

LETTER TO THE EDITOR

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# Radiotherapy for gynecologic cancer in nonagenarian patients: a framework for new paradigms

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## Abstract

No consensus exists regarding the role of radiotherapy in the management of gynecologic cancer in nonagenarian patients. We retrospectively reviewed the outcomes of 19 consecutive nonagenarian patients with gynecologic cancer (6 endometrial cancers, 6 cervical cancers, 4 vulvar cancers, and 3 vaginal cancers) who were treated with radiotherapy. Radiotherapy was performed mainly in a palliative setting ( $n = 12$ ; 63.2%), with a median dose of 45 Gy (range, 6–76 Gy). Infrequent major acute or late toxicities were reported. Among 19 patients, 9 (47.4%) experienced tumor progression, 5 (26.3%) experienced complete response, 2 (10.5%) experienced stable disease and/or partial response. At last follow-up, 12 patients (63.2%) had died; most deaths ( $n = 9$ ) occurred because of the cancer. These results suggest that radiotherapy is feasible in the treatment of nonagenarian patients with gynecologic cancer.

**Keywords:** Gynecologic cancer, Nonagenarians, Female genital tract, Radiotherapy, Geriatrics

## Background

Radiotherapy is a cornerstone in the management of gynecologic cancer. Because patients 65 years of age or older are often excluded from clinical trials, little is known about the therapeutic index (efficacy/toxicity ratio) of radiotherapy in the geriatric population [1]. For patients at high risk of local recurrence or who have unresectable or locally advanced disease, radiotherapy can be performed with the intent to cure [2–6]. Radiotherapy can also be performed in a palliative setting. A few studies reported radiotherapy-caused complications in nonagenarian patients, but data on efficacy are still scarce. The objective of the present study was to report efficacy and toxicity data on the radiotherapy treatment of nonagenarian patients with gynecologic cancer.

## Patients and methods

This retrospective study was conducted at two public and two private comprehensive cancer centers in France. Institutional review boards approved the study, which was conducted in compliance with the Declaration of Helsinki.

## Patient population

We reviewed the medical records of consecutive nonagenarian patients who received external-beam radiotherapy for the treatment of gynecologic cancer between 2003 and 2012. Patient, tumor, and radiotherapy characteristics were analyzed. The total biological equivalent dose in 2-Gy fractions (EQD2) was calculated using the linear quadratic model and an alpha/beta ratio of 10 Gy for tumors.

## Toxicity evaluation

Patients were assessed for toxicity every week during the radiotherapy treatment and every 6 months thereafter.

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Toxicities were graded using the Common Terminology Criteria for Adverse Events (version 4.0). Toxicities that occurred within 6 months of the beginning of radiotherapy treatment were considered acute toxicities; toxicities that occurred after 6 months were considered late toxicities. Follow-up and survival durations were calculated from receipt of the last radiotherapy fraction.

## Results

### Patient characteristics

We analyzed the data of 19 nonagenarian patients with gynecologic cancer. At the time of radiotherapy treatment, the patients' median age was 91.4 years (range, 90.0–98.6 years). Before radiotherapy, 11 patients (57.9%) had an Eastern Cooperative Oncology Group Performance Status score of 2 or higher. Nine patients (47.4%) were nursing home residents. Among the 19 patients, histologic diagnosis revealed 6 (31.6%) endometrial cancers, 6 (31.6%) cervical cancers, 4 (21.0%) vulvar cancer, and 3 (15.8%) vaginal cancers; primarily 15 (78.9%) with a locally advanced tumor (T3–T4 or N+) or metastatic disease. Seven patients (36.8%) underwent surgery before radiotherapy, and one patient (5.3%) had previously received radiotherapy for the same indication. Patient characteristics are shown in Table 1.

### Radiotherapy characteristics

Three-dimensional conformal radiotherapy was used for palliation, and intensity-modulated radiotherapy

was used for curative intent. The median delivered dose was 45 Gy (range, 6–76 Gy), and the median EQD2 was 44.2 Gy<sub>α/β = 10</sub> (range, 8–84 Gy<sub>α/β = 10</sub>). The median number of fractions was 18 (range, 1–36 fractions), and the median dose per fraction was 3 Gy (range, 1.5–6 Gy). Palliative treatments were mainly hemostatic radiotherapy (8 of 19, 42.1%), followed by decompression radiotherapy (1 of 19, 5.3%) and postoperative radiotherapy (1 of 19, 5.3%); the intent of radiotherapy was not reported in two patients (10.5%). Radiotherapy was performed with the intent to cure for seven patients (36.8%).

### Efficacy and toxicity data

Median follow-up time was 18 weeks (range, 0–116 weeks). At last follow-up, seven patients (36.8%) achieved tumor control (defined as stable disease and/or partial response and/or complete response), including five complete responses; 12 patients (63.2%) treated with radiotherapy for palliative intent died, mainly because of disease progression ( $n = 9$ ; 47.4%).

One patient who underwent 15 Gy of irradiation (total prescribed dose: 50 Gy) developed grade 5 bladder perforation and peritonitis and died after surgery for stage IV endometrial cancer); this represented 8.3% (1 of 12) of all deaths. One patient (5.3%) who underwent 44 Gy of irradiation (total prescribed dose for cervical cancer: 44 Gy) developed grade 4 diarrhea, and one patient (5.3%) developed grade 3 diarrhea. Two patients (10.5%) developed grade 2 asthenia, and one patient (5.3%) developed grade 2 epithelitis. There were two (10.5%) treatment disruptions: one caused by grade 5 toxicity, the other caused by grade 3 toxicity. One late grade 2 toxicity was observed (lower limb edema).

## Discussion

Based on these real-life findings, radiotherapy seems feasible in nonagenarian patients, either with intent to cure or in palliative setting. In this study, we retrospectively assessed the safety and efficacy of radiotherapy for 19 nonagenarian patients with gynecologic cancer. We observed only infrequent infield toxicities (5.3% grade 5, 5.3% grade 4, and 5.3% grade 3). At last follow-up, disease was controlled in 36.8% of the patients. Currently, little is known about the therapeutic index (efficacy/toxicity ratio) of radiotherapy in patients 65 years of age or older. Toxicities in small populations of geriatric patients were reported, but these studies employed outdated radiotherapy techniques [7, 8]. To our knowledge, our study is one of the largest to analyze the effects of radiotherapy on nonagenarian patients with gynecologic cancer. As expected, hypofractionated techniques were widely used, since they reduce acute toxicities (in cell populations with a high turnover, such as mucosal membranes)

**Table 1 Characteristics of 19 nonagenarian patients with gynecologic cancer**

Characteristic	No. of patients (%)
PS score	
0–1	8 (42.1)
2	5 (26.3)
3	6 (31.6)
Living place	
Home	9 (47.4)
Institution	9 (47.4)
Not reported	1 (5.2)
Primary site	
Endometrium	6 (31.6)
Cervix	6 (31.6)
Vulva	4 (21.0)
Vagina	3 (15.8)
Stage	
Localized (T1–T2 N0)	5 (26.3)
Locally advanced (T3–T4 or N+)	10 (52.7)
Metastatic	2 (10.5)
Not reported	2 (10.5)

PS performance status; N+ positive lymph node

and favor radiotherapy completion [9]. Our results suggest that radiotherapy is feasible in nonagenarian patients with gynecologic cancer, but geriatric assessment could probably reduce treatment disruption and death rates. Although no consensus exists regarding the role of brachytherapy in the management of gynecologic cancer in patients 65 years of age or older, it should probably be considered a favorable option for geriatric patients because of its good results in terms of efficacy [10–12] and, when compared to external-beam radiotherapy, the fact that it causes fewer toxicities [11].

#### Authors' contributions

NM, CC, PA, AA, OC, CB, JPI, GdL, and PF conceived of the study and participated in its design and coordination. SMN, JBG, AV, and JCT performed the data acquisition. RR, AV, SE, and GM interpreted the data. BM, AF, and AV drafted the manuscript. NM reviewed the manuscript. All authors read and approved the final manuscript.

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#### Competing interests

The authors declare that they have no competing interests.

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#### References

- Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *N Engl J Med*. 1999;341:2061–7.
- Undurraga M, Loubeyre P, Dubuisson JB, Schneider D, Petignat P. Early-stage cervical cancer: is surgery better than radiotherapy? *Expert Rev Anticancer Ther*. 2010;10:451–60.
- Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, et al. Carcinoma of the corpus uteri. FIGO 26th annual report on the results of treatment in gynecological cancer. *Int J Gynaecol Obstet*. 2006;95:S105–43.
- Keys HM, Roberts JA, Burnetto VL, Zaino RJ, Spirtos NM, Bloss JD, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a gynecologic oncology group study. *Gynecol Oncol*. 2004;92:744–51.
- Hogberg T, Signorelli M, de Olivera CF, Fossati R, Lissoni AA, Sorbe B, et al. Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer—results from two randomized studies. *Eur J Cancer*. 2010;46:2422–31.
- Greven K, Winter K, Underhill K, Fontenesi J, Cooper J, Burke T, et al. Final analysis of RTOG 9708: adjuvant postoperative irradiation combined with cisplatin/paclitaxel chemotherapy following surgery for patients with high-risk endometrial cancer. *Gynecol Oncol*. 2006;103:155–9.
- Halle JS, Rosenman JG, Varia MA, Fowler WC, Walton LA, Currie JL. 1000 cGy single dose palliation for advanced carcinoma of the cervix or endometrium. *Int J Radiat Oncol Biol Phys*. 1986;12:1947–50.
- Hodson DI, Krepert G. Once monthly radiotherapy for the palliation of the pelvic gynecological malignancy. *Gynecol Oncol*. 1983;16:112–6.
- Friberg S, Rudén BI. Hypofractionation in radiotherapy. An investigation of injured Swedish women, treated for cancer of the breast. *Acta Oncol*. 2009;48:822–31.
- Magné N, Mancy NC, Chajon E, Duvallard P, Pautier P, Castaigne D, et al. Patterns of care and outcome in elderly cervical cancer patients: a special focus on brachytherapy. *Radiother Oncol*. 2009;91:197–201.
- Nout RA, Putter H, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LC, van der Steen-Banasik EM, et al. Five-year quality of life of endometrial cancer patients treated in the randomised post operative radiation therapy in endometrial cancer (PORTEC-2) trial and comparison with norm data. *Eur J Cancer*. 2012;48:1638–48.
- Wang Y, Ye WJ, Du LH, Li AJ, Ren YF, Cao XP. Dose-volume parameters and clinical outcome of CT-guided free-hand high-dose-rate interstitial brachytherapy for cervical cancer. *Chin J Cancer*. 2012;31:598–604.

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