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# A prospective trial of real-time magnetic resonance–guided catheter placement in interstitial gynecologic brachytherapy

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**ABSTRACT**

**PURPOSE:** To present outcome and toxicity results of the first real-time intraoperative MRI-guided interstitial approach to gynecologic cancer.

**METHODS AND MATERIALS:** From February 2004 to December 2006, 25 patients with gynecologic malignancies were enrolled and treated in a prospective clinical trial of real-time MRI-guided interstitial brachytherapy. This was followed by a confirmatory CT imaging scan. Statistical analyses included Kaplan–Meier estimates for overall and relapse-free survival.

**RESULTS:** MRI visualization of needles during placement permitted accurate placement with no inadvertent insertions. This prevented unnecessary normal-tissue perforation as confirmed by CT simulation. With a mean followup of 3.8 years (range, 2–6.8), 1-, 2-, and 3-year overall survival rates were 80%, 60% and 43%, respectively; corresponding relapse-free survival rates were 79%, 65%, and 59%, respectively. Actuarial acute toxicity rates for any grade were 0% at 0–14 days and 80% (all grade 1) at 14–90 days. Long-term (>180 days) actuarial toxicity rates were 8% gastrointestinal, 4% bladder and 4% vaginal.

**CONCLUSIONS:** Real-time MRI guidance during insertion of interstitial needles followed by 3D-planning maximized opportunities for tumor targeting and sparing of normal tissues. Although image guidance requires additional anesthesia time, clinical outcomes indicate potential for a successful reduction in toxicity using 3D image-guided in addition to 3D image-planned brachytherapy. 

*Keywords:* Interstitial brachytherapy; Gynecologic malignancies; Toxicity

## Introduction

Gynecologic brachytherapy, the placement of radioactive isotopes into the tumor, vagina, or uterine canal, escalates the radiation dose to the tumor more than to the surrounding normal tissues and significantly increases patient survival when executed properly and added to external-beam radiation (1–4). Interstitial gynecologic brachytherapy was first reported by Abbe (5) in 1913. It refers to the placement of hollow needles directly into tumor-bearing tissues, which are afterloaded with radioactive source(s). Although the technique as originally described used $^{226}$Ra (5), the most commonly used isotope is $^{192}$Ir. Both high-dose-rate (HDR) and low-dose-rate (LDR) techniques are used. Interstitial brachytherapy is typically used for gynecologic malignancies presenting with a large vaginal lesion thicker than 5 mm, vesicovaginal or rectovaginal fistulas, posthysterectomy recurrences or recurrence in a previously irradiated area, tumors with extensive distal vaginal involvement, or bulky cervical or vaginal disease with extensive parametrial involvement (6).

To date, the role of real-time MRI-guided insertion of interstitial implants, in addition to treatment planning, remains unexamined. Several institutions have reported on the use of MRI in cervical cancer after insertion to assist

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This trial is registered through ClinicalTrials.gov, registration # NCT00112307: http://clinicaltrials.gov/ct2/show/NCT00112307.

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with contouring (7) and for optimization of brachytherapy treatment planning (8); this approach allows careful assessment of the planned dose of radiation in relation to the tumor and normal tissues (9–12). However, when using a real-time MRI-guided approach, the available MR images may allow the physician to properly position an applicator and alter the dose distribution to conform to the tumor volume and avoid the organs at risk (OARs). This provides unique opportunities to direct the applicator into the areas of disease as seen on MRI. The postinsertion three-dimensional (3D) image then allows dose optimization of radiation to the contoured target volume.

In 2006, we reported preliminary feasibility results of MRI-guided treatment for recurrent endometrial cancer (13). Our initial publication demonstrated that a real-time MRI-guided approach is a safe and reliable method for protecting the OAR, as inadvertent needle penetration was avoided, and plans were optimized to ensure comprehensive tumor coverage. The current report presents the final outcome results of all the 25 enrolled patients with gynecologic cancer, including survival results not previously reported. Other novel analyses include the time required for the procedure; treatment planning parameters, including the dose–volume histogram (DVH) results for the OAR (bladder, rectum, and sigmoid); and outcome results, including relapse and toxicity to the OAR using a real-time intraoperative MRI-guided interstitial approach to gynecologic malignancies.

## Methods and materials

From February 2004 to December 2006, 25 women with gynecologic malignancies were enrolled in a study at the Dana–Farber Cancer Institute and the Brigham and Women's Hospital (BWH). This prospective study was listed on ClinicalTrials.gov by the National Institutes of Health (NCT#00112307), and, therefore, accrued patients from around the United States.

The project was reviewed and approved by the Dana–Farber Cancer Institute Institutional Review Board (IRB), Assurance # FWA00001121. During the review of this project, the IRB specifically considered (*1*) the risks and anticipated benefits, if any, to the subjects; (*2*) the selection of subjects; (*3*) the procedures for securing and documenting informed consent; (*4*) the safety of subjects; and (*5*) the privacy of subjects and confidentiality of the data. Informed consent was obtained in writing from all participants involved in the study. Data were collected prospectively starting with registration, continuing during treatment and followup until a minimum of 2 years for all survivors. The primary endpoint was prevention of any inadvertent insertion of the applicator into the rectum or bladder. The secondary endpoints were 90- and 180-day toxicity analysis and assessment of local relapses after response, as well as survival. Any gynecologic cancer patient without distant metastases at diagnosis and who was eligible for interstitial implantation without MR guidance was considered eligible for this protocol. All patients had an Eastern Cooperative Oncology Group (ECOG) performance status of two or less, were aged 18 years or older, and had a histologic documentation of carcinoma. All pathology was reviewed at BWH. Patients were screened for MR compatibility, as no patients with pacemakers or other MR-unsafe materials were allowed into the MRI scanner. Patients with a significant history of silent myocardial ischemia were excluded, as the duration of anesthesia was slightly longer using MR. All preprocedural evaluations, the details of the magnetic resonance tomography (MRT) unit, the procedural details, and treatment planning have been previously described (13).

### *Real-time MR guidance*

Patients received both epidural anesthesia, which continued throughout the duration of their treatment, and general or spinal anesthesia, which was initiated on entering the MRT unit and stopped at the end of the applicator insertion. A baseline 0.5-T MR scan was obtained, including multiplanar T2-weighted (T2W) images and T1 images before and after the injection of i.v. gadolinium contrast. For some patients with an intact uterus, a CT-/MR-compatible tandem (Nucletron, Co., Veenendaal, The Netherlands) was placed into it using MR guidance to aid in placement of the tandem. The template's plastic obturator was placed over the distal end of the tandem and advanced along it. For patients who had undergone hysterectomy, the obturator was placed flush against the vaginal apex. A Syed disposable template (Best Medical Systems, Inc., Springfield, VA) was placed over the obturator and sutured to the perineum.

Each needle (ProGuide; Nucletron, 294-mm length) was placed using 0.5 T MR guidance; images of the needle as inserted were viewed in 4-s increments with either fast T2 sagittal or axial images displayed on the MR screens present above the operating area. The first needle was inserted in the most anterior location. Real-time imaging was performed using the fast T2 series in the sagittal and/or the axial plane immediately around the needle. Typically for the first needle, a real-time T2 sequence in the sagittal plane was performed to watch the depth of insertion. After insertion of each needle, a series of T2W images was obtained to confirm the precise location of the needle, and, if necessary, the needle was repositioned immediately. The image identified the needle as a black void; the needle was tracked during insertion until it reached the most superior aspect. The sagittal image was repeated for needle #1 to confirm the depth of insertion (Fig. 1). The depth was considered appropriate if the tumor was covered in its entirety with up to a 1-cm margin superiorly, with the caveat that the needle was not inserted into a superior normal-tissue structure. An axial image was obtained to identify the needle. Each subsequent needle was inserted to the same depth approximately as needle #1 based on