As imagens revelaram três áreas hipercaptantes ao gálio-67 em correspondência com áreas hipocaptantes ao fitato-99mTc, na mesma topografia das lesões assinaladas pela CT, reforçando o diagnóstico de recidiva tumoral. **Discussão:** A cintilografia hepática com hemácias marcadas é indicada para excluir a presença de hemangiomas. O gálio-67 exibe um padrão de hipercaptação em cerca de 90% dos HC. O estudo hepático com radiocolóides é útil no diagnóstico diferencial da hiperplasia nodular focal (HNF) e apresenta hipocaptação em lesões de outra natureza. O DISIDA-99mTc pode demonstrar hipercaptação precoce na HNF e tardia no HC. A pesquisa de shunt hepato-pulmonar é realizada através da cateterização da artéria hepática e infusão do MAA-99mTc. Tanto o FDG-18F quanto o acetato-11C são traçadores de PET utilizados na avaliação do HC. O tratamento paliativo do HC com lipiodol-131I apresenta taxa de resposta de 17 a 92%. Outra opção terapêutica, com eficácia semelhante, são as microsferas marcadas com 90Y. **Conclusão:** A MN pode contribuir de forma significativa para o diagnóstico e terapia de lesões de HC.

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BONE MANIFESTATION OF THE RICHTER'S SYNDROME (RS) – RARE PATHOLOGY ASSESSED BY THE NUCLEAR MEDICINE. CASE REPORT AND LITERATURE REVISION.

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Introduction: Patients with chronic lymphoid leukemia (CLL) rarely develop diffuse large B-cell lymphoma, known as RS. The transformation of CLL in lymphoma has incidence of 3 to 5% and they attack a lymph node, or more frequently, a group of lymph nodes. However, in some patients, the extranodal location has been observed. The prognostic regarding patients that develop RS is not a good one.

18F-FDG PET-CT in these patients and the findings suggest that therapeutic decisions in patients with MEC should include 18F-FDG PET-CT scanning in addition to conventional imaging and histological grading.

• Tema Livre •

IMPACT OF [F-18] FDG PET-CT ON THE MANAGEMENT OF PATIENTS WITH MALIGNANT MELANOMA.

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Introduction: A small number of studies have shown the impact of positron emission tomography (FDG-PET) on the management of patients with malignant melanoma, but none of them have addressed this issue with PET-CT. **Purpose:** The aim of this retrospective study was to assess the impact of FDG with PET-CT on the treatment of patients with malignant melanoma. **Methods:** The medical records of 56 patients (26 females, 20 males; ages ranging from 27 to 77 years, mean 53 years) were reviewed. Treatment planning before and after FDG PET-CT was evaluated for changes in the management of the disease. FDG PET-CT scans were performed in patients with stages II (6/56), III (14/56) and IV (36/56) disease. All patients were injected with 370 MBq of [F-18] FDG and imaged from head to feet 60 minutes later using oral contrast. Patients were required to fast for 4-6 hours and blood glucose levels were required to be below 140 mg/dl prior to the radiotracer injection. Images were performed in a 2-slice PET-CT (Siemens Biograph). **Results:** In 12/56 patients (21.4%) treatment was changed after the FDG PET-CT studies. Three of them (25%) were upstaged as a result of FDG PET-CT. Treatment was changed after FDG PET-CT in 4/14 (29%) stage III patients and in 7/36 (19%) stage IV patients. **Conclusion:** FDG PET-CT is most valuable in patients with stage III malignant melanoma, but may also be useful on stage IV disease.

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IN HOUSE PRODUCTION OF ^{99m}Tc-EDDA-HYNIC-[TYR3]-OCTREOTIDE FOR SOMATOSTATIN RECEPTOR SCINTIGRAPHY.

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Aim: Scintigraphy using ¹¹¹In-diethylene-triamine-penta-acetic-acid-D-Phe1-octreotide (DTPA-octreotide) gained widespread acceptance. Radio-labelling of peptides with indium-111 has some drawbacks, including suboptimal gamma energy. Recently, a new technetium labeled peptide was developed. The somatostatin analogue is an octreotide derivative with high specific tumor uptake, and showed promising results in the detection of neuroendocrine tumors. **Methods:** Reagents were purchased from Sigma-Aldrich. HYNIC-[Tyr3]-octreotide (HYNIC-TOC) was purchased from PiChem. ^{99m}TcO₄⁻ was obtained from commercial ^{99m}Mo/^{99m}Tc generator produced by G.E. Healthcare. Radio-labeling experiments were performed using the protocol issued by the University Hospital of Innsbruck. Overall the following formulation and labeling conditions with reproducible labeling yields of >90% were established: 20 mg HYNIC-TOC, 10mg EDDA, 20 mg tricine, 10 mg SnCl₂. 2H₂O, pH 6.5–7.5, labeled with 1200 MBq ^{99m}TcO₄⁻ in a total volume of 2 ml, reaction time: 10 min in boiling water. Quality control was performed as follows: HPLC: Reaction solutions were tested for radiochemical purity by HPLC. Column: Dionex Acclaim 300 ODS 5 µm, 4.6 mm x 250 mm. Mobile phase: linear gradient of increasing concentrations of ACN in 0.01 N phosphate buffer pH 6,2: 0–3 min

0% ACN, 3–5 min 0% 25% ACN, 5–18 min 25% ACN, 18–22 min 25%–70% ACN, 22–24 min 70%, 24–25 70%–0% ACN 25–30 min 0% ACN. Flow rate: 1 ml/min. Detection: a sodium-iodide detector interfaced to a multichannel analyzer (Raytest). Thin-layer chromatography: instant thin-layer chromatography on silica gel (ITLC-SG, Gelman Sciences) was performed using different mobile phases. Sep-Pak Purification: A C-18-SepPak-Mini cartridge (Waters) was activated using 5 ml ethanol, followed by 5 ml of water and 5 ml of air. The radiolabeling mixture was passed through the cartridge which was then washed with 5 ml of water. The radiolabelled peptide was eluted with 1 ml ethanol and 1 ml of water. **Results:** This method of preparation has been safely used in more than 30 patients in our Department with always a purity yield of more than 95% with a preparation time of approximately 30 minutes. **Conclusion:** The high specific tumor uptake, rapid blood clearance, and predominantly renal excretion make ^{99m}Tc-EDDA-HYNIC-TOC a promising candidate as an alternative to ¹¹¹In-DTPA-octreotide for tumor imaging.

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LINFOMA CUTÂNEO E SÍNDROME DE SÉZARY (SS) – PATOLOGIA AVALIADA E ESTADIADA PELA MEDICINA NUCLEAR. RELATO DE CASO E REVISÃO DE LITERATURA.

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Introdução: Linfomas de células T (LCT) representam cerca de 15% de todos os linfomas não-Hodgkin. Esses podem ser clinicamente agressivos e relativamente raros quando comparados aos linfomas B. Linfoma cutâneo de células T, conhecido como Mycosis fungoides (MF) é caracterizado pelo acometimento cutâneo local ou disseminado da doença. Em raros casos, evolui para forma sistêmica, onde outros órgãos são acometidos, caracterizando a Síndrome de Sézary. O prognóstico de pacientes com MF depende do estágio, do tipo, da extensão das lesões cutâneas e da presença de doença extracutânea. A expectativa de sobrevida em dez anos é de 98% em pacientes em estádios precoces, diminuindo em estádios mais avançados, sendo de 83% em pacientes com envolvimento superior a 10% da superfície da pele; 42% com tumoração e de 20% naqueles com envolvimento linfonodal. A cintilografia com gálio-67 é método efetivo com alta sensibilidade em localizar e determinar a atividade nos sítios de linfoma, sendo importante exame para estadiamento, seguimento e prognóstico dessa patologia. **Objetivo:** Relatar um caso de linfoma cutâneo disseminado com acometimento sistêmico – Síndrome de Sézary, por meio da cintilografia com gálio-67. **Relato de caso:** AHW, 65 anos, feminina, com queixa de lesão cutânea nodular em glúteo direito, iniciada há cinco meses, com posterior ulceração e disseminação para outras regiões cutâneas. A biópsia revelou linfoma maligno não Hodgkin difuso de células T. O hemograma mostrou leucocitose com predominância linfocítica de 64%. O esfregaço evidenciou presença de linfócitos de tamanho médio, núcleos com contornos irregulares, alguns convolutos, cromatina com maturação intermediária, citoplasma com microvacúolos. Essas células representaram maioria da população linfóide. As sombras nucleares foram raras. A imunofenotipagem das células do sangue periférico revelou presença de 94% de linfócitos T e 1% de linfócitos B-CD19+. Os linfócitos T apresentaram o seguinte perfil CD3+, CD2+, CD5-, CD7+, CD4+, CD8-, CD1-, TCR alfa/beta+, CD16-, CD56-, CD57-. Este fenótipo é compatível com síndrome de Sézary (SS). O mielograma foi compatível com diagnóstico de infiltração de medula óssea por linfócitos. A cintilografia com gálio-67 revelou múltiplas lesões gálio-captantes cutâneas e extracutâneas ativas, localizadas em mediastino; região infra-mamária, hemibacia, raiz da coxa (partes moles), glúteo e terço médio e distal do fêmur à direita; terço médio de coxas (partes moles) e região inguinal esquerda, sendo submetida ao esquema quimioterápico com Gemcitabina. **Comentários:** A cintilografia com gálio-67 foi imprescindível na de-

tal extremity and proximal of tibia and right tibia distal extremity. At the moment, patient undergoes a palliative treatment with oral Etoposide, plus pain relief. **Comments:** In this case report, bone scintigraphy was decisive in documenting the monostotic to multicentric evolution evidencing the disease aggressiveness in agreement with literature.

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URINARY FISTULA TO SEMINAL VESICLE DETECTED BY DEDICATED PET/CT: UNUSUAL CAUSE OF FALSE-POSITIVE FINDING. CASE REPORT.

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Objective: To report on a case of urinary fistula to seminal vesicle detected by dedicated PET/CT and the importance of performing a fully diagnostic intravenous contrast-enhanced CT. **Method:** 65-year-old heavy smoker male with history of rising in blood tumor markers and benign prostatic hyperplasia treated with trans-urethral resection. Ultrasonography detected a possible thickening of the bladder wall. Patient was submitted to a whole body PET/CT study 1 hour after an intravenous injection of 288.6 MBq (7.8 mCi) of 18F-FDG in a dedicated PET/CT scanner. Fully diagnostic intravenous contrast-enhanced CT images were acquired immediately after PET images. Delayed PET/CT images of the pelvic region were also acquired approximately 40 minutes after an intravenous injection of furosemide to improve lesion detection in the bladder wall. **Results:** Images showed a spiculated pulmonary nodule in the left upper lobe and large bulky mediastinal lymph adenopathy, all of them with markedly increased 18F-FDG uptake. Delayed post-furosemide PET images showed a focal area of moderately increased 18F-FDG uptake in the right hemi pelvis that corresponded to the right seminal vesicle on the CT images, which was fulfilled with iodinated contrast. These abnormalities were not present in the first set of images. **Conclusions:** The use of intravenous iodinated contrast in the CT images allowed the precise characterization of the 18F-FDG concentration in the right seminal vesicle that was noted only in the delayed images, and corresponded to a urinary fistula to the right seminal vesicle. Have we not injected the intravenous contrast for the fully diagnostic CT images, this abnormality would be incorrectly characterized as a lesion with increased metabolic activity.

error of 40% between experimental and theoretical exposure rates. The best measurements were obtained when performed at 2.0 meters in front of the patients. With this approach, the error was about 2% between experimental and theoretical values and the determination of the activity retained by patients' body yield more accuracy and precision following the measures at 2.0 meters instead 1.0 meter. These findings suggest a new methodology for patients' measurement in nuclear medicine and could be useful for personal monitoring in cases of radiological emergencies involving 131I ingestion.

• Tema Livre •

EVALUATION OF THE ABSORBED DOSE FROM PATIENTS BASED ON WHOLE-BODY 131I CLEARANCE IN THYROID CANCER THERAPY.

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The evaluation of the absorbed dose from radioactive patients during the treatment of thyroid disease is an important factor to establish precautions in these procedures, and the 131I retention/excretion by patients' body provides additional information to medical and radioprotection service. In 94 patients, the measurement of the exposure rates was performed over the 7 days after Na131I administration and the rates permitted to study the dynamic of excretion and the potential dose evaluation. The administered activities ranged from 3.7 GBq (100 mCi) to 16.65 GBq (450 mCi) and the results proved that the majority of the activity is excreted by patients in first three days after Na131I administration. The average 131I activity excreted at 24, 48, 72, 96 and 120 hours after oral administration was (72 ± 10), (91 ± 6), (97 ± 3), (98.9 ± 1.5) and (99.6 ± 0.7)% respectively. According to the administered activity, the evaluation of the accumulated absorbed dose from patients ranged from 3.0 ± 0.7 to 8.4 ± 1.1 mSv at one meter and 1.2 ± 0.4 to 3.2 ± 0.4 mSv at two meters. The data reported here are important to radioprotection policy and to add and improve on the guidelines reported in USNRC Regulatory Guide 8.39.

• Tema Livre •

SCHISTOSOMIASIS HAEMATOBIA: CLINICAL ASPECTS AND SCINTIGRAPHIC IMAGES IN BRAZILIAN PATIENTS.

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The *Schistosoma haematobium* is a trematode that cause schistosomiasis haematobia and resides in venous plexus around the vesicle bladder, where the eggs are deposited. The aim of this study was to evaluate the scintigraphic alterations trying to identify obstructive uropathy and its modifications during clinical evolution, because the worsening of renal function is related to the intensity and duration of the obstruction. In this study, 19 male Brazilian patients aged from 26 to 36 years, infected in Mozambique, were evaluated. Clinical and laboratorial diagnosis was done in a period of few months to 7 years after the contact with parasite. They underwent dynamic renal scintigraphy with 99mTc-DTPA and tubular function with 99mTc-DMSA. Among results there were 2 patients had abnormal scintigraphy 12 months after beginning of symptoms. Other 2 patients had normal exams 24 months after being symptomatic. Among patients being symptomatic for 48 months only one had obstructive pattern and renal scar, two had obstructive pattern and one presented a normal exam. We can be concluded that the alterations are randomic in relation to duration of symptoms, depending more on individual response, parasite charge, then others. This favors the idea

Outros

• Tema Livre •

A NEW PROPOSAL FOR MONITORING PATIENTS IN NUCLEAR MEDICINE.

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The measurement of the exposure rates is fundamentally important in the release of patients given radioactive material and for keeping the exposures of others as low as reasonable achievable (ALARA). Similar measurements methodologies have generally been used for point and extended sources, but this approach may lead to methodological errors in calculating radiation dose estimates. In this study, nuclear medicine patients (n=122) who received activities of Na131I for therapy (0.74 to 16.6 GBq, 20 to 450 mCi) were monitored using different measurement methodologies and the results showed that the usual measurement performed at 1.0 meter in front of the body resulted in a mean

of close clinical and scintigraphic evolution because alterations non-detected earlier increases morbidity and irreversible damage to patient.

Radiobiologia/Instrumentação

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CORRELAÇÃO ENTRE A VARIAÇÃO DE TEMPERATURA, UMIDADE, TENSÃO, CORRENTE E UNIFORMIDADE EM UM SISTEMA SPECT.

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Objetivo: O objetivo deste trabalho foi analisar temperatura, umidade, tensão e corrente para verificar se dentro das condições atuais de funcionamento de um determinado sistema SPECT é possível detectar variações significativas na Uniformidade do sistema. A Uniformidade avalia a diferença de resposta do detector em diferentes pontos do campo visual, sendo um dos parâmetros mais importantes no desempenho de um sistema SPECT. **Metodologia:** O estudo do comportamento dos valores da Uniformidade foi realizado num sistema SPECT dotado de dois detectores. Este equipamento está sujeito a variações térmicas e umidade devido à região climática em que se encontra. As variações de tensão e corrente foram analisadas, pois a rede elétrica que alimenta este equipamento é a mesma que alimenta todos os equipamentos de radiodiagnóstico. Este equipamento tem sua Uniformidade analisada diariamente conforme recomendações do IAEA e do fabricante. Registraram-se diariamente os valores de Uniformidade, temperatura e umidade ambiente, tensão e corrente. **Resultados:** Por meio do termohigrômetro e do MUG, verificamos a possível constância das grandezas avaliadas. A variação de temperatura ocorre entre os 23 e 25 °C e a umidade entre 36,5 e 51%, o que indica uma faixa de variação muito reduzida. Apesar da umidade apresentar certa variação, quando confrontado com a Uniformidade percebe-se que esta não é significativa. O fabricante sugere que não se exponha o detector a variações de temperatura superiores a 5 °C/hora e que os limites sejam de 15 e 27 °C. A temperatura média verificada foi de 20,55 °C, não havendo variação de 5 °C e a variação de umidade indicada pelo fabricante é de 20 a 80%, e em nossa análise verificamos uma média de 44,75%. O fabricante define a tensão de entrada 120 V ($\pm 10\%$) e a média encontrada foi de 112 V ($\pm 6\%$). A corrente de entrada é fixada em 5 A ($\pm 10\%$), sendo que a média foi de 6,16 A ($\pm 1,2\%$). **Conclusões:** Neste trabalho, percebemos que todas as grandezas analisadas não interferem na Uniformidade medida para este sistema SPECT. Além disso, constatamos que não há porque imaginar que possa haver desgaste elétrico no sistema, se o nobreak estiver em bom funcionamento, bem como atribuir à falta de qualidade da imagem, à tensão e a corrente recebida ou a variações de temperatura e umidade se essas grandezas permanecerem controladas e constantes. Verificamos, a partir da análise realizada, que as variações percebidas na Uniformidade são muito pequenas (para este sistema) de modo que as grandezas analisadas não interferem significativamente na mesma.

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EFFECT OF RECOMBINANT TSH (rTSH) ON IODINE-131 RESIDENCE TIME AND DOSIMETRY ON THYROID GLAND: FINAL RESULTS.

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Introduction: Patients with total thyroidectomy are strongly depended on hormone reposition therapy to maintain a normal metabolic status. The hormone therapy is mandatory for serum TSH levels suppression and for avoiding undesirable symptoms of hypothyroidism such as tiredness and slowness. However, patients with differentiated thyroid carcinoma need at least two whole body iodine-131 surveys within the first 2 years of total thyroidectomy, which requires increased levels of serum TSH to residual thyroid tissue or even metastases. Recombinant human thyrotropin (rTSH) was developed to avoid the interruption on hormone therapy, which brings comfort and safety to the patient. **Objective:** Our purpose was to estimate the effect of rTSH on thyroid-absorbed dose and total glandular residence time after an oral administration of iodine-131. **Methodology:** In this experimental model, 27 Wistar rats, 200 g of weight each, received 11,1 MBq of I-131 orally. Nine of these animals received rTSH (IPEN-CNEN) and, nine received Thyrogen (Gensyme), respectively, on the day before. Twenty four hours urine was collected for each animal. The urine was collected in metabolic cages and the tube collectors that contained the urine were verified on hourly basis. A CRC-15R Capintec dose calibrator was used to determinate their activities. The accumulated activity in thyroid and the residence time were calculated by MIRD standards. The absorbed dose was calculated by the Monte Carlo Method through the program MCNP-4C. **Results:** The accumulated activity of 9 rats who received I-131 without rTSH stimulus was: $\bar{A} = 2087,50 \pm 374,11$ MBq.h and the average residence time was: $RT = 188,00 \pm 33,69$ h. The 9 rats who ingested I-131 preceded by Thyrogen presented accumulated activity on thyroid: $\bar{A} = 2105,26 \pm 328,01$ MBq.h. The residence time was: $RT = 189,70 \pm 29,56$ h. The 9 rats who ingested I-131 preceded by rTSH/IPEN presented accumulated activity on thyroid: $\bar{A} = 2291,11 \pm 514,40$. The residence time was: $204,80 \pm 46,57$ h. The absorbed dose in thyroid was respectively: $D = 2.295,8$ Gy (I-131), $2.315,4$ Gy (Thyrogen) and $2.522,6$ (rTSH – IPEN). **Conclusions:** These data suggest that rTSH promotes rates of accumulated activity of I-131 in the thyroid gland and also prolongs the residence time of iodine in normal glands, in this case about 10%. So far, these preliminary results had not been associated with an increase in the genetic damage.

• Painel •

HIGH SPATIAL AND TEMPORAL RESOLUTION SCINTIGRAPHIC IMAGES OF SMALL VOLUMES USING CODED MASKS AND STANDARD CLINICAL GAMMA CAMERAS.

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Rationale: Non invasive imaging techniques, used in experimental protocols with small animals, are very powerful tools for making sequential in vivo studies on the same subject, so reducing research time and costs and providing more reliable results. These techniques can be very useful for studies of human diseases, and discovery and development of new drugs. **Objectives:** Given the small size of some animal organs, we propose to implement hardware and software techniques which allow us to obtain high spatial (better than 1 mm) and temporal (equivalent to that of clinical studies) resolution scintigraphic images of small volumes using conventional clinical SPECT gamma cameras. The proposed techniques include coded mask-based multipinhole collimators and iterative image restoration algorithms. **Method:** In order to reach high spatial resolution in scintigraphy, it is necessary to reduce the collimator hole size (in pin-hole or parallel-hole collimators), conveying a simultaneous reduction in camera's sensitivity. Initially, we have made Monte Carlo simulations (MCS) of a pinhole collimator camera with inserts of different sizes to gain a better understanding of those effects. After that, MCS of the effect of a multipinhole collimator (1-mm size), based on a MURA 7x7 coded mask, were carried out. We built and tested this collimator with a Siemens Orbiter NaI(Tl)-based clinical gamma

camera, obtaining images of small-size phantoms in different configurations. The images were reconstructed by using a Richardson-Lucy-based image restoration algorithm. All the phantoms were imaged with the same magnification factor of 4. **Results:** MCS and images of small objects were obtained and reconstructed including: point sources, sets of point sources and small-size continuous sources. The resulting images show spatial resolution better than 1 mm on the object, and temporal resolution equivalent to that of a 4-mm diameter single pinhole. Additionally, the simulations show that, using this kind of collimator, identification of individual planes perpendicular to the camera's axis is possible. In this way, we can perform tomography with a single image. **Conclusions:** We have shown that, by using small-size, multipinhole collimators, in combination with a clinical gamma camera, it is possible to obtain, simultaneously, high spatial and temporal resolution images of small volumes, which can be used in dynamic studies of radio-tracers. Given the collimator configuration, tomography can be done with a single image.

• Painei •

X PHARMACOKINETIC AND TISSUE DISTRIBUTION OF NEUTRON IRRADIATED PENTAVALENT ANTIMONIALS AS ANTI-LEISHMANIAL DRUGS.

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Introduction: Visceral Leishmaniasis (VL) is a systemic protozoan parasite infection of tropical and subtropical areas, which afflicts a million people each year and may be fatal if untreated. Despite lengthened treatment regimes, parenteral administration and toxic side effects, the pentavalent antimonial meglumine antimoniate or sodium antimony gluconate have remained the first-line treatment for VL. Besides over half a century of clinical use, their mechanism of action, toxicity and pharmacokinetics data remain unknown. **Objectives:** The aim of the present study was to compare the pharmacokinetic and the tissue distribution of non-complexed pentavalent antimony and of meglumine antimoniate. **Methods:** Both drugs were neutron irradiated inside IEA-R1 nuclear reactor (IPEN-CNEN-SP). Two radioisotopes of antimony - ^{122}Sb and ^{124}Sb , were produced and were suitable for use in biodistribution studies. Healthy or mice experimentally infected with *Leishmania chagasi* received a single intraperitoneal dose of either drugs. At different times after injection, the tissues and the organs were excised and activity measured in a NaI (TI) scintillation counter. **Results:** Analysis of the curve of the concentration in blood after administration of meglumine antimoniate showed two compartments, a distribution in the central compartment and other associated to drug equilibrium and excretion. It was found higher uptake in the liver of healthy or infected mice, where approximately 55% of the injected activity at 30 minutes is accumulated and retained. At 24h post injection, no significant activity was seen in any major organ other than liver, which could also be associated with selective anti-parasitic effect. The elimination is mostly by biliary excretion with a small and fast proportion of the drug excreted by kidney. Free pentavalent antimony showed fast elimination predominant by kidney and great proportion of the drug is excreted by biliary route, thus indicating that complexed drug favors the distribution of antimony in organs and increases its residence time in tissues. This would explain the superior antileishmanial efficacy of this formulation compared to those of the free drug in mice. **Conclusions:** The use of the radiotracers, easily created by neutron irradiation, could be an interesting tool to solve important questions in antimonial pharmacology. Besides its useful results for leishmaniasis treatment, this radiopharmaceutical system has great potential for evaluating various kinds of drugs. This work was supported by CNPq Proj.476666/2004-0 and SETB fellowship PhD Program Proj.142839/2005-1.

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• Painei •

SITUAÇÃO DO PET NO BRASIL.

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O objetivo deste trabalho é analisar a situação dos tomógrafos PET (positron emission tomography) no Brasil, do ponto de vista do licenciamento. Os Serviços de Medicina Nuclear utilizam em sua rotina calibradores de radionuclídeos para medir a atividade de soluções contendo radiofármacos como I-131, Ga-67 e Tc-99m, entre outros. Estas soluções são administradas a pacientes com o propósito de obter o diagnóstico de doenças ou sua terapia; o procedimento é simples: a dose de radiofármaco a ser administrada ao paciente é medida no calibrador de radionuclídeo e, após a administração e absorção do medicamento, o paciente realiza uma tomografia computadorizada. O PET é um tomógrafo de geração mais avançada que o tomógrafo computadorizado e detecta dois fótons num sistema de coincidência; para tal, utiliza o F-18, um radiofármaco que emite dois fótons de 511 keV. A realização de exames com o F-18 é semelhante a outros exames de medicina nuclear, mas o projeto de uma instalação com PET requer uma série de cuidados que não se aplicam num Serviço de Medicina Nuclear convencional. Entre esses aspectos, podemos destacar o tratamento do paciente injetado com F-18, a dosimetria dos indivíduos ocupacionalmente expostos e a blindagem da instalação. Existe uma grande lacuna na literatura brasileira sobre este assunto e, inclusive nas Normas da Comissão Nacional de Energia Nuclear (CNEN), órgão que licencia instalações nucleares e radioativas no Brasil, não existem itens específicos contemplando instalações com PET. Este trabalho pretende minimizar esta lacuna e evidenciar a necessidade de estudos direcionados à realidade brasileira no tocante ao PET.

• Painei •

X STUDY OF DOSIMETRY AND TOXICITY OF ^{177}Lu -DOTA-Y3-OCTREOTATE IN RATS.

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Introduction: It has been demonstrated that radiolabeled somatostatin analogs bears some effectiveness for targeted radiotherapy of somatostatin receptor tumor in rat's models and humans. Usually, one of the radionuclides used in this purpose for cancer therapy is the ^{177}Lu (β^- 100% and $T_{1/2} = 6.6$ days). Reasonable therapeutic efficacy of the somatostatin analog ^{177}Lu -DOTA-Tyr3-octreotate (DOTA-Y3-TATE) has been demonstrated on many studies published in the literature. **Objective:** To evaluate the toxicity and dosimetry of ^{177}Lu -DOTA-Y3-TATE through an experimental tumor model in rats. **Methodology:** Total activity of 1.11 MBq of ^{177}Lu -DOTA-Y3-TATE was administered in 15 NUDE Swiss rats and sequentially complete total blood counts were obtained 24 hours after the IV injection. The biodistribution of ^{177}Lu -DOTA-Y3-TATE was determined using a well detector and a scintillation camera dedicated to experimental studies. The dosimetry (accumulated activity and residence time in target organs) was calculated using MIRD method. **Results:** No overt signs of toxicity were observed. The absorbed dose in tumor was determined in comparison with the other organs in the total body. The average absorbed dose on the rat tumor was estimated to be 0.44 ± 0.04 mGy/MBq. The absorbed dose in pancreas was 0.43 ± 0.04 mGy/MBq, kidneys was 0.22 ± 0.03 mGy/MBq and total body 0.029 ± 0.006 . **Conclusions:** These preliminary data suggest that ^{177}Lu -DOTA-Y3-TATE bears adequate dosimetric and lack of toxicity enough to rise clinical interest for its indication as an alternative modality of treatment for somatostatin receptor-positive tumors.

11816 v

Radiofarmácia/Radioquímica

• Painei •

A GAS CHROMATOGRAPHY TECHNIQUE FOR ANALYSIS OF RESIDUAL SOLVENTS IN 18F-FDG PREPARATION.

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Aim: Positron emission tomography (PET) with 18F-2-deoxy-2-fluoro-D-glucose (FDG) has been investigated as a means of detecting primary tumors in recent years. The analysis of 18F-FDG has focused on the detection of chemical, radiochemical and radionuclidic purities and little attention has been paid to the analysis of residual solvents involved in the preparation of 18F-FDG. Any residual solvent with potential toxic, physiologic or pharmacological effects must be evaluated. The aim of this study was to develop a quantitative method for residual acetonitrile, ethanol and isopropanol in 18F-FDG using gas chromatography. **Materials and methods:** Analysis was carried out on a Shimadzu 17AA gas chromatography equipped with a flame ionization detector (FID) and an auto-sampler. The injection was configured for split sample injection at a ratio 20:1 and operated at 250°C. It was used a J&W DBWAX column 30 m x 0.25 mm and operated at a temperature range between 50-85°C. Helium was used as the carrier gas (flow rate 2.0 mL/min). The detector was operated at 250°C and injection sample volume was 1.0 µL. Standard solutions were prepared with high purity solvents in purified water. Calibration curves were prepared with concentration range of 0-600 ppm. Three injections of each standard were made to obtain the data. 50 samples of different batches were stored in sealed vials at room temperature and analyzed. **Results and discussion:** The analysis time was 3.75 min. The retention time for isopropanol, ethanol and acetonitrile were 2.20, 2.25 and 2.69 min, respectively. The USP 28 and FDA specified that the permissible levels of the residual solvents in the final preparation of 18F-FDG might not exceed 400 ppm for acetonitrile and 5000 ppm for ethanol and diethyl ether. In the considered process isopropanol is used instead of diethyl ether for cleaning. The correlation coefficients of the calibration curves were 0.9990 for isopropanol, 0.9988 for ethanol and 0.9979 for acetonitrile. In the 50 analyzed samples all the levels were below the allowable limit described for USP and FDA. The obtained range for isopropanol, ethanol and acetonitrile in the samples of 18F-FDG were 9.09-40.12 ppm, 27.23-515.28 ppm and 22.07-150.71 ppm, respectively. **Conclusion:** Gas chromatography is an excellent technique for determination of the residual solvents in the final preparation of 18F-FDG. The levels observed in the samples were in accordance with the permissible levels proposed for the USP and FDA.

• Tema Livre •

A SIMPLE METHOD FOR BONE MARROW-DERIVED MESENCHYMAL STEM CELLS LABELING WITH Tc-99m.

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Background: The ability to incorporate readily available radio-nuclides with optimal decay characteristics into tracer molecules has been the foremost consideration in development diagnostic radiopharmaceuticals. In this respect, 99mTc has become the mainstay of diagnostic nuclear medicine and in some chemical form is used in the majority of the diagnostic scans performed each year in hospitals. This preferential use of 99mTc radiopharmaceuticals reflects the ideal nuclear properties of the isotope, as well as its convenient availability from commercial generator columns. Employment of radiolabeled stem cells

can provide many important contributions in the monitorization of cell delivery. It may also prove to constitute in the future an important ancillary procedure in the procession of the treatment of several chronic diseases. **Objective:** To evaluate homing and retention of the stem cells into human body organs. **Methods:** Approximately 10% of these cells were labeled with technetium 99m (370 MBq) by incubation in saline solution of SnCl₂. Scintigraphic images were obtained one, three and twenty four hours after cell injection. **Results:** The radio labeling of stem cell with Tc-99m was obtained with high efficiency (89%). Imaging of 99mTc-stem cell following intravenous injection into normal rat showed the accumulation of radioactivity in liver, kidneys, lungs and spleen. When 99mTc-stem cells were injected into the heart of a chagasic patient, the radioactivity was accumulated in the liver, lungs and heart. When 99mTc-stem cells labeled were injected into hepatic artery by angiography in cirrhotic patients we could observe their homing by scintigraphy during 24 hours. **Conclusion:** 99mTc-stem cell is simple to prepare and uses a labeling agent for 24 hours distribution studies of injected stem cells.

• Tema Livre •

ASSESSMENT OF THE ANIMAL BIODISTRIBUTION OF SEVEN GLUCOSE APPENDED [99mTc]TECHNETIUM COMPLEXES IN A MURINE MELANOMA TUMOR MODEL.

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Objective: In this work we prepared seven carbohydrate-appended [99mTc]technetium complexes, including two bisoxo-bisdiamine ([99mTc(O)₂(Ldam)₂]⁺), two diamine-tricarbonyl ([99mTc(Ldam)(CO)₃]⁺) and three 2,2'-dipicolylamine-tricarbonyl ([99mTc(Ldpy)(CO)₃]⁺) complexes, as candidate for (18F)FDG substitution in nuclear medicine imaging in tumor detection. The biodistribution of each one was assessed in a tumor animal model. **Methods:** Ligands Le = 2,3-diamino-1-propyl-β-D-glucopyranosyl, Lpen = 1,3-diamino-2-propyl-β-D-glucopyranosyl, Lpy = 2-(bis(2-pyridinylmethyl)amino)ethyl-β-D-glucopyranosyl, LpyN = 2-(bis(2-pyridinylmethyl)amino)acetyl-α-D-1-amineglucopyranosyl and LpyS = 2-(bis(2-pyridinylmethyl)amino)ethyl-β-D-2-thiogluco-pyranosyl were synthesized and characterized previously. [99mTc(O)₂(Len)₂]⁺ and [99mTc(O)₂(Lpen)₂]⁺ complexes were prepared by the reduction of TcO₄⁻ with Sn²⁺ in alkaline medium; [99mTc(Len)(CO)₃]⁺, [99mTc(Lpen)(CO)₃]⁺, [99mTc(Lpy)(CO)₃]⁺, [99mTc(LpyN)(CO)₃]⁺ and [99mTc(LpyS)(CO)₃]⁺ were prepared from an Isolink[®] kit, through transchelation. Radiochemical purity was determined by HPLC or thin layer chromatography. The biodistribution of each complex was assessed in a C57BL6 mouse with implanted B16F10 murine melanoma tumor cells. Animals (n=3 to 5) were anesthetized, killed and organs were excised at 15, 60, 120 and 240 minutes after complexes injection and the concentration of the compounds was calculated as % dose/g organ. **Results:** Radiochemical purity of all complexes were over 95%. All complexes showed insignificant cardiac and cerebral uptake, the main organs of FDG metabolism. In general, [99mTc(Ldam)(CO)₃]⁺ and [99mTc(Ldpy)(CO)₃]⁺ complexes have hepatobiliary system as principal elimination route, whereas [99mTc(O)₂(Ldam)₂]⁺ complexes were eliminated by the kidneys. Best data for tumor concentration (a) and tumor/blood ratio (b), were taken at 120 minutes, and the best results were given by the following complex: [99mTc(O)₂(Lpen)₂]⁺ (a) = 1.30±0.40% and (b) = 1.39 ± 0.57%; [99mTc(Len)(CO)₃]⁺ (a) = 1.22±0.61% and (b) = 1.88 ± 0.66%; [99mTc(Lpyr)(CO)₃]⁺, (a) = 0.43 ± 0.12% and (b) = 1.53 ± 0.68%. Our general results permit to observe that less lipophilic complexes ([99mTc(O)₂(Lpen)₂]⁺ and ([99mTc(Len)(CO)₃]⁺) have

higher tumor accumulation in relation to more lipophilic ($[^{99m}\text{Tc}(\text{Lpyr})(\text{CO})_3]^+$) but, on the other hand, the last one has a fast blood pool washout. **Conclusion:** The concentration of these complexes in the tumor and tumor/blood ratio, is comparable to data published in the literature for other glucose appended ^{99m}Tc complex, but it is improbable they will be used in clinical trials due to the high uptake in surrounding organs. The insignificant cardiac and cerebral concentrations suggest that these compounds were not metabolized as glucose or (18F)FDG. So, research in this area must be continued to understand the uptake mechanisms and to rationalize the development of new products.

• Painel •

DEVELOPMENT OF IODINATION METHODOLOGIES FOR THE OBTENTION OF 5-[^{123}I]IODOURACIL AND IODOAROMATIC COMPOUNDS.

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The substance 5-iodouracil is a derivative of the heterocyclic base, pyrimidine. Uracil is a pyrimidine base found in RNA, whereas 5-iodouracil may act as an analog of thymine, a pyrimidine base found in DNA. Aromatic halides have been used in organic synthesis for more than 100 years and they are therefore important intermediates in synthetic organic chemistry. Aromatic halides are used as intermediates for the obtention of other functional groups on the aromatic ring either by substitution reactions or via aromatic organometallic reagents. **Aim:** This study aimed to investigate the development of radiochemical synthetic methodologies for the obtention of 5-[^{123}I]iodouracil. As well as the synthesis of 5-[^{123}I]iodouracil, the iodination of aminobenzonitrile derivatives was investigated using potassium dichloroiodate as the iodination reagent. As well as the preparation of the ^{123}I labeled molecule, this study aimed to investigate the use of the molecule as radioactive tracer for imaging in tumor cells. **Methods:** The radiochemical synthetic methodologies used were electrophilic substitution and isotopic and non-isotopic exchange reactions. **Results and discussion:** Inexpensive and readily available oxidants were employed in the electrophilic substitution reactions: chloramine T, Oxone®, ammonium and cerium nitrate, trichloroisocyanuric acid were purchased, and potassium dichloroiodate was synthesized. The optimal reaction conditions were generally mild and resulted in good radiochemical yields. For the exchange reactions, isotopic and non-isotopic methodologies were developed. In order to develop the non-isotopic exchange 5-bromouracil was prepared, so as to obtain the product of interest in a carrier free state. In this study it was found that the exchange methodologies gave inferior radiochemical yield when compared with electrophilic substitution reactions. The iodination of aminobenzonitrile derivatives was investigated using potassium dichloroiodate as the iodination reagent. The results obtained confirmed the versatility of this reagent and the reactions gave satisfactory chemo- and regio-selective results. **Conclusions:** The iodinated aminobenzonitrile derivatives could be used as precursors for the synthesis of radiopharmaceuticals used in imaging. The labeled molecule, 5-[^{123}I]iodouracil, was found to have good prospects for use in imaging in Nuclear Medicine.

• Tema Livre •

^{111}In -DTPA-OCTREOTIDE: PRODUCTION AND QUALITY CONTROL.

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Recent advances in receptor mediated-tumor imaging have resulted in the development of somatostatin analogues. Somatostatin binds with

high affinity to all hsstr-subtypes and undergoes rapid “in-vivo” degradation compared with octreotide. Octreotide, an octapeptide analog of somatostatin, has a longer biological half-life, which makes it more suitable for labeling and imaging. Octreotide can be radioiodinated or labeled with radiometals: In-111; Ga-67; Cu-64; Y-90 and Tb-161. The successful use of radiolabeled somatostatin analogues in imaging promoted further studies in utilizing them in radiopeptide therapy. The aim of this work is to establish and validate the labelling, the quality control procedures and evaluate the “in-vitro” stability for routine production and clinical application of ^{111}In -DTPA-Tyr3-Octreotide (^{111}In -DTPA-Oct). The labeling of DTPA-Oct with In-111 ($^{111}\text{InCl}_3$) was performed in a “glove-box” under GMP condition, with 1850 - 3700 MBq of $^{111}\text{InCl}_3$ at pH 4.5, using radionuclide:peptide ratios of 122 MBq/10 μg in sodium acetate buffer, at room temperature for 30 minutes. All solutions were prepared with WFI water. Radiochemical purity was determined by ITLC-SG using 0.1M sodium citrate, pH 5.5, as solvent. The labeled peptide migrates from the origin $R_f = 0.4 - 0.5$ and the radionuclide migrates with the solvent front $R_f = 1.0$. Radiochemical purity was also determined using Sep-Pack silica cartridge. The free radionuclide was eluted with 5 mL of 0.1M sodium acetate, pH 5.5, and the labeled peptide with 5 mL of methanol. The stability of the final product was evaluated immediately, 24 and 48 hours kept under refrigeration. Sterility and pyrogen tests are performed by the microbiology procedures in different culture medium and the aprotogenicity by the “in-vitro” Limulus test (LAL). The final product presents the following characteristics: radioactive concentration of 185 MBq/mL; chemical concentration of 15–16 $\mu\text{g}/\text{mL}$; specific activity of 12.21 MBq/ μg ; validation and calibration time of 48 hours. The stability of the radio-labeled peptide (^{111}In -DTPA-Oct) was high even 48 hours under refrigeration, exceeding a radiochemical purity of 98%, determined in both systems. Sterility and pyrogen tests were negative in all the delivered vials, which are considered suitable for clinical applications. The efficient procedure to obtain ^{111}In -DTPA-Oct was confirmed in the first clinical groups.

• Painel •

INVASIVE EVALUATION OF $^{99m}\text{Tc}(\text{CO})_3$ -THYMIDINE ANALOG IN A LUNG CANCER MODEL.

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Introduction: The use of $[^{99m}\text{Tc}(\text{CO})_3]^+$ as a radiopharmaceutical precursor opens new routes in the labeling of biomolecules. Labeled thymidine is used for tumor imaging, since it is incorporated into DNA and therefore provides a measure of cell proliferation. For the current study thymidine was functionalized at the C5' position of the sugar moiety with the tridentate iminodiacetic acid chelator for complexation and radiolabeling with $^{99m}\text{Tc}(\text{I})$ -tricarboxyl core. A lung cancer model was selected because this is one of the most lethal of cancers worldwide causing up to 3 million deaths annually. **Aim:** The aim was a biodistribution study of the complex $^{99m}\text{Tc}(\text{CO})_3$ -thymidine analog in nude mice bearing lung cancer tumor. **Methods:** The preparation of the organometallic technetium precursor was done under mild reaction following the procedures of Alberto et al. (1998) protocol, where gaseous carbon monoxide and sodium borohydride were used. Then the ligand iminodiacetic acid thymidine was radiolabeled with previously prepared ^{99m}Tc -carbonyl. Athymic male nude mice were inoculated with a human non-small-cell lung carcinoma cell line (A549). Ten days after the inoculation the radioactive complex was injected and one and half hour after the administration of the drug the animals were sacrificed and the invasive studies performed. **Results:** Yield of the $[^{99m}\text{Tc}(\text{CO})_3]^+$ was $98.3 \pm 0.8\%$. Radiochemical purity of $[^{99m}\text{Tc}(\text{CO})_3]$ -thymidine analog was $97.3 \pm 0.4\%$. Biodistribution studies in mice bearing tumor showed

the highest uptake by intestine, followed by liver and kidneys. It was observed that blood clearance was not very fast after 1.5 hour. Tumor/blood and tumor/muscle ratios were 0.2 and 1.4 respectively. Uptake by the tumor was $0.3 \pm 0.02\%ID/g$. **Conclusion:** Despite the good radiochemical profile of the complex, the uptake in lung tumor was low. Other tumor models should be used in the search for better results.

• Painel •

PREPARAÇÃO E CONTROLE DE QUALIDADE DO GLUCARATO- ^{99m}Tc .

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As doenças cardiovasculares encontram-se entre as maiores causas de morbidade e mortalidade no adulto. O infarto agudo do miocárdio continua sendo freqüente, apesar dos avanços da medicina preventiva. O diagnóstico baseia-se normalmente na tríade: dor anginosa típica, alterações do eletrocardiograma e elevação das enzimas cardíacas no soro. Muitos casos podem, no entanto, cursar sem a síndrome completa. A dificuldade do diagnóstico diferencial é por si só causa adicional de eventos fatais. Portanto, o desenvolvimento de ensaios não-invasivos para a detecção dos danos do miocárdio é de extrema importância. Os danos celulares podem ser identificados pela técnica cintilográfica utilizando, entre outros radiotraçadores, o glucarato- ^{99m}Tc (GLA- ^{99m}Tc). O ácido glucárico, também conhecido como ácido sacárico, é um ácido dicarboxílico análogo da glicose. Ele é estruturalmente similar à frutose e penetra na célula através do sistema de transporte D-frutose, sendo desprezível em condições não isquêmicas. O objetivo principal foi estudar as condições de preparação, controle de qualidade, estabilidade e biodistribuição do reagente liofilizado GLA marcado com ^{99m}Tc . O reagente de GLA foi preparado sob a forma liofilizada, em condições assépticas sob fluxo laminar. Cada frasco contém: 12,00mg de ácido glucárico; 0,50mg de $SnCl_2 \cdot H_2O$; 0,50mg de ácido genticônico com pH final igual a 5,0. A pureza radioquímica foi avaliada em dois sistemas cromatográficos: 1) papel Whatman 3MM como suporte e acetona como solvente ($R_f = 1,0$ para $^{99m}TcO_4^-$ e $R_f = 0,0$ para $^{99m}TcO_2^-/GLA-^{99m}Tc$); e 2) ITLC-SG (fibra de vidro) como suporte e cloreto de sódio 0,9% como solvente ($R_f = 1,0$ para $^{99m}TcO_4^-/GLA-^{99m}Tc$ e $R_f = 0,0$ para $^{99m}TcO_2^-$). Foram obtidos resultados maiores que 97% aos 30, 60 e 120 minutos após a marcação utilizando 37, 370, 1850 e 3700MBq/ 3-5mL de $^{99m}TcO_4^-$. O produto manteve-se estável por 12 meses, armazenado a temperatura de 2°C a 80°C. A pureza radioquímica verificada nos ensaios de estabilidade em plasma aos 30, 60 e 120 minutos de incubação foi superior a 98%. A biodistribuição em camundongos Swiss demonstrou rápido clareamento sanguíneo, eliminação renal elevada e baixa captação em órgãos adjacentes e sistema ósseo, confirmada através das imagens cintilográficas em ratos Wistar aos 30, 120 e 360 minutos após a injeção de 18,5MBq de GLA- ^{99m}Tc . O produto apresentou pureza radioquímica, estabilidade e biodistribuição adequadas para sua implantação nos ensaios clínicos, estando em fase de validação os processos de liofilização e controle de qualidade, a fim de estender o protocolo em produção rotineira.

• Painel •

PREPARATION AND QUALITY CONTROL OF 18F-FDG.

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The most important radiopharmaceutical used routinely worldwide in clinical PET studies is the 2-[^{18}F]fluoro-2-deoxy-D-glucose (18F-FDG), for brain, heart and tumors studies, as well as in basic research.

The compound has provided a valuable tool for the study the glucose metabolism in both normal and disease tissue. The synthesis is achieved by a nucleophilic substitution reaction in automatic module available for production. The main advantages of this method are the high purity of the final product, the reduced synthesis time and the decrease radiation exposition to the workers. The aim of this work is to describe the procedure developed and validated, for the routine production and quality control of 18F-FDG. The 18F- is obtained by the nuclear reaction $^{18}O(p,n)^{18}F$ using enriched $H_2^{18}O$ (97%). At the end of bombardment the fluoride is transferred directly to the automatic module. All the reagents are with ultra-pure degree and provided as a "reagents kit" that must be fit 15-20 minutes before the start of the synthesis. The automatic synthesis is achieved in 25 minutes. The impurities are trapped automatically and the labeled precursor is washed away and sterilized by 0.22 mm Millipore filter. The resulting neutral eluent (16 ± 0.6) ml of 18F-FDG is dispensing in a sterile glass vial. Thin layer chromatography system is carried out for radiochemical and chemical determination, in TLC using acetonitrile:H₂O (95:5) and NH₄OH: MeOH (1:9) as solvents, respectively. Stability of 18F-FDG is determined immediately and 10 hours at the end of synthesis (EOS). Sterility and pyrogen tests are performed by the microbiology procedures outlined in the pharmacopoeias in different culture medium. The apirogenicity is evaluated using the "in-vitro" Limulus test (LAL). The yield of synthesis was higher than 55%. The radiochemical purity of 18F-FDG were ($99.04 \pm 0,96\%$) and ($95.91 \pm 4,09\%$), immediately and 10 hours EOS, respectively. The Kriptofix level was below the detection limit of color spot test. Sterility and pyrogen tests were negative in all delivered vials. During the first five months in 2006, the Radiopharmacy Center has produced 92,500 – 110,000 MBq/batch of 18F-FDG at the end of synthesis (EOS) and distributed 3,201 doses at nuclear medicine services in Brazil.

• Painel •

PREPARATION AND QUALITY CONTROL OF ^{99m}Tc -DMSA.

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^{99m}Tc -dimercaptosuccinic acid (DMSA) is considered an excellent kidney imaging agent and is indicated for evaluation of renal parenchymal disorders. After intravenous injection in humans, ^{99m}Tc -DMSA becomes loosely bound to plasma protein (75% at 1 hour after injection, increasing to 90% by 24 hours), with little or no diffusion into red cells. Renal excretion is slow, with only 16% of the dose in urine 2 hours after injection. This report describes the validation of a new formulation of DMSA for routine production and quality control, in lyophilized form for labeled with ^{99m}Tc with 37 at 3,700 MBq. The process was done under vacuum and low temperature in Super Modulyo – "Edwards" lyophilizer and each lyophilized vial contains: 1.0 mg of DMSA; 0.44 mg $SnCl_2 \cdot H_2O$; 0.7 mg ascorbic acid and 50.0 mg inositol, pH = 2.5. The radiochemical purity was evaluated by thin layer chromatography system in Whatman 3MM paper (1 x 8 cm) and TLC-SG (Al) 1.5 x 12.5 cm, using acetone and 0.9% NaCl as solvents, respectively, at 30, 60, 120 and 240 minutes after labeling. The R_f value in acetone is 1.0 for $^{99m}TcO_4^-$ and 0.0 for $^{99m}TcO_2^- / ^{99m}Tc$ -DMSA and the R_f value in 0.9% NaCl is 1.0 for $^{99m}TcO_4^- / ^{99m}Tc$ -DMSA and 0.0 for $^{99m}TcO_2^-$. The stability was evaluated during 6 months and the validation performed in 6 batches. The sterility and pyrogen tests were performed by the microbiology procedures outlined in the pharmacopoeias and by the "in-vitro" Limulus test, respectively. Biological distribution was evaluated in Wistar rats by i.v. of 8.8MBq/0.100 mL. The % dose / organ in different tissues was determined at 1 h after dose. The method was validated for routine production at Radiopharmacy Center, with a stability of 6 month kept at 2–8°C and with a radiochemical purity higher than 90%. The biological distribution in rats

showed an uptake higher than 40% and 6% of injected dose in kidney and rate kidney/liver+spleen, respectively. Sterility and pyrogen tests were negative in all the delivered lyophilized vials. During the first 6 months in 2006, were distributed more than 1,200 lyophilized "kits" of DMSA at clinics and hospitals of nuclear medicine in Brazil.

• Painel •

PREPARATION OF 90Y-CITRATE (90Y-CIT) FOR SYNOVECTOMY.

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Radyosinovectomy is a therapy used to relieve pain and inflammation from rheumatoid arthritis and related diseases. It has been shown that the intra-articular injection of a radioisotopic B-emitter can be used to control synovial inflammation. Synoviorthesis with radioisotopes is indicated when joint inflammation is not totally controlled by drug prescription. Ideal radiopharmaceuticals for this type of treatment would be one, which is pharmaceutically stable, which destroys only the synovial membrane and which is confined to the intra-articular space. Several publications have shown the efficacy of Y-90 for treatment of the knee joint in rheumatoid arthritis. The ideal particle size range was considered to be from 2 - 10 microns and the dose of 148MBq seems to be efficient. The aim of this work was to study the preparation, the quality control and the stability of 90Y-citrate (90Y-Cit) for synovectomy of knee joint. The labeling process is carried out as described previously in literature using 90YCl₃ from Nordion. The 90YCl₃ solution is evaporated to nearly dryness at 150 C. After cooled at room temperature is added 1.5mL /2mM Y(NO₃)₃, 0.1mL /10mM sodium citrate and 2.4mL of sterile water for injection USP. The pH was adjusted to 7.0 with 0.1N NaOH. The solution was gently agitated via rotation, heated at 100 C for one hour and then cooled at room temperature. Radiochemical purity was determined by paper chromatograph system in Whatman 3MM and in TLC-AL, using 0,9% saline solution as a solvent, at 30, 60 and 120 minutes after labeling. In these systems the Rf of 90Y-Cit = 0.0 while the Rf of 90YCl₃ = 1.0. The final product showed radiochemical purity greater than 99% with particle size less than 5 microns. The 90Y-Cit was stable for 5 days at room temperature. Further studies on radiochemical purity, physical, biological and chemical evaluation will be make to compare characteristics and efficacy of 90Y-Cit and the 90Y-HA for synovectomy.

• Painel •

PREPARATION OF HIDROXIAPATITE (90Y-HA) FOR SYNOVECTOMY.

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It is estimated that about 3% of the population worldwide is affected by rheumatoid arthritis. Radiation synovectomy is a method of treatment in non-surgical operation damages, by intra-articular application of b-emitting radioisotopes. An ideal radiopharmaceutical for this type of treatment would be one, which is pharmaceutically stable; which destroys only the synovial membrane and which is confined to the intra-articular space. There are several radionuclides available for this treatment such as Y-90; Sm-153; Dy-165; Ho-166 and Re-188/186. However, Yttrium-90 is often believed to be among the most useful of the radionuclides that have been considered for therapeutic applications, with a half-life of 64.1h and beta rays of high-energy 2.3MeV, with no gamma rays, and decays to a stable daughter (90Zr). The aim of this work is to establish the methodology of preparation, the quality control and stability of 90Y-hydroxyapatite (90Y-HA) for synovectomy. The labeling process was carried out as described previously in literature using 90YCl₃ from Nordion. In a conical glass vial containing 40 mg of

HA from Bio-Rad, with particles in the desirable size range (20mm), dissolved in 0.75 mL sterile water, is added 74-370 MBq of 90Y in citrate form. The vial is sealed and mixed for 30 minutes at room temperature. The suspension is centrifuged twice at 1000 rpm for 3-5 minutes, the liquid was discarded and the precipitated resuspended with 5 mL of saline solution. The final precipitate (90Y-HA) is resuspended in 5-8 mL of sterile saline solution (pH = 6.0), sealed and autoclaved for 30 minutes at 121°C. The percentage of bound activity is determined by measuring the activity of particles (90Y-HA) and supernatant (90Y+++) solution in a dose calibrator in order to calculate the yield of labeling procedure. The radiochemical quality control is evaluated by chromatography system using ITLC-SG and Whatman 3MM paper (1 x 10cm) as support and 0.9% and 8.4% saline solution and acetate buffer as solvents. Radiochemical purity was carried out 30; 120; 240 minutes after labeling to assess the stability of the 90Y-HA. Filters of different sizes (1.2; 5; 8 and 12 mm) were used for particle size determination. The labeling yield of 90Y- HA was (92.1 ± 1.4)% (n = 9). The final product presents a radiochemical purity > 98.9% with particle size > 8mm and "in-vitro" stability of 5 days at room temperature.

• Painel •

PRODUÇÃO E AVALIAÇÃO DE KIT PARA OBTENÇÃO DO 99mTc-HEDP.

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Objetivos: Complexos de tecnécio com difosfonatos são largamente utilizados em cintilografia óssea. Dois produtos são aprovados pelo FDA-USA para uso em humanos, o 99mTc-MDP, o qual é produzido no Brasil, e o 99mTc-HEDP, que somente pode ser obtido sob importação. Neste trabalho, buscamos sintetizar o ligante 1-hidroxi-1,1-difosfonato-etano (HEDP), preparar o complexo de tecnécio e comparar a biodistribuição deste com o 99mTc-MDP. **Métodos:** O ligante foi sintetizado pela reação entre tricloreto de fósforo e ácido acético, seguido por neutralização com NaOH, e foi caracterizado por análise elemental e RMN. Kit para marcação com [99mTc]tecnécio foi preparado com 5,0 mg do ligante, 0,75 mg de SnCl₂.2H₂O e 1,5 mg de ácido ascórbico, a pH = 6,0. Marcações foram realizadas utilizando atividades de até 18,5 GBq (500 mCi) e a eficiência de marcação e estabilidade da ligação foi avaliada por cromatografia em ITLC-SG utilizando solução fisiológica e acetona como fases móveis. Imagens estáticas da biodistribuição do produto, em coelhos Nova Zelândia, foram adquiridas nos tempos de 1, 2 e 3 horas após a administração do radiofármaco, utilizando câmara à cintilação LEM-Ziemens, equipada com colimador LEAP. Para comparação, imagens de 99mTc-MDP foram realizadas utilizando os mesmos parâmetros e as imagens foram analisadas por dois profissionais com experiência na área. **Resultados:** A síntese do ligante forneceu 67% de rendimento, com o produto apresentando análise elemental teórico C = 7,40%; H = 3,40% e obtido C = 7,67%; H = 2,87% e 1H-RMN (D₂O, 300 MHz), δ = 1,6 (t, 3H). A eficiência de marcação para o produto marcado com 500 mCi (n = 5) foi de 98,76 ± 1,15%, após 30 minutos, e 98,95 ± 0,87%, após 14 horas. A relação entre a captação no osso e partes moles, para os tempos de 2 e 3 horas, foram de: 1,68 e 2,50 para o 99mTc-MDP e 1,86 e 2,82 para o 99mTc-HEDP. Análise visual não permitiu diferenciar entre a utilização dos dois produtos. **Conclusões:** A síntese do ligante é de relativa facilidade e o produto obtido apresentou características adequadas. O kit pôde ser marcado com alta atividade, superior àquela definida para o MDP, fornecendo produto com alta pureza radioquímica e estabilidade. A qualidade das imagens é equivalente, demonstrando que o kit produzido pode ser uma alternativa ao uso do 99mTc-MDP, principalmente em clínicas em que são realizadas grande Tema de cintilografias ósseas.

• Painel •

PRODUCTION OF I-131 BY DRY-DESTILLATION OF IRRADIATED TELLURIUM OXIDE.

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One of the more important radioisotopes for use in Nuclear Medicine is I-131. It can be produced in nuclear reactors, by two different reactions: fission of U-235 or neutron activation of Te in different forms, such as telluric acid, tellurium oxides and the elementary tellurium. The reaction of choice was the neutron activation of Te because it provides I-131 with high radioactive concentration, high specific activity and lower amount of waste (radioactive or not) when compared to the U-235 fission. The irradiation parameters that could be varied were the mass of the target, the neutron flux and length of irradiation. The objective of this work was to study the production of I-131 using the dry distillation technique for its separation from targets of tellurium oxide (TeO₂) irradiated at IPEN's IEA-R1 Nuclear Reactor. After the irradiation the targets were heated inside a resistive oven at temperatures higher than its melting point for an adequate period of time. In this condition, I-131 is sublimated and carried by a flow of oxygen gas and further trapped onto water cooled diluted NaOH solution (pH 11). The variables studied in this procedure were the time and the temperature of distillation and the effect of the mass of the target to be processed. The results shown that the best conditions of distillation occurred with oven temperatures between 800°C and 750°C and with the distillation time between 2h and 4h. For the temperature of 750°C, the total I-131 activity produced was in average 468.346 MBq (12658 mCi), while at 800°C the average value was 361.453 MBq (9769 mCi). The distillation apparatus could handle up to 3 targets (150 g of TeO₂). Quality control studies showed that the I-131 produced had the proper conditions to be used in Nuclear Medicine. Nowadays a total activity of nearly 777 GBq (21 Ci) of I-131 can be produced every week using this technology that represents about 60% of the total demand of I-131.

• Tema Livre •

PRODUCTION OF ¹⁷⁷Lu-DOTA-TYR3-OCTREOTATE TO CLINICAL APPLICATION IN NEUROENDOCRINE TUMORS.

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Radiolabeled receptor-binding peptide is an important class of radiopharmaceuticals for tumour diagnosis and therapy. The new somatostatin analogue Tyr3-octreotate has an increased receptor affinity compared with octreotide and Tyr3-octreotide. Suitable radionuclide as Lutetium-177 (Lu-177) with a medium energy β emitter (0.5 MeV), a low abundance and half life of 6.7 days is one of the most frequently radioisotope used in peptide receptor radiotherapy (PRRT). The aim of this work is to validate the preparation and quality control of Tyr3-octreotate labeled with Lu-177, using DOTA as chelating agent, for clinical application. The labeling of DOTA-Tyr3-Octreotate with Lu-177 was performed, under GMP condition, in a "glove-box" with ¹⁷⁷LuCl₃ (IDB-Holland) at pH 4.5, using radionuclide:peptide ratio of 279 MBq/18 μ g in sodium acetate buffer, at 100°C for 30 minutes. Radiochemical purity was determined by ITLC-SG in 0.1M sodium citrate, pH 5.5, as solvent. The labeled peptide migrates from the origin R_f = 0.1-0.3 and the radionuclide migrates with the solvent front R_f = 1.0. The stability of the final product was evaluated immediately and for 3 days, kept under freezing condition. Sterility and pyrogen tests were performed by microbiology procedures in different culture medium and the apirogenicity by the "in-vitro" Limulus test (LAL). The ¹⁷⁷Lu-DOTA-Tyr3-Octreotate was stable for 3 days with a radiochemical purity of (98.6 \pm 3.3)%; (98.8 \pm 6.6)% and (98.5 \pm 0.5)%; first day, 24 and 48 hours, respectively, kept under freezing condition. Sterility and pyrogen tests were negative, which are considered suitable for clinical applications.

The clinical study were successfully performed and the scintigraphic images were compared with ¹¹¹In-DTPA-Oct, showing a similar distribution in the same patient.

• Painel •

QUALITY ASSURANCE IN RADIOPHARMACEUTICAL PRODUCTION.

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Radiopharmaceuticals must be manufactured in accordance with the basic principles of Good Manufacturing Practices (GMP) for sterile pharmaceutical products as recommended by the World Human Organization (WHO). **Objective:** The aim of this paper is to discuss the Quality Assurance in radiopharmaceutical production based on WHO recommendations and in USA and Europe regulations. **Methods and results:** Quality Assurance is a wide ranging concept which covers all matters which individually or collectively influence the quality of a product. GMP means the part of Quality Assurance which ensures that products are consistently produced and controlled in accordance with the quality standards, appropriate to their use. The GMP in USA are part of the "Code of Federal Regulations" - CFR 21, parts 210 and 211. Radioactive drugs are regulated to the same extent that other drugs. The European Commission adopt the Directive 2003/94/C to regulates GMP. The GMP in Brazil were published in the Resolution ANVISA, RDC 210, 2003. Some aspects of the GMP applied to radiopharmaceutical production are of special interest: Personnel: personnel should be trained in GMP, safe handling of radioactive materials and radiation safety procedures. Premises and equipment: Laboratories for the handling of radioactive materials must be specially designed to take into consideration aspects of radiation protection, cleanliness and sterility. The production of sterile radioactive products should be carried out under negative pressure surrounded by a positive pressure zone ensuring that appropriate air quality requirements are met. Production: Careful consideration should be given to the validation of the process, process control and monitoring of the established parameters, specially from the environment. Quality Control and Quality Assurance: principal responsibilities: (a) instructions for each test /analysis and revision of procedures/specifications; (b) identification and segregation of test samples to avoid mix-ups and cross-contamination; (c) environmental monitoring and equipment and process validation for evaluating the adequacy of the manufacturing conditions; (d) release or rejection of starting materials, intermediate products, packaging and labelling materials, and each batch of finish preparation; (e) evaluation of stability of the finished products and establishment of expiry dates; (f) retaining samples of radiopharmaceuticals products and keeping adequate records of the distribution. **Conclusion:** Because of their short half-lives, many radiopharmaceuticals are released and administered to patients shortly after their production, so that quality control (e.g. tests for sterility, endotoxin, radionuclidic purity, etc) may sometimes be retrospective. The implementation of and compliance with the Quality Assurance Programme are therefore essential.

• Painel •

STUDY OF PREPARATION OF GENERATORS OF ⁹⁹Mo-^{99m}Tc BASED TO GELS OF MOLYBDENUM WITH ZIRCONIUM, TITANIUM, CERIUM AND HAFNIUM.

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Generator of ⁹⁹Mo-^{99m}Tc is a system formed with these two radioisotopes, where the molybdenum, by radioactive decay, produces the technetium that must be separated from molybdenum. ⁹⁹Mo can be produced by several nuclear reactions in particles accelerators or nuclear reactors. ^{99m}Tc has ideal nuclear properties for organ imaging in nuclear

medicine, due to its nuclear characteristics: short half-life (6.04 h), emission of gamma radiation of low energy (140 keV), absence of beta emission, 100% of decay by isomeric transition for ^{99m}Tc . This work presents the preparation of gel generators of molybdenum with zirconium, titanium, cerium and hafnium and characterization of the gels: mass ratio between molybdenum and cation, particles size and elution percentage of ^{99m}Tc after irradiating the gels. Gels had been prepared in different temperatures (25 and 50 °C), NaOH concentrations (2 and 4 mol/L), mass ratio (Mo/Zr = 3.29, Mo/Ti = 1.80 and 2.25, Mo/Ce = 0.31 and 0.38, Mo/Hf = 0.24) and final pH of 3.5 and 4.5. The analysis of the results proved that these gels are adequate for preparation of the generators of ^{99}Mo - ^{99m}Tc : Zr: Mo/Zr = 3.29, NaOH concentration = 2 mol/L, 50°C and final pH = 4.5 Ti: Mo/Ti = 2.25, NaOH concentration = 2 mol/L, 25°C and final pH = 3.5 Ti: Mo/Ti = 2.25, NaOH concentration = 4 mol/L, 50°C and final pH = 3.5 Hf: Mo/Hf = 0.24, NaOH concentration = 4 mol/L, 50°C and final pH = 4.5 Percentages of molybdenum in the molybdenum with zirconium gels and the two molybdenum with titanium gels are similar, which is not observed in the molybdenum with hafnium gel, since the molybdenum percentage is lower. If the activation of the molybdenum during the irradiation is considered, the totality of ^{99}Mo produced will be similar in the molybdenum with zirconium and molybdenum with titanium gels and will be lower in the molybdenum with hafnium. An adequate gel for the preparation of the molybdenum generators must possess particles of size between 0.106 and 0.150 μm and all gels are adequate. ^{99m}Tc elution is a process that consists of passing saline solution through the irradiated gel to remove the ^{99m}Tc and the elution yield are high and similar for all gels, demonstrating good performance. The results have shown a good performance of molybdenum with titanium gels and molybdenum with hafnium gels, when compared with the molybdenum with zirconium gels.

• Painei •

* STUDY OF THE VIABILITY OF THE PRODUCTION OF ^{177}Lu IN NUCLEAR REACTOR.

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The beta- emitter ^{177}Lu is an important radioisotope, for research and investigational purposes as a diagnostic and radiotherapy agent in the treatment of several malignant tumors. The nuclear properties of ^{177}Lu are advantageous compared to other therapeutic radionuclides, e.g. ^{90}Y , and it can label several biomolecules, such as peptides. The objective of this work is to study the production of ^{177}Lu in the nuclear reactor located at IPEN using the two different methods: direct and indirect route. In the first reaction, Lu_2O_3 is irradiated in the reactor producing ^{177}Lu . The second route employs targets of Yb_2O_3 are irradiated in the reactor producing ^{177}Yb that decays to no-carried-added ^{177}Lu . This paper shows the results of the production yields of ^{177}Lu using the two nuclear reactions, and the extrapolations to real production conditions. Targets of Lu_2O_3 and Yb_2O_3 were irradiated in the nuclear reactor under different neutron fluxes and irradiation times. After the irradiation the targets were analyzed by g-ray spectroscopy using a hiperpue Ge detector. The direct method gives a lower specific activity $4,92 \times 10^8 \text{ Bq/g}$ compared to the indirect one, $7,14 \times 10^8 \text{ Bq/g}$, but the later can not achieve the total activity required for a routine production.

• Painei •

* ^{99m}Tc DIRECT RADIOLABELING OF MONOCLONAL ANTIBODIES: REDUCING AND PURIFICATION OF ANTIBODIES.

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Monoclonal antibodies (Mabs) have been used for diagnostic and therapeutic treatment of some types of tumors. Nuclear medicine is one the best tools among the diagnostic modalities in the cancer diagnosis and the radionuclide technetium- ^{99m}Tc (^{99m}Tc) is extensively used

in radiodiagnostics in nuclear medicine. The direct labelling method of Mabs with ^{99m}Tc depends on the free disulfide bridges (-SH) obtained after the reduction of the antibody (Ab). The objective of this work was to study the reduction process of Mabs and their purification before labelling with ^{99m}Tc . The -SH bridges of the Ab molecule were broken by using the reducing agent 2-mercaptoethanol (2-ME) and converting them into free -SH groups. The mixture of Ab (CEA-1 and EGF/R3) and 2-ME was incubated at room temperature and after the reaction time the resulting solution was purified on a Sephadex PD-10 column using phosphate buffered saline (PBS)(pH 7.4) purged with nitrogen as mobile phase and fractions of 1 mL were collected (12 fractions). These fractions were analysed by HPLC using a Protein-Pak Diol (OH) column and PBS as solvent, measuring the UV signal at 254 nm. The results showed that the reduction time of 30 min is enough when the native Ab is a fresh one. After some storage time, the reduction time had to be increased in order to improve the labelling efficiency. A relation with the mass of Ab was established as follows: for 5 mg of Ab the reduction time was 1 hour and for 10 mg of Ab was 2 hours. The HPLC showed a good separation between the Ab peaks (Retention time of 7.84 min for CEA1 and 6.67 min for EGF/R3) and the 2-ME peak (Retention time of 12.22 min). In the purification system, the reduced Ab was in the fractions 3 to 5 and sometimes it appeared in the fraction 6 together with 2-ME. From the fraction 7 on, only 2-ME appeared in the HPLC analysis. As conclusion, the Ab reducing process must produce a number of free -SH bridges enough to label it with ^{99m}Tc with a good radiochemical yield. The HPLC analysis is very important to make sure that the right fractions of the purification process are collected for further use, otherwise 2-ME will be present, a contaminant that interferes in the labelling reaction.

• Painei •

UV-VIS SPECTROPHOTOMETRIC QUANTIFICATION OF $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ IN LYOPHILIZED KIT FOR ^{99m}Tc TECHNETIUM LABELING.

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Objectives: Before the use as radiopharmaceuticals, lyophilized kit for ^{99m}Tc technetium labeling are considered pharmaceuticals preparations. By the way, biological and physico-chemical analysis must be performed, including quantification of the major component. Although the HPLC is the choice method for this analysis, sometimes UV-VIS spectrophotometry is the used method, once it is low cost and fast analytical procedure. In this work we assessed the UV-VIS spectrophotometric method for quantification of $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ in lyophilized preparations used for obtention of the radiopharmaceutical $[[^{99m}\text{Tc}](\text{MIBI})_6]^+$, the important agent for myocardial perfusion studies. **Methods:** Standard of $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ was synthesized and characterized by $^1\text{H-NMR}$, Infrared spectrometry, elemental analysis, melting point and HPLC. A calibration curve was generated from concentration between 5 μg to 80 $\mu\text{g/mL}$, in water, with absorbance measured at 218 nm, using water as reference. Vials content were evaluated dissolving lyophilized products Cardiolite[®] (n = 6), MIBI-CMN prepared at CMN-FMUSP (n = 6) and MIBI-IPEN prepared at IPEN-CNEN/SP (n = 2) in water and samples were measured at 218 nm using the others kit components as reference. **Results:** Analytical data for $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ standard are in agreement with structure and purity for desired compound. The calibration curve showed linear regression of $R^2 = 0,9986$ and concentration of the $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ in the samples were: $1,07 \pm 0,03 \text{ mg}$ for Cardiolite[®], $0,97 \pm 0,07 \text{ mg}$ for MIBI-CMN and $1,07 \pm 0,04 \text{ mg}$ for MIBI-IPEN. **Conclusions:** The use of UV-Vis spectrophotometry for quantification of $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ in lyophilized preparations allowed a fast and inexpensive analysis, and the results obtained are in concordance with established values of concentration and deviation of $1,00 \pm 10\% \text{ mg}$ of $[\text{Cu}(\text{MIBI})_4]\text{BF}_4$ for all products.