Sudan University of Science and Technology

College of Graduate Studies

Evaluation of ^{99m}Tc- labeled Radiopharmaceuticals Quality Control Procedures in the Radiation and Isotopes Center of Khartoum.

تقويم اجراءات ضبط الجودة للمواد الصيدلية المرقومة بعنصر التكنيشيوم 99م في المركز القومي للعلاج بالأشعة والطب النووي

Thesis submitted for the award of PhD in Nuclear Medicine Technology

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2016

Dedication

This study is dedicated to all people who saved no effort and no advice in encouraging and assisting me in the commencement and completion thereof. Most of all , the study is particularly dedicated to the members of my family , colleagues and friends to whom my love , sincerity and devotion will last forever .Special dedication is sent to all people who are interested in nuclear medicine technology , and who may find something which deserves attention in this modest study.

Acknowledgement

Many research would not be written without the inspiration and encouragement provided by colleagues and friends. I am, therefore, grateful to all people who have contributed in so many ways towards the accomplishment of this study. Special gratitude is extended to my supervisor, Dr. Sediek M. Mustafa and the co-supervisor, Dr. Mohammed El fadil. Without their instructions and advice, the study would not have been conducted. I must acknowledge the considerable assistance provided by the staff members of the nuclear medicine department of RICK, particularly the nuclear medicine technologists, who provided free access to the hot lab and other places at any time to carry out the tests and experiments. I am really indebted to the physicists of RICK who deserve special recognition for putting their measurement devices and tools at my disposal throughout the study period. Sincere thanks and gratitude are extended to the dean and my colleagues in the College of Medical Radiologic Science, for their continuous assistance, advices and encouragement.

List of abbreviations

^{99}Mo /moly	Molybdenum-99
IAEA	International Atomic Energy Agency
QC	Quality Control
RICK	The Radiation and Isotopes Center of Khartoum
WHO	World Health Organization
^{99m}Tc O_4	Technetium pertechnetate
Lab	laboratory
NaI (Tl)	sodium iodide- Thallium activated
US	The United States
CFR	Code of Federal Regulations (US)
GM	Geiger and Muller
mR	milli-rem
Hr /h	hour
µCi	micro-Curie
mCi	milli-curie
Z	atomic number
Kev	Kilo-electron volt
Nacl	Sodium chloride
$Sncl_2$	stannous chloride
OH.	Hydroxy free radical
MDP	Methyline Diphosphate
DTPA	diethlyline triamine penta- acetic acid

EDTA	ethylene diamine tetra acetic acid
HMPAO	Hexamethyl propylamineoxime
HEDP	hydroxy ethethylidenediphosphonate
DMSA	dimercapto succinic acid
^{226}Ra	Radium-226
^{68}Ge	germanium-68
^{68}Ga	gallium-68
^{81}Rb	rubidium-81
^{68}Zn	zinc-68
^{81}Kr	krypton-81
^{113}Sn	tin-113
^{113}In	indium-113
^{132}Te	tetanium-132
^{132}Xe	xenon-132
^{82}Sr	strontium-82
$Al_2 O_3$	alumina (aluminum oxide)
Na $^{99m}TcO_4$	sodium pertechnetate
LET	linear energy transfer
IDA	iminodiacetic acid
GH	glucoheptonte
MIAA	Micro- aggregated albumin
MAA	macro- aggregated -albumin
PYP	pyrophosphate

RBC	red blood cell
WBC	white blood cell
MIBG	metaiodobenzylguanidine
RIA	Radio-immuno- assay
SPECT	single photon emission computed tomography
SC	sulfer colloid
HAM	human albumin microsphere
MBq	Mega Becquerel
MAG-3	mercapto-acetyl-triglycine
ITLC	instant thin layer chromatography
HEDP	hydroxy ethylidene diphosphate
FOV	field of view
BBB	blood brain barrier
^{18}F-FDG	fluoro deoxy glucose
USP	United States pharmacopoeia
RISA	radio-iodinated serum albumin
LEGP	low energy general purpose (collimator) .
QA	quality assurance
RHTC	hydrolyzed reduced technetium
BP	British pharmacopoeia
EP	European pharmacopoeia
MEK	methyl ethyl Ketone
LAL	limulus amebocyte lysate

mR	milli- Roentgen
NM	nuclear medicine
CPS	counts per second
dpm	disintegration per minute
AAEED	annual average effective equivalent dose
NCRP	National Commission of Radiation Protection (USA).
USNRC	United States Nuclear Regulatory Commission.
Fig.	Figure
SSN	Supra sterna notch

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Abstract

This study was conducted at the nuclear medicine department of the Radiation and Isotopes Center of Khartoum (RICK), during the period from 2010 to 2016. The main objective of the study was to study the situation of ^{99m}Tc – radiopharmaceuticals QC procedures in RICK. The data were collected from many experimental and observational procedures which were done for the first time, to the best of the researcher's knowledge. These procedures included measurements of radiation exposures and contamination rates at different areas of the department. All the measured radiation exposures in the different areas of the department were within the permissible limits, except the waiting room of the injected patients, in which the radiation exposure rates were high owing to the large number of patients and the narrow area. Physical inspection of ^{99m}Tc eluate appearance for color, particles size and turbidity was performed which revealed no abnormality in these variables. Measurement of remaining (unused) activities were performed on different elution yields, and revealed that the total unused activities from 13 elutions were 3999.4 mCi (57%) out of the total eluted activities (7008.7 mCi), 32% of the unused activities were prepared (mixed with the chemical agent) and 74% were unprepared. These unused activities constitute a radiation hazard, in addition to the economical aspect. The researcher measured the external radiation exposure emanating from a new generator, and the generator package surface contamination of two generators, and the tests showed no abnormal results. The measurements, as well, included the radiation doses received by some body organs during elution of generators, injection and imaging of patients. Pyrogenicity test on three mature rabbits was done, and revealed a total temperature increment by 0.9 C^0, which was an evidence of the presence of pyrogens within the tested radiopharmaceutical. The study also included the ^{99}Mo breakthrough test which revealed that the amounts of molebdenum-99 within the eluate were within the internationally acceptable limits, and there was no justification to sacrifice the eluate of the first elution of each generator.

The lack of personnel radiation monitoring devices, and the undetermined regular working hours of the staff members made the specification of accurate received doses very difficult, in spite of the attempts made by the researcher to estimate these doses, depending on assumptions.

The study concluded that no regular ^{99m}Tc radiopharmaceuticals QC procedures were performed in the nuclear medicine department of RICK and that most of radiation doses in different areas were within the internationally permissible limits. The results and recommendations of the study may constitute a great benefit to the department, and a start point to design and implement a comprehensive program of QC procedures in this domain at daily, weekly,

monthly and annual fashion. Future studies in this domain are encouraged.

المستخلص

اجريت هذه الدراسة فى قسم الطب النووى بالمركز القومى للعلاج بالأشعة والطب النووى , قى الفترة بين عامي (2010) و(2016) , وكان الهدف الأساسي من الدراسة هو دراسة و تقويم وضع اجراءات ضبط الجودة لعنصر التكنيشيوم 99م المشع والمواد الصيدلية المرتبطة به . تم جمع البيانات عن طريق الملاحظة والتجارب المعملية والقياسات التي تجرى لأول مرة بالقسم على حد علم الباحث بغرض تحقيق أهداف الدراسة . اشتملت التجارب و القياسات على قياس معدلات التعرض والتلوث الاشعاعى فى محتلف الأماكن داخل المبنى . أوضحت الدراسة أن تلك المعدلات كانت فى الحدود المسموح بها عالميا ماعدا غرفة انتظار المرضى المحقونين التى سجلت معدلات عالية . اجريت دراسة استكشاف بصرى على المادة المشعة المستخرجة من المولد الاشعاعى عدة مرات , حيث أوضحت الدراسة عدم وجود أى تغيير فى اللون أو درجة النقاء أو حجم الجزيئات .

قام الباحث بقياس النشاط الاشعاعى للمواد المشعة المتبقية (غير المستخدمة) لعدد (13) استحلاب من المولد , حيث كشفت الدراسة أن جملة النشاط الاشعاعى لتلك المواد بلغت (3999.4) ملى كورى بنسبة 57% من جملة النشاط الاشعاعى للمواد المستحلبة وهى (7 .7008) . هناك نسبة 32% من المواد غير المستخدمة مخلوطة بالمواد الصيدلية و نسبة 74% غير مخلوطة (تكنيشيوم فقط).

تشكل هذه المواد غير المستخدمة خطرا اشعاعيا وهدرا اقتصاديا , لأنها يمكن أن تكفي لعدد (800) فحص تقريبا للغدة الدرقية مثلا.

أجري الباحث قياسا للتعرض الاشعاعى الخارج من اثنين من المولدات الاشعاعية الجديدة ,حيث أوضح القياس أن التعرض كان فى الحدود المسموح بها عالميا . قام الباحث كذلك بقياس الجرعات الأشعاعية التى تتعرض لها بعض أعضاء الجسم أثناء استحلاب المواد المشعة , وأثناء الحقن والتصوير .

أحضر الباحث عدد ثلاثة أرانب بالغة لاختبار تلوث المادة الصيدلية الشعاعية بعد حقنها. كشف الاختبار ارتفاع درجة الحرارة في كل أرنب , وارتفاع مجموع درجات الحرارة للأرانب الثلاثة بمقدار(2.3درجة مئوية) , بينما الزيادة المقبولة ينبغي ان تكون أقل من 1.4 درجة مئوية , وهو مؤشر علي وجود تلوث بالمادة المحقونة.

تم اجراء قياس النشاط الاشعاعى لعنصر الموليبدينوم- 99 (وهو من الشوائب) الخارج مع مستحلب التكنيشيوم 99م , بما في ذلك المستحلب الأول للمولد, وكشف القياس الذي اجرى علي عشرة مستحلبات مختلفة ,عند زمن الاستحلاب وزمن الحقن , أن كمية الموليبدينوم-99 كانت في الحدود المسموح بها عالميا, ولا يوجد مبرر لعدم الاستفادة من المتحلب الأول في جراء الفحوصات.

خلصت الدراسة الي أنه لاتوجد اختبارات ضبط جودة منتظمة لمادة التكنيشيوم-99م والمواد الصيدلية المرتبطة به بقسم الطب النووي مكان الدراسة , وأن نتائج وتوصيات الدراسة من شأنها أن تشجع القسم والأقسام المشابهة في السودان علي تصميم وتنفيذ برنامج متكامل لاجراءات ضبط الجودة في هذا المجال بصورة يومية واسبوعية وشهرية وسنوية .

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