بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

البقرة الآية ٣٢

Stem Cell Injection in Surgical Management of Ischemic Heart Patients with Non-Contractile or Ungraftable Cardiac Segments

Thesis

Submitted for Partial Fulfillment of a MD
in **Cardiothoracic Surgery**

Presented by

Motaz Sobhi Ahmad Rabie
Master Degree in General Surgery-
Ain Shams University

Under Supervision of

Prof. Dr. Mohammed Magdy Mostafa
Professor of Cardiothoracic Surgery
Faculty of Medicine - Ain Shams University

Prof. Dr. Alaa Ismail Abdel-Mottaleb
Professor of General Surgery
Faculty of Medicine - Ain Shams University

Prof. Dr. Mohammed Mohammed El-Fiky
Professor of Cardiothoracic Surgery
Faculty of Medicine - Ain Shams University

Dr. Ayman Mahmoud Ammar
Professor of Cardiothoracic Surgery
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2012

إستخدام الحقن الجراحي للخلايا الجذعية لعلاج مرضى قصور الشرايين التاجية

رسالة

توطئة للحصول على درجة الدكتوراة في جراحة القلب والصدر

مقدمة من

الطبيب/ معتز صبحي ربيع
ماجيستير الجراحة العامة ـ كلية الطب- جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ محمد مجدي مصطفى
أستاذ جراحة القلب و الصدر
كلية الطب- جامعة عين شمس

الأستاذ الدكتور/علاء اسماعيل عبد المطلب
أستاذ الجراحة العامة
كلية الطب- جامعة عين شمس

الأستاذ الدكتور/ محمد محمد الفقي
أستاذ جراحة القلب و الصدر
كلية الطب- جامعة عين شمس

الدكتور/ أيمن محمود عمار
مدرس جراحة القلب و الصدر
كلية الطب- جامعة عين شمس

كلية الطـــب
جامعة عين شمس
٢٠١٢

Acknowledgement

First of all, thanks to **Allah** who granted me the ability to accomplish this work.

I would like to express my deepest and utmost thanks to **Prof. Dr. Mohammed Magdy Mostafa,** Professor of Cardiothoracic Surgery for his sincere guidance, kind supervision and great help. I was honored to be his candidate and to be guided all through this work by his kind and valuable advices. You've always been like a father to all of us, thank you so much.

I wish also to express my great gratitude and utmost appreciation to **Prof. Dr. Alaa Ismail Abdel-Mottaleb,** Professor of General Surgery, for his valuable participation and instructions. The whole idea of this study started when I listened to one of his lectures & was impressed by the way he believes in his work. There is always a lot to be learnt from you, thank you so much.

I wish also to express my great appreciation to **Prof. Dr. Mohammed Mohammed El-Fiky,** Professor of Cardiothoracic Surgery, for his efforts. Since day one, your guidance & instructions have been the main factor for this study to end by the way it looks today, thank you so much.

Also, I would like to express my appreciation to **Prof. Dr. Ayman Mahmoud Ammar,** Assistant Professor of Cardiothoracic Surgery, for his sincere advice and his open-mind. Your support and help in solving any problem facing me during the progress of this work would never be fogetten, thank you so much.

I must also dedicate this work to the following professors for their valuable participation in this study. I will never forget your efforts that helped this study to become a reality.

Cardiothoracic Surgery department:

Prof. Dr. Ezz El-Dien Mostafa, for being so understanding & supportive.
Prof. Dr. Ahmad Hassouna, for being so generous in giving his effort & time to help in the statistics & results of this study.
Prof. Dr. Ahmad El-kerdany, for taking care of all of us. You are a kind of persons who *LOVES* to help others.
Prof. Dr. Tarek El-Sayegh, for his particiration in the study.
Prof. Dr. Walaa Saber, for his particiration in the study.
Prof. Dr. Mostafa Abdel-Azim, for his particiration in the study.
Prof. Dr. Saeed Refaat, for his particiration in the study.

Cardiology department:

Prof. Dr. Zeinab Abdel-Salam, for being supportive & flexible in performing Dobutamine stress echocardiography for the whole 31 patients included in this study.

Radiology department:

Prof. Dr. Waheed Tantawy, a great professor & a great person as well who finds happiness in helping others, it was my pleasure to deal with him *before* & throughout the study.
Prof. Dr. Ahmad Samir, for being so skillful, helpful & devoted, you never hesitate to do all the best for patients.
I was honored that our cases included in this study were some of the first cases in all Egypt that had cardiac MRI done. Thank you both for giving me this chance.

Finally, I would like to thank **Mr. Ali Abdel-Bar** for his help, not only as the provider of *Harvest Technologies Kits* & the centrifugal system but also as a partner and above all as a friend.

I was lucky enough to work with such a great team….

Thank You All

Dedication

In the beginning, I dedicate this work to my parents, the reason of any good thing that happened or would ever happen to me. Any achievement I had is mostly because of your help and endless prayers to me, thank you so much.

Second, I wish to thank my wife **Dr. Hala** *for her generous help, support, effort, time, advice and wishes. Without you non of this would ever be done, thanks God for giving me the pleasure of having you in my life.*

I also dedicate this work to my beautiful children **Marwan, Yassin and Logine** *they are the real motive for every step I take. The world is really nice with you in it.*

I must also dedicate this to my brothers who are always arround me whenever I need them.It always makes me feel safe & secured.

In fact, I am glad and proud to have this great family beside me. Without you, my life would be much more difficult.

God bless you all

List of Contents

List of abbreviations

ABMMNCs	Autologus Bone Marrow Mononuclear Cells
AECs	Amniotic epithelial cells
AMI	Acute Myocardial Infarction
BLI	bio-luminescence imaging
BM	Bone Marrow
BMCs	Bone marrow derived cells
CABG	Coronary Artery Bypass Grafting
CAC	Canadian angina classification
CAD	Coronary Artery Disease
CCU	Coronary Care Unit
CD	Cluster of Differentiation
CMRI	Cardiovascular magnetic resonance imaging
CSCs	Resident cardiac stem cells
CT	Cardiac computed tomography
DE	Delayed Enhancement
DNMT3B	DNA (cytosine-5-)-methyltransferase 3 beta
DSE	Dobutamine stress echocardiography
EAPCs	Endogenous adult stem/progenitor cells

EBAF	Endometrial bleeding associated factor
EBs	Embryoid bodies
EDD	End Diastolic Diameter
EF	Ejection Fraction
EPC	Endothelial progenitor cells
ESCs	Embryonic stem cells
ESD	End Systolic Diameter
EuroSCORE	European System for Cardiac Operative Risk Evaluation
FACS	Fluorescence activated cell sorting
FDG	Fluorodeoxyglucose
FGF2	Fibroblast growth factor 2 protein
FSCs	Fetal Stem Cells
G-CSF	Granulocyte-colony-stimulating factor
HDF	Human dermal fibroblasts
hES	Human embryonic cells
HLA	Human leucocyte antigen
HSCs	Heamopoietic stem cells
IC	Ischemic Cardiomyopathy
ICMs	Inner cell masses
IGF-1	Insulin-like growth factor-1

IHD	Ischemic Heart disease
iPS	Induced pluripotent stem
LAD	Left Anterior Descending Artery
LCX	Left Circumflex
LIMA	Left Internal Mammary Artery
LV	Left ventricle
MEF	Mouse embryonic fibroblasts
MHC	Major histocompatability complex
MR	Mitral regurge
MSC	Mesenchymal stem cells
MVD	Multivessel disease
NYHA class	New York Heart Association Classification
Oct-4	Octamer-binding transcription factor 4
PBSCs	Peripheral blood stem cells
PCI	Percutaneous coronary intervention
PDA	Posterior Descending Artery
PET scan	Positron emission tomography
RCT	Randomized Controlled Trial
SCID	Severe Combined Immunodeficiency
SCNT	Somatic cell nuclear transfer
SCs	Stem Cells

SDF-1α	Stromal cell-derived factor-1 alpha
SOX2	(sex determining region Y)-box 2
SPECT	Single photon emission computed tomography
SSEA	Stage-specific embryonic antigen
STS	Society of Thoracic Surgeons mortality risk score
SVG	Saphenous Venous Graft
SYNTAX	SYNergy between PCI with TAXUS™ and Cardiac Surgery
TGFβ	Transforming growth factor beta
TMLR	Transmyocardial laser revascularization
TRA	Tumor-rejection antigen
TTE	Transthoracic Echocardiography
UCB	Umbilical cord blood
UCCs	Umbilical cord cells
UCE	Umbilical cord epithelium

List of Figures

List of Tables