A novel technique with a flexible applicator for MRI-based brachytherapy of cervical cancer

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Summary

Purpose: To introduce a novel technique for magnetic resonance (MR)-based 3-dimensional planned high-dose rate intracervical brachytherapy (BT).

Materials and methods: During 2002, 16 patients received external beam radiotherapy and BT as part of radiochemotherapy for cervical cancer. A special adjustable applicator device was designed and used for BT. The isodose distribution was calculated from MR images with the applicator in place.

Results: The planning target volume coverage was adequate and the radiation burden on the organs at risk was within acceptable limits. Complete regression was achieved in two patients (12.5%), and partial regression in ten (62.5%) patients. The overall response rate for the complex treatment was 93.75%. In three cases the disease was considered to be stable.

Conclusion: The MR-compatible, flexible applicator allows safe and reproducible cervical radiotherapy with no added discomfort or hazard for the patient.

Key words: Cervix; Adjustable applicator; Dose distribution.

Introduction

In advanced, surgically inoperable cases, the treatment of cervical cancer is based on a combination of external beam radiotherapy (EBRT) and brachytherapy (BT) with concomitant chemotherapy. Considerable problems may arise because of the potential underdosage of the tumorous tissue resulting in a poor treatment outcome. At the same time, the overdosage of normal tissues has resulted in a substantial rate (up to 20%) of grade 3-4 sequelae [1].

The inherent positional uncertainties and inhomogeneous dose distribution in BT pose dosimetric problems. The optimal imaging modalities, treatment technique and device still remain to be attained. The latter should satisfy many criteria, e.g. the possibility of multiple, exact positioning in terms of volumetric dose distribution and reproducibility; the avoidance of perforation or a massive bleeding risk; an improvement in patient convenience; applicability for a cervix narrowed by the tumor mass; compatibility for the magnetic resonance imaging (MRI) and visibility on MRI, computed tomography (CT), ultrasonography (US) and X-ray imaging. This communication describes an adjustable applicator device that complies with the above criteria, and reports the early experience with this treatment technique.

Materials and Methods

Patients

During 2002, 16 patients received concomitant radiochemotherapy as standard treatment for FIGO Stage IIB-IVA squamous cell cervical carcinoma. The mean age of the patients was 51 years (range: 36-69 years). Chemotherapy was applied on a standard cisplatin-based protocol once weekly during EBRT.

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External beam radiotherapy

Therapy was started with a four-field box technique of EBRT on a Mevatron Primus 15 MV linear accelerator (Siemens, Erlangen, Germany). CT-based three-dimensional (3D) treatment planning was performed after body fixation with a thermoplastic mask. A median dose of 50.6 (range: 50-54) Gy was delivered to the initial planning target volume (PTV1) in 26 (range: 25-28) fractions with a median fraction dose of 1.96 (range: 1.8-2) Gy (Figure 1). PTV1 consisted of the gross tumor volume (GTV), the uterus, the parametria, the internal and common iliac lymph nodes and the whole of the vagina.

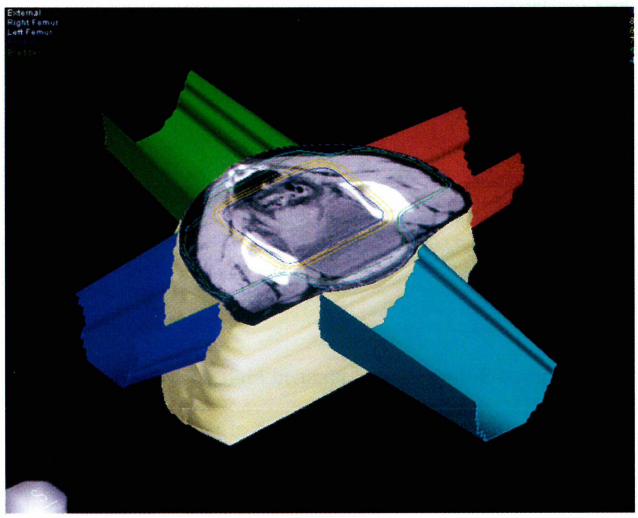
The volume of the boost radiotherapy (PTV1-boost) was determined on the basis of a control CT examination. PTV1-boost was always smaller than PTV1, and included GTV and the involved part of the parametria. The boost was delivered with a median dose of 9 Gy (range: 7.2-14.4), in 5 fractions (range: 4-8) with a fraction dose of 1.8 Gy. The organs at risk (OARs) taken into consideration were the intestinal tract (especially the sigmoid and the rectum) and the bladder.

Insertion of the brachytherapeutic applicator

Following the EBRT, a flexible 5 F (1.65 mm) interstitial cervical applicator (Cook® BFCS-6.OR-30-STB-25, Bloomington, USA) (Figure 2) was inserted without dilatation under local anesthesia in the Department of Gynecology and Obstetrics, Kaposvár. Its accurate position was maintained under visual, fluoroscopy and extracorporal US control. After insertion, the flexible applicator was fixed into the cervix for the whole period of the BT with a surgical suture.

The vaginal part of the applicator device (Figure 2) consists of a cylindrical holder with one central and four circumferential channels for the flexible applicators. Inserted through the central channel on the previously fixed flexible applicator, the vaginal holder was positioned only for non-barrel-shaped tumors, or when residual parametrial involvement was presumed from gynecological or CT examinations.

Fig. 1a



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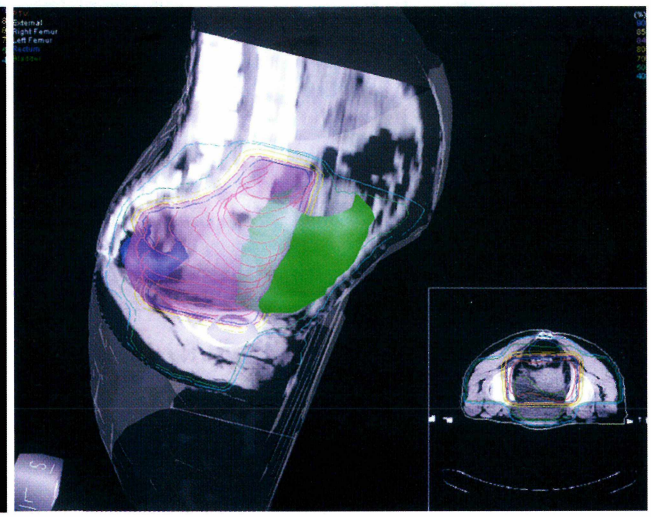


Fig. 1c

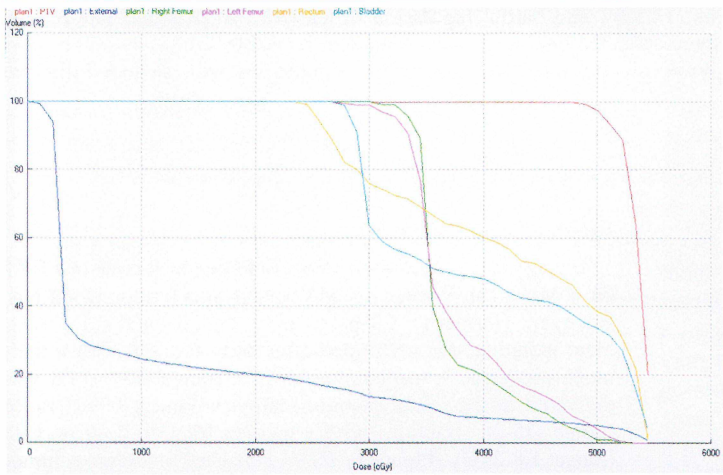


Figure 1. — CT-based 3D-treatment plan. (a) Axial view with the isodoses and the entering beam projections. (b) PTV1 (red lines), and the OARs; the rectum and the bladder (respectively, blue and green solid surface) are presented with the isodose coverage (transparent violet) on a sagitally and axially opened 3D reconstruction. (c) Dose-volume histograms; red line - PTV1; yellow – rectum; light-blue – bladder; green - right femur head; violet - left femur head; blue - skin surface.

Figure 2. — Applicators for cervical HDR BT. (a) The flexible instrument and a standard cervical applicator. (b) The vaginal cylinder holder of the device with four circumferential channels positioned on the cervical applicator through the central channel.

Fig. 2a

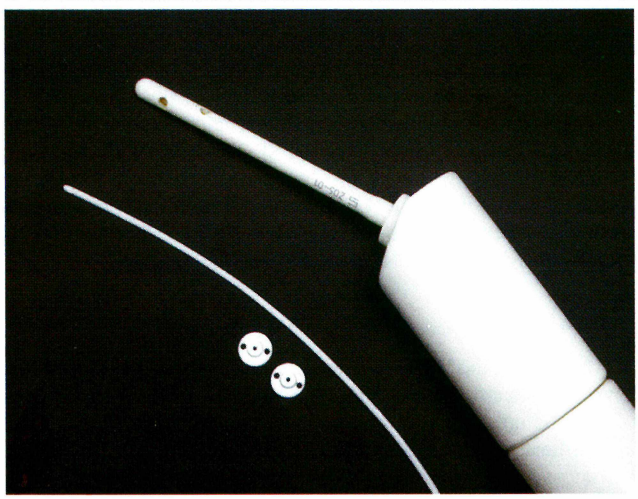
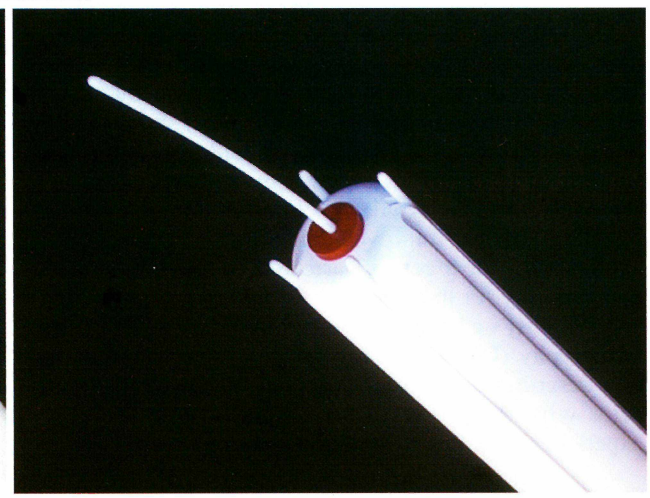


Fig.



Brachytherapy planning and implementation

T2-weighted pelvic MRI was carried out in the axial and sagittal planes with the patient and the adjustable applicator in the treatment position. For a better evaluation and orientation in BT planning, volumetric 3D reconstruction of the anatomical structures was taken into consideration before the irradiation plan was accepted (Figure 3). DICOM-compatible sequential MR images were used to delineate PTV for the BT (PTV2) and the OARs in all planes. The PTV2 was identical with the MRI-defined GTV.

A conformal BT plan was calculated with the Abacus™ dose-planning system (MDS Nordion®, Quebec, Canada). The generated isodose lines and PTV2 contours were overlaid for each axial MR image and were also reconstructed in the sagittal and coronal views to visualize the 3D coverage (Figure 4). Dose adaptation to PTV2 was based on the volumetric measurements for GTV and the critical organs. The limits defined for the OARs (rectum and bladder) were 4 Gy per fraction for tissue volumes of 2 and 4 cm^3, respectively.

g. 3a

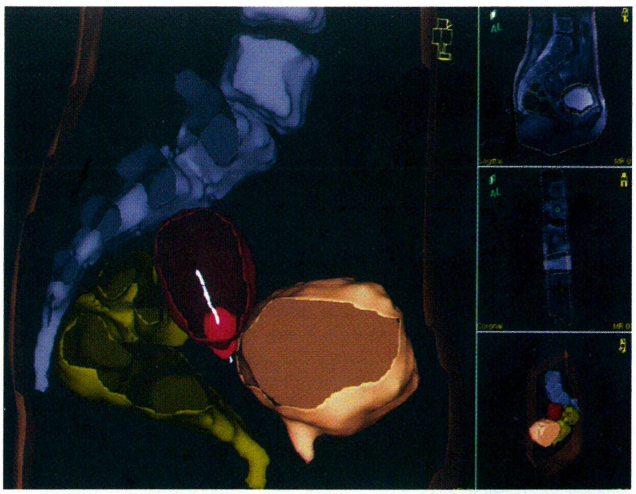
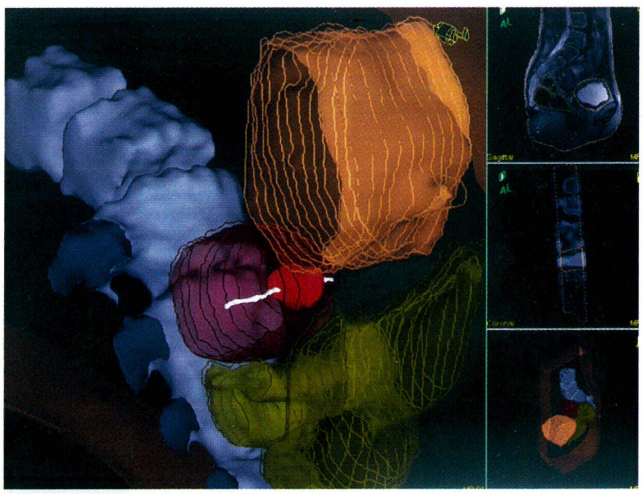
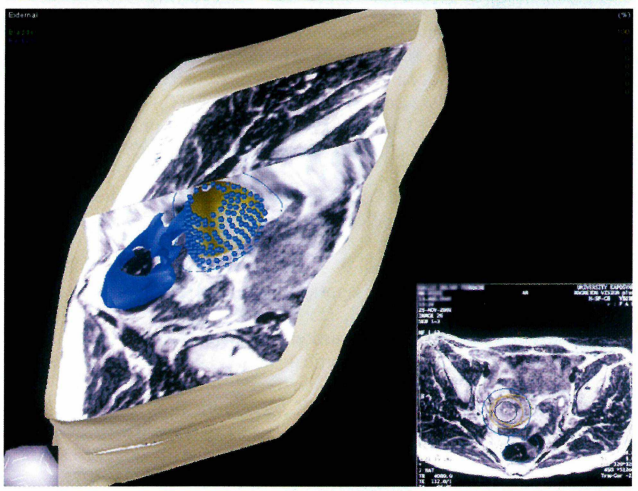


Fig. 3b



g. 4a



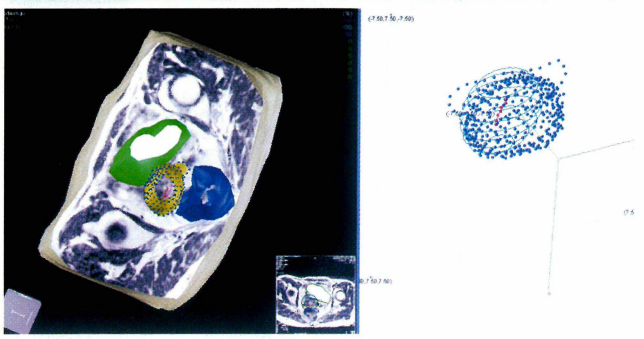


Fig. 4b

Figure 3. — 3D volume-rendering reconstruction of the treatment site. (a) The applicator (white), the PTV2 (red), the uterus and the OARs; the rectum and the bladder (respectively, dark-red, yellow and beige), and the spinal column (gray) are presented. (b) Rotation and different modes of windowing facilitate better visualization of the relationship between the structures and the applicator position and volume.

Figure 4. — MRI-based conformal HDR BT plan. (a) MR image with the applicator in treatment position and the prescribed dose. Delineation of PTV2 (beige) and the OARs; the rectum and the bladder (respectively, blue and green solid surface) on the sectional images are imported directly into the treatment planning system, and the dose-volume association is evaluated. (b) 3D volumetric representation of the dwell positions for the ^{192}Ir source (red dots), PTV2 (GTV), the OARs and the isodose coverage (blue dots).

High dose rate (HDR) intracavital BT was carried out with a GammaMedplus™ after-loading machine (Varian Medical Systems Inc. Palo Alto, USA), with ^{192}Ir stepping sources in 3 fractions, twice weekly, with a total dose of 12 Gy prescribed to ≥ 90% of PTV2 (Figure 4).

Evaluation

As primary end-points, the coverage of the PTVs, the dose to the OARs, the acute toxicity and the local tumor control were evaluated. Acute toxicity was graded on the basis of Common Toxicity Criteria Version 2.0 (NCI CTC). The overall response was determined according to the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines [2].

Results

The treatment proved feasible and was tolerated well by all patients. The PTV1, PTV1-boost and PTV2 median coverage was 97.4%, 98.8% and 93.2%, respectively. The prescribed total dose, calculated from the parameters of the two irradiation modalities was received by 17.7% and 13.3% of the total volume of the OARs' (the rectum and the bladder respectively). Thus, both the coverage of the PTVs and the radiation burden on the OARs were within acceptable limits.

Grade 1 diarrhea (with occasional abdominal pain) occurred in six patients (36%) during the fourth week of EBRT. Following a decrease of the daily dose and strict adherence to the proposed diet, the clinical signs had disappeared by the first week after completion of the irradiation. Bladder complications were less frequent (3 patients, 18%), but more severe (grade 2; acute sterile cystitis with bladder spasm) in the last week of the EBRT. Antibiotics, antispasmolytic treatment and an extensive daily fluid intake led to normalization of the patients' conditions. Insertional or acute complications related to BT were not observed.

In accordance with the RECIST guidelines, the overall response to the complex oncological treatment was identical with the response of the target lesion. Complete regression was attained in two patients (12.5%), and partial

regression in ten patients (62.5%). The overall response rate for the complex treatment was 93.75%. In three cases (18.75%) the disease was regarded as stable, and one (6.25%) patient displayed progression of the disease.

Discussion

The most frequent criticism of BT relates to inaccurate doses in the PTV as a result of difficulties in correct *positioning and repositioning* of the applicator within the cervical and vaginal lumens. The commercially available applicators used for the treatment of cervical cancer are rigid and from a physical point of view function like "second-order levers". Movement of the proximal end causes an indefinable trajectory of the short arm of the lever and has an unpredictable mechanical effect on the tumor structure. The proposed technique, with a flexible, adjustable cervical applicator and the single stable positioning, overcomes the mentioned problems and improves patient convenience during BT.

The presented technique also gives an opportunity for the *conversion of intracavitary BT to intersititial BT* by means of a simple change of the applicators located in the adjustable vaginal cylinder holder to plastic needles. This may be of appreciable importance in patients with disease that can not be optimally encompassed by intracavitary BT [3].

A further advantage for both patient and physician is the use of *local anesthesia instead* of the general anesthesia required with rigid applicators, with a resultant lowering of the rate of complications associated with the insertion. The standard rigid intracavitary applicators demand dilatation up to Hegar 6-7. As the outer *diameter* of the flexible applicator used is 1.65 mm, dilatation is not required. The single insertion of a thin applicator involves a lower *risk of infection, perforation and bleeding*, as compared with the multiple, extensive insertion of a large device.

Misplacement of the cervical applicator can be lowered significantly by US guidance during insertion [4] especially when the applicator is thin and flexible. In order to avoid direct contact with the fundus wall, it must be at least 1-1.5 cm shorter than the cavity length and still cover the total length of the tumor. With our novel approach, the length of the intracervical applicator is adjustable and *the cavity is visualized* during and after applicator insertion.

Over and above the undisputable diagnostic role of MRI in staging, restaging and therapy monitoring in cervical cancer *MRI* is being increasingly *utilized in radiation therapy.* MRI data are extensively used for gynecological EBRT [5-11], whereas data relating to conformal MRI-based BT with the applicator in situ are scarcely to be found [12-15]. For BT planning, *we applied MR images to delineate the OARs and the PTV2.* MRI high spatial resolution in soft tissue is essential in controlling the relationship between tumor and applicator. Moreover, the treatment planning too was facilitated, since the radiation dose to the PTVs and OARs could be calculated accurately, which allowed more efficient tumor treatment, with maximal protection of the normal tissues.

To summarize, the MRI-compatible, flexible applicator and novel technique reported here allow efficient MRI-based treatment planning and convenient, safe and reproducible cervical BT. This technique may also be suitable for other intraluminal applications, e.g. endometrial, bile and pancreatic duct, and ureteral tumor treatment.

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