Using Digitally Reconstructed Radiographs from MRI (MRI-DRR) to Localize Pelvic Lymph Nodes on 2D X-ray Simulator-Based Brachytherapy Treatment Planning

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ABSTRACT

Purpose: Many of the available brachytherapy treatment planning systems in developing countries are not equipped with CT (or MRI) simulator; therefore, 3D treatment planning cannot be performed. In this project a new procedure has been introduced for utilizing the 2D digitally reconstructed radiograph from MRI images in brachytherapy treatment planning. This procedure enables us to localize the tumor volume and delineate the extent of critical structures in vicinity of tumor volume.

Methods: Pelvic lymph node chain position was delineated from transverse MRI images, and transferred into Digitally Reconstructed Radiograph (DRR) and then onto the X-ray images obtained from conventional simulator unit. These images were then imported to Brachytherapy treatment planning system to evaluate the dose to be applied to these organs in cervix Brachytherapy. The accuracy of the matching process was evaluated by phantom study, having known 3D geometric information and landmark assertion.

Results: The statistical variations obtained from distance mismatch in phantom and patient studies were in the range of clinically applicable error of registration (< 2mm). The results showed a large variation of the nodal dose when dose calculation is performed based on point B dose which is the geometrical reference point for calculating the dose to the pelvic lymphatic system. The result also shows that the dose to point B is usually underestimated to represent external iliac maximum dose, and overestimated for representation of external iliac minimum dose.

Conclusion: The results indicated that the DRR images can produce comparable accuracies in tumor localization reported in 3D MRI or CT based treatment planning procedures. Therefore, this technique could be used as a feasible approach where a 3D treatment planning is not available.

1. Introduction

A typical pathway for spread of cervical cancer is through the pelvic lymph node chain especially external iliac lymph nodes. The treatment of these lymph nodes is typically accomplished through a combination of external beam radiation therapy boosted by intracavitary brachytherapy [1]. Due to rapid dose fall off from an internal source, the accurate delineation of target of interest is essential in brachytherapy system. This is secondary to the fact that many of the available brachytherapy treatment

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planning systems in some developing countries are still based on 2D radiographic images. The limited availability of 3D simulator images, results poor visualization of lymph nodes during treatment planning process.

The objective of treatment planning in cervical brachytherapy is to achieve the maximum uniform dose to the tumor volume, delivering a prescribed dose to the pelvic lymph chain according to the stage of cancer. The best non-surgical method for localizing the positions of the pelvic lymph nodes is lymphangiography which is itself an invasive method for routine use [2]. Alternatively, Ted and Meredith [3] used x-ray radiographs and defined anatomical points A and B relative to an applicator, to estimate doses to the target volume and pelvic lymph nodes, respectively. Point A is regarded as the crossing of uterine artery and urethra, and point B is used as a reference point for the pelvic lymph nodes. Later on, they used an arrangement of various tools (applicator, Tandem, Ovoid) called Manchester system [4] or similarly Fletcher Suit Device. In this system, point A is the major critical point for dose specification in intracavitary brachytherapy and its prescribed dose is offered by the oncologist. This prescribed dose is also intended to guarantee the adequacy of radiation dose delivered to local lymphatic areas. Point B in Manchester frame can be defined on radiographic film to be at a level 2 cm above the flange on the tandem, and 5 cm to the right (BR) or to the left (BL) of mid-sagittal line of the patient. If the applicator is set exactly midline with equal separation between ovoids, dose to BR and BL should be identical.

In the current era of modern treatment planning techniques, the dose definition should be based on delineated tumor volume and anatomical extent of important structures rather than on an arbitrary-point based system which is none-patient-specific. Since accurate anatomical delineation of the lymph node chain can only be obtained by using a 3D image data set such as CT or MR, it is not expected to calculate direct dose to pelvic lymph node chain using a 2D x-ray simulated image as used routinely in some radiotherapy centers. It was shown by the GEC ESTRO working group II [5] that the treatment aims which including target coverage and sparing of organs at risk can be significantly improved, if radiation dose is prescribed to a 3D image-based clinical target volume. Niloy and Christopher [6, 7] showed that in using a 2D planning system, bladder and rectal doses defined by ICRU 38 are significantly underestimated in 90% of bladder cases and 95% of rectal cases. Also they showed that dose prescription based on Point A could lead to uncertainty and mostly dose underestimation to the tumor. Mizoe and Schoeppel [8, 9] similarly demonstrated the dose underestimation to some organs at risk such as bladder and rectum in the Manchester system. Moreover, the only reference point representing the pelvic lymph node chain in a 2D treatment planning based on Manchester system is point B. unfortunately, the position of this point determined based on point A, can itself be uncertain.

The aim of this study is to define a new procedure using DRRs to register 3D imaging system into 2D treatment planning images in order to locate the anatomical regions of interest accurately while the 2D planning system using Manchester apparatus is applied. This helps to evaluate the dose to pelvic lymph node chain and to compare its variation to the dose in point B. The process involves DRR which is a two dimensional image computed from a 3D dataset such as Computed Tomography (CT-DRR) or Magnetic Resonance Imaging (MRI-DRR). DRRs have many applications in diagnosis, radiation treatment and other treatment techniques because it provides anatomical information comparable to x-ray simulator images for radiotherapy applications. Our belief is that this technique can offer an opportunity to fuse anatomical information such as lymph nodes from MRI images to the x-rays simulator radiographs taken when the patient is implanted with the Manchester apparatus. Hence, a more accurate computation of dose to anatomical landmarks can be achieved in 2D brachytherapy treatment planning system. This can provide an increased reliability for delineating anatomical layouts and dose calculations in brachytherapy centers of the developing countries which lack any 3D imaging simulators and 3D simulation system. However, there is a limitation in regard to geometric distortion in MRI which is unavoidable. Fortunately, most of this distortion can be reduced using various MR acquisition parameters and post processing corrections (e.g. bandwidth, phase direction, field map correction, etc).

2. Methods

To use MRI-DRR for localizing pelvic lymph node on x-ray simulator radiographs, we need to take two series of images from the pelvis using 3D MRI scanner and 2D simulator system. Appropriate pulse sequences as routine studies need to be applied in order to visualize pelvic lymph node precisely in MRI. MRI examinations were performed on a 1.5 T Signa GE system (GE Healthcare, USA). Axial and coronal planes were taken using T1-weighted fast spoiled gradient recall acquisition sequence in phantom study and T2 fat saturated sequence for patient study with 2mm slice thickness

without any inter slice gap. Then, an orthogonal set of radiographs was acquired using x-ray simulator unit and entered into the registration process.

The locally developed software was implemented to perform ray tracing through the 3D MR data set considering the same geometric parameters as those in 2D simulator system such as isocenter distance, target skin distance, and patient positioning. DRRs are commonly generated by tracing rays through the volumetric datasets and by integrating the intensity values along these rays.

Our initial task was to reconstruct the DRR from the MRI images most similar to the one obtained from x-ray simulator image. This reconstruction effort is highly dependent on finding the best camera geometry (view point) to produce the DRR with the characteristics most identical to the planar film obtained from the simulator. In this process a large number of DRRs are generated using different viewpoints. Each projection image is then registered to the x-ray simulator image and its mismatch is evaluated. The aim of this registration process is to find the best transformation parameters for transferring anatomical information from MRI-DRR to their corresponding positions on 2D x-ray image.

2.1. Registration Process

DRR reconstruction process is first performed using predefined set of geometric parameters initially used in x-ray simulator unit (e.g. SAD, SSD). In this approach, the first iteration of DRR is started in order to roughly correct the mismatch according to known orientation of the central ray of the Simulator system. For this purpose, initial co-central ray alignment and scaling are performed manually by adjusting appropriate translation, rotation, and scaling parameters predicted from the simulator set up. Then, optimum fine rotation and translation of the DRR is performed in an iterative process, and the mismatch value is evaluated.

The mismatch error is measured according to the distances between some corresponding marker points on the two data sets. Spherical seeds consisting of fatty fluid (E-Zavit from Zahravi pharmaceutical Co, Iran) are good markers which were implanted in specific locations on the patient body surface before the imaging process. In this manner, the geometric coordinates of the corresponding landmarks are taken and Euclidean distances between them are obtained. Then, all distances from all landmark pairs are used to measure their mean square distance value (MSD) as the mismatch error.

In order to transfer anatomical information from MRI-DRR projection to 2D simulator radiograph, the best geometric transformation values obtained at final registration process are used. Consequently, it is possible to localize all critical points such as the lymph nodes or target volume on the x-ray simulator radiograph in routine brachytherapy treatment planning.

2.2. Validation Procedure

Phantom studies were performed to validate our 3D-to-2D image registration algorithm. A cubical shaped phantom with dimensions of $15\times15\times15$ cm^3 was manufactured from PMMA material and filled with water. Spherical seeds consisting of fatty fluid which are visible in both x-ray and MRI were implanted in specific locations inside the cubic phantom in order to resemble the 3D distribution of markers in real cases.

2.3. Patient Study

External markers were used on five patients who underwent cervix brachytherapy. Point based image registration was applied using the algorithm explained above. After attaching external markers, each patient was scanned from the L4-L5 inter-vertebral disc to inferior of the symphis pubis. The axial MRI images were used to define the anatomical contours from internal, external and common iliac vasculature. The iliac vessels are easily visible on axial MRI images. The iliac lymph nodes embrace these vessels. Since the lymph nodes are not easily distinguished from their nearby vessels, the contour of vessels can be used as the location of the lymph node chain (Figure 1).

After Point based 3D-to-2D image registration using the algorithm explained above, the final superimposed image showing both, the reference points (A and B) and contour of iliac vessels, are used for new treatment planning approach (Figure 2). Using this procedure, the dose to the iliac vessels/lymph nodes can be calculated using position of brachytherapy isodose curves in relation to the position of these organs on the final registered image.

In order to use this technique routinely in brachytherapy centers, some technical considerations must be taken into account. We considered the following technical matters in various steps of the process.

Preparation: Attention was given to the selection of anatomical landmarks or fixation of external markers in order to prevent missing them due to dissimilar FOV set up between the two imaging modalities.

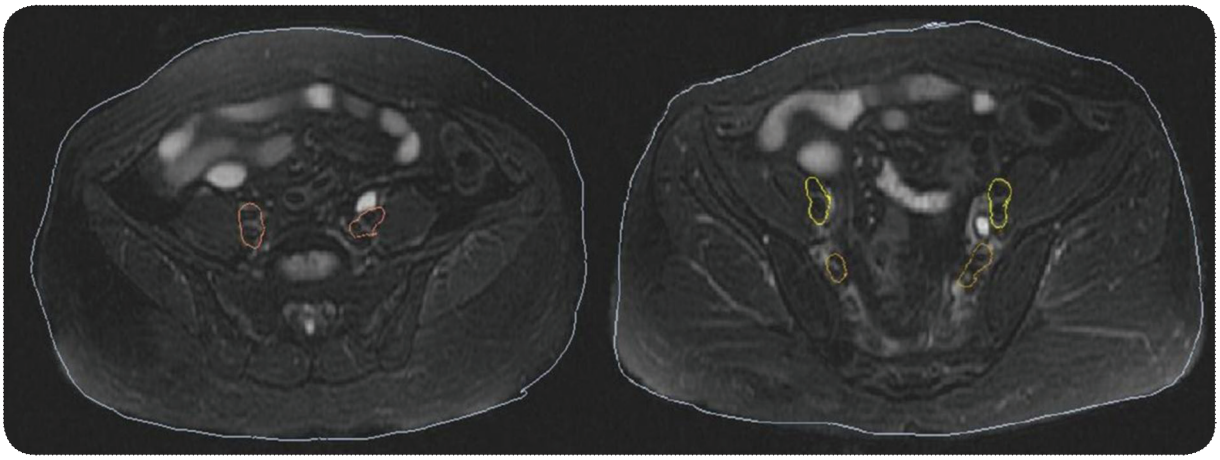

Figure 1. MRI images of iliac vessels acquired immediately before taking the simulation radiograph. (Left) common iliac vessels, (Right) the external and internal iliac vessels.

Imaging system: DRR reconstruction technique can be performed on any 3D image dataset, obtained from MRI or CT scan. Modality selection entirely depends on the accessibility of the systems, and the type of information required for 3D-to-2D registration. However, CT is not capable to delineate lymph nodes very well. In our technique, MRI was used to better visualize the pelvic lymph nodes, and respiratory gating was applied.

DRR Reconstruction: Special attention was paid to apply the same source-detector geometry (e.g. initial transformation parameters) as in x-ray simulator when reconstructing DRR from 3D MR slices.

X-ray Simulation: Minimum possible object-to-film distance was set in order to prevent magnification and, therefore, facilitates registration step.

Registration: The optimum geometric transformation parameters and acceptance criteria were considered based on a clinically acceptable accuracy level. An attention should be taken into consideration during the

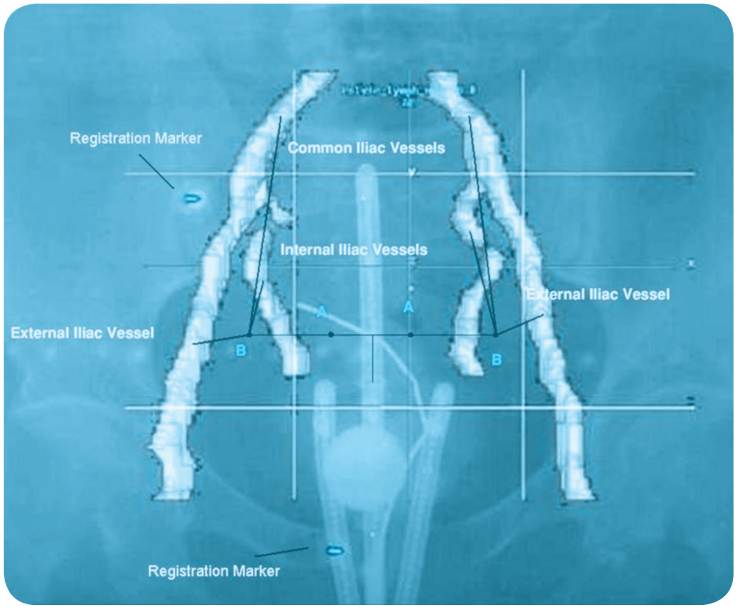

Figure 2. Registration of MRI-DRR of pelvic on simulator radiograph used for treatment planning. This shows position of pelvic lymph node chain. Iliac vessel and point A and B are also shown

registration process when using T1 weighted images. These images are susceptible to chemical shift distortion particularly in fatty fluid markers position. Therefore, an increased RF bandwidth with the minimum possible FOV should be set to minimize this distortion (which can be limited to an order of one millimeter).

3. Results

To investigate the reproducibility of using the DRR procedure, we performed five MRI examinations of phantom at different days and used five simulator radiographs with similar parameters. Their statistical variations obtained from distance mismatch (MSD errors) between all corresponding marker points were then measured. We found a reasonable mismatch error of 1.48±0.13mm with a maximum and minimum value of 1.77mm and 1.32mm respectively.

A comparison of dose at iliac lymph node chains versus point B was performed. Table 1 summarizes these reference point doses on the DRR registered radiographs. These doses were observed using routine treatment planning isodose curve calculation. The results are presented as a percentage of dose rates at point A, in order to make the result less dependent upon the loading differences. Maximum and minimum dose to the internal and external lymph node chain were first obtained, and dose variations in these points were measured between 5 subjects.

As presented in Table 1, maximum and minimum doses of the internal and external iliac lymph nodes show large variation in comparison to point B. Since point B is defined geometrically at a constant distance from the applicator instead of anatomically, the factors affecting this variation may be due to the different source loadings, applicator characteristics, and other physical or geometrical parameters between the patients.

Moreover the large variation of the nodal dose on the left side than on the right is due to a lack of symmetry of the tandem with respect to the patient mid-sagittal causing a higher dose gradient in the left side of the body.

The dose non-uniformity on nodal chain is also confirmed in Figure 3, which shows the pelvic lymph node in one side can receive more doses in relation to the other side.

MSD errors for 3 external markers in five patients was found to be less than 2mm (i.e. 1.61± 0.13 mm). Therefore, a small positional error of about 2 mm can be expected for locating iliac lymph node chain on 2D original x-ray simulator images.

Table 1. Average percentage dose (D) of specific points IImax, IImin, EImax, and EImin (II and EI stand for internal iliac and external iliac, respectively, as shown in Figure 3) and their standard deviation (SD), for 5 subjects. The doses were normalized to the dose in point A (as 100% dose).

Position	Patient's Left Side		Patient's Right Side	
	D (%)	SD (%)	D (%)	SD (%)
II max	45	32	69	29
II min	32	25	42	17
EI max	43	32	38	21
EI min	27.4	13	22	6
Point B	30	4	28.8	2

Patient-to-patient variation of dose to external and internal iliac nodes relative to dose in point B is presented in Figure 4. Large variations of doses are evident in nodal lymph chains when dose calculation is performed based on point B dose from routine 2D planning system. The results also show that the dose to point B usually underestimates the actual external iliac maximum (EImax) dose, and overestimates the external iliac minimum (EImin) dose. In the internal iliac lymph node chain, the results also confirm a large uncertainty in the doses. These dose variations can be due to the position of nodes in a region of large dose gradient, where radiated from internal sources in brachytherapy.

4. Discussion

Using MRI-DRR registered to a 2D x-ray simulation image, we calculated the dose to external and internal iliac nodes. We found that point B does not represent the delivered dose to pelvic lymph node chain very well. It was found that the dose delivered to this point can be only considered as an average dose over all parts of the pelvic lymph node chain. However, this is not acceptable in brachytherapy of cervical carcinoma because, each point of the lymph nodes should receive a minimum required dose. In other words, this point can represent neither the whole chain nor a point with a minimum delivered dose. Nevertheless, using point B has a long history and its use is still being recommended for 2D treatment planning in some brachytherapy centers lacking 3D systems. Since our results indicated that this point cannot be regarded as a good reference point for accurate nodal dose in brachytherapy planning, we proposed incorporating DRR images from 3D MRI in order to overcome the deficiencies in the routine 2D planning systems.

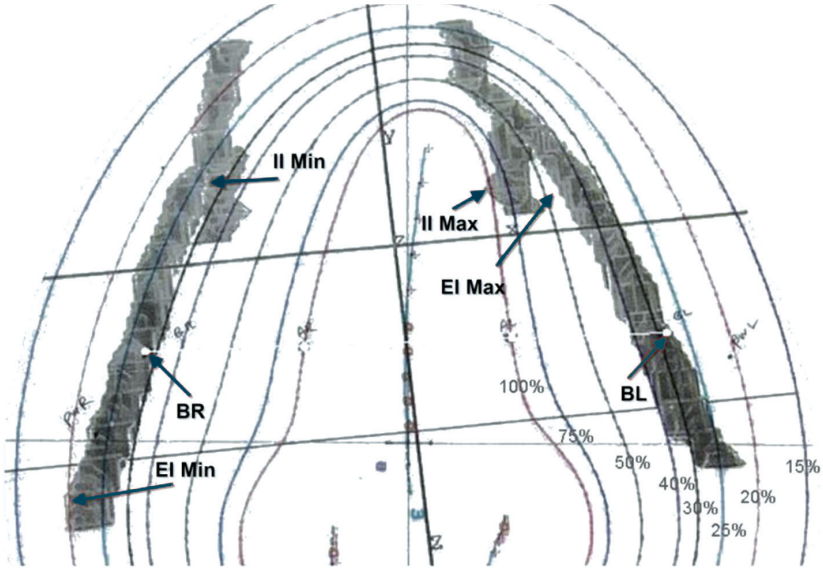

Figure 3. Non-uniformity of dose to the pelvic lymph node in patient's right and left side due to fact that the tandem in the Manchester frame may not be centered about the patient's mid-sagittal line. The percentages of dose in isodose curves in relation to dose at point A are shown. A large variation of percentage doses can be seen along the lymph node chains.

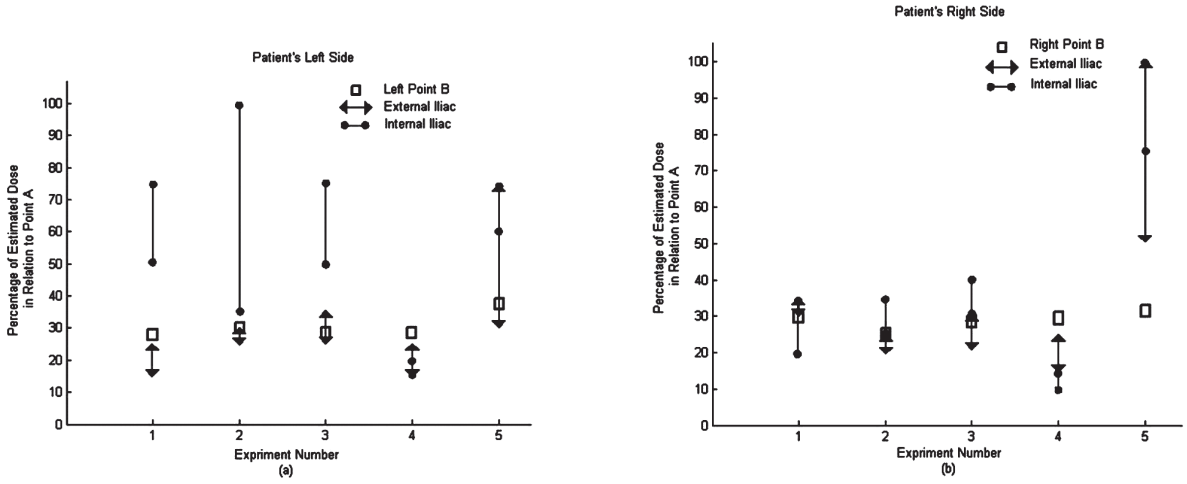

Figure 4. Comparison of the doses in internal and external iliac lymph nodes in relation to the Point B in five subject patients: (a) patient's left side, (b) patient's right side

Gebara W. G. et al. [10] showed the deficiency in calculation of dose to the pelvic lymph node chain based on point B, using CT simulator and 3D planning system. He found that the dose value to this point is different from the minimum dose received by some parts of the chain. He recommended that using a 3D imaging system can help to prevent such deficiencies in dose calculation. Unfortunately, many brachytherapy centers in developing countries are not equipped with CT or MRI simulation technologies, although CT is not fully capable to delineate the lymph nodes. Alternatively, using MRI-DRR based simulation planning as defined in this

study can be useful in such centers. Then, to guarantee sufficient dose delivered to the pelvic chain, one should ensure that a minimum prescribed dose is delivered, either by brachytherapy or external beam radiotherapy.

This study presents the results from dose estimation to the iliac lymph nodes in brachytherapy of cervical carcinoma. This is important, because in routine 2D brachytherapy planning systems, definition of some anatomical target organs (e.g. iliac lymph nodes) are based on the position of reference points which are themselves supported by a flexible apparatus. We investigated the usefulness and reliability of 3D MRI-DRR on both phantom and a number of patients, to overcome the inherent deficiency of planar simulator images for spatial localization. This technique showed promising results in phantom study and worked well for the lymph nodes. However, in order to apply this technique in clinical application, more evidences should be provided to compare this method with delineating the lymph nodes at the time of brachytherapy on MRI or CT as a benchmark study.

To visualize tumor volume and its related target tissues on a 2D treatment planning film, MRI-DRR with beam's eye view similar to that of simulator image was proposed for accurate dose calculation. Chemical shift miss-registration, if applicable, can be calculated and corrected before the registration, and T2 weighted protocol and non-fatty markers can be also considered to reduce this potential shift artifact. Upon obtaining a successful registration between MRI and x-ray simulator image, this method can be used routinely in brachytherapy or any other treatment planning center. Since there is a correlation between dose, disease control, and complication rates in radiation therapy, 3D-to-2D image registration may improve our ability to reduced failure and complications. It is expected that developing and applying this technique in brachytherapy centers, where no 3D planning system is available, would help better dose delivery to the lymph node chain.

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