

ROLE OF BRACHYTHERAPY IN THE TREATMENT OF HEAD AND NECK MALIGNANCIES

ESSAY

Submitted for the fulfillment of the master degree in Clinical Oncology

Presented by

Karim Nabil Mashhour

M.B.B.Ch. Cairo University

Under the supervision of

Prof. Dr. Ehsan Gamal El-Din El-Ghoneimy

Professor of Clinical Oncology

Director of NEMROCK

Faculty of medicine

Cairo University

Prof. Dr. Magda Moustafa Kamal

Professor of Clinical Oncology

Faculty of medicine

Cairo University

Prof. Dr. Hesham Atef Zaki

Professor of Clinical Oncology

Faculty of medicine

Cairo University

Faculty of medicine

Cairo University

2009

Abstract

Both primary and recurrent squamous cell carcinoma of head and neck cancers are classic indications for brachytherapy. A high rate of local tumor control at the cost of limited morbidity can be achieved with brachytherapy through good patient selection, meticulous source implantation and careful treatment planning.

With the aid of new technologies such as three dimensional imaging (3D) and image guided brachytherapy it is now easier, safer and much more accurate improving the conformality of treatment.

Keywords:

Head and neck cancers, brachytherapy, three dimensional imaging (3D)

Contents

pg

Acknowledgement.....	3
List of Figures and Tables	4
List of Abbreviations.....	8
Introduction.....	10
Aim of Work.....	13
Review of literature	14
I- Overview of Head and Neck malignancies.....	15
II- Principles of Brachytherapy.....	51
III- Role of Brachytherapy in the treatment of Head and Neck Malignancies...	98
IV- Imaging, Optimization and future prospectives in Brachytherapy.....	143
Summary and Recommendations	179
References.....	182
Arabic Summary	210

ACKNOWLEDGEMENTS

First and foremost, my deepest praises are due to Almighty “**ALLAH** “ who enabled me to finish this piece of work appropriately.

I would like to express my deep thanks and gratitude to **Prof. Dr. Ehsan Gamal El-Din El-Ghoneimy** for her continuous meticulous supervision apart from her motherly spiritual support that paved the way to the achievement of this work.

My sincere appreciation to **Prof. Dr. Magda Moustafa Kamal** for her unlimited scientific help, remarkable advices removing any obstacle and continuous encouragement throughout my work.

I also feel deeply indebted to **Prof.Dr. Hesham Atef Zaki** for his precious valuable advices and close supervision. I shall always be proud to have worked under his guidance.

Finally, I would like to express my infinite gratitude and my deepest appreciation to all staff members and to my colleagues at Clinical Oncology department for their support.

Karim Mashhour

List of Figures and Tables

Number	Title	Page
Fig 1	Global incidence of head and neck cancer.	16
Fig 2	Relative risk for oropharyngeal cancer for males according to amount of tobacco and alcohol use.	19
Fig 3	Anatomic sites and subsites of the head and neck.	24
Fig 4	Midsagittal section of head shows nasopharynx and related structures.	25
Fig 5	Oral cavity and Oropharynx.	26
Fig 6	Anatomy of the Larynx.	27
Fig 7	The salivary glands.	29
Fig 8	Levels of the neck as determined by lymphatic drainage patterns.	31
Fig 9	Invasive squamous cell carcinoma.	33
Table 1	TNM staging system for carcinomas of the pharynx.	35
Table 2	Histopathological negative prognostic factors in HNSCC.	38
Fig 10	Image quality hampering by artifacts arising from dental fillings in computed tomography.	44
Fig 11	PET/CT helps regional staging by detecting cervical metastasis.	46
Fig 12	One of the first remote afterloading machines.	53
Fig 13	The three different treatment schedules in Brachytherapy.	58
Table 3	Physical characteristics of radionuclides used in Brachytherapy.	59

Fig 14	Different types of sources used in Brachytherapy.	60
Fig 15	Iodine -125 seed.	64
Table 4	Reference air kerma rate for some sources.	66
Fig 16	Systems of implant dosimetry.	71
Fig 17	Plastic tubes in an oral cavity carcinoma.	73
Fig 18	Guide gutters in a lateral border of a mobile tongue carcinoma.	73
Fig 19	Modern Afterloading Machines used for PDR/HDR.	76
Table 5	Dose limits required for radiation protection in brachytherapy.	77
Fig 20	Relative Therapeutic Ratio as a function of dose rate.	82
Fig 21	Effect of fractionation (a) on tumor (b) on late-responding normal tissue.	83
Fig 22	Effect of changing dose rate (a) on tumor (b) on normal tissue.	84
Fig 23	Survival curves in early-responding tissues and in late responding normal tissues according to the linear-quadratic model.	88
Fig 24	The effects of repair of sublethal damage, progression in cell cycle, and repopulation on survival rate, according to dose rate.	90
Fig 25	A custom-designed dental shield lined with lead.	100

Fig 26	Basic design of gutter guide and technique for insertion of the iridium wire.	104
Fig 27	Typical hypodermic needle implant of the lip.	106
Fig 28	A remote high dose rate afterloader system.	110
Fig 29	A transpalatal flap approach for nasopharyngeal brachytherapy.	114
Fig 30	A plain film x-ray of an ^{125}I seed implant of a nasopharyngeal tumor.	116
Fig 31	A patient with a small squamous cell carcinoma of the lower lip approaching to commissure with a single plane low dose rate implant using angiocatheters loaded with ^{192}Ir.	119
Fig 32	A patient with squamous cell carcinoma of the oral tongue. Using a plastic tube looping technique, the entire tumor volume is implanted.	121
Fig 33	A patient with squamous cell carcinoma of the floor of mouth.	125
Fig 34	Base of tongue low-dose rate implant.	132
Fig 35	Intraoperative high dose rate brachytherapy.	141
Fig 36	Treatment planning system showing axial computed tomography scan isodose distribution about lip with a highly conformal dose.	143
Fig 37	Localization films taken with dummy sources for dosimetric planning.	145
Fig 38	Treatment planning for a brachytherapy boost in tongue cancer based on clinical examination and MRI.	147
Fig 39	The computed tomography (CT) scanner fixed in the middle of a dedicated brachytherapy suite.	148
Fig 40	Clinical implant in the head with five plastic flexible catheters.	150

Fig 41	Digitally reconstructed radiograph of lateral projection.	151
Fig 42	3D view of the result of autoactivation showing the active source dwell positions and the PTV surface.	152
Fig 43	Isodose lines generated relative to the target volume and surrounding anatomy.	153
Fig 44	Dose distributions generated in three dimensional view.	154
Fig 45	ICRU recommendations on interstitial Brachytherapy dosimetry.	156
Fig 46	The reference dose.	163
Fig 47	The geometric relationships among the dwell positions.	166
Fig 48	The differential DVH.	168
Fig 49	The cumulative DVH.	168
Fig 50	Source specific cumulative dose-volume histogram for a continuous line source.	170

List of Abbreviations

3D : Three dimensional

AAPM : American Association of Physicists in Medicine

AJCC : American Joint Committee on Cancer

BT : Brachytherapy

CI : Conformity Index

CN : Cranial nerves

CT : Computed Tomography

CRT : Conformal radiation therapy

CTV : Clinical Target Volume

DRR : Digitally reconstructed radiograph

DVH : Dose Volume Histogram

EBRT : External beam radiation therapy

FDG : Fluorodeoxyglucose

FNA : Fine needle aspiration

FOM : Floor of mouth

GEC-ESTRO : Groupe Europeen de Curietherapie- European Society of
Therapeutic Radiation Oncology

GTV : Gross Target Volume

HDR : High dose-rate

HNSCC : Head and Neck Squamous cell carcinoma

ICRP : International Commission on Radiological Protection

ICRU : International Commission on Radiation Units and Measurements

IGRT : Image guided radiation therapy

IMBT : Intensity modulated Brachytherapy

IMRT : Intensity modulated radiation therapy

IOHDBT : Intra-operative high dose Brachytherapy

IORT : Intra-operative radiation therapy

IRR : Ionising Radiations Regulations

LAHNC : Locally advanced Head and Neck Cancer

LDR : Low dose-rate

LQ model : Linear quadratic model

MCD: Mean Central dose

MDR : Medium dose-rate

MRI : Magnetic Resonance Imaging

MRS : Magnetic Resonance Spectroscopy

OER : Oxygen enhancement ratio

PET : Positron Emission Tomography

PDR : Pulsed dose-rate

PTV : Planning Target Volume

RAKR : Reference air kerma rate

SCC : Squamous cell carcinoma

SPECT : Single Positron Emission Computed Tomography

TRAK : Total reference air kerma

Introduction

The overall incidence of head and neck cancer varies between countries ranging from 8 to 22% in males and from 1 to 8% in females. During the last several decades, head and neck cancer rates have been increasing, particularly between 1950 and 1970, with a slight decrease thereafter. (**Wartell et al. 1990**)

During the last fifty years, incidence of head and neck cancers worldwide was the first regarding males population and the sixth regarding the females, the mortality resulting from these cancers appears stable ; representing 9% of cancer mortality in men and 2% in women. (**Boyle et al. 1995**)

Radiotherapy is a main line of treatment that contributes to the cure or palliation of Head and Neck malignancies. Most patients present with a locally advanced disease; in this situation, radiotherapy has an important role in local control, improving survival and in relief of local symptoms. (**Dobbs et al 1999**)

Many tools are available for the treatment of Head and neck Malignancies including (Surgery, radiation therapy and concomitant chemo-radio modality) depending on the initial presentation of the disease. Radiation therapy forms are external beam radiation therapy and brachytherapy. (**Gerbaulet et al. 1999**)

Brachytherapy will continue to play an important role in the multidisciplinary approach in the treatment of head and neck cancers. (**Dutreix et al.1998**)

Brachytherapy is the delivery of radiation therapy using sealed isotopic sources which are placed as close as possible to the site to be treated. The principal advantages of brachytherapy lie in the physics of the dose distribution around a radiation source, which results in a high concentration of dose immediately around the source and a rapid fall-off of dose away from the source with distance according to the inverse square law. By implementing adequate immobilization of the area to be treated; thus eliminating the need of adding margins in radiotherapy planning to account for target mobility, it could be an ideal form of conformal treatment. (**Joslin et al 2001**)

Head & Neck Brachytherapy has a place in several key clinical situations as in:

- (A) As a primary treatment of small T1 and T2 squamous cell cancers,
- (B) In combination with external beam radiotherapy boosting the primary site,
- (C) Re-irradiation in previously treated areas either for recurrence or second primaries in the same area or site. (**Sedky et al. 2001 and Spiro et al. 2002**)

With the aid of new technologies such as three dimensional imaging (3D) and image guided application; brachytherapy became now more easier, safer and much more accurate. All of these approaches require delineation of the target volume and critical structure surfaces from 3D imaging studies, allowing the integration of 3D imaging data and 3D dose distributions and hence improving the conformality of treatment. (**Martel et al. 2006**)

Brachytherapy in its various forms remains an excellent tool for achieving control and cure for locally confined head and neck cancers. The high degree of conformality cannot be equaled even by modern day external beam radiotherapy (EBRT) techniques like intensity modulated radiation therapy (IMRT) and image guided radiation therapy (IGRT). Proper patient selection, experience and skill are of utmost importance in ensuring the best outcome. **(Shrivastava et al. 2006)**

Aim of work

The aim of the work is to overview the applications of brachytherapy as an established technique in treating head & neck cancers and the recent advances in technology that improved radiation planning and delivery of such a technique; throwing light upon modern brachytherapy which is highly selective and adaptive as a competitive tool in the multidisciplinary treatment of head & neck malignancies.

Review Of Literature