THE ROLE OF PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN TREATMENT OF HEMATOLOGICAL MALIGNANCY

Essay Submitted for the Partial Fulfillment of the Master Degree in Radiotherapy and Nuclear Medicine

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بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا،
إنك أنت العليم الحكيم

صدق الله العظيم

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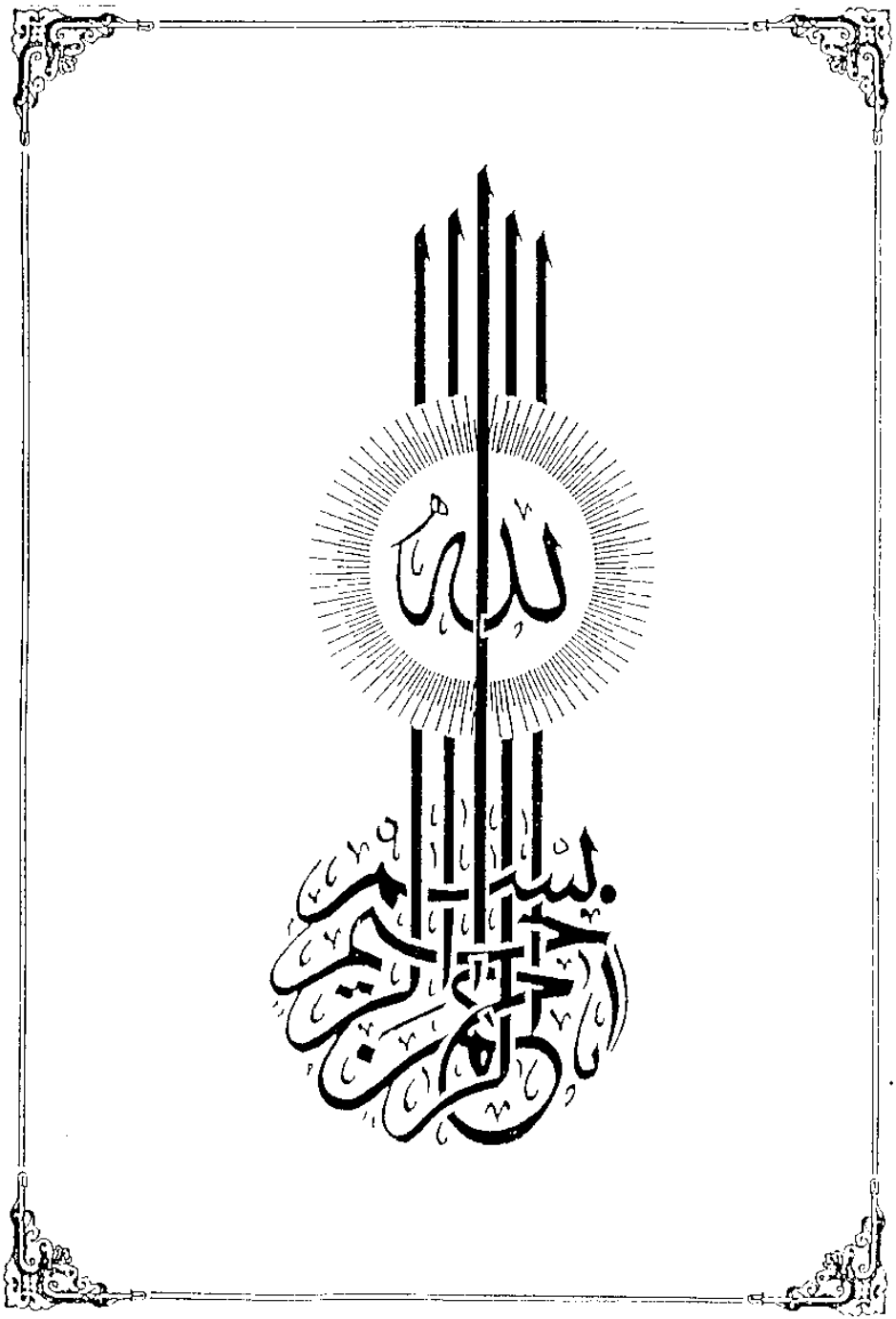

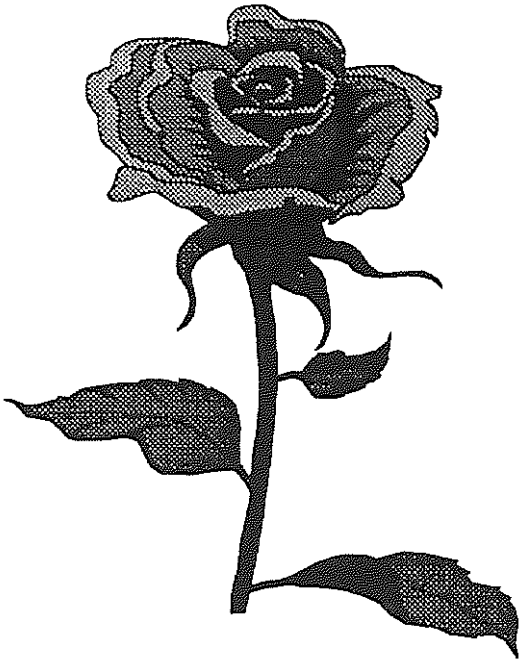

To My Family

Acknowledgment

First of all thanks to God for helping me to complete this work.

I wish to express my deep gratitude and thanks to Prof. Dr. Soheir Helmy, Professor of Radiation Oncology and Nuclear Medicine Department, Ain Shams University, for her encouragement as well her support throughout the whole work.

I am deeply grateful to Dr. Mohamed Essam Saleh, Lecturer, of Radiation Oncology and Nuclear Medicine, Ain Shams University, for his faithful assistance and kind cooperation during this work.

I was fortunate enough to carry out this work under the guidance of Dr. Anwaar Rady, Colleague of Radiation Oncology and Nuclear Medicine Department, Ain Shams University for her help.

Lastly, I would like to thank all senior staff and my colleagues of Radiation Oncology and Nuclear Medicine Department, Ain Shams University for their sincere help and cooperation during the accomplishment of this work.

Gehan Ibrahim El-Sharrany

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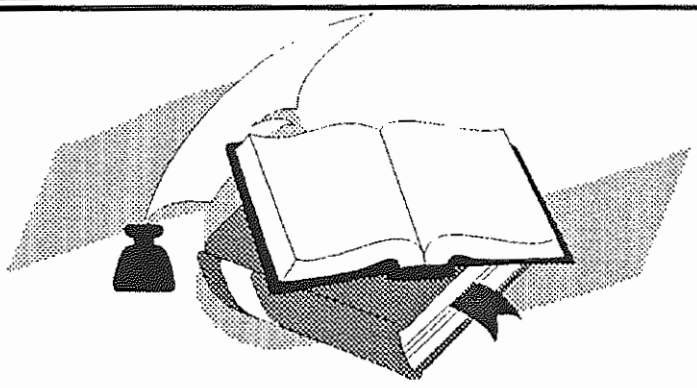
List of Abbreviations

ABMT	Autologous bone marrow transplantation
ABSCT	Autologous blood stem cell transplantation
ACD-A	Acid citrate dextrose formula-A
ALL	Acute lymphoblastic leukemia
AML	Acute myeloblastic leukemia
ANLL	Acute non-lymphoblastic leukemia
AP	Accelerated phase
ara-c	Cytosine arabinose
ASCO	American Society of Clinical Oncology
BC	Blastic crisis
BCGF-II	B-cell growth factor-II
BCNU	Bischlorethyl nitrosourea
BFU-E	Burst forming unit-erythroid
BFU-Meg	Burst forming unit-megakaryocyte
BM	Bone marrow
BM MNC	Bone marrow mononuclear cells
BSC	Blood stem cell
BSF-1	B cell stimulating factor-1
Bu	Buslphan
CE	Etoposide
CEP	Cisplatin
CFU	Colony forming unit
CFU-Bas	Colony forming unit-basophil
CFU-blasts	Colony forming unit-blast
CFU-E	Colony forming unit-erythroid
CFU-Eo	Colony forming unit-eosinophil
CFU-G	Colony forming unit-granulocyte
CFU-GM	Colony forming unit-granulocyte macrophage
CFU-M	Colony forming unit-macrophage
CFU-Meg	colony forming unit-megakaryocyte
CFU-S	Colony forming unit-spleen
CML	Chronic myeloid leukaemia
CMV	Cytomegalovirus
CR	Complete remission
CSF	Colony stimulating factor
CY	Cyclophosphamide
d	Delton

Dexa-BEAM	Dexamethasone, BCNU, etoposide, cytarabine, melphalan
DFS	Disease-free survival
DMSO	Dimethyl sulfoxide
EDF	Eosinophil differentiation factor
EPO	Erythropoietin
FDC	Follicular dendritic cell
GM-CSF	Granulocyte macrophage-colony stimulating factor
GVHD	Graft versus host disease
HDM	High dose melphalan
HGFs	Haematopoietic growth factors
HM	Hematopoietic microenvironment
HPP-CFC	High proliferative potential-colony forming cell
HSC	Haematopoietic stem cell
ICDs	Interdigitating cells
IL	Interleukin
IP-10	Interferon-inducible protein-10
KD	Kilodelton
LIF	Leukemia inhibitory factor
LTC-IC	Long term culture-initiating cell
M-CSf	Monocyte-colony stimulating factor
MALT	Mucosa-associated lymphatic tissue
MDS	Myelodysplastic syndrome
Mel	Melphalan
MHC	Major histocompatibility complex
MIP-1α	Macrophage-inflammatory protein-1 alpha
MIP-1ß	Macrophage-inflammatory protein-1 beta
MMC	Marrow mononuclear cells
MNC	Mononucleated cell
MZ	Marginal zone
NAP-2	Neutrophil activating peptide-2
NHL	Non-Hodgkin's lymphoma
NK	Natural killer
P	Probability factor
PBPC	Peripheral blood progenitor cell
PBSC	Peripheral blood stem cell
PC	Plasma cells
PCR	Polymerase chain reaction
PDGF	Platelet derived growth factor
PF4	Platelet factor-4
ph	Philadelphia chromosome
ph+	Philadelphia chromosome positive

PSCs	Peripheral stem cells
PSR	Progenitor stimulating rate
rHGM-CSF	Recombinant human granulocyte-macrophage colony stimulating factor
rHuG-CSF	Recombinant human granulocyte-colony stimulating factor
RLP	Recirculating lymphocyte pool
RP	Red pulp
TBI	Total body irradiation
TNF-α, ß	Tumor necrosis factor- α, ß
TPO	Thrombopoietin
TRF	T-cell replacing factor
TT	Thiotepa
VOD	Veno-occlusive disease
WBC	White blood cell
WP	White pulp



Introduction and Aim of the Work

INTRODUCTION

For the last decade, peripheral blood stem cell transplantation has been increasingly used for treatment of haematological malignancy ***(Körbling et al., 1995a).***

The biology of bone marrow transplantation (BMT) is determined by the different cell types transplantation from the donor, mature T-lymphocytes, lymphoid stem cells and haemopoietic stem cells, the biology of different cell types defines the clinical and biological events that occurs following transplantation ***(Parkman, 1993).***

The use of haematopoietic growth factors in particular, colony stimulating factor, granulocytes (CSF-G) and colony stimulating factor granulocyte-macrophages (CSF-GM) to accelerate haematopoietic recovery following peripheral blood stem cell transplantation (PBSCT) is becoming more prevalent ***(Devereux et al., 1989).***

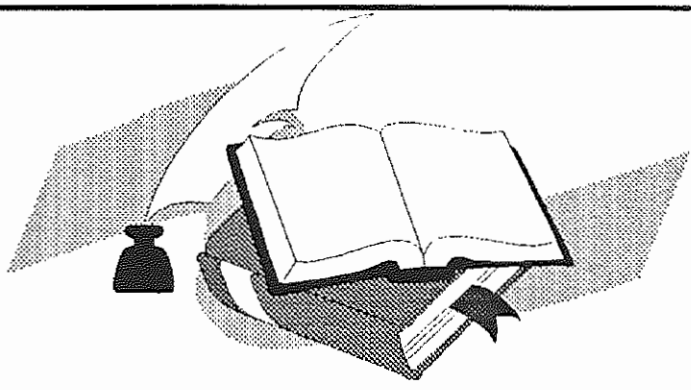
Filgrastim (G-CSF) stimulated allogenic peripheral blood stem cells (PBSC) may be a suitable alternative to allogenic marrow for transplantation for refractory leukaemia and lymphoma with advantage of more rapid platelet recovery ***(Korbling et al., 1995b).***

There are also several major clinical indications for autologous blood stem cell transplant: acute non-lymphoblastic leukaemias, low-grade non-Hodgkin's lymphomas, multiple myeloma, chronic myeloid leukaemia and even some solid tumors ***(Hénon, 1993).***

A retrospective comparison with bone marrow transplantation (BMT) in advanced haematological malignancies suggests that compared to marrow transplantation from HLA-identical donors allogenic blood stem cell transplantation (PBSCT) from HLA identical donors is associated with faster engraftment, fewer transfusions and no greater incidence of acute or chronic graft versus host disease (GVHD) ***(Bensinger et al., 1996b).***

AIM OF THE WORK:

Revision of the role of peripheral blood stem cell transplantation (PBSCT) in treatment of haematological malignancies.



Histology of Haematopoietic Tissues