



شبكة المعلومات الجامعية

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



شبكة المعلومات الجامعية
@ ASUNET



شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of
15-25- c and relative humidity 20-40%

بعض الوثائق الأصلية تالفة

بالرسالة صفحات لم ترد بالاصل

2007

Risk Associating of Patients with Radiopharmaceuticals in Nuclear Cardiology

(In vivo and In vitro)

THESIS

**Submitted for the partial fulfillment of
Ph D Degree in Medical Biophysics**

By

MAHMOUD HANY KHEDR

**Physicist in Nuclear Cardiology Unit
Critical Care Department
Cairo University Hospitals**

TO

**Biophysics department
Faculty of Science
Cairo University**

2007

APPROVAL SHEET

TITLE OF THE PH.D. THESIS

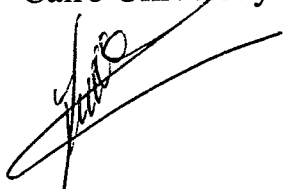
**Risk Associating Injection of Patients with
Radiopharmaceuticals in Nuclear Cardiology
(In vivo and In vitro)**

NAME OF THE CANDIDATE

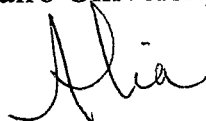
Mahmoud Hany Khedr

SUPERVISION COMMITTEE

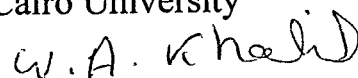
Prof. Dr. Fadel M. Ali
Professor of Biophysics
Faculty of Science
Cairo University




Prof. Dr. Alia H. Abdel-Fattah
Professor of Critical Care Medicine
Head of Critical Care Department
Director of Nuclear Cardiology Unit
Cairo University



Prof. Dr. Wafaa M.A. Khalil
Professor of Biophysics
Faculty of Science
Cairo University



Assist. Prof. Dr. Reem H. El-Gebaly
Assistant Professor of Biophysics
Faculty of Science
Cairo University



Head of Biophysics Department
Prof. Dr/ Osiris Wanis

Acknowledgment

Thanks to **Allah** who gave us patience and, skill to continue this work with this success.

I would like to thank the great **Professor Dr Fadel M.Ali** who offered us all the facilities and encouraged us to get this work to light, he is always innovative,updated, taking new technologies cautiously and courageously, he taught us how to be patient, to work not only hard but also in a meticulous, skilled and efficient way. I am really unlimitedly indebted to him.

I would like to thank to **Professor DR Wafaa M. Ahmed Khaleel** for her encouraging me to initiate this work and her patience intelligent,continuous supervision through revision of this thesis

I would like to thank **Professor Dr Alia Abd El-Fattah** for her endless support and her sincere help and training in the field of nuclear cardiology, she always has new ideas work in a meticulous, hard and very active way and tries to innovate, update and actively participate in every part concerning her work.

Many thanks to **professor assistant Dr Reem H. El- Gebaly** who supported, encouraged and taught me how to think and how to work in a friendly way and helped me in data collection, actively participated in every part of this work, reviewed with me every single step from A-Z. I owe her much.

Many thanks to **my great family** they not only participated in this work as much as I did, they are every thing in my life I would never be able to reward them any part of what they give me.

I carry a big debt to **my colleagues, the team of nuclear lab** they were always beside me encouraging ,helping,working,following with great care.

Mahmoud Hany Khedr

CONTENTS

	Page
List of Figures	I
List of Tables	V
List of abbreviations	VII
ABSTRACT	IX
INTRODUCTION	1
CHAPTER ONE: LITERATURE REVIEW	
1.1 Radiation Biological Effects	2
CHAPTER TWO: BASIC ASPECTS	
2.1 Radiopharmaceuticals	12
A-Radiopharmaceutical characteristics	13
B-Factors Influencing the Design of Radiopharmaceuticals	13
2-2 $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Generator	15
A- Production of Molybdenum-99	17
B-Performance of the $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Generator	18
2-3 Technetium $^{99\text{m}}\text{Tc}$ Pharmaceuticals	20
2-4,Myocardial Perfusion Radiopharmaceuticals	21
• ^{201}Tl -Thallous Chloride	22
• $^{99\text{m}}\text{Tc}$ -MIBI (Cardiolite)	24
• $^{99\text{m}}\text{Tc}$ -Tetrofosmin (Myoview)	25
• Other Perfusion Radiopharmaceuticals	26
2-5 Internal Radiation Dosimetry	28
▪ Calculation of Radiation Absorbed Dose	28
▪ Calculation Effective Dose	31
2-6 Gamma Camera	32
2-7 Blood	35

a) Erythrocytes (red blood cells)	35
b) Hemoglobin	36
c) The Erythrocyte Membrane	39
2-8 Theory of Dielectric Relaxation	41
2-8-1. Basic Concepts of Dielectric Properties	43
2-8.2 Cole-Cole Equation	48
2-8-3. Kramers - Kronig Relations	49
2-8.4 Molecular Interpretation of the Dielectric Behavior of Biological Material	50
2-9 Solubilization of red blood cells by detergent	51

CHAPTER THREE: MATERIALS AND METHODS

<i>3-1, Patients studies</i>	53
<i>A- in vivo studies</i>	53
<i>B-In vitro studies</i>	55
<i>3-2 Animals. Studies</i>	56
3.3 Red Blood Cell Membrane Solubilization test	57
3.4 Osmotic Fragility	58
3.5 Hemoglobin Extraction	60
3.6 Dielectrics: -	60

CHPTER FOUR: RESULTES

4-1 Statistical analysis	62
4-2 Patients Results	62
A – in vivo	62
I. Solubilization studies	62
II. Osmo-fragility Studies	67
III. Dielectric studies	76
IV. Hemoglobin absorption spectra	77
V. Blood film	82
B – in vitro	87
i. Solubilization studies	87
ii. Osmo-fragility Studies	89

iii. Dielectric studies	92
iv. Hemoglobin absorption spectra	93
v. Blood film	95
4-3 Animal Results	96
i. Solubilization studies	96
ii. Osmo-fragility Studies	102
iii. Dielectric studies	119
iv. Hemoglobin absorption spectra	120
v. Blood film	126
CHAPTER FIVE: DISCUSSION AND CONCLUSION	
Discussion	132
Conclusion	146
Appendix I	147
Appendix II	163
Appendix III	169
REFERENCES	190
ARABIC ABSTRACT	---

List of Figures

	Page
Figure (2-1)	16
Figure (2-2)	16
Figure (2-3)	18
Figure (2-4)	25
Figure (2-5)	33
Figure (2-6)	34
Figure (2-7)	36
Figure (2-8)	38
Figure(2-9)	38
Figure (2-10)	39
Figure (2-11)	42
Figure (2-12)	45
Figure (2-13)	46
Figure (2-14)	48
Figure (2-15)	50
Figure (4-1)	63
Figure (4-2)	64
Figure (4-3)	65
Figure (4-4)	66
Figure (4-5)	68
Figure (4-6)	68
Figure (4-7)	69
Figure (4-8)	70
Figure (4.9)	70
Figure (4-10)	71
Figure (4-11)	71
Figure (4-12)	72
Figure (4-13)	72
Figure (4-14)	73
Figure (4-15)	73

Figure (4-16)	Osmotic fragility curve for one patient from group IV, pre injection	74
Figure (4-17)	Osmotic fragility curve for one patient from group IV, 24 hr, post injection	74
Figure (4-18)	Osmotic fragility curve for one patient from group IV, 3 days post injection	75
Figure (4-19)	Osmotic fragility curve for one patient from group IV, 12 days post first injection	75
Figure (4-20)	Absorption spectra of Hb molecules for one patient from group I	78
Figure (4-21)	Absorption spectra of Hb molecules for one patient from group II	79
Figure (4-22)	Absorption spectra of Hb molecules for one patient from group III	80
Figure (4-23)	Absorption spectra of Hb molecules for one patient from group IV	81
Figure (4-24)	Blood film for one patient from group I	83
Figure (4-25)	Blood film for one patient from group II	84
Figure (4-26)	Blood film for one patient from group III	85
Figure (4-27)	Blood film for one patient from group IV	86
Figure (4-28)	The variation of the turbidity of RBCs as a function of the detergent concentration for one sample from group V	88
Figure (4-29)	Osmotic fragility curve for one sample from group V pre adding radiopharmaceuticals	89
Figure (4-30)	Osmotic fragility curve for one sample from group V, 24 hr post adding ^{99m}Tc	90
Figure (4-31)	Osmotic fragility curve for one sample from group V, 24 hr post adding ^{99m}Tc -MIBI	90
Figure (4-32)	Osmotic fragility curve for one sample from group V, 24 hr post adding ^{99m}Tc -Terofosmin	91
Figure (4-33)	Osmotic fragility curve for one sample from group V, 24 h post adding ^{201}Tl	91
Figure (4-34)	Absorption spectra of Hb molecules for one sample from group V	94
Figure (4-35)	Blood film for group V	95
Figure (4-36)	The variation of the turbidity of RBCs as a function of the detergent concentration for one rat from group 1.	97
Figure (4-37)	The variation of the turbidity of RBCs as a function of the detergent concentration for one rat from group 2.	98
Figure (4-38)	The variation of the turbidity of RBCs as a function of the detergent concentration for one rat from group 3.	99
Figure (4-39)	The variation of the turbidity of RBCs as a function of the detergent concentration for one rat from group 4.	100
Figure (4-40)	The variation of the turbidity of RBCs as a function of the detergent concentration for one rat from group 5.	101
Figure (4-41)	Osmotic fragility curve for one rat from group 1 pre injection	104
Figure (4-42)	Osmotic fragility curve for one rat from group 1 24 hr, post 1 st injection	104
Figure (4-43)	Osmotic fragility curve for one rat from group 1 24 hr, post 2 nd injection	105

Figure (4-44)	Osmotic fragility curve for one rat from group 1 one week post 1 st injection	105
Figure (4-45)	Osmotic fragility curve for one rat from group 1 two weeks post 1 st injection	106
Figure (4-46)	Osmotic fragility curve for one rat from group 2 pre injection	107
Figure (4-47)	Osmotic fragility curve for one rat from group 2 ,24 hr, post 1 st injection	107
Figure (4-48)	Osmotic fragility curve for one rat from group 2, 24 hr, post 2 nd injection	108
Figure (4-49)	Osmotic fragility curve for one rat from group 2 one week post 1 st injection	108
Figure (4-50)	Osmotic fragility curve for one rat from group 2 two weeks post 1 st injection	109
Figure (4-51)	Osmotic fragility curve for one rat from group 3 pre injection	110
Figure (4-52)	Osmotic fragility curve for one rat from group 3 24 hr, post 1 st injection	110
Figure (4-53)	Osmotic fragility curve for one rat from group 3 24 hr, post 2 nd injection	111
Figure (4-54)	Osmotic fragility curve for one rat from group 3 one week post 1 st injection	111
Figure (4-55)	Osmotic fragility curve for one rat from group 3 two weeks post 1 st injection	112
Figure (4-56)	Osmotic fragility curve for one rat from group 4 pre injection	113
Figure (4-57)	Osmotic fragility curve for one rat from group 4 24 hr, post 1 st injection	113
Figure (4-58)	Osmotic fragility curve for one rat from group 4 24 hr, post 2 nd injection	114
Figure (4-59)	Osmotic fragility curve for one rat from group 4 one week post 1 st injection	114
Figure (4-60)	Osmotic fragility curve for one rat from group 4 two weeks post 1 st injection	115
Figure (4-61)	Osmotic fragility curve for one rat from group 5 pre injection	116
Figure (4-62)	Osmotic fragility curve for one rat from group 5 24 hr, post 1 st injection	116
Figure (4-63)	Osmotic fragility curve for one rat from group 5 24 hr, post 2 nd injection	117
Figure (4-64)	Osmotic fragility curve for one rat from group 5 one week post 1 st injection	117
Figure (4-65)	Osmotic fragility curve for one rat from group 5 two weeks post 1 st injection	118
Figure (4-66)	Absorption spectra of Hb molecules for one rat from group1	121
Figure (4-67)	Absorption spectra of Hb molecules for one rat from group2	122
Figure (4-68)	Absorption spectra of Hb molecules for one rat from group3	123
Figure (4-69)	Absorption spectra of Hb molecules for one rat from group4	124
Figure (4-70)	Absorption spectra of Hb molecules for one rat from group5	125
Figure (4-71)	Blood film for one rat from group 1	127
Figure (4-72)	Blood film for one rat from group 2	128
Figure (4-73)	Blood film for one rat from group 3	129
Figure (4-74)	Blood film for one rat from group 4	130
Figure (4-75)	Blood film for one rat from group 5	131
Figure (5-1)	Differentiation of solubilization curve for one patient from group I	136
Figure (5-2)	Differentiation of solubilization curve for one patient from group II	137
Figure (5-3)	Differentiation of solubilization curve for one patient from group III	138
Figure (5-4)	Differentiation of solubilization curve for one patient from group IV	139
Figure (5-5)	Differentiation of solubilization curve for one sample from group V	140

Figure (5-6)	Differentiation of solubilization curve for one rat from group 1	141
Figure (5-7)	Differentiation of solubilization curve for one rat from group 2	142
Figure (5-8)	Differentiation of solubilization curve for one rat from group 3	143
Figure (5-9)	Differentiation of solubilization curve for one rat from group 4	144
Figure (5-10)	Differentiation of solubilization curve for one rat from group 5	145