City St George's, University of London
Northampton Square
London
EC1V 0HB
United Kingdom

T +44 (0)20 7040 5060

Optimisation of organ preservation techniques for muscle invasive bladder cancer

Thesis presented in accordance with the requirements for the degree of Doctor of Philosophy

By

Liam Mannion

Student number: 1301157

B. Abstract

Introduction

Bladder cancers mostly originate within the inner lining of the bladder (urothelium). In advanced cases, the cancerous cells will invade into the smooth muscular layer of the bladder wall. Treating muscle invasive bladder cancer (MIBC) can and often does involve a multimodality approach. Combining chemotherapy, surgery, and radiotherapy. The optimal way to treat MIBC is highly debated and a key difference between treatment regimens is whether the patient retains their bladder or not. This thesis was undertaken to assess the role of organ-sparing trimodality treatments that included a brachytherapy boost (TMT-BT) for MIBC. With an aim to explore how current organ sparing techniques could be optimised.

Methods

A systematic review was first undertaken to evaluate the clinical effectiveness of BT for solitary urinary bladder tumours in terms of overall survival, local recurrence rates, and adverse events. Following this, a retrospective cohort study of patients who received radical treatment for MIBC: radical cystectomy and lymph node dissection (RC-LND), or radical radiotherapy +/- chemotherapy (C-RT) to determine what proportion of patients would have been suitable for TMT-BT if it were available. As a secondary objective we also assessed the accuracy of clinical tumour diameter measurements, which is a key selection criterion for choosing patients. Building upon this information we next focused on what was important to patients who have, are yet to, or are in post-

radical follow up after undergoing, treatment for MIBC. The final project was a feasibility study, in which we assessed the planning feasibility of using HDR-brachytherapy to treat muscle invasive bladder cancer.

Results

Our systematic review demonstrated that patients who underwent TMT-BT had an overall survival % at 5 years of 60%. Disease-specific survival of 75% at 5 years and local control ranged from 0% to 32%. In our retrospective study (over the ten-year period) 703 patients received radical treatment: 562 RC-LND, 141 C-RT. From these, 96 would have been suitable for TMT-HDR: 54 RC-LND, 42 C-RT. Diagnostic imaging and TURBT estimates of tumour diameter were all found to fall within 0.5cm of the RC-LND histology measurements hence diagnostic imaging and TURBT diameter measurements are clinically appropriate for guiding patient selection.

When we assessed patient preferences, our results showed that when deciding on the type of treatment, increased life expectancy is the most important consideration for people with MIBC. Our study also highlighted that patients are willing to accept long-term complications after treatments to improve other treatment outcomes. Understanding patient preferences is important for shared decision-making, which has an impact on quality of care for people living with MIBC. In terms of dosimetric feasibility, we were able to produce plans for 13/15 CTV volumes with a median EQD2 (Gy) CTV D90% of 24.36 Gy (11.7-41.7). The median EQD2 (Gy) delivered to the small bowel was 32.4 (25.9-48.3) and to the rectum 24.9 (22.7-31.6).

Conclusions

The overall aim of this research was to provide evidence on ways to optimise organ preservation techniques for MIBC. Organ sparing techniques such as TMT were the focus, with the new research exploring optimisation of these techniques with a brachytherapy boost. The work within this thesis has demonstrated that brachytherapy as part of TMT is an effective treatment in experienced centres for a select patient population who wish to preserve their bladder. In such patients, TMT-BT is well tolerated with an acceptable safety profile. Approximately 10 patients per year who would have undergone a RC or TMT could have been offered TMT-BT. With further work into the streamlining the selection process this number could be increased. Estimating tumour size is something that is essential to selecting the right patients, we demonstrated that measurements taken at TURBT are accurate to use. MIBC patients have a strong preference for treatments that increase their life expectancy. Treatments that result in less changes to body image are also something that influences choice hence organ preserving TMT-BT is something that requires further development and implementation. HDR-BT planning is feasible for solitary tumours (less than or equal to max diameter 5cm) located in the anterior dome of the bladder. Achieving suitable catheter placement and subsequent treatment is difficult for tumours in the lateral walls and should be considered on an individual case basis.