

FEASIBILITY INVESTIGATION OF VIRTUAL PATIENT GUIDED RADIATION THERAPY (VPGRT)

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# FEASIBILITY INVESTIGATION OF VIRTUAL PATIENT GUIDED RADIATION THERAPY (VPGRT)

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## Abstract:

This study investigated the feasibility of virtual patient guided radiation therapy (VPGRT). VPGRT means the application of advanced virtual human modeling techniques in radiation therapy. Four main topics were included in this dissertation.

First, a set of three-dimensional (3D) virtual human models were applied for internal electron dosimetry. The concept, Specific Absorbed Fraction (SAF), was applied to evaluate the average absorbed dose in a target organ as a result of radioactive materials deposited in a source organ. The SAF is commonly used to calculate doses to internal organs from nuclear medicine studies. Our study reported a new set of SAF values for internal electron emitters ranging from 10 keV to 4 MeV from various internal organs to the fetus based on Monte Carlo method and three newly developed pregnant female models. These models, named RPI-P3, RPI-P6 and RPI-P9, represent the anatomy of a reference female at 3<sup>th</sup>, 6<sup>th</sup> and 9<sup>th</sup> month pregnancy respectively. Linear log relationship was observed between SAF values and electron energies. Since the RPI-P models had finer details of human anatomy and more realistic organ volumes and geometries following the latest ICRP reference values, this study may improve the dosimetric accuracy for pregnant women and their fetuses undergoing nuclear medicine studies.

The second topic was dosimetric and biological modeling of electronic brachytherapy. The model S700 Axxent™ x-ray device developed by Xoft Inc. is a low energy electronic brachytherapy source which has been used in high dose rate (HDR) intracavitary accelerated partial breast irradiation (APBI) as an alternative to an Ir-192 source. The prescription dose and delivery schema of electronic brachytherapy APBI are the same as the Ir-192 HDR. However, due to its lower mean energy than the Ir-192 source, Axxent has dosimetric and biological features different from Ir-192 source. Current brachytherapy treatment planning methods may have large errors in treatment outcome prediction for an electronic brachytherapy plan. Two main factors contribute to the uncertainties: the dosimetric influence of tissue heterogeneities and the enhancement of relative biological effectiveness (RBE) of electronic brachytherapy. Our study quantified the effects of these two factors and revisited the plan quality of electronic brachytherapy APBI. Influence of tissue heterogeneities was studied by Monte Carlo method and heterogeneous virtual patient phantoms created from CT images and structure contours. Effect of RBE enhancement in treatment outcome was estimated by biologically effective dose (BED) distribution. Ten electronic brachytherapy APBI cases were studied. The results showed that, for electronic brachytherapy cases, tissue heterogeneities and patient boundary effect decreased dose to the target and skin but increased dose to the bones. On average, the target dose coverage PTV  $V_{100}$  reduced from 95.0% in water phantoms (planned) to only 66.7% in virtual patient phantoms (actual). Actual maximum dose to the ribs was 3.3 times higher than planned; actual mean dose to the ipsilateral breast and maximum dose to the skin were reduced by 22% and 17% respectively. Combining the effect of tissue heterogeneities and RBE enhancement, BED coverage of the target was 89.9% in virtual patient phantoms with RBE enhancement (actual BED) as compared to 95.2% in water phantoms without RBE enhancement (planned BED). About 10% increase in source output was required to raise BED PTV  $V_{100}$  to 95%. By using heterogeneous virtual patient models in dose calculation and biologically effective dose in plan evaluation, this study improved the dosimetric accuracy and facilitated the outcome prediction for electronic brachytherapy.

In the third topic, we applied dosimetric modeling to a novel brachytherapy treatment method: 3D intensity modulated brachytherapy (IMBT). The feasibility of IMBT to improve dose conformity for irregularly shaped targets has been previously investigated by researchers by means of partially shielded sources. However, partial shielding does not fully explore the potential of IMBT. Our study introduced the concept of 3D IMBT and solved two fundamental issues regarding the application of 3D IMBT treatment planning: the dose calculation algorithm and the inverse treatment planning method. A 3D IMBT treatment planning system prototype was developed. This

system consisted of three major components: (1) a comprehensive IMBT source calibration method with dosimetric inputs from Monte Carlo (EGSnrc) simulations; (2) a “modified TG-43” (mTG-43) dose calculation formalism for IMBT dosimetry; and (3) a physical constraint based inverse IMBT treatment planning platform utilizing a simulated annealing optimization algorithm. The Axxent electronic brachytherapy source was simulated in this application. Ten intracavitary APBI cases were studied. For each case, an “isotropic plan” with only optimized source dwell time and a fully optimized IMBT plan were generated and compared with the original patient treatment plan. The results showed that IMBT showed superior plan quality compared with the original plans and the isotropic plans in all cases. In an extremely difficult APBI case with a small breast and small distances to the ribs and skin, the IMBT plan reduced the high dose volume PTV  $V_{200}$  by 16.1% and 4.8% respectively compared with the original plan and the isotropic plan. The conformity index for the target was increased by 0.13 and 0.04 respectively. The maximum dose to the skin was reduced by 56 cGy and 28 cGy respectively per fraction. Also, the maximum dose to the ribs was reduced by 104 cGy and 96 cGy respectively. The mean doses to the ipsilateral and contralateral breasts and lungs were also slightly reduced by IMBT. The limitations of IMBT are the longer planning and delivery time.

At last, we applied motion modeling techniques to 4D radiation therapy and proposed a novel 4D treatment planning strategy: 4D model-based planning (4DMP). 4DMP predicts the 3D deformable motion of the target and critical structures as a function of time during radiation therapy delivery and then adjusts the delivery beam apertures formed by the dynamic multi-leaf collimators (DMLC) to account for the motion. The key feature of 4DMP is the application of a dynamic virtual patient model (4D model) in motion prediction, treatment beam adjustment and dose calculation. A lung case was chosen to demonstrate 4DMP. For the lung case, a dynamic virtual patient model was first developed based on the patient’s 4DCT images. The 4D model was capable of simulating respiratory motion of different patterns. A model based registration method was then applied to convert the 4D model into a set of deformation maps and 4DCT images for dosimetry purposes. Based on the 4D model, 4DMP treatment plans with different respiratory scenarios were developed. The quality of 4DMP plans was then compared with two other commonly used 4D planning methods: maximum intensity projection (MIP) and planning on individual phases (IP). The results showed that, under regular motion, 4DMP offered similar target coverage as MIP with much better normal tissue sparing. At breathing amplitude of 2 cm, the lung  $V_{20}$  was 23.9% for an arc MIP plan and 16.7% for an arc 4DMP plan. The plan quality was comparable between 4DMP and IP. Under a real time irregular breathing pattern, 4DMP had the best plan quality of all three 4D planning methods. PTV  $V_{97}$  was 90.4%

for an arc MIP plan, 88.6% for an arc IP plan and 94.1% for an arc 4DMP plan. Lung  $V_{20}$  was 20.1% for the arc MIP plan, 17.8% for the arc IP plan and 17.5% for the arc 4DMP plan. In summary, 4D model-based planning, which applies dynamic virtual patient models in IMRT treatment planning, can account for the real time deformable motion of tumor under different breathing conditions. The plan quality of model-based planning method was superior to MIP and IP.

This study showed a few examples of using advanced virtual human modeling techniques in radiation therapy and the advantages were obvious: using 3D virtual patient models improved dosimetric accuracy in nuclear medicine and brachytherapy. Biological modeling gave a better estimation of treatment outcomes for brachytherapy. Virtual modeling techniques also enabled the development of novel radiation therapy techniques. 3D IMBT largely improved dose uniformity in targets and reduced dose to critical structures for APBI. 4D model-based planning improved intra-fraction motion management. Model based 4D plans showed superior target coverage and normal tissue sparing to two other 4D planning methods under realistic respiratory motion. Based on these results, it is expected that using advanced virtual human modeling techniques in radiation therapy will largely benefit current radiation therapy research and clinical applications. As the complexity of radiation therapy techniques increases, more and more advanced virtual modeling techniques will be developed and incorporated into radiation therapy.

#### List of publications:

1. Bingqi Guo, X George Xu, and Chengyu Shi, "Real time 4D IMRT treatment planning based on a dynamic virtual patient model: proof of concept" **38(5)** 2011.
2. Jun Xu, Chengyu Shi, Bingqi Guo, and Nikos Papanikolaou, "Deformable Multi-Phase (DMP) Delivery: A novel 4D MLC-based IMRT with non-rigid motion compensation" Under revision, Physics in Medicine and Biology.
3. Chengyu Shi, Bingqi Guo, Chih-Yao Cheng, Tony Eng and Nikos Papanikolaou, "Applications of Tissue Heterogeneity Corrections and Biologically Effective Dose Volume Histograms in Assessing the Doses for Accelerated Partial Breast Irradiation Using an Electronic Brachytherapy Source" Physics in Medicine and Biology, 55(18) 2010.
4. Chengyu Shi, Bingqi Guo, Chih-Yao Cheng, Carlos Esquivel, Tony Eng and Nikos Papanikolaou, "Three dimensional Intensity Modulated Brachytherapy (IMBT): dosimetry algorithm and inverse treatment planning" Medical Physics, **37** (7) 2010.
5. Bingqi Guo, X George Xu, and Chengyu Shi, "Specific absorbed fractions for internal electron emitters derived for a set of anatomically realistic reference pregnant female models" Radiation Protection Dosimetry, **138**(1) 2010.