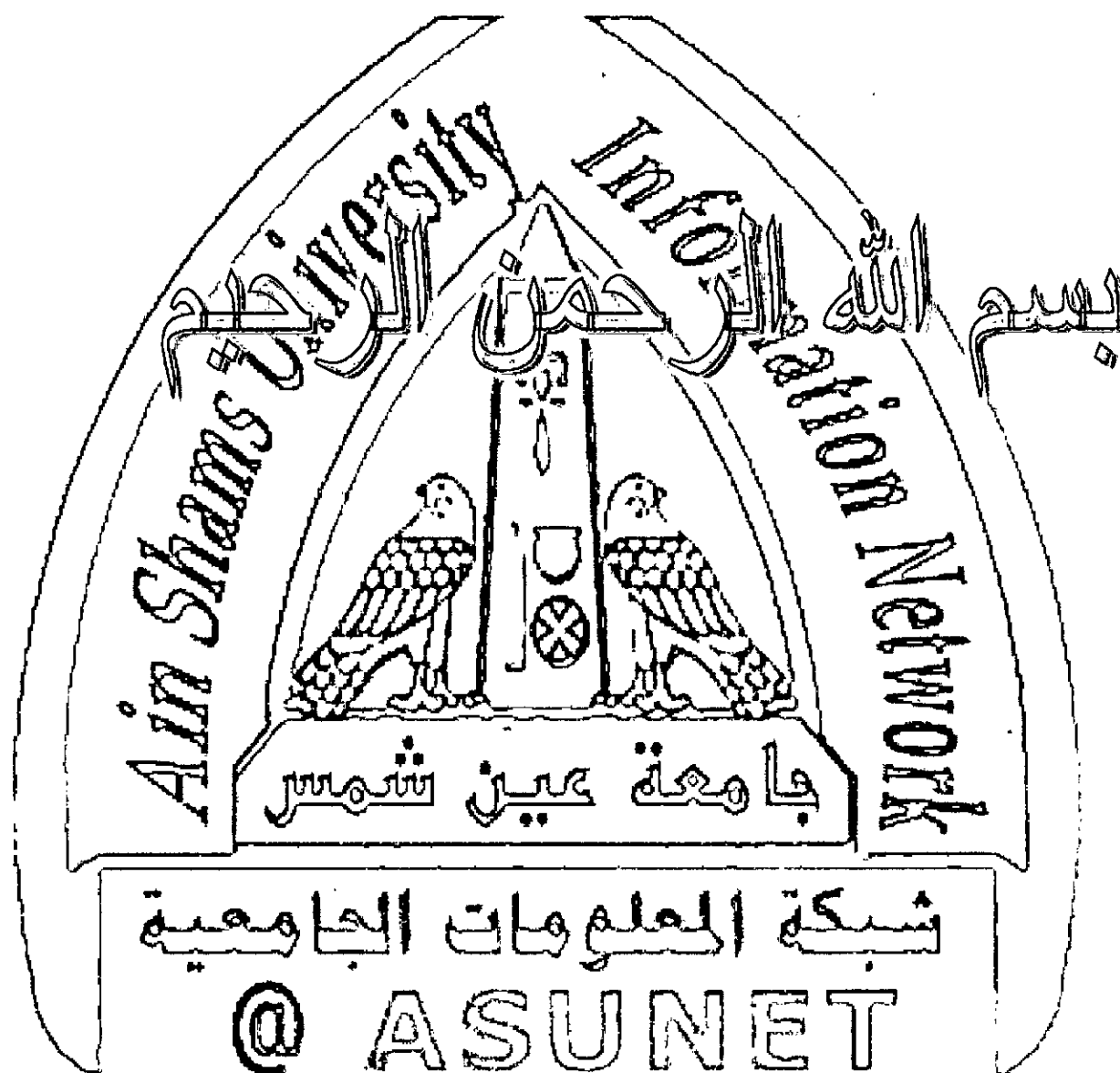




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6

BLADDER PRESERVING APPROACH BY CHEMO- RADIOTHERAPY IN PATIENTS WITH MUSCLE INVADING TRANSITIONAL CELL CARCINOMA

*Thesis submitted for partial fulfillment
of M.D. degree in radiation oncology*

By

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2004

684211

To...

My Patients,

Who taught me by their courage and suffering.

My Teachers,

Who inspired me with their knowledge and insight.

My Family,

Who unselfishly endured my endeavors.

M. abdel hameed abo giada

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ABRIVATION

- AI: Apoptosis index.
- BC: Bladder cancer.
- BCG: Bacilles bilie de Calmette- Guerin.
- cCR: Clinical complete response .
- CCRT: Concomitant chemo-radiotherapy.
- CIS: Carcinoma in situ
- DFS: Disease free survival
- DRE: Digital rectal examination.
- GTV: Gross target volume.
- HPV: Human papilloma virus.
- ICRU: International commission on radiation units and measurements.
- MCV: Methotrexate, Cisplatin, vinblastine
- MGH: Massachusetts General Hospital.
- MIBC: Muscle-invasive bladder cancer.
- M-VAC: Methotrexate, vinblastine, Adriamycin, Cisplatin.
- OS: Overall survival.
- PS: Performance status.
- PR: Partial response.
- PCR: Pathological complete response.
- PORT: Post operative radiotherapy.
- pRb: Retinoblastoma protein.
- PTV: Planning target volume.
- RCT: Radio-chemotherapy.
- RFS: Recurrence free survival.
- RTOG: Radiation Therapy Oncology Group.
- SD: Stationary disease.
- UICC: International union against cancer.
- XRT: External beam irradiation.

*Introduction
And Aim
Of The Works*

INTRODUCTION

Bladder Cancer constitutes 4% of all cancer in United State, and represents 30.3% of all cancer cases treated at Egyptian National Cancer Institute (Nazli et al., 2001). South Egypt cancer institute reported a relative frequency of 18.5% from year 2000-2002 (Alia, 2003).

The relative frequency of histological subtypes of bladder carcinoma depends on the clinical setting. About 90% -95% of bladder carcinoma reported from the west are transitional cell type (Shipley et al., 2002). In large series reported from Egypt, squamous cell carcinoma accounted for 59% - 73% of bilharzial bladder cases (Awwad et al., 1992, Ghoneim et al., 1997 and El-Bolkainy et al., 1998).

The prognosis and treatment outcome depend on the depth of bladder-wall invasion. Superficial disease has an excellent prognosis, whereas the survival rate decreases significantly for deeply invasive tumors (Shipley et al., 1997).

Muscle-invasive bladder cancer (MIBC) is a disease associated with a relatively low cure rate. The optimal management of MIBC has been a continuous subject of controversy. Radical cystectomy represents the most frequent treatment approach. Despite great advances in surgical techniques and better perioperative support, even a neovesica cannot substitute for the patient's original bladder without entailing a high risk of infection and consequential renal failure, metabolic disorders, and sexual dysfunction. The other drawback of this treatment approach lies in the fact that over half of the patients will die with distant metastases (Raghavan et al., 1995). Local recurrence represented

50%-60% of the causes of failure after radical cystectomy (Zaghloul et al., 2003).

In view of these problems, several clinical studies were conducted using a bladder-sparing approach to the treatment of this disease. In the past decade, the most promising advance has been achieved using transurethral surgery (TUR) and combined chemo-radiotherapy regimens. This treatment approach uses the advantages of the favorable effects of cisplatin-based chemotherapy as well as the synergistic effects of chemotherapy and radiotherapy (Joica Ervek et al., 1998).

In selected patients, bladder preserving treatment with TUR, radiation therapy and concurrent chemotherapy offers a probability of long term cure and overall survival at 5-years is comparable to cystectomy-based approaches (49% to 63% at 5 years) in patients of similar clinical stage and age. Five-year survival with bladder preservation is 38% to 45%. In addition, these selective bladder-preserving approaches result in approximately 80% of the long-term survivors maintaining a normal functioning bladder (Michaelson and Zietman, 2003).

Evolving data show that the categorical recommendation of surgically removing the bladder in all cases with invasive disease is outdated. It is nevertheless important to stress that the primary goal of treatment is survival, and sparing the bladder is justified only when it has a high likelihood of eradicating the tumor in the bladder, the risk of recurrence is low, and bladder function is not compromised. Many groups have reported favorable cure rates with bladder-preserving methods in selected patients with tumors who met certain criteria. Cystectomy reserved for those who do not meet these criteria (Harry et al., 2001).