Ph.D. Thesis Abstract for Alonso N. Gutierrez
Department of Medical Physics
University of Wisconsin-Madison

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Clinical Applications of Image Guided-Intensity Modulated Radiation Therapy (IG-IMRT) for Conformal Avoidance of Normal Tissues

Alonso N. Gutierrez

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Recent improvements in imaging technology and radiation delivery have led to the development of advanced treatment techniques in radiotherapy. These advances have opened the door for novel therapeutic approaches to improve the efficacy of radiation cancer treatments. Among these advances is image-guided-intensity modulated radiation therapy (IG-IMRT). In which, imaging is incorporated to aid in inter-/intra-fractional localization of target volumes and to ensure accurate delivery of precise and highly conformal dose distributions. In principle, clinical implementation of IG-IMRT should improve normal tissue sparing while permitting significant biological effective dose escalation through the enhanced ability to localize and treat target volumes with highly conformal dose distributions. This in theory should open the radiation therapeutic window and lead to increases in survival through improvements in local control of primary diseases.

A critical element in improving the therapeutic index in radiotherapy is the minimization of normal tissue irradiation. Laparoscopically implanted tissue expander radiotherapy (LITE-RT) has been developed to enhance conformal avoidance of normal tissue during the treatment of intra-abdominal/pelvic cancers. LITE-RT incorporates three components: (1) a site-specific, custom-shaped tissue expander (2) a minimally-invasive laparoscopic surgery for tissue expander placement, and (3) a form of image-guided radiation therapy (IGRT) for accurate delivery of precise dose distributions. LITE-RT functions by geometrically displacing surrounding normal tissue and isolating the target volume thru the interfractional inflation of the tissue expander throughout the course of treatment. The geometric displacement of normal tissue achievable with the custom shaped tissue expander allows for: (1) application of larger PTV margins to compensate for inter- and intra-fractional target motion without increasing normal tissue dose, (2) uniform or non-uniform dose escalation without increasing normal tissue dose, or (3) reduction of normal tissue dose and associated toxicities with current deliverable target doses. In a veterinary phase I trial, LITE-RT was shown to reduce the clinical presentation of gastrointestinal radiation morbidities during the treatment of bladder transitional cell carcinoma in canines and provided the means for a future dose escalation trial.

The unique delivery geometry of helical tomotherapy, a novel form of IG-IMRT, enables the shaping of conformal dose distributions to multiple tumor structures while at the same time provides the ability to conformally avoid critical structures. These capabilities have been utilized to develop a new delivery method for the management of patients with multiple brain metastases. The large number of radiation delivery projections intrinsic to helical tomotherapy permits the delivery of whole brain radiotherapy (WBRT) with hippocampal avoidance, hypothesized to reduce the risk of memory function decline and improve the patient�s quality of life, and simultaneously integrated boost to multiple brain metastases to improve intracranial tumor control. A treatment planning and delivery study verified that a composite tomotherapy plan in which a homogeneous whole brain dose distribution equivalent to conventional WBRT, conformal hippocampal avoidance without loss of whole brain coverage, and radiosurgically-equivalent dose distributions to individual metastases could be generated and delivered.

IG-IMRT uniquely allows for the escalation of biological dose to targets through integrated, selective subvolume boosts. Subvolume boosting has been shown to be an efficient method of increasing the dose to the tumor volume without significantly increasing the dose to adjacent normal tissue. Helical tomotherapy was used to test the planning feasibility of delivering a simultaneously integrated subvolume boost to canine nasal tumors to improve local control. A treatment planning study showed that treating the entire nasal cavity while simultaneously boosting visible gross disease significantly increase the estimated tumor control probability (TCP) at 1-year without increasing the dose to the adjacent eyes, so as to preserve vision, and to the brain, so as to reduce neuropathy. This approach may be translated to human application to further improve local tumor control.

Details of the development of these clinical applications made solely possible with IG-IMRT radiation delivery techniques are presented.

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