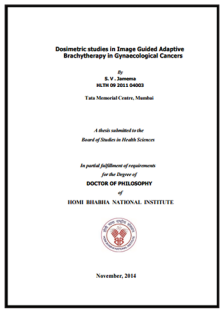
Dosimetric Studies in Image-Guided Adaptive Brachytherapy in Gynecological Cancers: A Journey to Successful Implementation


Dosimetric studies in Image Guided Adaptive Brachytherapy in Gynaecological Cancers

By

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Implementation of Image-guided adaptive brachytherapy (IGABT) in India and other developing countries is a major challenge due to the resources, expertise and financial constraints. The basis of this thesis was to address various issues related to transition and successful implementation of IGABT in clinical routine.[1] Tata Memorial Hospital (TMH), Mumbai has a long tradition of being active in international collaborative research. Various fellowship programs for both clinicians and physicists have been the basis for successful collaborative research. Within many such projects, TMH is one of largest participating centers in the ongoing multi-centric collaborative international study on magnetic resonance (MR) imaging-guided brachytherapy in locally advanced cervical cancer. The study was designed to evaluate the dose-effect relationship on local control/morbidity of the tumor and toxicities of organs at risks (OAR) when MR images were used for cervical cancer brachytherapy. This thesis reiterates that, like any other advanced techniques, IGABT too requires systematic clinical implementation taking into account various technological, dosimetrical, and clinical issues. Systematic transition and appropriate implementation of IGABT for locally advanced cervical cancers may result in better outcome.

Specific Objectives of the Work Undertaken in this Thesis

1. To analyze the dosimetric difference between the standard loading, manually optimized and inverse optimized dosimetric plans using Inverse Planning Simulated Annealing (IPSA) and Hybrid Inverse Planning Optimization (HIPO) for various applications in IGABT in gynecological cancers for various types of applications:
   a. Intracavitary brachytherapy – Tandem and Ovoid and Tandem and Ring applicators
   b. Combined intracavitary and interstitial (IC + IS) Vienna applicator
   c. Interstitial template for gynecological applications – Martinez Universal Perennial Interstitial Template (MUPIT).
2. To analyze the inter application variation for
   a. Orthogonal Radiograph Image Based Brachytherapy
   b. MR image-based brachytherapy using rigid registration
   c. MR image-based brachytherapy using deformable image registration.

This thesis has been divided into five chapters; the first chapter describes about brachytherapy history, technological developments, and implantation techniques. The second chapter describes the conventional methods of treatment planning, its limitations and the newer developments such as MR-IGABT, the processes involved in the transition and its rationale. The third chapter describes the application of inverse planning for various gynecological applications. The fourth chapter addresses the uncertainties in IGABT, especially, organ motion related to inter-application variation in multi-fractionated brachytherapy in both radiograph-based and volumetric imaging-based brachytherapy environments. Finally, fifth chapter summarizes the important findings of this thesis and also discusses the future direction of research.

Inverse Planning Algorithms

The use of inverse planning algorithms in external beam therapy is an established procedure and widely accepted in the clinics, while in brachytherapy, its use is dependent on the specific application. Interstitial implants with many needles providing a high degree of freedom have a substantially different dose distribution compared to intracavitary implants. The technique has been successfully implemented in prostate brachytherapy, while its use in gynecological brachytherapy is unclear. There are certain issues with currently available inverse planning algorithms, especially for intracavitary brachytherapy, which need to be clearly understood for various clinical situations before clinical implementation. For example, the loading pattern resulting from these algorithms

has a large deviation from the conventional pattern which may not be clinically acceptable when substantially changing the spatial dose distributions and dose gradients within the target volumes, OARs and healthy tissues. The first part of this thesis addresses issues related to inverse planning for various clinical scenarios in IGABT using two commercially available inverse planning algorithms, IPSA and HIPO.[2-4] Dosimetric and clinical evidence have to be collected to obtain as much knowledge as possible which may be useful to integrate into future inverse planning tools.

The major findings of this section are summarized as follows. For intracavitary applications, inverse planning with HIPO and/or manual optimization offers improved plans in terms of OAR sparing while maintaining target coverage when compared to standard clinical plans. However, the average loading pattern was found to deviate from a traditional standard Fletcher loading. The tandem loading was decreased compared to the ovoids mainly due to high sigmoid dose. For combined intracavitary and interstitial applicators, inverse planning with IPSA resulted in plans with higher volumes of high dose regions. Without help structures, the treatment time in the needles was high resulting in highly modified spatial dose distributions, which was significantly reduced when help structures were included. For interstitial gynecological implants based on MUPIT template, IPSA resulted in significant sparing of normal tissues without compromising the target coverage as compared to geometrically and graphically optimized plans.

Uncertainties of Organ Motion

The second part of this thesis addresses the uncertainties in IGABT, which have not been adequately addressed so far.[5,6] It is essential to identify these uncertainties, their magnitude, and their impact on the overall uncertainty of dose delivery to the patient. This knowledge may provide correct dose assessment in IGABT, dose-effect modeling, and subsequently improved clinical outcome when using better planning aims with dose and volume constraints. In multi fractional brachytherapy, inter-application/fraction variations occur between different treatments/applicator insertions, both in terms of geometric and dosimetric parameters. These parameters have been identified as bladder and/or rectal filling, movements of sigmoid colon, and variation in vaginal packing among others. The current practice of determining the D_{2cm^3} cumulative dose to OARs during brachytherapy is based on what has previously been called "the worst-case scenario," which is the assumption that the D_{2cm^3} regions are located in the same anatomical part of the organ in each fraction. This assumption implies that the cumulated brachytherapy dose can be calculated by adding D_{2cm^3} values for each fraction. This approximation can lead to OAR dose overestimation when different organ parts are exposed to a high dose in different fractions. This question has been addressed systematically for orthogonal radiograph based dosimetry and IGABT using MR images with rigid and deformable image registration in this thesis.

The major findings of this section are as follows. For orthogonal radiograph image-based dosimetry, the inter application dose variation for the International Commission on Radiation Units and Measurement (ICRU) rectum and bladder was found to be 10%. ICRU rectal point was more stable as compared to the ICRU bladder point. Similarly, in MR image-based dosimetry using rigid registration, the inter application variation of the spatial location of D_{2cm^3} volumes was found to be most stable for rectum and to a large extent for the bladder. Minimal to moderate geometric changes in sigmoid are seen in the majority of the patients resulting in maximal variation in the spatial location of D_{2cm^3} volumes which may lead to over estimation of doses during the direct Dose Volume Histogram (DVH) addition. The results of dose accumulation using deformable image registration indicate that the current DIR algorithms are not robust enough to handle large deformations in rectum and bladder. For the sigmoid, it was, in general, not feasible to perform DIR due to significant deformations. DIR based dose accumulation based on different DIR algorithms resulted in large discrepancies on the accumulated dose for bladder and rectum. It is, therefore, recommended to use direct DVH addition for estimation of total dose, while DIR is not recommended for dose accumulation.

Summary and Conclusion

IGABT has evolved into a high-technology modality of radiotherapy incorporating modern imaging, advanced brachytherapy applications using newer applicators and advanced computational algorithms. Various processes involved in the implementation of IGABT have been established while some concerns about uncertainties related to imaging, treatment planning, dose delivery, and anatomical variations have been raised. These are current areas of research by various groups. This thesis is a hallmark for addressing few of the issues enumerated above and has provided some insight into the IGABT processes. The significant findings of the thesis are as follows: (1) Manual dose optimization significantly improves the dose as compared to standard point A prescription. (2) Application of inverse dose optimization has major pitfalls; hence, inverse planning is not recommended for IGABT for cervical cancers. (3) Dose accumulation across fractions can be done with a good precision for bladder and rectum by direct DVH additions. However, the sigmoid dose may be overestimated with direct DVH addition, and special care should be taken during plan evaluation depending on imaging findings for sigmoid. Image-guided adaptive brachytherapy is a high technology modality within radiotherapy which can be performed with the promising outcome and economical gain in India.[7-10]

Dissemination of this promising technique should be addressed systematically for a smooth transition from conventional to IGABT approach in cervical cancer. This can be achieved through continuing teaching and training

efforts through national/regional and hospital based hands-on workshops as well as teaching courses in collaboration with various national (AMPI/AROI/IBS) and International societies (ESTRO). This thesis supports the implementation of high-quality treatment planning and dose reporting for IGABT in cervical cancer.

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