Brachytherapy Treatment Planning for Cervical Cancer Patients Using a Lower Magnetic Field MR Scanner

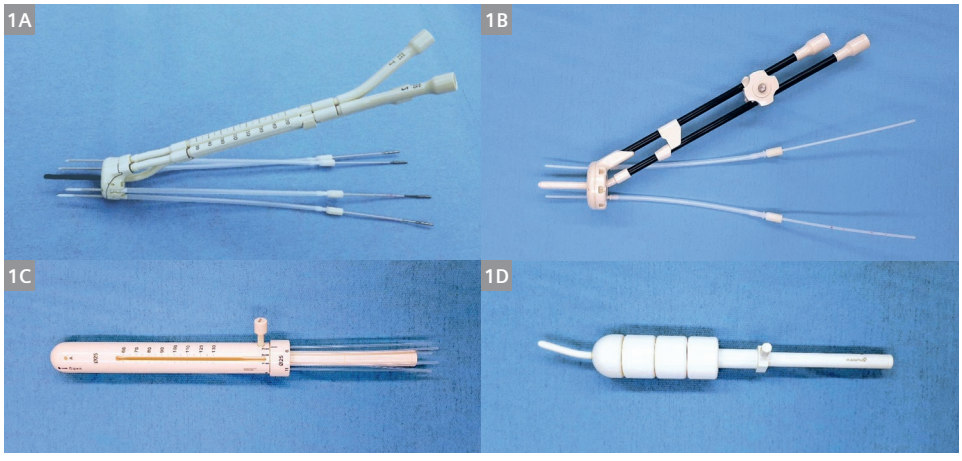
Tibor Major[1,2,3]; Júlia Vizkeleti[1]; Péter Ágoston[1,2]; Zoltán Takácsi-Nagy[1,2,3]; Csaba Polgár[1,2,3]

[1]Radiotherapy Centre, National Institute of Oncology, Budapest, Hungary
[2]Department of Oncology, Semmelweis University, Budapest, Hungary
[3]National Institute of Oncology and National Tumor Biology Laboratory, Budapest, Hungary

Introduction

Brachytherapy (BT) has long been used successfully in the treatment of various cancers, with excellent clinical results. Although its use has recently declined, its favorable dosimetric properties make it a successful alternative to high-tech external-beam radiotherapy (EBRT) [1]. For BT, the most common treatment sites are the gynecological cancers. Currently, delivering a radiation boost with BT after EBRT is considered mandatory for the treatment of locally advanced cervical cancer. MRI is the method of choice for BT treatment planning, but due to the limited availability of MR scanners, CT is still the main imaging modality for treatment planning. However, MRI is superior to CT imaging in many respects, especially because of its better soft-tissue visualization [2, 3]. Currently, image-guided adaptive brachytherapy (IGABT) is considered state-of-the-art treatment for cervical cancer patients, with excellent clinical outcomes [4, 5]. For cervical cancer, pre-treatment MRI without an applicator can help to determine the size of tumor shrinkage after EBRT and to define BT target volume on CT images depending on the disease stage. However, MRI with an applicator in place is recommended for optimal BT treatment planning [6]. There is growing clinical evidence that IGABT not only leads to improved clinical outcomes, but also to a reduction in treatment-related morbidity [4]. Combined intracavitary/interstitial brachytherapy provides excellent local control and overall survival rates, with acceptable toxicity [7].

The MAGNETOM Free.Max (Siemens Shenzhen Magnetic Resonance Ltd., Shenzhen, China) MR scanner has a field strength of 0.55 Tesla and is supported by deep learning software technologies and advanced image processing. It offers a number of advantages for treatment planning in radiation oncology. The 80 cm wide patient bore is useful for scanning extremely obese and claustrophobic patients, and is especially beneficial when planning brachytherapy for gynecological cancer patients. The large aperture allows the use of a leg support system during imaging, which provides the same patient positioning as during applicator insertion and dose delivery. The scanner is very compact, takes up little space, and requires only 0.7 liters of liquid helium without a quench pipe.



1 MR-compatible GYN applicators: Advanced Gynecological Applicator-Venezia **(1A)**, Interstitial Ring CT/MR Applicator **(1B)**, Vaginal CT/MR Multi Channel Applicator **(1C)**, Vaginal CT/MR Applicator **(1D)**.

The National Institute of Oncology in Budapest is the only comprehensive cancer center (CCC) in Hungary to be accredited by the Organisation of European Cancer Institutes (OECI). The institute's Radiotherapy Centre has seven linear accelerators: two TrueBeam, two VitalBeam, one Unique, one Ethos (Varian, A Siemens Healthineers Company, Palo Alto, CA, USA), and one CyberKnife (Accuray, Sunnyvale, CA, USA). In EBRT, the majority of patients are treated with intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT with RapidArc, Varian, A Siemens Healthineers Company, Palo Alto, CA, USA), in combination with image-guided radiotherapy (IGRT). In 2022, a special treatment, adaptive radiotherapy (ART), was introduced using the Ethos system. Stereotactic radiosurgery (SRS), and in most cases stereotactic body radiotherapy (SBRT), is performed with the CyberKnife. Small tumors of the lung or pelvic region are treated with the Synchrony system (Accuray, Sunnyvale, CA, USA) using a tracking method. A SOMATOM go.Sim (Siemens Healthineers, Forchheim, Germany) and an Optima CT 580 (GE HealthCare, Chicago, IL, USA) CT simulator are used for treatment planning. Our center treats nearly 6,000 patients with EBRT every year.

We also have an active BT program. Patients are treated with a Flexitron high-dose-rate (HDR) afterloader (Elekta Brachytherapy, Veenendaal, The Netherlands). The most common tumor site is gynecological (GYN) cancer, but prostate, breast, head and neck, bronchus, and esophageal cancers are also treated. We also perform permanent seed implantation with I-125 isotopes for prostate cancer. At our center, the number of patients treated with BT is around 330 per year, with more than 1,000 fractions. For treatment planning, we use the SOMATOM go.Sim CT simulator, and an ultrasound system (BK Medical, a GE HealthCare company, Harlev, Denmark) for prostate BT. Recently, two new imaging devices have become available to us: an ImagingRing (Elekta Brachytherapy, Veenendaal, The Netherlands) that uses X-ray with a cone beam CT (CBCT) option, and a MAGNETOM Free.Max 0.55T MR scanner. The ImagingRing is located in the BT treatment room and the MR scanner is very close to the BT suite. A few years ago, we started 3D treatment planning for GYN BT using a CT simulator and have since gained a lot of experience. We are now exploring how we can effectively introduce the two new imaging modalities into our BT workflow.

In this paper, we present our preliminary experience with the MAGNETOM Free.Max MR scanner, which is used to plan BT treatments for cervical cancer.

Clinical application

In the radiotherapy management of patients with cervical cancer, MR imaging after EBRT helps to determine the extent and topography of the tumor and the extent of its shrinkage, even if the treatment planning is CT-based [8]. For CT-based planning, we also routinely applied this method by visually comparing MR and CT images side by side. Although MR-based BT is considered the gold standard treatment modality, post-implant MR imaging with the inserted applicator is not available in many centers. The best results, however, can be expected with true MR-based planning, when imaging is performed after the applicator/needles are implanted. With the installation of the MAGNETOM Free.Max in our center, we were able to start MR-based BT planning for cervical cancer. In some cases, patients underwent parallel CT and MR imaging, and the two image series were coregistered. The advantage of this technique is that the reconstruction of the applicator can be performed more accurately on CT images, while MR images are better for delineating the target volume and organs at risk (OAR). However, in our experience, the uncertainty of image fusion can be as large as the uncertainty of the reconstruction of the applicator in MR images. Furthermore, any additional imaging is logistically challenging and requires extra time, including image registration. Because of these difficulties, we started using only MR images for treatment planning.

In external beam radiotherapy, MR images are mainly used to determine the target volume, while CT images are used for dose calculation. This requires coregistration of MR images and CT scans. In brachytherapy, however, MR images alone can be used for treatment planning, as the commonly used TG 43 dose calculation algorithm does not take tissue inhomogeneities into account [9]. Dose distribution is always calculated in water, and MR imaging is only used for tissue segmentation, target volume determination, and reconstruction of applicators/catheters/needles. This geometrical information must be accurate, because small inaccuracies can cause large dose differences. The main factor in determining the dose distribution around a BT source is the distance measured from the source (inverse square law).

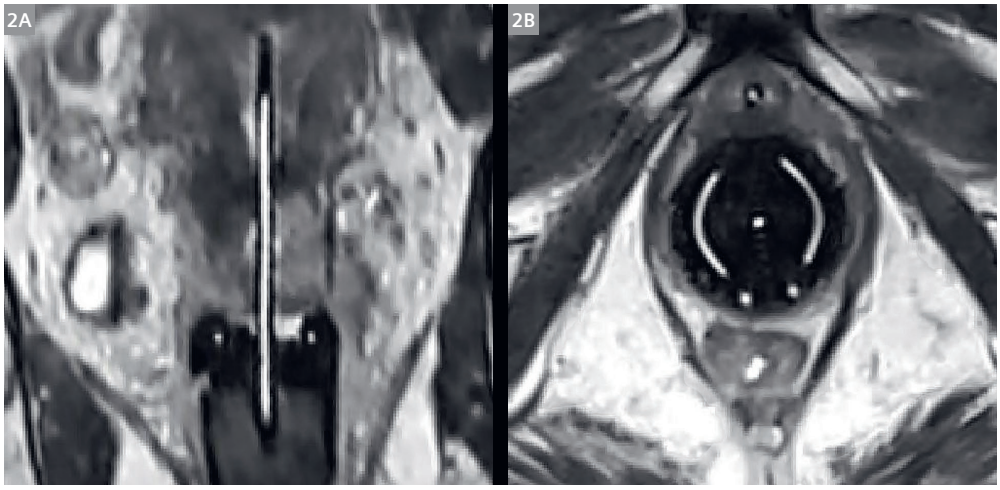
Brachytherapy applicators for the treatment of cervical cancer

The standard GYN BT applicators are made of steel for long-lasting use thanks to their rigidity and mechanical strength. They can be used for CT-based planning with small artifacts, but MR imaging requires MR-compatible applicators made of plastic or titanium [10]. We have four types of non-metallic MR-safe applicators: Advanced Gynecological Applicator-Venezia, Interstitial Ring CT/MR Applicator, Vaginal CT/MR Multi Channel Applicator, Vaginal CT/MR Applicator (Elekta Brachytherapy, Veenendaal, The Netherlands) (Fig. 1). For small tumors, it is sufficient to use only an intracavitary applicator. For larger, irregular

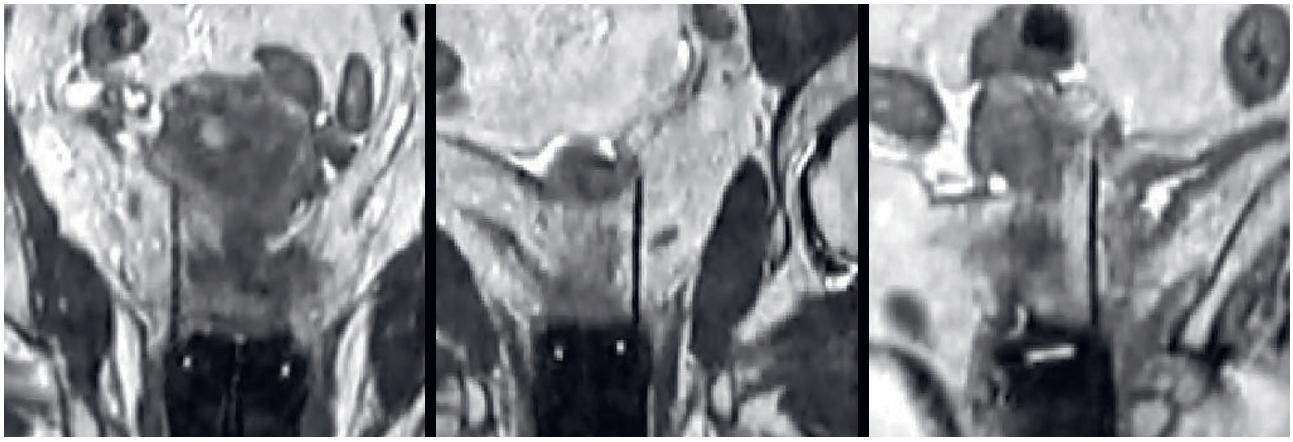
tumors with parametrium infiltration, however, intracavitary and interstitial techniques should be combined. With the Venezia and Ring applicators, plastic needles (ProGuide Needles, Merit Medical Systems, South Jordan, UT, USA) with a rigid tungsten alloy obturator can be inserted peripherally through the ovoids. The number of needles and their locations depend on the laterality and extent of the tumor. The insertion of the applicator/needles is performed in the BT suite, and the patient is then transferred to the MR scanner using a T-180 MR Trolley (Troyka Med Inc., Ankara, Turkey).

MR imaging and treatment planning

Fifteen minutes before the applicator insertion, 1 mL of Buscopan (hyoscine butylbromide) is given intravascularly to the patient to reduce bowel motility during imaging. As the MR table does not have a leg support, the patient's legs are lowered and placed on a knee support. Note that the same patient position is maintained during irradiation. To achieve a better signal-to-noise ratio, a pelvic surface coil is wrapped around the pelvis. To improve the visibility of the applicator, MR line markers are placed in the central and two lateral ovoid tubes (Fig. 2). The needles do not have an MR marker and are therefore empty, so without signal the air makes them visible (negative contrast) (Fig. 3). Any arbitrary oblique plane can be created in the treatment planning system by selecting a special coordinate system. By rotating the coordinate system axis, the needles can be displayed in the plane parallel to them. This technique helps to easily reconstruct the needles. Following the recommendations of the GEC-ESTRO GYN Working Group, T2-weighted images are acquired in a para-axial (perpendicular to the long axis of the cervical canal) and a sagittal (parallel to the long axis of the cervical canal) slice orientation [11]. No contrast media is used. After the images are exported to the Oncentra Brachy planning system (Elekta Brachytherapy, Veenendaal, The Netherlands), the treating physician outlines the bladder, rectum, sigmoid colon, and intestines as OAR, the high-risk clinical target volume (HR-CTV), and sometimes the gross tumor volume (GTV) [12]. The physicist then reconstructs the applicator and the needles, if relevant. For an intracavitary applicator



2 MR line markers inserted into a Venezia applicator, in an intrauterine tube **(2A)** and in two lateral ovoid tubes **(2B)**.



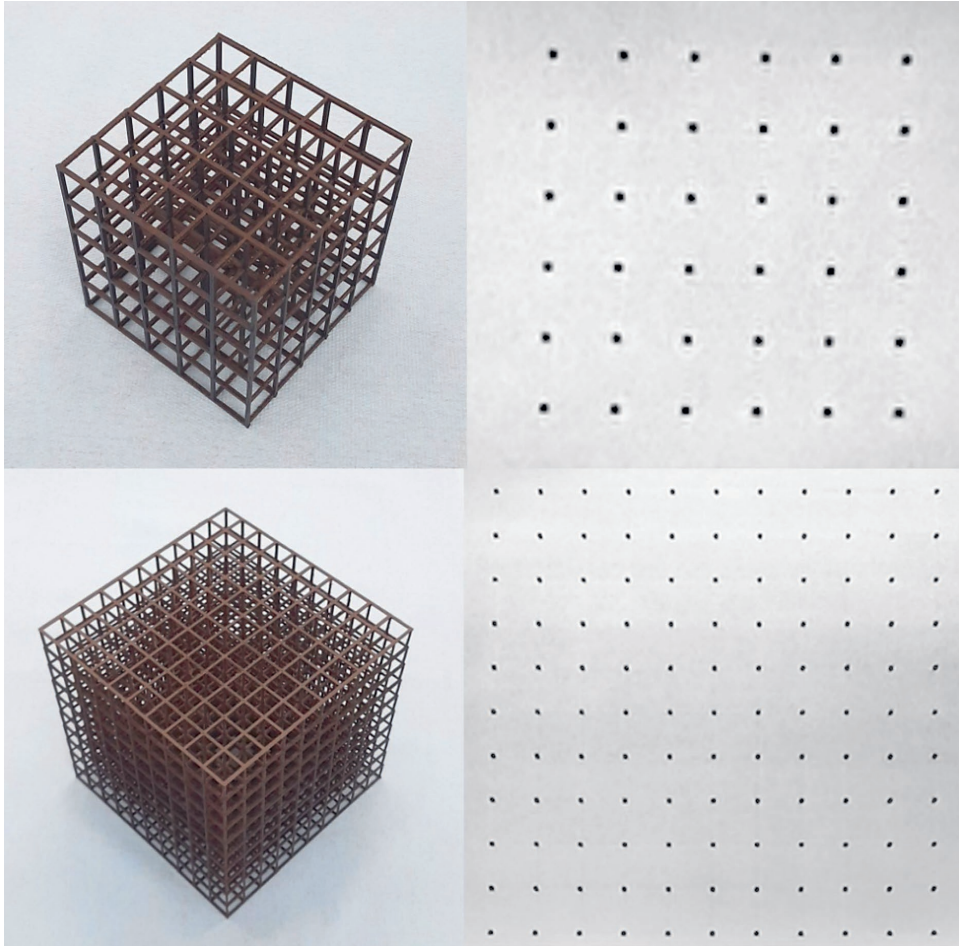
3 Visualization of three plastic needles with only air (no markers) in reconstructed planes parallel to the needles.

only, geometrical and graphical optimization is performed, followed by DVH-based dose prescription. The goal is that the clinical target volume (CTV) receives at least 90% of the prescribed dose (PD) while meeting the dose constraints for the OARs. The fractional dose to the most exposed 2 cm^3 volume (D2cm3) of bladder, rectum, and sigmoid colon should not exceed 5 Gy, 3.5 Gy, and 4 Gy, respectively. If interstitial needles are also used, hybrid inverse planning optimization (HIPO) is applied, followed by graphical optimization for minor adjustments, if necessary. Our BT dose prescription after EBRT is 4 × 7 Gy.

Image distortions

For accurate applicator reconstruction and tissue segmentation using MR alone, images must be free of distortion. We performed distortion checks using special 3D-printed phantoms. The cubic grid-like phantoms are made of plastic (PLA, polylactic acid), which does not give an MR signal. The phantoms consist of a grid structure with 2 cm between the grid points. We made two phantoms measuring 10 × 10 × 10 cm and 20 × 20 × 20 cm (Fig. 4, left).

When the phantoms were embedded in the water and scanned, the structures of the phantoms were drawn out due to the lack of signal (negative contrast) (Fig. 4, right). We performed 3D imaging, and the distortions in the MR images were visually evaluated and the distances between the furthest grid points in all three main directions were measured in each slice. Figure 4 shows that the grid points are arranged in a regular, square geometry, with virtually no distortion. With the smaller phantom, in the volume measuring 10 × 10 × 10 cm, all distortions were less than a millimeter. With the larger phantom, the maximum distortion within a volume measuring 15 × 15 × 15 cm was less than 2 mm. Such accuracy has been reported by others and is acceptable [13]. It is worth noting, however, that the region of interest in BT is only a few centimeters from the center of the applicator/catheters or the sources, as the dose is very small at greater distances due to the inverse square law. Further studies using different scanning protocols are needed to investigate the distortions in more detail.



4 Our own grid phantoms to investigate the distortion of MR imaging. Photos of the phantoms (left) and their MR image in a central axial slice (right). The distance between the grid points is 2 cm for both phantoms. The size of the small phantom is 10 × 10 × 10 cm (top), and the large one is 20 × 20 × 20 cm (bottom).

Clinical cases

Patient 1

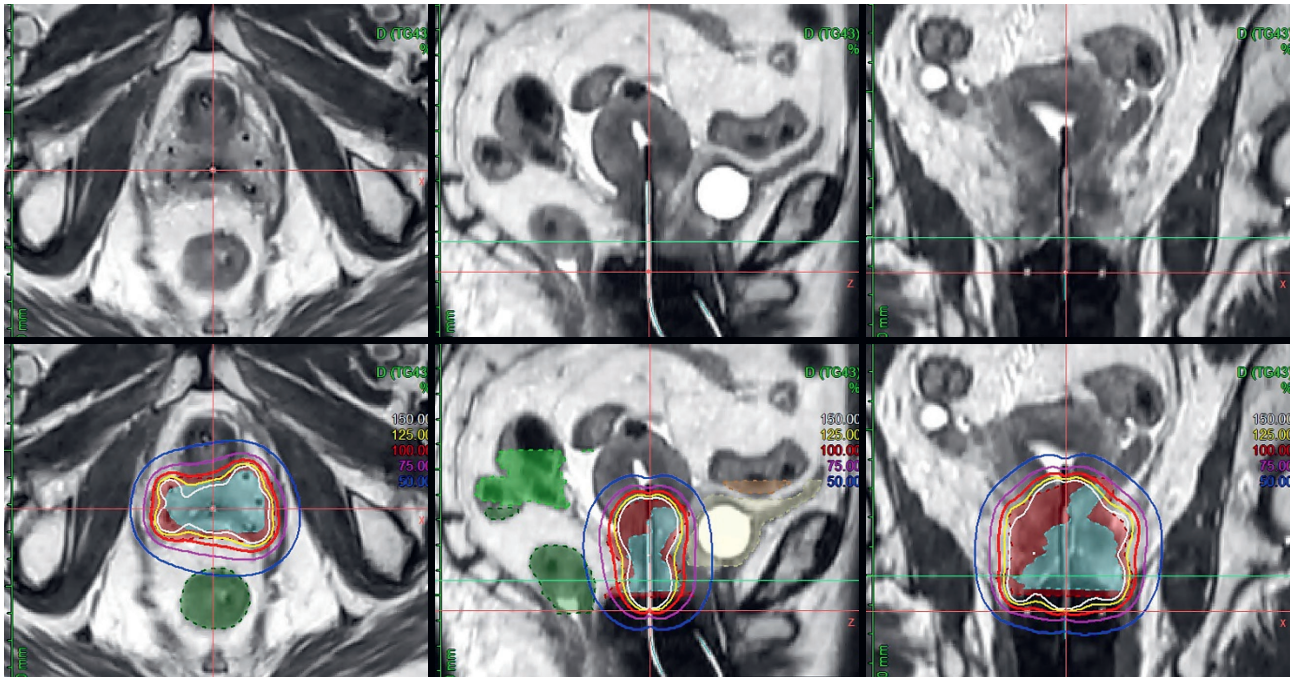
A 65-year-old patient with T2bN2M0 (St. IIIC2) squamous cell cervical cancer was first treated with EBRT (25 × 1.8 Gy to the pelvis and 25 × 2.24 Gy to the suspected lymph nodes) in combination with cisplatin-based chemotherapy. The residual tumor, measuring 2.7 × 1.4 × 1.8 cm, was then irradiated with a Venezia applicator with five interstitial needles inserted under intravenous anesthesia. The BT dose was 4 × 7 Gy. No grade 2 or higher side effects were registered. Control PET-CT imaging showed complete metabolic regression. The top row of Figure 5 shows the anatomy and the location of the applicator and the five needles in the axial (left), sagittal (middle), and coronal (right) planes. The needles are represented by small black holes on the axial slice, while the intrauterine tube inserted in the cervix is shown by the white color of the MR marker on all three slices. The bottom row of Figure 5 shows the outlined OARs, HR-CTV, and GTV for the corresponding three slices and the dose distribution. The 100% isodose line corresponds to 7 Gy. The D2cm3 of bladder, rectum, and sigmoid colon is 4.4 Gy, 2.7 Gy, and 1.3 Gy, respectively.

Patient 2

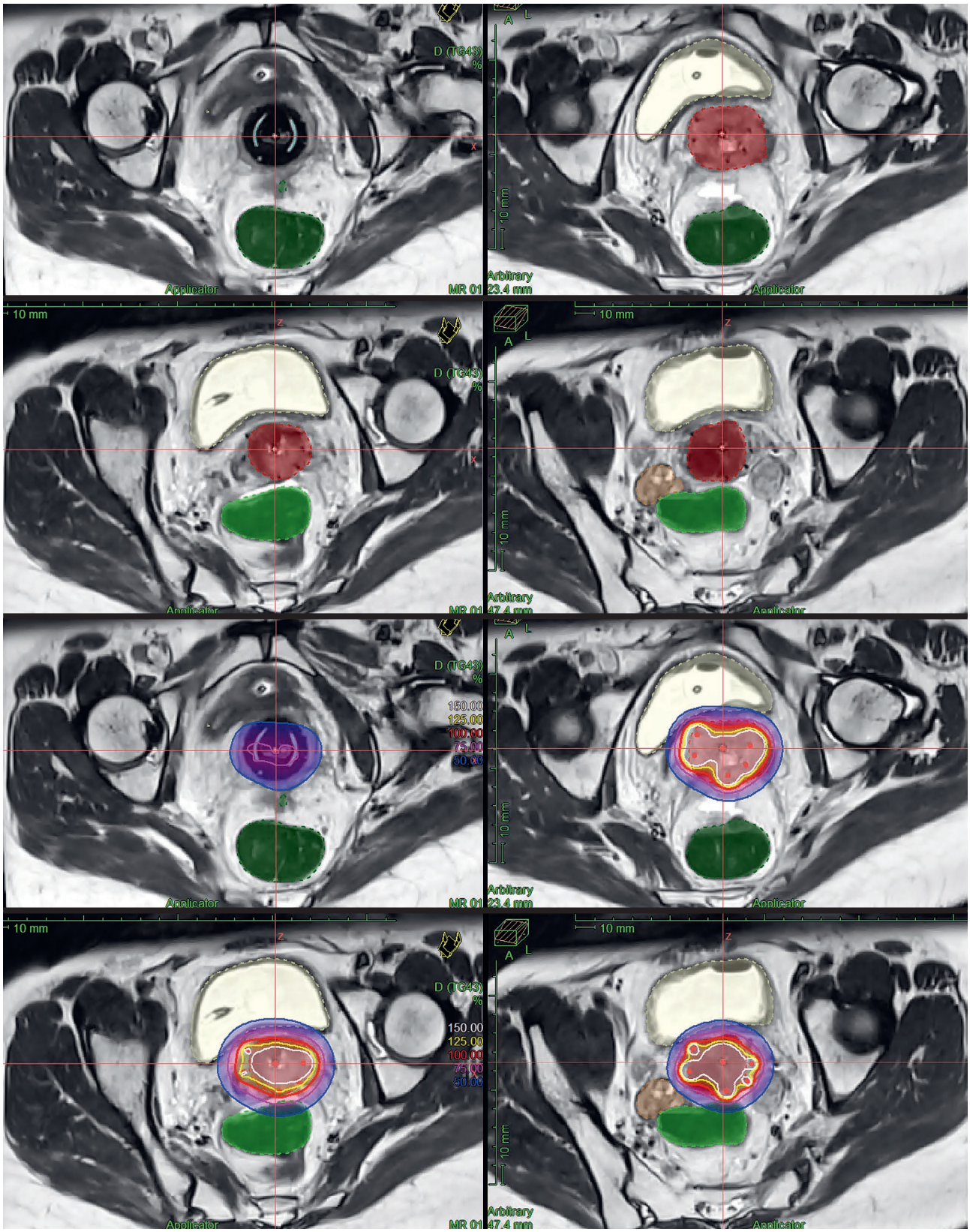
A 43-year-old patient with T2bN1M0 (St. IIIC1) squamous cell cervical cancer was first treated with EBRT (25 × 1.8 Gy to the pelvis and 25 × 2.24 Gy to the bilateral pelvic lymph nodes) in combination with cisplatin-based chemotherapy. Control pelvic MRI showed a residual tumor measuring 3.0 × 3.1 × 4.0 cm. The BT treatment, with a dose of 4 × 7 Gy, was performed using a Venezia applicator with five interstitial needles inserted under intravenous anesthesia. No grade 2 or higher side effects were registered. Control pelvic MRI showed complete clinical regression. The top four images in Figure 6 show the anatomy with the outlined OARs and HR-CTV, as well as the location of the Venezia applicator and the five needles in four axial planes. The top left image clearly shows the two ovoids with the MR markers. The conformal dose distribution is shown in the bottom four images. The 100% isodose line corresponds to 7 Gy. The V100 = 93%, and the D2cm3 of bladder, rectum, and sigmoid colon is 3.8 Gy, 1.8 Gy, and 3.6 Gy, respectively.

Discussion and conclusions

Previous experience has confirmed that low-field (0.1–0.5T) and high-field (1.0–1.5T) MR scanners can meet the requirements of MR-based BT planning [11, 14]. Although the magnetic field in MAGNETOM Free.Max is only 0.55T, the image quality is quite good and the low field means that magnetic susceptibility differences between tissues



5 A representative clinical case with an axial, sagittal, and coronal MR slice (top) and relative dose distribution (bottom) with a Venezia applicator and five interstitial needles. The 100% isodose line corresponds to 7 Gy. An MR line marker is inserted into the intrauterine tube, and the needles contain only air. The colors indicate the OARs (dark green: rectum; light green: sigmoid colon; yellow: bladder; light brown: intestines; red: high-risk CTV; cyan: GTV).



6 Four axial MRI scans with outlines of OARs (top). The bladder is marked in yellow, the rectum in dark green, the sigmoid colon in light green, the intestines in light brown, and the high-risk CTV in red. The bottom four images show the relative dose distribution in the same slices as above. The 100% isodose line corresponds to 7 Gy.

and air have less effect on image distortions, and the potential heating effect of the titanium applicator is also less than in high-field MRI machines [10]. In terms of patient comfort, this scanner is less noisy, and the large bore can reduce patient anxiety and claustrophobia, and causes less interference with implanted devices. Based on our experience, the image distortion of the MAGNETOM Free.Max is no more than 1 mm in the volume of interest, including the applicator region and relevant anatomy.

The introduction of MR-based BT treatment planning for cervical cancer was relatively easy after our experience with CT-based planning. Despite the lower magnetic field strength, the image quality is good enough to determine the target volume and organs at risk. MR markers make it easier to identify the intracavitary applicator, but the interstitial needles can also be made visible without a marker, just by the air inside. Image distortions occurred only in the regions away from the applicator, which does not affect the accuracy of applicator reconstruction and the delineation of anatomical organs. Based on our initial experience, we believe that the MAGNETOM Free.Max MR can help to implement and expand image-guided adaptive brachytherapy for cervical cancer worldwide. This is thanks to its appropriate image quality, large patient aperture, compact design, advanced software solutions, and cost-effectiveness. The potential use of MR-based planning for other cancer sites (breast, head and neck, prostate) is being investigated.

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Contact

Professor Tibor Major, Ph.D.
National Institute of Oncology
Radiotherapy Centre
Ráth György u. 7-9
Budapest 1122
Hungary
Tel.: +36 1 224 8600
major.tibor@oncol.hu

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