Corrigendum: Study of the Radiotherapy Treatment Margins in Prostate Cancer with Fuzzy Logic Model
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In addition, throughout the paper it draws upon a work first published in [1]. The authors apologise for failing to include this source in the reference list.

[1] Bongile Mzenda; Mir Hosseini-Ashrafi; Alex Gegov; David J. Brown, (2010), 'Implementation of a fuzzy model for computation of margins in cancer treatment', International Conference on Fuzzy Systems, 10.1109/FUZZY.2010.5584468.'
Study of the Radiotherapy Treatment Margins in Prostate Cancer with Fuzzy Logic Model

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Abstract. Start your abstract here…External beam radiation therapy (EBRT) is a process in which therapeutic radiation dose is delivered to target tissues whilst seeking the risk of healthy normal and critical organs is minimal. In case of Complex radiation therapy technique such as volumetric modulated arc radiotherapy (VMAT), there is requirement of precise and optimal treatment margin selection so that not only the resulting dose distributions gives high tumor control probability (TCP) but also dose close to critical organs will get minimal. A fuzzy logic application was used here to derive the optimal radiotherapy treatment margins to be used in radiation therapy treatment planning. Here major all possible radiotherapy uncertainties accounted such as translational set-up, organ delineation and organ motion-induced errors for calculating the quantitative variations in target volume radiobiological parameters for treatment plans using fixed step sized increments of treatment margins up to maximum possible variations of tumor volumes. Therules and membership functions were adopted from dosimetric results of treatment planning for the fuzzy inference system. The imprecision and smoothness of the original fuzzy output was corrected with application of a convolution technique. The results demonstrate that performance of the applied fuzzy model margins against current used radiotherapy margins was consistent in lower range of error magnitude but beyond that a significant non-linearly margin performance was found when considering the normal tissue complication probability (NTCP) and constraint factors into account in the margin recipe formulation. With the new margins obtained then applied for the study of prostate cancer treatment planning and results were compared well with current volumetric modulated arc radiotherapy (VMAT) technique.

Key words: PTV (Planning target volume), TCP, NTCP, volumetric modulated arc radiotherapy (VMAT).

1. Introduction

In the external beam radiotherapy, the therapeutic radiation dose is delivered to target tissues whilst seeking the risk of healthy normal and critical organs is minimal. Before the treatment, the area of interest to be irradiated, all target volumes and normal structures should be
delineated clearly. The inability of current imaging modalities may lead to the inter and intra-observer variability when considering the microscopic tumor spread for particular type of cancer. In the external beam radiotherapy treatment planning the energy, geometry of radiation beam, dose prescription and optimization are considered to achieve the therapeutic gain of treatment. During the fractionated radiotherapy treatment course, many variations such as translational set-up, organ delineation and organ motion errors affect the planned treatment volume with actual treatment volume so that as a result the delivered dose to planned volumes which may differs from the actual received dose to planned volumes. To avoid this significant dose variation, treatment volumes must be defined with precise margins so that to achieve the therapeutic gain of treatment by maintain the geometrical accuracy. Many standard recommendations for the definition of margins applied in radiotherapy treatment planning are available via ICRU reports 50 and 62 [1-5] and formulations are based on probabilistic dose distributions. The gross tumor volume (GTV) which is the identifiable or palpable tumor and a clinical target volume (CTV) is defined with extra margin to GTV to considering the effects of microscopic growth of tumor, whilst the inclusion of additional margin to CTV for geometrical accuracy results is the planning target volume (PTV). The radiobiological concepts for tumor volumes and normal structures are control probability (TCP) which is the probability of killing all tumor cells in a volume. Thenormal tissue complication probability (NTCP) which is the damage that occurs to normal tissues and critical organs respectively. These biological parameters are calculated to get the possible radiation therapy rationale or probability of cure without complications which is obtained by estimating the Uncomplicated Tumor Control Probability using the margin recipe formulation.

In the present study we considered uncertainties i.e. translational set-up, organ contouring and organ motion errors to estimate the required margins in radiotherapy with fuzzy inference system. To quantify mathematically relationship between the above said radiobiological parameters, radiotherapy margins as well as radiotherapy uncertainties difficult, however the distinct advantage of fuzzy logic is that allow the linkage of these parameters through the use of fuzzy rules and membership functions to have possible output [5,6-8]. Advanced radiotherapy treatment delivery techniques such as intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) and Tomotherapy required precise treatment margins so that treatment volumes must be defined with precise margins to achieve high dose close to critical organs and dose escalation. The application of the derived fuzzy margin was applied this study and compared to currently used margins to assess such a clinical situation.

2. Materials and methods

The TheSugeno type fuzzy inference system was used considering knowledge based rules and Gaussian membership functions in the PTV margin modeling as it gives results which would be consistent with the expected output. From various studies [9-10], the possible variations of prostate tumor motion displacement was observed to be 0-15 mm. With help of earlier sources and our institutional image guiding techniques the procedure first started with defining variable PTV margins (0mm to 16 mm) symmetrically with treatment planning system (TPS) using typical incremental error magnitudes as obtained during radiotherapy treatment. For each PTV, the treatment plans were generated for prostate cancer treatment. The dosimetric statistics of each plan were used to calculate baseline values of TCP and NTCP as starting point used for comparisons in Matlab program and also subsequent calculations of new TCP and NTCP values corresponding to each plan which has new
PTV margin with stepped symmetrical increment. The crisp output was evaluated with final defuzzification and taken care for smoothness of the fuzzy output processing with Gaussian convolution kernel. Then using final PTV margin estimated from the fuzzy model, the VMAT treatment planning was performed using the commercial Eclipse 15.6 (Varian Medical Systems) treatment planning system (TPS) in which the AAA algorithm is configured in the Eclipse Beam Configuration task to provide the increased speed and accuracy required for modern treatment techniques. Then final plan was compared with currently applied van Herk margins for prostate cancer. All treatment plans planned with different PTV margins which were varying symmetrically from 0 to 16 mm in 2 mm step sized increment from minimum to maximum possible variation of PTV. The dose prescription was set as conventional dose fractionation with 70 Gy. The plan passing criteria so that 95% isodose line covered the PTV on all slices to achieve the high conformity of dose distribution. For each plan the dosimetric results of the prostate volume (CTV) and major normal structures (rectum and bladder) were calculated. The Equivalent Uniform Dose (EUD) modeling, which was recommended for the true radiobiological outcomes and here was used to calculate the radiobiological parameters TCP and NTCP using a Matlab-based simulation tool based on the concept EUD which is defined as the uniform dose distribution giving an equivalent survival fraction to that of a heterogeneous dose distribution. In calculation of radiobiological parameters i.e. loss of prostate TCP which corresponding to the difference between new TCP and baseline value \( TCP_0 \) and the increase in rectal NTCP which corresponding to the difference between new NTCP and baseline value \( NTCP_0 \) for each plan. The loss of prostate TCP and increase in rectal NTCP were denoted as \( \Delta TCP \), \( \Delta NTCP \) respectively. For each of the treatment plans using the different PTV margin with stepped increment size, \( \Delta TCP \) and \( \Delta NTCP \) were calculated. The fuzzy rules were defined based mainly on expert knowledge and clinically assessable so that the balance which allows the risk between increase in NTCP and reduction of the PTV margin also the loss in and increasing the PTV margin size respectively. Here the loss of prostate TCP and increase in rectal NTCP were chosen as two inputs for Fuzzy system and one output, i.e. PTV margin for each normal tissue nearby prostate PTV. Six membership functions i.e. Very High, High, Medium, Small, Very Small, Almost Zero and were chosen for the input and output values considering knowledge based and existing normal tissue toxicity limitations. Preselected increase in rectal NTCP as well as the irradiated volume of the anterior wall of rectum were chosen so as to allow the algorithm to select margins for rectal complications. The optimization of fuzzy rules derived from the input data and using the conditions imposed on the margin limits. The weighted average technique was used to calculate the final output of the Sugeno FIS.

3. Results and discussion

The resulted output function of the Sugeno FIS obtained from the defuzzification as 3D surface view in which each PTV margin point corresponds to a specific value of two inputs, i.e. \( \Delta TCP \) and \( \Delta NTCP \) from a matrix representation of the output function from 3D surface of particular OAR and target sub volumes of OAR combination. Also it was observed when \( \Delta NTCP \) increasing, the results in a PTV margin decreases. Also the loss in TCP increasing the resultant PTV margin would be increasing as satisfying the preselected margin requirements. The plan with resultant fuzzy model PTV margin was compared to the plan with PTV commonly used margin recipe van Herk et al. Considering the modeling uncertainty into consideration, it was observed that good agreement but between the conventional PTV margin based on van Herk et al’s formulation and fuzzy model PTV margin up to 5.5 mm s.d. equivalent errors but on average 0.5 mm bigger margin of fuzzy model than the conventional margin in the considerable clinical range. Due to the conditions imposed in our margin formulation, the fuzzy PTV margin apparently not exceeding approximately 12.5 mm for errors above 4.5-5 mm s.d. The fuzzy PTV margin observation was linear up to 11 mm range which shows insignificant variation from van Herk margin but variation was observed non-linearly greater than
5mm s.d. as shown in Figure-1. This was due to introducing of knowledge based fuzzy rules, the normal tissue complication rates, rectal tolerance constraints and related biological factors were incorporated into the margin formulation.

To assess the performance of fuzzy derived PTV margin against current margins, The VMAT treatment planning using appropriate plan geometry was performed with new derived fuzzy margin and compared with VMAT in which conventional PTV was sat as target volume based on van Herk formulation. As the fuzzy margin on an average 0.5mm bigger than the conventional margin in the considerable range of clinical acceptance. But higher the error magnitude greater than 5-5.5mm s.d. clinically fuzzy margin would be significant depending on clinical imposed and existing patient related factors. The dose-volume results of the VMAT plans for the prostate PTV, the dose volume histogram (DVH) was shown in Figure-2(a), which demonstrates more or less similarity was observed between the plans as they were considered in lower s.d. variation depends on tumor staging and growth characteristics of current prostate case. In case of critical organs, rectum was observed as organ at risk to be spared. The dose volume histogram (DVH) of the rectum shown in Figure-2(b), in which intermediate volumes may significant but overall insignificant differences were observed. But as posterior margins increases, biological based fuzzy margins may have significant ΔNTCP results of OARs.

![Figure 1](image1.png)

Figure 1. Comparison of van Herk et al and fuzzy model based PTV margins, in terms of the standard deviation of total displacement errors, using the same corresponding uncertainties as inputs.

![Figure 2](image2.png)

Figure 2(a) and 2(b)show the dose volume histogram (DVH) for the prostate and rectum respectively.
Figure 2(a). DV(dose-volume) Histograms for the prostate PTV and Figure 2 (b) rectum for plans using the conventional (van herk) and expected fuzzy margins.

4. Results and discussion

The application of fuzzy logic based PTV margin in the treatment plans was dictated to produce more or less similar results compared to plans using current treatment margins but might be favorable clinical endpoints for organ motion uncertainties when higher the error magnitudes. Here the practical usefulness and advantage of using fuzzy logic was addressed under practical limitation on the margin size as proposed fuzzy approach using not only physical dose constraints but also radiobiological data to optimize the required margin to estimate true outcomes whereas the most existing margin models considering mostly physical dose-volume data alone. Apart of that the fuzzy model is not only relatively simple to implement also gives accurate margin sizes and so applicable to all other volumes of interest to be treated and have organ motion related errors and risk estimation of sub volumes. Consistency of the fuzzy margin compared with the classical van Herkbased margin recipe showed nearly similar. The new fuzzy margin was applied in VMAT treatment planning. The results were compared to classical plans showing good consiste

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