

## ARTICLE

# The use of MRI in planning radiotherapy for gynaecological tumours

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### Abstract

Parameters that significantly influence results in radiation treatment of gynaecological malignancies are mainly related to the tumour characteristics and the radiotherapy technique used. High-dose radiotherapy requires accurate localisation of the tumour volume and its relationship to surrounding normal tissues. For many years the standard technique used for irradiation of the pelvic area was the four-field box technique which offered the potential benefit of the lateral fields to shield the rectum and small bowel. However, this conventional technique was designed according to bony landmarks and offered limited information regarding the topography of the tumour and the flexion of the uterus which are influenced by the tumour burden and bladder and rectal filling. CT and MRI enable the visualisation of the cervix, uterus, vagina, iliac vessels and organs at risk, but MRI allows tumour depiction in all planes. In the early 1990s, several studies reported on the value of pelvic MRI in designing the lateral fields of the box technique. They demonstrated that conventional lateral portals would have resulted in a marginal tumour miss and incomplete coverage of the uterine fundus in more than 50% of cases, thus leading to the conclusion that if a box technique is used its design should be based on sagittal MRI. CT-based 3D planning systems are now routinely used in the vast majority of radiotherapy departments. Target volumes and organs at risk are delineated by the physician on each CT slice in order to conform the radiotherapy fields to the tumour volume. For several reasons, such as distortion and lack of electron density which is essential for dose calculation, the implementation of MRI into radiation treatment planning has its limitations. However, MRI can still be used if planning systems integrate tools for CT/MR image registration. There is little experience in the literature for gynaecological malignancies demonstrating that image fusion allows an improvement of the definition of the target and the organ at risk compared to CT alone. Only a few papers in the literature report on the use of CT/MR image registration in planning the external irradiation of gynaecological tumours. Most demonstrate feasibility, but they fail to quantify the improvement for volume definition compared to the use of CT alone. Finally, recent possibilities offered by MRI technology are promising in the area of brachytherapy planning as the full potential of individually defining and evaluating GTV and CTV based on tumour extent and anatomical structures is exploited.

**Keywords:** *Cervix carcinoma; 3D conformal technique; brachytherapy; image registration.*

### Introduction

The effectiveness of radiation therapy in the management of cervical cancer of all stages is well established. Radiation therapy usually consists of a combination of

external beam therapy and brachytherapy. At present, radiotherapy is also the only adjuvant treatment that is really effective in improving the results of local control of endometrial carcinoma with poor prognosis factors on surgical specimen. Patients non-operable for

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medical reasons or patients with unresectable cancer are benefiting from radiotherapy alone.

Parameters that significantly influence results in radiation treatment, especially for carcinoma of the cervix, are related to tumour size, tumour extension and the radiotherapy technique used. The endpoint of radiation technique is tumour control obtained with the minimum amount of toxicity. For external beam therapy, the four-field box technique has long been a standard technique. Conventional radiation fields were designed according to bony landmarks. Because of lateral ports, the technique offered the possibility to shield the rectum and small bowel and to reduce the dose to organs at risk. However, without knowledge of the precise tumour volume it was potentially dangerous because of the risk of geographical miss of the tumour. Many observations indicating potential inadequate coverage of tumour volume have been substantiated by investigators using lymphangiography, computed tomography (CT) or magnetic resonance imaging (MRI)<sup>[1-7]</sup>. The aim of this paper is to describe the impact of MRI on the planning of radiotherapy before and after the availability of 3D imaging-based treatment planning systems.

### MRI in planning radiotherapy for patients treated with a conventional four-field box technique

For at least 20 years the most common technique used for irradiation of the whole pelvis was the two-field A-P/P-A approach. The four-field box technique was introduced in the early 1980s with the aim of reducing the treated volume and increasing the dose to the tumour volume. The use of lateral ports allowed the shielding of part of the posterior wall of the rectum, part of the anterior wall of the bladder and some of the small bowel, thus resulting in a significant decrease of the dose administered to these critical organs. Radiographic and anatomical guidelines for definition of the border of A-P/P-A fields were well established. The superior border was usually at the level of the L4 and L5 interspace in order adequately to cover the common iliac node level; the inferior border was defined by the lowest part of the obturator foramen, or with at least a 2 cm margin from the lowest extension of the tumour (Fig. 1). Lateral margins were set 1.5–2 cm from the widest aspect of the bony pelvis; however, in 1993 Pendlebury *et al.* reported, based on lymphangiography examinations, that in 90% of patients a margin of 2.5 cm beyond the pelvic side wall would be required to cover pelvic lymph nodes<sup>[4]</sup>. Conversely, guidelines for the lateral pelvic ports were not always clearly defined and based on bony landmarks that can be identified radiographically. A review of literature that showed the variability of portal arrangements, especially with regard to the posterior border, concluded that standard lateral ports did not

exist<sup>[8-10]</sup>. The commonly used definition of standard field borders for the lateral fields was the anterior aspect of the symphysis and the S2/S3 interspace (Fig. 2). Ports defined by these guidelines appeared to be not always suitable for the individual patient's anatomy. Greer *et al.* concluded, based on intra-operative measurements, that in order to cover the areas at risk, the entire anterior sacral silhouette should be included in the lateral field, owing to a posterior extension of the parametria<sup>[1]</sup>.



Figure 1 Four-field box technique: typical A-P/P-A fields.

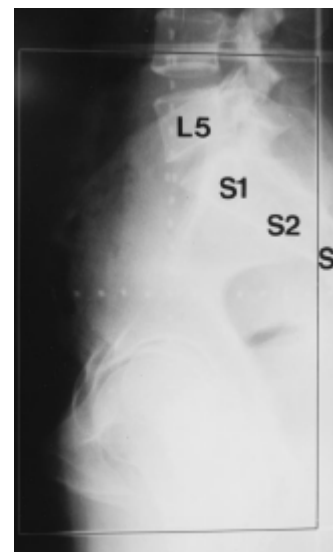
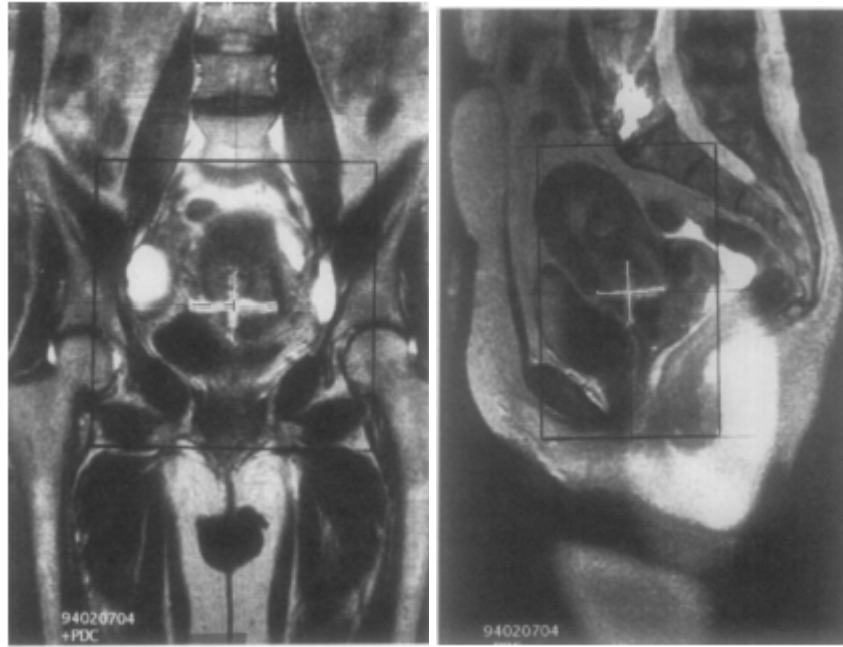


Figure 2 Four-field box technique: typical lateral field.

As high-dose radiotherapy requires accurate localisation of tumour volume and its relationship to surrounding normal tissues, several attempts to improve treatment planning have been made to take into account the individual anatomy of the patient. Conventional radiographic treatment planning with contrast medium in the bladder and rectum offered only limited information regarding the localisation of tumour and uterus. Computed tomography



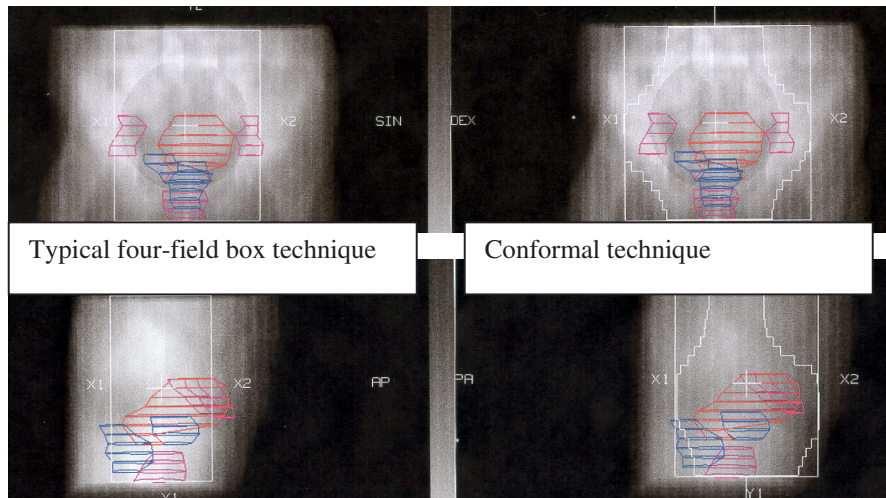
**Figure 3** Anterior and lateral simulated field. Superimposed on mid-coronal and mid-sagittal MRI<sup>[6]</sup>.

section enables the visualisation of the cervix, uterus, vagina, iliac vessels and organs at risk such as bladder, rectum and intestine. Kim *et al.* conducted a prospective study on 34 patients with cervix carcinoma<sup>[2]</sup>. All patients were first simulated for conventional four-field pelvic portals using the standard field limits. Customised blocks were used to spare the posterior half of the rectum and a portion of small bowel using the barium silhouette of those organs. The diagnostic CT was then used to identify the tumour volume on each CT slice. The extension of the tumour volume relative to the central ray on each CT slice was determined and the tumour volume was reconstructed on the simulator films. Finally, measurements from the tumour to the field's borders were taken. All 34 patients had adequate tumour margins on the A-P/P-A portals. In contrast, an inadequate posterior margin that ranged from 39% to 50% was seen. The most common site of inadequate coverage was at the customised rectal block, followed by the posterior border on the lateral fields. With a median follow-up of 36 months, pelvic control for adequate and inadequate margins was 100% and 71% for stage IB, 88% and 50% for stage IIB.

Although all the necessary information was contained in a series of CT scans, this information was difficult to integrate in a three-dimensional space so as to derive the optimum size of the beams. Russell *et al.*, in 1992, reported for the first time on the value of pelvic MRI in designing the lateral fields of the box technique<sup>[5]</sup>. MRI offers the possibility of visualising the anatomy of the pelvis on all planes and enables much better evaluation of soft tissue structures and tumour depiction than CT<sup>[11–16]</sup>. Russell and colleagues found that conventional

lateral portals would have resulted in a marginal miss in more than 50% of patients and incomplete coverage of the uterine fundus in 62.5%. Overall, with standard portals, adequate coverage of the tumour volume was obtained in only 44% of patients. Three more recent studies (Mayr *et al.* in 1993, Thomas *et al.* in 1997 and Zunino *et al.* in 1999) have confirmed these results<sup>[3,6,7]</sup>. Zunino *et al.* found that the borders of the lateral portals failed to involve PTV in over 50% of cases owing to uterus flexion and associated pathology (myoma, endometriosis, pyometra)<sup>[7]</sup>. Thomas *et al.* concluded that diagnostic MRI was a helpful tool for designing the irradiation fields but was not entirely sufficient because it did not fit the special needs of radiotherapy (Fig. 3). In their study, MRI images were also acquired in the treatment position in 39% of patients (flat table, skin marking of radiation ports labelled with MR detectable tubing to access the adequacy of port placement). This dosimetric MRI added new information in the majority of cases meaning that MRI in treatment position alone could assess the simulated fields because it gave a perfect correlation between the morbid anatomy and the simulated fields<sup>[6]</sup>.

According to these series, the modification of normal anatomy caused by tumour mass as well as uterus flexion (observed on MRI) called into doubt the application of a standard four-field irradiation technique based only on references to normal anatomy. The potential benefit of the lateral fields to shield the rectum and small bowel was outweighed by the loss of tumour margins.



**Figure 4** The beam's eye view technique allows the optimal design of individually shaped fields. Uterus in anteфлекed position. Anterior border traverses the uterus fundus.

### MRI in planning radiotherapy for patients treated with 3D conformal radiotherapy

CT-based 3D planning and the use of the beam's eye view (BEV) are now available in the majority of radiotherapy departments. 3D conformal radiotherapy should be considered as the reference technique for irradiation of gynaecological malignancies. Target volumes and organs at risk are delineated by the physician on each CT slice. The gross tumour volume (GTV) includes macroscopic tumour extension whereas the clinical target volume (CTV) includes structures with clinically suspicious but unproven involvement. The planning target volume (PTV) is obtained by adding safety margins to compensate for expected physiologic movements and variation in size, shape and position of the CTV during therapy and to account for uncertainties in patient positioning and beam alignment during treatment delivery<sup>[17]</sup>. The CTV usually includes the GTV + a margin of 0.5 cm, the whole uterus, parametria, part of the vagina according to caudal tumour extension, and regional lymph nodes. The PTV is defined as CTV + 1 cm margin, but in order to take into account the movement of the corpus uteri a 1.5 cm margin in the cranial direction should be considered. The beam's eye view technique enables an accurate visualisation of the topographic relationship of target volumes and organs at risk, defined in the original transverse CT scan, which allows the optimal design of individually shaped fields (Fig. 4). It offers the potential both to avoid geographical misses on the one hand and to reduce the dose to organs at risk on the other. Gerstner *et al.* have shown adequate target volume coverage and in addition a reduction of bladder (up to 34%) and bowel volume (up to 254 cm<sup>3</sup>) receiving more than 70% of the prescribed dose. When replacing the standard portals by BEV-based individually shaped portals a mean reduction

of treated volume (inside 90% isodose) of 7% was observed. In contrast to what was shown for bowel and bladder, however, the rectum volume receiving more than 70% of the prescribed dose increased with the use of the BEV technique, especially in patients with involvement of more than half of the parametria<sup>[18]</sup>.

For several reasons, such as distortions and lack of electron density for dose calculation, the implementation of MRI into radiation planning has its limitations<sup>[19]</sup>. However, MRI can still be used if the planning system integrates tools for CT/MR image registration. CT is essential to ensure a precise calculation of dose distribution since CT gives the electronic density of the tissues. Registration will be usable only if the images from each modality are taken with the patient in the treatment position. When a CT image is registered with an MR image, each image keeps its own properties; the MR image is used for delineation and the calculation can be made on CT. Image registration is also called image fusion by some authors, but this is a misuse of the word as fusion of images is only a way of displaying registered images on a screen. This only allows the acquisition of a single volume of voxels from those of the registered images but this volume is not usable in radiotherapy since it only partially retains the contributions of the CT and MR images. However, it does enable one to draw and save a set of volumes for a precise delineation of the CTV. There is little in the literature on its use in gynaecological malignancies. Percez *et al.* performed an automatic rigid fusion followed by a deformable soft tissue fusion allowing an improvement in the definition of both the target and the organs at risk when compared to CT alone. The automatic fusion was usually achieved in approximately 5 min, providing a high degree of anatomical correlation<sup>[20]</sup>.

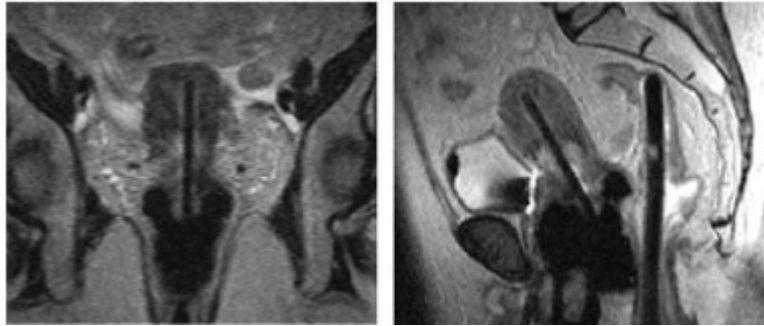


Figure 5 Coronal and sagittal MRI with applicators *in situ* [23].

### MRI in planning radiotherapy for patients treated with brachytherapy

Intracavitary brachytherapy plays a crucial role in the management of invasive cervical cancer or in the management of inoperable endometrial carcinoma. Recently, 3D treatment planning systems have been increasingly used in brachytherapy facilities. CT and/or MRI compatible applicators allow a sectional image-based approach with a better assessment of GTV and definition and delineation of CTV compared to traditional approaches (Fig. 5).

CT-based methods accurately localise intracavitary applicators and demonstrate the 3D anatomical relationship between the applicators and neighbouring structures, thereby obtaining the dose delivered to the tumour volume and surrounding organs. But again, CT images have significant limitations when visualising the tumour volume, especially with regard to the applicator in the vagina.

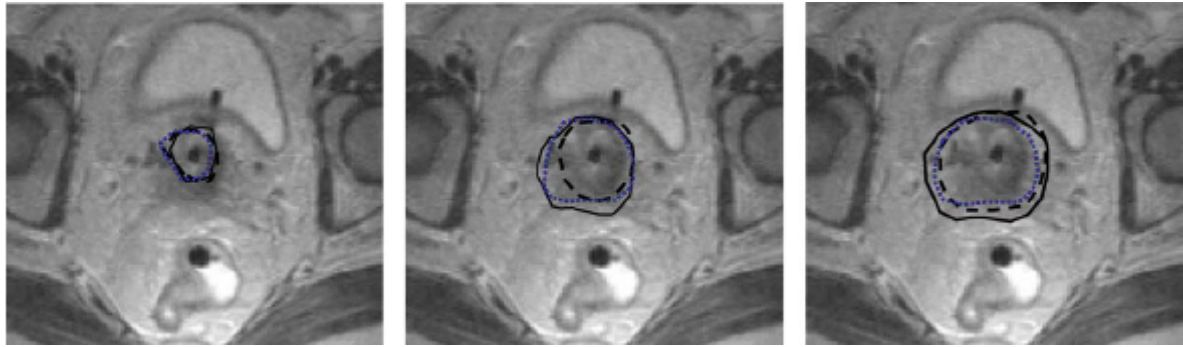
First reports on the use of MR images for brachytherapy treatment planning of cervical cancer were published in 1992 when Schoepfel *et al.* discussed the problem of tumour delineation on MR images after external irradiation [21]. While tumours of the cervix typically demonstrate increased signal intensity on T2-weighted images this can be changed by tumour necrosis, increased oedema and tumour shrinking. MRI, which became available for treatment planning in 1998, was at that time systematically introduced into daily clinical practice in the brachytherapy department of the university hospital of Vienna. From their considerable experience in this area we have learned that MRI provides information for precise topographic definition and delineation of patho-anatomical structures and organs at risk in relation to the applicator in more than 90%. We have also learned that with MRI we are able to visualise the tumour volume covered insufficiently by the dose distribution much better than with CT [22].

During the last 5 years, concepts and parameters have been prospectively developed for brachytherapy treatment planning. Because MRI provides superior soft tissue resolution compared to CT and because

electron density does not play a role in dose calculation in brachytherapy, the Gynaecological (GYN) GEC-ESTRO Working Group and the American Image-Guided Brachytherapy Working Group have proposed that T2-weighted MRI be used for imaging using a pelvic surface coil with image-compatible brachytherapy applicators in place for cervical implants. Since 2000, these two groups have been working on recommendations for recording and reporting 3D image-based brachytherapy (BT) for cervical cancer [23,24]. The recommendations on definition and delineation of GTV and CTV are based on clinical experience and different dosimetric concepts. Development of 3D image-based treatment planning includes a comprehensive approach with systematic description of GTV and topography at diagnosis and at time of BT, taking into account its evolution over time. The full potential of individually defining and evaluating CTV based on tumour extent and anatomical structures has been exploited. According to the GYN ESTRO Group the GTV for BT (GTVB) includes macroscopic tumour extension at the time of BT as detected by clinical examination and as visualised on MRI (high signal intensity mass(es) (FSE, T2) in cervix/corpus, parametria, vagina, bladder and rectum). High-risk CTV for BT (HR CTV) carrying a high tumour load includes GTVB, always the whole cervix, and the presumed extracervical tumour extension at the time of BT defined by means of clinical examination (visualisation and palpation) and/or residual grey zones in parametria, uterine corpus, vagina or rectum and bladder on MRI. No safety margins are added. Intermediate-risk CTV for BT (IR CTV) carrying a significant microscopic tumour load encompasses HR CTV with a safety margin of 5–15 mm (Fig. 6). The amount of the safety margin is chosen according to tumour size and location, potential tumour spread, tumour regression and treatment strategy [23].

### Conclusion

In the light of present knowledge, individual 3D imaging-based treatment planning for gynaecological malignancies is necessary to avoid geographical misses.



**Figure 6** Example of delineation for GTV (left), HR CTV (middle) and IR CTV (right)<sup>[23]</sup>.

In 2006, there is no getting away from CT planning as CT gives the electronic density of the tissues, which is essential to ensure a precise calculation of dose distribution. Beam's eye view-based 3D treatment planning for external beam therapy enables a reduction of bowel and bladder volumes receiving more than 70% of the prescribed dose and, additionally, an adequate coverage of the planning target volume. The use of MRI, which provides us with direct and accurate images of tumours, taking into account the real spatial relationship between tumour and normal anatomy, undoubtedly improves the accuracy of the drawing of the CTV. At the very least, diagnostic MRI should be systematically used, but dosimetric MRI in the treatment position adds more accurate information. Therefore, the process of CT-MRI image registration should be more widely used. Recent possibilities offered by MRI technology are promising in the area of brachytherapy planning as the full potential of individually defining and evaluating CTV based on tumour extent and anatomical structures is exploited.

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