EJGO European Journal of Gynaecological Oncology

Intensity modulated radiotherapy and brachytherapy for a cervical cancer after renal transplantation

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Summary

Radiotherapy and surgery are important radical treatment options for cervical cancer, but the presence of a pelvic kidney complicates the situation. Fine radiation technique can help avoiding side effects. Radiation to the modified pelvis using intensity modulated radiotherapy (IMRT) followed by brachytherapy, while avoiding the renal allograft is technically feasible which ensures adequate target volume and reduces side effects. Here, the authors report a 45-year-old patient with invasive cervical cancer with a pelvic kidney who was treated by pelvic IMRT in combination with high-dose rate brachytherapy. There was no evidence of disease and with normal kidney function currently at 12 months.

Key words: Brachytherapy; Cervical cancer; Intensity modulated radiation therapy; Pelvic radiotherapy; Renal transplantation.

Introduction

Cancer is considered to be an important long-time complication of kidney transplantation. The administration of intense immunosuppression therapy is thought to be playing a main role. The developing of specific cancers is even higher due to the activation of oncogenic viruses. Radiotherapy and surgery are important radical treatment options for cervical cancer, but the anatomical position of a renal allograft in the pelvis complicates the situation. Fine radiation technique can help avoid side effects. Radiation to the modified pelvis using IMRT, while avoiding the renal allograft is technically feasible which ensures adequate target volume and reduces side effects. Here, the authors report a case of invasive cervical cancer treated by pelvic IMRT in combination with high-dose rate brachytherapy with a pelvic kidney.

Case Report

A 45-year-old Chinese female with invasive squamous carcinoma of cervix was referred to Zhejiang Cancer Hospital on May 28th, 2014. Her native kidneys were non-functional due to polycystic kidney disease since she was 35-years-old. She had received a living donor kidney transplantation. The renal vessels were grafted to the right external iliac vessels, and the kidney was placed in the right iliac fossa. She then received cyclosporine A at 125 mg per day and mycophenolate mofetil at 125 mg per day up to now. Her renal function has been stable since then.

The patient was admitted with a chief complaint of irregular vaginal bleeding for two months with no explanation. She weighed 63 kg, was 162 cm tall, and gynecological examination showed a 2×2 cm cauliflower-like lesion on the anterior lip of cervix. Cervical biopsy revealed invasive squamous carcinoma of cervix at 3, 6, 9, and 12 o'clock position. She was staged as FIGO IB1 cervical cancer. Enhancement CT scan of chest and abdomen, pelvic magnetic resonance were negative besides the lesions on cervix. Surgical and radiation therapy options were proposed initially. After careful consideration, radiation therapy was chosen. The clinical target volume (CTV) included entire gross target volume (GTV), entire cervix, entire uterus, entire parametrium, the upper third of the vagina, and nodal CTV included draining nodal groups (common, internal, external iliac, obturator, and presacral lymph nodes). The planning target volume (PTV) included a margin of 1.0 cm around the CTV, and a margin of seven mm around the nodal CTV with an exclusion of the transplanted kidney.

The patient received pelvic radiotherapy with 45 Gy at 1.8 Gy for 25 fractions with seven fields to a modified field from Jun 16th to July 20th, 2014 (Figure 1, Table 1). No fields were directed through the kidney. A second intracavitary (tandem insertion) system was placed using Ir192 source. The dose received was less than 20 Gy for one-third of the transplanted kidney, and less than 6 Gy for two-thirds (Figure 2).

Pelvic magnetic resonance revealed that the tumor was remarkably reduced after treatment (Figure 3). Renal function tests were normal during and after treatment. The patient was followed

Table 1. — *Treatment dose and volume for the irradiated organs.*

Organ	Volume (cc)	D95 (Gy)	D01 (Gy)	Mean dose (Gy)
CTV	707.93	45.27	47.45	46.03
PTV	1164.92	45.00	47.36	45.89
Rectum	31.73	11.59	46.59	38.94
Bladder	90.74	30.83	46.67	41.27
Sigmoid	33.44	42.28	47.15	45.06
Pelvic kidney	240.33	1.06	38.41	13.83

Revised manuscript accepted for publication September 29, 2015

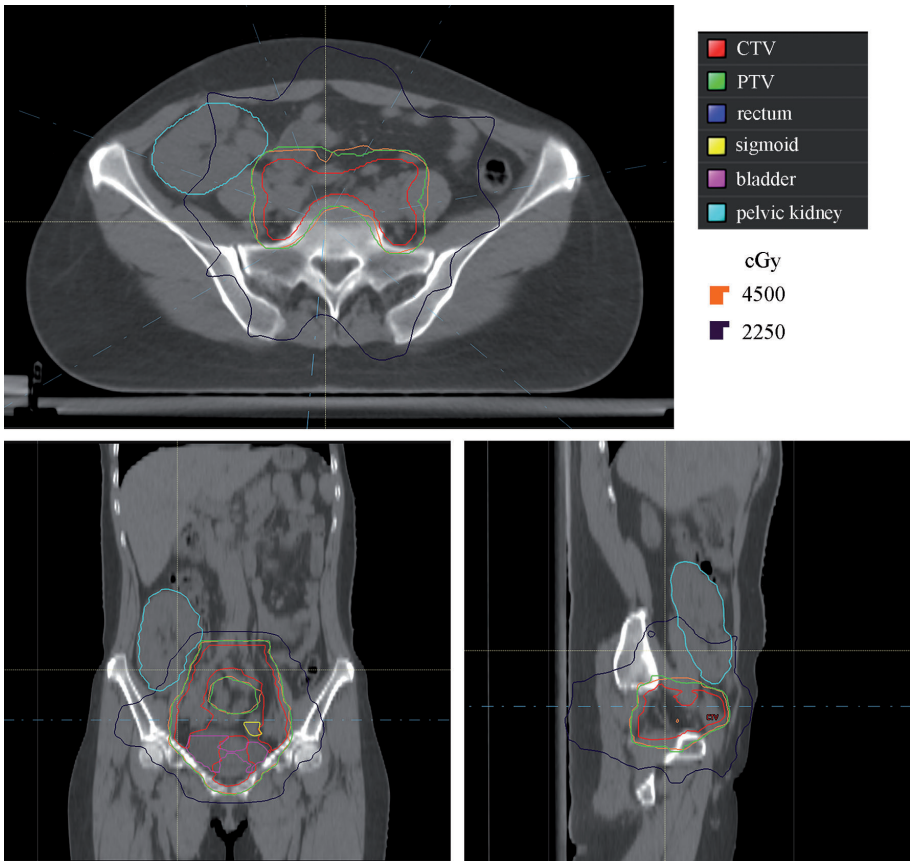

Figure 1. — Dose distributions (for 45 Gy and 22.5 Gy).

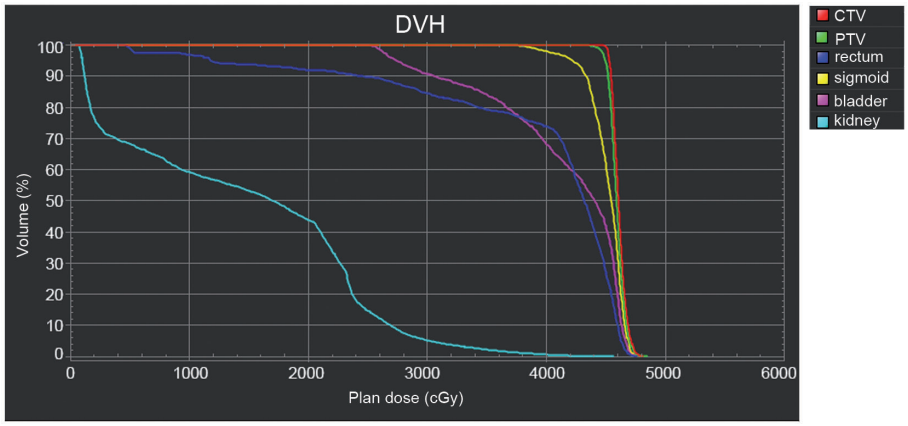

Figure 2. — Dose volume histogram (DVH) of percentage dose to transplanted kidney, rectum, bladder, sigmoid, CTV, and PTV.

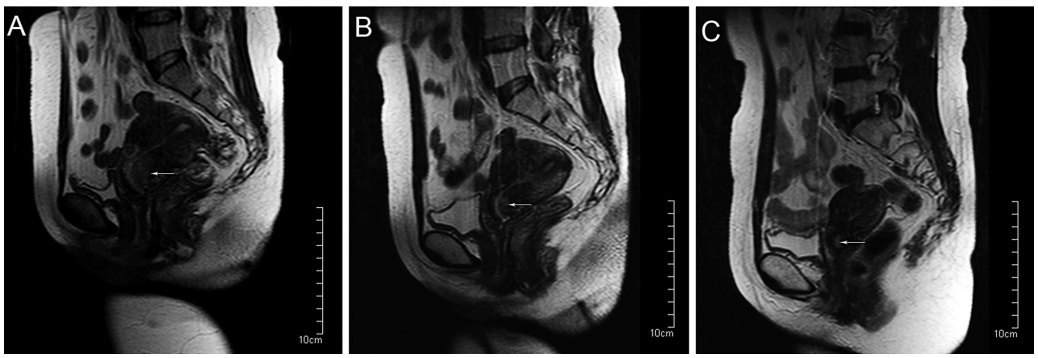

Figure 3. — Sagittal magnetic resonance imaging of pelvis before (A, Jun 6th, 2014), during (B, July 25th, 2014) and after (C, January 26th, 2015) radiation therapy.

with exams every three months after radiation therapy and was without evidence of disease and with normal kidney function currently at 12 months.

Discussion

Cancer is considered to be a confirmed and important long-time complication of kidney transplantation [1-3]. There is a large increase of the incidence of malignancies due to the improved long-term survival of renal transplant recipients. The administration of lifelong intense immunosuppression therapy is thought to play a main role in malignant transformation in transplant recipients and the developing of specific cancers is even higher due to the activation of oncogenic viruses. Renal transplant recipients are more often affected with HPV infections than in general population, with an incidence rate of mucosal infections between 22% and 63%, and are more often with multifocal infection [4, 5]. Intraepithelial lesions of the cervix has a 14-fold increased incidence, cervical cancer between 2.3- and 8.6-fold increased incidence, vulvar cancer has a 50-fold increased incidence, and anal cancer has a 100-fold increased incidence in renal transplant recipients compared to the general population [6-8].

For Stage IB2 to IIA2 cervical cancer, the standard treatment is radiation therapy or surgery. However, for renal transplant recipients, it is difficult to make treatment decisions. Radical surgery is challenging because the pelvic lymph nodes are difficult to be reached and risk of injury to the ureter and transplant vascular supply is increased. Radiation dose or field delivered to the iliac and obturator lymph nodes should be limited in order to preserve renal function. After careful discussion, the present authors chose radiation therapy for safety consideration.

Roth *et al.* [9] reported a patient who had bilateral pelvic kidneys and Stage IIB cervical cancer that underwent anterior exenteration; however, the patient was complicated by urinary conduit leakage and eventually left nephrectomy for hemorrhage. The patient showed no evidence of disease and normal renal function after 14 months.

Rosenshein, Abouna, and Bakri *et al.* [10-12] suggested nephrectomy or reimplantation or translocation out of the pelvis into the upper abdomen before radiation or surgery. However, the attempts to move a pelvic kidney out of the radiation field can be complicated by an aberrant blood supply to the kidney and a short ureter. Also, unlike in the present case, these patients had a normal functioning kidney on contralateral side and had not undergone immunosuppression treatment.

Ripley *et al.* [13] reported radiation therapy for a case of adenocarcinoma of the cervix in a renal transplant patient in 1994. They performed anterior-posterior/posterior-anterior fields at 2 Gy per fraction with 18 MeV photons to a dose of 40 Gy applied to a modified field excluding the transplanted kidney and common iliac. Then intracavitary system (low dose rate) was used. The total dose received by the kidney was calculated to be 600 cGy to the lower pole and 200 cGy to the upper pole. The tumor recurred at the right presacral area, straddling the border of the radiation field about 22 months later.

Castilho *et al.* [14] reported the first use of IMRT in the postoperative treatment of an endometrial cancer patient with a congenital pelvic kidney in 2006. The kidney was located in the central pelvis at the level of sacro-iliac joints. The prescribed dose to cover 95% of the target volume (whole pelvic drainage and vaginal vault) was 45 Gy at 1.8 Gy per fraction with seven fields. The target volume excluded the entire pelvic kidney and covered pelvic lymphatics from L5 down. Dose volume histogram showed that the whole pelvis kidney received 13 Gy, two-thirds received 21 Gy, and one-third received 31 Gy. The patient was free from disease and with normal kidney function at 18 months. In the present case, the transplanted kidney was located in the right iliac fossa, which is common.

Mohiuddin *et al*. [15] reported the use of adjuvant pelvic IMRT in a recurrent cervical adenocarcinoma in an immunosuppressed patient with a transplanted kidney. The CTV incorporated the preoperative masses and the post-surgical pelvic seromas. PTV1 included the CTV and was expanded to the whole pelvis and lymphatics but excluded the transplanted right kidney with a five- to ten-mm margin. PTV2 equaled the CTV plus one-cm expansion with similar renal exclusion. PTV1 received 45 Gy at 1.8 Gy daily with nine fields as the "modified whole pelvis." PTV2 was a small field boost of 14.4 Gy with seven fields. The CTV received 59.4 Gy total. No more than 28% of the kidney received 10 Gy on dose volume histogram. Despite relapse in the upper abdomen two months later, there has been no pelvic recurrence after adjuvant radiation therapy 36 months later.

The current report presents the first use of pelvic IMRT in combination with high-dose rate brachytherapy in a primary cervical cancer patient with a pelvic kidney. With the development of radiation technology, we can now use IMRT to evaluate the treatment dose and volume more precisely as in compared with Ripley *et al.*'s case [13]. To prevent renal complications, the present authors formulated a modified pelvic radiation plan with adequate coverage to pelvic lymphatics. The dose delivered to the transplanted kidney was less than 20 Gy for one-third and eventually less than 6 Gy for two-thirds. The patient was without evidence of disease and renal damage up to now for 12 months.

In conclusion, IMRT is qualified to both complete adequate pelvic radiation plan and spare a kidney in a complex situation. For primary cervical cancer patients, in case of damage of graft vasculature and the urinary tract with surgery, IMRT combined with high dose rate brachytherapy can be a good alternative.

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