Medical Dosimetry 41 (2016) 70–74

Medical Dosimetry

journal homepage: www.meddos.org

Using individual patient anatomy to predict protocol compliance for prostate intensity-modulated radiotherapy

Hannah Caine, B.Med.Rad.Sc. (RT),* Deborah Whalley, M.B.Ch.B., F.R.A.N.Z.C.R.,* Andrew Kneebone, M.B.B.S., F.R.A.N.Z.C.R.,*† Philip McCloud, Ph.D.,‡ and Thomas Eade, M.B.Ch.B., F.R.A.N.Z.C.R.*†

*Radiation Oncology, Royal North Shore Hospital, Northern Sydney Cancer Centre, New South Wales, Australia; †Northern Clinical School, University of Sydney, Camperdown, New South Wales, Australia; and ‡McCloud Consulting Group, New South Wales, Australia

ARTICLE INFO

Article history:
Received 12 February 2015
Received in revised form
12 May 2015
Accepted 11 August 2015

Keywords:
Prostate cancer
IMRT
Plan quality
Knowledge based
Radiotherapy planning
Multivariate analysis

ABSTRACT

If a prostate intensity-modulated radiation therapy (IMRT) or volumetric-modulated arc therapy (VMAT) plan has protocol violations, it is often a challenge knowing whether this is due to unfavorable anatomy or suboptimal planning. This study aimed to create a model to predict protocol violations based on patient anatomical variables and their potential relationship to target and organ at risk (OAR) end points in the setting of definitive, dose-escalated IMRT/VMAT prostate planning. Radiotherapy plans from 200 consecutive patients treated with definitive radiation for prostate cancer using IMRT or VMAT were analyzed. The first 100 patient plans (hypothesis-generating cohort) were examined to identify anatomical variables that predict for dosimetric outcome, in particular OAR end points. Variables that scored significance were further assessed for their ability to predict protocol violations using a Classification and Regression Tree (CART) analysis. These results were then validated in a second group of 100 patients (validation cohort). In the initial analysis of the hypothesis-generating cohort, percentage of rectum overlap in the planning target volume (PTV) (%OR) and percentage of bladder overlap in the PTV (%OB) were highlighted as significant predictors of rectal and bladder dosimetry. Lymph node treatment was also significant for bladder outcomes. For the validation cohort, CART analysis showed that %OR of $< 6\%$, 6% to 9% and $> 9\%$ predicted a 13%, 63%, and 100% rate of rectal protocol violations respectively. For the bladder, %OB of $< 9\%$ *vs* $> 9\%$ is associated with 13% *vs* 88% rate of bladder constraint violations when lymph nodes were not treated. If nodal irradiation was delivered, plans with a %OB of $< 9\%$ had a 59% risk of violations. Percentage of rectum and bladder within the PTV can be used to identify individual plan potential to achieve dose-volume histogram (DVH) constraints. A model based on these factors could be used to reduce planning time, improve work flow, and strengthen plan quality and consistency.

© 2016 American Association of Medical Dosimetrists.

Introduction

Intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) for prostate cancer allow the creation of highly complex plans to achieve dose escalation while maintaining low doses to organs at risk (OAR).[1,2] However, inverse planning continues to have large variation for both plan quality and the time needed to plan each patient across centers and individual dosimetrists.[3,4] Due to the complex nature of IMRT and VMAT, it can be difficult to accurately assess the potential of each plan. Where patients have certain unfavorable characteristics, it might not be possible to achieve the same dose expectations as for other patients, and it can be difficult to know when the optimization software could achieve any greater OAR sparing without sacrificing target coverage. This ambiguity of individual plan potential leads to a cyclical process of attempting plan improvement, which is likely to incur time expenditure that outweighs the overall clinical gain.

Evidence is emerging that by using knowledge of past plans, it is possible to predict the dose-volume histogram (DVH) outcomes for patients based on anatomical information before the optimization process has begun.[4] The purpose of this study was to establish independent patient anatomical variables and their

Reprint requests to Thomas Eade, M.B.Ch.B., F.R.A.N.Z.C.R., Northern Sydney Cancer Centre, Radiation Oncology, Level 1 ASB, Royal North Shore Hospital, Reserve Road, St Leonards, New South Wales 2065, Australia.
E-mail: Thomas.Eade@health.nsw.gov.au

http://dx.doi.org/10.1016/j.meddos.2015.08.005
0958-3947/Copyright © 2016 American Association of Medical Dosimetrists

potential relationship to target and OAR end points. We hypothesized that these variables could be used to accurately predict planning outcomes for individual patients and aimed to create a model that would identify plans more likely to have protocol violations, thus assisting in time management. Through the creation of clinically usable models, it is anticipated that we can achieve a reduction in planning time, improve work flow, and strengthen planning consistency.

Material and Methods

Patient selection and radiation technique

All patients treated at the Northern Sydney Cancer Centre with IMRT or VMAT for prostate cancer are enrolled in a prospective ethics-approved clinical database, including both clinical and dosimetric data (Northern Sydney Local Health District Human Research Ethics Committee 0708–159M). This study included 200 consecutive patients from this institution treated with definitive dose-escalated radiotherapy from July 2012 to January 2014 (Ethics approval LNR/14/HAWKE/290). The subjects were divided sequentially into a hypothesis-generating cohort ($n = 100$) and a validation cohort ($n = 100$). A proportion of patients underwent SpaceOAR Hydrogel spacer insertion and were included in the analysis.

Simulation and planning have been previously detailed [5] but in summary, all patients were simulated with an empty rectum and a comfortably full bladder. Patients were planned to receive a dose of 80 Gy in 40 fractions to > 95% (D_{95}) of the planning target volume (PTV), created from a 7-mm uniform expansion of the clinical target volume (CTV) of the prostate and the proximal seminal vesicles, except a 5-mm expansion posteriorly. The rectum (contoured as a solid structure from the inferior ischial tuberosities to the rectosigmoid junction) was prescribed to receive a dose of 65 Gy to < 17% and 40 Gy to < 35% of the volume. The bladder was planned to receive a dose of 65 Gy to < 25% and 40 Gy to < 50% of the volume. Patients having their pelvic lymph nodes treated received a dose of 60 Gy in 40 fractions to a low-dose PTV, created from a 7-mm expansion of the CTV of the lymph node volume, including distal seminal vesicles and periprostatic, obturator, iliac, and pre-sacral lymph nodes. All patients were treated using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) using 7 to 9 beam angles for IMRT or 2 arcs for VMAT.

Individual patient plan data were retrieved to collect the doses to 99% of the PTV (D_{99}), PTV mean dose, prostate size, and dose to 100% of the prostate (D_{100}). The bladder and the rectum were assessed for organ size (cm^3), 1-cm^3 maximum dose, and percentage of volume receiving a dose of 65 ($V_{65\ Gy}$) and 40 Gy ($V_{40\ Gy}$). An overlap structure was created to measure the volume (cm^3) and percentage (%) of overlap of bladder (OB) and overlap of rectum (OR) within the PTV.

Statistical methods

An iterative model was used, whereby a series of tests were performed, each one applying the results of the previous test. The statistical analyses were generated with TIBCO Spotfire S+ 8.1 software.

Identification of predictive factors

To identify predictive factors, radiotherapy plans from the hypothesis-generating cohort were analyzed to identify those variables that might predict for dosimetric outcome. For the bladder, dosimetric outcome measures included the 1-cm^3 maximum dose, $V_{40\ Gy}$, and $V_{65\ Gy}$, which were correlated with bladder volume, OB (cm^3), OB (%), volume of prostate (cm^3), Hydrogel (yes or no), and lymph node treatment (yes or no). For the rectum, dosimetric outcome measures included the 1-cm^3 maximum dose, $V_{40\ Gy}$, and $V_{65\ Gy}$, which were correlated with rectal volume, OR (cm^3), OR (%), volume of prostate (cm^3), Hydrogel (yes or no), and lymph node treatment (yes or no).

The relationships between the anatomical variables and the corresponding dosimetric outcome were assessed with scatterplots, univariate linear regression, multivariate linear regression, and simple correlation. The scatterplots included a locally weighted least squares regression line (LOWESS) to assess the linearity of the relationships.

Hypothesis-generating model

Anatomical variables that scored significant dosimetric correlations in part 1 were further assessed with a Classification and Regression Tree (CART) analysis for their ability to predict planning violations. Planning violations were defined as plans that did not meet the PTV and the OAR criteria, as described in the section Patient selection and radiation technique, earlier. For each dosimetric outcome, the classification tree selects the anatomical variable or variables with their corresponding optimal cut points that predict the likelihood of protocol violations in treatment plans. The predictions can then be compared with the actual results to determine the sensitivity, specificity, positive predictive value, and negative predictive value of the classification tree. As the CART algorithm searches through many combinations of anatomical variables and cut points to find the optimal classification rule, the estimated values of the classification parameters (sensitivity, specificity, positive predictive value, and negative predictive value) would be overly optimistic. Therefore, CART analysis was conducted with the 2 data sets previously mentioned, beginning with the hypothesis-generating cohort to derive the optimal classification rule for that data set.

Validation model

The classification rule was then applied to a CART analysis of the validation cohort in part 3, to estimate realistic values for the classification parameters. The classification parameter values from the validation cohort therefore reflect the outcome if the classification rule were to be applied to other independently collected data sets.

Results

Determining predictive variables

Volume of OR was significant for all factors on univariate analysis, but it became nonsignificant on multivariate analysis (Table 1). Percentage of the OR was significant for 1 cm^3 maximum dose, $V_{40\ Gy}$, and $V_{65\ Gy}$ on both univariate and multivariate analyses ($p < 0.001$). Bladder total volume was significant on univariate analysis for $V_{40\ Gy}$ and $V_{65\ Gy}$ ($p < 0.001$) but not for 1 cm^3 maximum dose ($p = 0.165$) (Table 2). Volume of OB was not significant on multivariate analysis. Percentage OB was significant on both univariate and multivariate analyses for $V_{40\ Gy}$ and $V_{65\ Gy}$ ($p < 0.001$) and 1 cm^3 maximum dose ($p = 0.004$ multivariate).

Lymph node treatment had a significant influence on bladder $V_{40\ Gy}$, bladder $V_{65\ Gy}$, and rectal $V_{40\ Gy}$ on both univariate and multivariate analysis (Tables 1 and 2). In the 32 patients who had SpaceOAR Hydrogel inserted, the presence of the spacer was associated with significant improvement ($p < 0.001$) for all rectal end points. The rectal spacer decreased both the volume and the percentage of overlap between the rectum and the PTV, confirming that a reduced OR or %OR, whether natural or assisted by rectal spacers, improves the dosimetric outcomes. The volume of the prostate was not predictive of bladder or rectal dosimetry, nor was it significant in terms of PTV or CTV coverage.

CART analysis model with the hypothesis-generating cohort

Part 1 highlighted %OR and %OB as important variables in the potential prediction of all dose points tested. It also showed that the addition of lymphatic treatment influenced the DVH. These factors were therefore selected for entry into the CART analysis in parts 2 and 3. Bladder total volume (cm^3) was only statistically significant on univariate analysis, but it is an adjustable patient variable so it was also included. The total volume of rectum, volume (cm^3) of OR and OB, and prostate (CTV) size were excluded from the CART model. Hydrogel was also excluded because the % OR accounted for the same effect.

For both the rectum and the bladder CART analyses, the algorithm was able to separate and define different groups of patients in a useable format with useful prediction values. It formulated that rectal violations could be predicted from varying amounts of %OR. The most important factors predictive of bladder violations were %OB and the presence or absence of lymph node treatment. The CART analysis also showed that a minimum bladder volume of 170 mL was an important contributor to the achievement of bladder constraints. Only 19 of the 100 patients had a bladder volume less than this value, but 14 of these patients had violations compared with a 19% rate of violations for patients with bladder volumes greater than 170 mL.

Final model determined by the validation cohort

The final CART analysis results closely reflected the hypothesis-generating cohort values, consequently confirming its relevance to

Download English Version:

https://daneshyari.com/en/article/1884773

Download Persian Version:

https://daneshyari.com/article/1884773

Daneshyari.com