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The use of MRI deformable image registration for CT-based brachytherapy in locally advanced cervical cancer

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ABSTRACT

PURPOSE: Incorporation of MRI into image-based brachytherapy (IBBT) is limited by logistics, reimbursement, and workflow demands. Our goal is to determine if deformable image registration (DIR) using a preimplantation MRI is feasible to construct a high-risk target volume during IBBT.

METHODS AND MATERIALS: From 2010 to 2013, 20 patients were treated with high-dose-rate IBBT for cervical cancer. A preimplantation MRI was fused to the planning CT, and DIR was performed using MIM v6.1. The gross tumor volume (GTV) and high-risk clinical target volume were contoured on the MRI (HR-CTV MRI), and a separate high-risk clinical target volume was made from the deformable image registration of the preimplantation MRI to the planning CT (HR-CTV′). The treated target volume from the planning CT without the DIR or fusion (HR-CTV BT) was compared with the HR-CTV′. The geometric means of the GTV, HR-CTV MRI, HR-CTV′, and HR-CTV BT were analyzed. Statistical analysis using Wilcoxon rank and analysis of variance were performed.

RESULTS: There was a significant larger difference between the GTV and the HR-CTV MRI, HR-CTV′, and HR-CTV BT ($p < 0.0001$). There was also a significant difference between the HR-CTV MRI vs. the HR-CTV BT ($p < 0.040$). There was no significant difference between the HR-CTV MRI and HR-CTV′. DIR was advantageous in the setting of residual disease pre-IBBT.

CONCLUSIONS: DIR is feasible to define an HR-CTV for MRI-guided, CT IBBT. The HR-CTV MRI predicted a smaller treatment volume in comparison with the HR-CTV BT. DIR is limited by patient anatomy and is most beneficial in patients with gross disease. Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Image-based brachytherapy; Cervical cancer; MRI; HDR brachytherapy

Introduction

The use of image-based brachytherapy (IBBT) for cervical cancer is increasing with most centers using CT-based treatment planning. The recent American Brachytherapy Society survey showed that CT-based three-dimensional (3D) planning for cervical brachytherapy is used by most radiation oncologists (55%) in the United States. Two-dimensional (2D) radiograph (43%) and MRI-based (2%) planning represent smaller portions of used dose specification techniques (1). An international practice pattern survey from 2009 also demonstrated a shift with 57% of respondents using CT-based planning and 25% of centers using of MRI, more than half of which obtained an MRI scan before the first treatment fraction (2).

Enhanced image guidance has furthered the field of gynecologic brachytherapy. MRI more appropriately assesses tumor size and shape compared to clinical examination and CT scan for cervical carcinoma (3, 4). The transition from 2D to 3D brachytherapy for locally advanced cervical cancer was one of the major considerations of the GEC-ESTRO Working Group Recommendations, a guideline for image-based definition, assessment, and delineation of gross tumor volume (GTV) and clinical target volume (CTV), beyond traditional approaches of prescribing to Point A (5, 6). The GEC-ESTRO Recommendations have been used in several prospective trials, including a large

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Conflicts of interest: None.

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clinical series that demonstrated improved local control, decreased morbidity, and higher survival rates compared to historical controls which excluded MRI-guided brachytherapy (7, 8). Unfortunately, widespread utilization of MRI-guided cervical brachytherapy is often limited by restricted reimbursements, logistics, and constrained demands on workflow.

Deformable image registration (DIR) is a useful tool for IBBT. Specifically, image sets of a patients anatomy acquired from two separate imaging procedures, and often from different modalities, are transformed into spatial alignment (9). This coregistration allows the radiation oncologist to use information from each scan to evaluate target structures, organs at risk (OARs), and anatomical changes. This can increase radiation therapy accuracy, reduce normal tissue dose, and allow dose escalation (10). Deformable registration is beneficial when matching images of a patient acquired by different imaging technologies because the relative position of the soft tissue anatomy to bony anatomy can change between studies, especially with the presence of a brachytherapy applicator. A multiinstitutional deformable registration study, by Brock *et al.*, analyzed multiple algorithms for accuracy, reproducibility, and computational performance in lung, liver, and prostate. Most deformable registration algorithms performed with acceptable accuracy, showing potential to improve treatment planning and delivery (11).

In an effort to incorporate the benefits of HR-CTV–based volumetric planning with MRI, while recognizing the difficulty of acquiring MRI during a brachytherapy procedure, we explore the utility of DIR. The aim of this work is to evaluate the use of DIR of preimplantation MRI images to intraprocedural CT images for delineation of a validated high-risk target volume for the treatment of locally advanced cervical cancer to achieve CT-planned MRI-guided brachytherapy.

The intent of this study is to contribute to the knowledge base of DIR in gynecologic brachytherapy. Hayashi *et al.* (12) review the role of DIR in obtaining rectal doses for intracavitary brachytherapy, but do not explore the use of DIR for image guidance. Because of the novel nature of the strategy applied in this research, a principle component of this work is demonstrating proof of concept and evaluating the feasibility of CT-planned MR-guided brachytherapy. One specific aspect we address is the limitation of using the available DIR for registering the entire pelvic region. We define an intermediate and integrative high-risk clinical target volume (HR-CTV BT′) by qualitative assessment of the clinical target when transitioning between imaging modalities for the DIR, specifically from MR to CT. It is the authors' hope that in further work using DIR in brachytherapy, there would be less of a need for this qualitative intermediary step, as we encourage and partner with industry to recognize the current limitations of DIR software design, specifically for brachytherapy.

Methods and materials

Patient selection

Locally advanced cervical cancer patients treated with chemoradiation therapy were retrospectively reviewed with the permission of the Institution Review Board. Patients received concurrent weekly cisplatin chemotherapy with external beam pelvic radiation therapy followed by high-dose-rate (HDR) brachytherapy to the cervix. Of the 120 patients reviewed, 20 patients had an MRI performed within 7 days before the first brachytherapy implant from 2010 to 2013.

All patients were treated with a tandem and ring applicator for HDR brachytherapy, receiving a mean dose of 657 cGy (range 550–800) to the high-risk CTV, in a median of four fractions (range 2–5). Planning was performed using 3D CT-based brachytherapy. A high-risk clinical target volume from the planning CT without the DIR or fusion (HR-CTV BT) was defined on the planning CT by a single radiation oncologist at the time of the implantation planning, with this volume determined by the patient's clinical examination, prebrachytherapy MRI, and planning CT. The ^{192}Ir brachytherapy source dwell position and dwell times were specified using a standard loading pattern and then manually optimized for each patient using BrachyVision (Varian, Palo Alto, CA) software. Forward

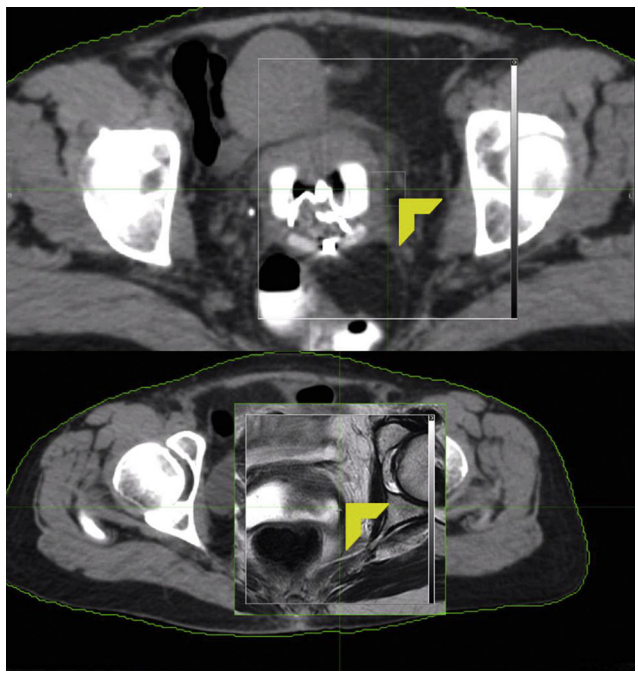

Fig. 1. Visual depiction of the local alignment point selected for image deformation. The *superior arrow* points to the reference point selected on the planning CT, and the *inferior arrow* demonstrates the corresponding point on the registered MRI. The point is near the periphery of the cervix, adjacent to the parametrium. Additionally, the sidewalls of the upper vagina were optimal reference points as a result of the visibility of the vagina on MRI and CT secondary to aqueous vaginal gel and radio-opaque packing, respectively.