OMICS Journal of Radiology
ISSN: 2167-7964

Wolfson, OMICS J Radiology 2013, 2:6
DOI: 10.4172/2167-7964.1000134

Review Article Open Access

Image-Guided Whole Abdominal Radiation Therapy in Gynecologic Cancers

Aaron H Wolfson*

University of Miami Miller School of Medicine, USA

Abstract

The use of adjuvant Whole Abdominal Radiation Therapy (WART) in gynecologic cancers has not achieved widespread use for a variety of reasons. Several phase III trials comparing WART with adjuvant chemotherapy (CT) in both uterine and ovarian cancers have demonstrated marginal improvement in survival favoring CT over WART. However, the dose of conventionally delivered WART has been historically limited due in large part to the low threshold of normal organ tolerance in the upper abdomen associated with significant late effects of the bowel and kidneys in particular. Yet, with the advent of Image-Guided Radiation Therapy (IGRT), the possibility of dose reduction to nearby organs at risk along with the potential to increase target volume dose is now obtainable. This paper will review the current data related to IGRT WART for several different patient populations of gynecologic cancers.

Keywords: Whole abdominal radiation therapy; Image-guided radiation therapy; Gynecologic cancers

Introduction

The use of full-dose, adjuvant Whole Abdominal Radiation Therapy (WART) in gynecologic cancer has been evaluated in patients with pathologically staged III and IV endometrial carcinoma [1-4], most stages of optimally debulked uterine carcinosarcoma [5], fallopian tube carcinoma [6] and in various stages of ovarian carcinoma [7-12]. However, the dose in most of these studies to the upper abdomen was limited to approximately 30 Gy at 1.2 Gy-1.5 Gy per fraction delivered either daily or twice-daily to sterilize microscopic disease due to the real concern of serious chronic adverse toxicities, especially obstruction requiring surgical repair [13]. Thus, it is not surprising that recurrence rates and even survival endpoints have been at best no better and even inferior when compared to chemotherapy regimen in prior clinical trials for some of these patient populations [4,5]. This paper aims to demonstrate how improvements in the delivery of WART that can be appropriately verified by the use of existing techniques of Image-Guided Radiation Therapy (IGRT) can have a potential impact in improving the outcome of these various patient populations.

Background

IGRT has been operationally defined as to the integration of image-based target volume identification methods, patient positioning instruments along with devices to guide the delivery of the radiation beam. These techniques provide the ability to deliver the radiation beam while accounting for intra-fraction organ movement, such as the diaphragm, during a given radiation treatment of an abdominopelvic target volume. In addition, IGRT approaches provide the means to ensure within given parameters to account for both internal target and organ movement and external patient movement and setup error from one treatment day to another. Examples of these IGRT systems include kV X-rays, cone beam CT (CBCT), and MV portal imaging. The use of fiducial markers for optical tracking, such as in Cyber Knife irradiation, or respiratory-gating systems, which involve either free-breathing approach or active breath control, have also been implemented to aid in the delivery of IGRT for abdominal tumors [14].

Techniques

Over the past 10 years, technological advances in the delivery of external beam irradiation have improved through the use of Intensity-Modulated Radiation Therapy (IMRT) that now allows a more precise radiation dose to be delivered to the peritoneal cavity, while potentially sparing critical organs at risk (OARs), namely bowel, kidneys, and bone marrow, from increased radiation damage [15]. One phase I/II study has previously investigated the feasibility and safety of using adjuvant IMRT/WART to deliver approximately 30 Gy over 20 daily fractions to the abdominal cavity in high risk patients with stage III ovarian carcinoma [16]. This latter study set out to enroll 8 patients into this treatment regimen. Although no updated results are available, it must be pointed out that there was no attempt to increase the total dose past 30 Gy. Also, this study did not specify the method of assuring appropriate real-time beam placement (image-guidance).

Another report did depict the delivery of IMRT/WART for a patient with resected stage IIIc ovarian carcinoma that employed helical tomotherapy to deliver both a homogenous total dose of 30 Gy over 20 daily fractions to the peritoneal surface as well as significantly sparing the exposure of the bowel, kidneys, and bone marrow. This case report is the first published instance of performing daily accuracy for patient positioning by means of the megavoltage Computed Tomography (CT) in 6 mm slice thickness, i.e. Image-Guided Radiation Therapy (IGRT) for WART in a gynecologic cancer. The authors stated that the daily radiation exposure from the CT scanning was approximately 0.01 Gy/day. Using the CT imaging in the tomotherapy unit provided real-time couch shifts in the lateral, vertical and longitudinal directions along with allowing for adjustments in patient "roll" on the table. However, this IGRT technique added about 15 minutes to daily patient setup. Of note, the authors stated that one downside of using helical tomotherapy in the delivery of IGRT/WART was the inability of this particular unit to accommodate a respiratory gating method to account for ongoing diaphragmatic excursion during treatment [17].

In order to get around the issue of variable fluctuations in

***Corresponding author:** Aaron H. Wolfson, University of Miami Miller School of Medicine 1475 NW 12th Avenue, D-31 Miami, FL 33136, USA, Tel: 305-243-4210; Fax: 305-243-4363; E-mail: awolfson@med.miami.edu

Received May 04, 2013; **Accepted** July 15, 2013; **Published** July 22, 2013

Citation: Wolfson AH (2013) Image-Guided Whole Abdominal Radiation Therapy in Gynecologic Cancers. OMICS J Radiology 2: 134 doi:10.4172/2167-7964.1000134

diaphragmatic positioning for IGRT/WART concerning a current linac-based treatment platform, one recently published approach involved the use of a blended MV-kV respiratory motion estimation technique using a computer simulation program. This approach required the implantation into the diaphragm of gold seed markers that were tracked using a shorter duration kV image similar to Cyber Knife stereotactic irradiation along with longer cine-MV imaging to optically track marker positioning. The modeling employed by these investigators clearly demonstrated accurate predicting of marker movements with real-time MV-kV imaging with respect to accurate monitoring of diaphragmatic movement during abdominal irradiation using a step-and-shoot IMRT technique. Furthermore, this approach yielded much less kV exposure to achieve its effect [18].

The overall treatment time of delivering IMRT to any target region has been significantly reduced by the introduction of volumetric arc therapy. One of the first reports to publish on this technique proposed to deliver approximately 33 Gy total dose over 22 total daily fractions to the whole abdomen, which involved a home-grown anatomy-based segmentation tool. However, this initial effort in Whole Abdominal Volumetric Arc Therapy (WAVAT) was limited by the technical limitations of the linac delivery system at that time [19].

Since doses greater than 30 Gy to the upper abdomen and 50 Gy to the lower abdomen/pelvis may be needed to improve control of microscopic/gross residual disease in both endometrial and ovarian cancers, the adaptation of a more recent approach at delivering WAVAT is indicated. The work of Mahantshetty and colleagues has focused on the use of RapidArc, RA for delivery of whole abdominal total dose of 25 Gy in 25 fractions with a simultaneous integrated boost of 45 Gy total dose to the pelvis over the same 25 fractions. These investigators demonstrated that the RA approach that involved two arcs of 360 degrees along with a third arc of 280 degrees (minus the posterior sector) was a superior solution to the delivery of abdominopelvic irradiation as compared to fixed field IMRT, especially concerning reduction of overall treatment time. More importantly, this novel technique of RA provided for more verifiable IGRT monitoring using either 2D planar kV or MV orthogonal real-time imaging [20].

Discussion

Thus, the application of WAVAT, especially using the RA treatment delivery platform, appears to be the most promising advancement for IGRT/WART for selected patients with gynecologic cancers. Continued investigations are indicated to validate this treatment technique under the auspices of appropriate clinical trial frameworks. Once the verification of dose delivery and dose escalation to the abdominal cavity along with demonstration of acceptable chromic toxicities have been conducted, then WAVAT using a RA treatment platform can be pitted against chemotherapy-base treatment regimens in multi-institutional phase III studies to improve the survival and/or quality of life indicators of these patients. Furthermore, the financial impact of WAVAT must be balanced against any possible outcome benefits to ensure appropriate implementation of this technology for selected patient populations.

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