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Ovarian transposition in young women and fertility sparing

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Abstract. – OBJECTIVE: Ovarian transposition is a highly effective surgical procedure used to preserve ovarian function in premenopausal patients with cancers requiring postoperative or primary pelvic radiotherapy. Pelvic irradiation determines severe damage of ovarian DNA and iatrogenic ovarian failure with premature menopause, necessity of long-term hormone replacement therapy and infertility.

MATERIALS AND METHODS: We conducted an extensive research of the literature in Medline between January 2000 and April 2015 using the key-words "ovarian transposition radiotherapy", "radiotherapy gonadal function", radiotherapy fertility sparing". The population included young women with normal ovarian function affected by cancers that required pelvic radiotherapy. We have examined 32 articles reporting on 1189 women undergoing ovarian transposition. Median age was 32.5 years, follow up was median 48 months. The procedure has been performed in patients less than 40 years of age. Surgery has been achieved by laparotomy or laparoscoy. We have analyzed effects of radiotherapy on ovarian function.

RESULTS: The proportion of women treated by ovarian transposition preserved ovarian function was 70%. About 86% of patients did not develop ovarian cysts and in 98-99% of cases did not occur any metastatic disease.

CONCLUSIONS: Ovarian transposition is associated with significant preservation of ovarian function and a low frequency of complications as cysts and metastasis. In 31% of cases the procedure can fail. Further studies are needed to evaluate the efficacy of ovarian transposition and the follow up. Ovarian transposition should be discussed at the time of cancer diagnosis in every premenopausal woman requiring pelvic radiotherapy.

Key Words:
Ovarian transposition, Radiotherapy, Ovarian function, Fertility sparing.

Introduction

Radiotherapy is a treatment involving the use of high-energy radiation. It's commonly used in the management of a lot of kind of cancers. Radiation therapy is commonly applied to the cancers because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. Radiotherapy can also be used before surgery to shrink dimension of cancer (known as neoadjuvant treatment), or after surgery to destroy residual neoplastic cells (known as adjuvant treatment)[1]. For people with incurable cancers, radiotherapy is also commonly used to control and palliate symptoms. Radiotherapy can be used, alone or in combination with chemotherapy. Radiotherapy aims to deliver a precisely measured dose of radiation to a defined tumor volume with minimum possible damage to the surrounding normal tissue[2]. Pelvic irradiation is often indicated in some women with Hodgkin's disease, genitourinary, or low intestinal malignancies[3]. Depending on the site and the extent of the disease, radiation can be administered locally or to a larger area. It is highly effective in patients with early stage cancers, and can improve survival in young women with pelvic malignant diseases. Radiotherapy in young patients with cancer has greatly enhanced the life expectancy of these patients. However the ovaries are very radiosensitive organs and pelvic irradiation can induce massive destruction of the ovarian tissue. Pelvic radiotherapy cause severe damage in ovarian DNA, resulting in premature ovarian failure, premature menopause with the necessity of long-term hormone replacement therapy and infertility[4]. The pool of ovarian primordial follicles declines from 2 million at birth to 500.000 at menarche. Between the age of 37 and 38 years there is an associated accelerated loss and an increased difficulty

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to spontaneous conception[5,6]. Primordial follicles are more radio-resistant than maturing follicles[7].

The human ovary contains a finite number of ovarian follicles, which are vulnerable to DNA damage induced by radiotherapy. After exposing to ionizing radiation by the ovaries most of the primordial follicles and granulose cells will die in microseconds. There is a loss of the cortical stromal cells and in time, the cortical volume is replaced by collagen. Only few cells can escape the damage, undergo repair, and still have their function[8-11].

The ovarian dose tolerance depends on many factors. The degree and persistence of ovarian damage and the suppression of its function are age and dose dependent[12]. The radiation dose inducing ovarian failure after treatment decreases with increasing age. Infact, the ovaries are more resistant in prepubertal girls. The estimated effective sterilizing dose at birth was 20.3 Gy; at 10 years 18.4 Gy; at 20 years 16.5 Gy and at 30 years 14.3 Gy. Irreversible ovarian failure is certain at delivery dose to both ovaries of 4 to 7 Gy in women older than 40 years[4]. But the same dose in fractioned modality can preserve the ovarian function. The risk of amenorrhea was of 80% in prepuberal women with 15 Gy and 10 Gy in postpuberal girls, 30-70% with 10-15 Gy in prepuberal and 5-10 Gy in postpuberal girls[7]. Furthermore, it has been reported[4] that with a dose of 12 to 50 Gy, primary amenorrhea occurred in 68% of cases treated at a mean age of 6.9 years. Winarto et al[13] reported that the cutoff dose for radiation-induced ovarian failure is around 8-20Gy. A dose >8 Gy causes permanent ovarian damage in patients older than 40 years. A dose >20 Gy causes permanent sterility in patients of any age, with disappearance of the primordial follicles.

If cancer doesn't include ovaries the preservation of ovarian function in premenopausal women is crucial so that their qualities of life could be improved. Early menopause is associated with osteoporosis and cardiovascular disease in addition to climacteric symptoms such as hot flushing, urogenital atrophy, and sexual dysfunction. Long-term hormone replacement therapy complications are increasing of cardiovascular events, breast cancer, and dementia[14]. Fertility preservation has become an issue in young female patients suffering from cancer. Various options are available to offer the opportunity of future pregnancies. Many strategies exist for fertility preservation and they should be assessed according to patient's age, type of cancer, and time available. Some techniques[15] are well established as embryo cryopreservation, oocyte preservation, ovarian tissue cryopreservation, and auto transplantation of the ovary to the upper extremity with creation of vascular anastomosis. A study by Gubbala[16] reported that ovarian function could be preserved by transposition but in literature there is a discordance between results. First transposition was described in 1958 by McCall et al[17].

Ovarian transposition is a highly effective surgical procedure used to preserve ovarian function in premenopausal patients with cancers requiring postoperative or primary pelvic radiotherapy that can cause iatrogenic ovarian failure[16]. Remove the ovaries from their anatomical site and transport them to a site out of the field of radiation is a useful method to minimize ovarian follicle exposure to radiation[4]. Generally this is done by laparotomy either as a part of surgical staging or as a separate procedure[18]. Ovarian transposition can be done by laparotomy or laparoscopy[19]. Many studies[20-22] showed that laparoscopic ovarian transposition is the best option. Ovarian transposition by laparotomy is associated with a large abdominal incision, a long hospital stay, a longest recovery time and an increased risk of adhesion formation, inflammation, and intestinal obstruction. Since laparotomy necessitates a longer postoperative recovery time, it significantly delays radiotherapy[19]. The ovary is mobilized to identify the ligament that can be sectioned[23]. However, attention should be paid to avoid torsion and extension of the ovarian vessels, which may reduce blood supply to the ovaries[13,24]. The ovaries are marked with metallic clips for radiologic identification and for indicate the site of new allocation to be preserved by radiations. The integrity of the fallopian tube was respected and the ovaries are sutured to peritoneum. The suture avoid the return of transposed ovary to natural site and the stitches were retrieved after irradiation.

It is important to define the site of new allocation of one or both ovaries to minimize the risks connected with radiotherapy. Ultrasonography or RMI can define the new position with satisfactory precision[4]. The ovaries have been transposed to a variety of sites and levels. Tulandi and AlTook[25] showed that steroid hormone production from only one ovary is enough to prevent ovarian function failure. Clough and Giacalone[21,26] showed that unilateral right ovarian transposition effectively preserves ovarian function in 85% of subjects. Additionally, unilateral ovarian transposition of the

right ovary to the paracolic gutter, as high as the subhepatic region, is technically easier, resulting in fewer complications. The ovaries can be transposed medially behind the uterus, laterally outside the radiation field, or to distant site[27].

In case of central pelvic irradiation ovaries should be located in lateral sites as paracolic gutters or near inguinal ring; in case of monolateral neoplasia the location of transposition in the opposite site; in some case of Hodgkin's lymphoma, if interested inguinal or low iliac chains, the ovaries are located in line with iliac crests. However, attaching the ovary to the flank produces more pain complaints than lateral transposition of the ovaries into the paracolic gutter, which is more widely accepted and results in minimal complications[28]. Lateral ovarian transposition to the paracolic gutter lateral to the ascending or descending colon is considered a simple standard procedure and can be done laparoscopically. If the ovaries are transposed laterally, about 3 cm above the pelvic inlet, they will receive only 1-10% of the total radiotherapy dose[29-31].

Therefore, the ovaries should be transposed at least to the level above the pelvic brim. Transposition to this level can be achieved easily without separating the fallopian tubes from its uterine origin. This allows the possibility of spontaneous conception[32]. Soda et al[33] analyzed data from 27 patients who underwent ovarian transposition after surgical treatment for uterine cancer. There were retrospectively analyzed the images acquired with TC at different times. The differences in ovarian position between the CT images were measured. The data suggest that bilateral ovaries need a planning risk volume margin of 2 cm in all directions. The study suggests that a transposed ovary needs the same planning risk volume margin as a normal ovary (2 cm). Even after transposition, the ovaries should be kept away from the radiation field to take into consideration the degree of ovarian movement.

The concerns of ovarian transposition are possibility of radiation-induced cancer, ovarian cyst formation and metastasis in the transposed ovaries[13,16]. Longer follow-up is required to assess the ovarian function. However, Irtan et al[4] showed how there are few studies that have followed these patients for long time in preservation of ovarian functions with this technique.

We conducted a comprehensive review of the existing literature and analyzed the effects of radiotherapy on the ovarian function, results in term of preservation of fertility and complications as cysts, metastasis and radiation-induced cancer on transposed ovaries.

Material and Methods

We conducted an extensive research of the literature in Medline between January 2000 and April 2015. We used the key-words "ovarian transposition radiotherapy", "radiotherapy gonadal function", radiotherapy fertility sparing". The list of references was based on recent date of publication and relevance to the scope of this Review as ovarian function preservation, ovarian cyst formation and metastatic ovarian diseases following ovarian transposition. The population interested in this review included young women with normal ovarian function affected by malignant diseases that required pelvic radiotherapy.

We have examined thirty-two articles reporting on 1189 women undergoing ovarian transposition. Median age was 32.5 years (range 1.2-38). Follow up was median 48 months (range 28 months-16 years). Were examined: publication date, type of study, duration of follow up, type of OT, retention of ovarian function, incidence of metastasis, ovarian cysts formation and associated complications. Patient's symptoms. All the studies were observational. No studies had a blinded assessment of the outcomes. Ovarian function was studied by serum FSH and 17-B-estradiol level and by morphological study of follicles with ultrasound. Some studies have considered patient's symptoms also.

In the majority of the studies, the procedure was performed in patients less than 40 years of age. Surgery was made by laparotomy or laparoscopy. In two studies the ovaries were transposed to the subcutaneous tissue.

Results

Pelvic irradiation is a highly effective treatment improving survival in young patients with early stage cancers. However, these treatments can induce massive destruction of the ovarian tissue inducing permanent loss of ovarian function. Ovarian transposition is indicated in premenopausal patients with tumors requiring pelvic radiation, in attempt to the preserve ovarian function.

Gubbala et al[16] computed the summary proportions for ovarian function preservation, ovarian cyst formation and metastatic ovarian disease following transposition.The ovarian preservation

was performed in 90%. More common complications were: 14% ovarian cysts, 0.9% metastasis.

For Irtan[4] several studies have reported results of ovarian transposition in preservation of ovarian function and fertility[21,30,34-37] but only few studies published long term follow up[38,39]. Overall the success in preservation of ovarian functionality seems to be located between 60 and 80%. New techniques in valuation of ovary as Inhibin B end anti-Mullerian hormone can increase the feasibility of future studies. Ovarian cysts are referred in 20-24% of cases[40]. Recent studies demonstrate a poor damage of ovarian function. Metastasis had a low occurrence.

Anderson et al referred that 104 premenopausal women, 42 years of age or less, with early stage carcinoma of the cervix had surgical management with ovarian retention. Only 17% of transposed and radiated patients have continued ovarian function. Only one patient developed a metastatic disease in the ovary at 17 months and 1 had a benign cystic teratoma at 62 months after treatment. They concluded that transposition was not successful in preserving ovarian function in patients who are likely to need radiation therapy and is, therefore, not indicated[30].

Thibaud et al[38] analyzed how ovarian transposition in adults has been shown to protect ovarian function in about 60% of cases by reducing ovarian exposure to less than 4 to 7 Gy. Therefore, the effect of ovarian transposition child or adolescent patients was evaluated. Eighteen girls had ovarian transposition performed at a mean age of 9.4 years (range 1.2 to 16 years). The ovarian transposition was bilateral in 15 patients and unilateral in 3 cases; in the latter the other ovary had been destroyed by the tumor or by abdominal irradiation. At the time of evaluation 16 patients had menstruation and 2 remained amenorrheic. The complications of ovarian transposition were present in four patients: intestinal occlusion, dyspareunia, functional ovarian cysts, and pelvic adhesions with tubal obstruction. The conclusion of the study was that ovarian transposition before abdominopelvic irradiation can preserve ovarian function[38].

Hwang et al[23] analyzed 53 patients with cervical cancer underwent ovarian transposition evaluating the effectiveness of ovarian transposition procedures in preserving the ovarian function in relation to the location of the transposed ovaries in patients who underwent surgery with or without pelvic radiotherapy with retrospective design. The conclusion confirmed that the location of transposed ovary higher than 1.5 above the iliac crest after pelvic irradiation in cervical cancer is recommended to avoid ovarian failure.

Shou et al[41] reported experience with laparoscopic ovarian transposition and ovarian function preservation in young women with cervical squamous cell carcinoma treated by primary pelvic irradiation. This work enrolled twenty-seven premenopausal patients treated with radiotherapy for a cervical squamous cell carcinoma. All of them underwent to bilateral or unilateral laparoscopic ovarian transposition. The ovarian preservation was achieved in 69.2% of patients. No patient was detected with immediate intraoperative or postoperative complications and ovarian metastasis at follow-up.

Pahisa et al[19] evaluated in his study the feasibility, efficacy and morbility of laparoscopic ovarian transposition. The study included 28 patients younger than 45 years, 93% of whom maintained normal ovarian function. Two patients developed benign ovarian cysts and there were no cases of ovarian metastasis.

Winarto et al[13] reported that lateral ovarian transposition is 44-85% effective in preserving the ovarian function and that complications such as symptomatic ovarian cyst formation range from 0% to 27%. Lateral ovarian transposition to the subcutaneous adipose tissue (20-27%) is more frequently associated to symptomatic cyst formation than after lateral ovarian transposition to the paracolic gutter. Ovarian metastasis is rare (0-1.2%) but is reported. The incidence of trocar insertion metastasis is <1%. As lateral ovarian transposition to the paracolic gutter is a simple and safe procedure for preserving ovarian function, its benefits outweighs the risks of complications[21,30,42-44].

Perri et al[45] in his study analyzed 30 patients and the ovarian function was preserved in 15 patients.

Terenziani et al[39] studied 11 women at a median age of 13 years. Fourteen pregnancies were recorder among these 11 patients. This result confirms that ovarian transposition can preserve ovarian function and enable future pregnancy in 60% of patients.

Bisharah et al[46] reported that laparoscopic ovarian transposition in women <40 years old is associated with preservation of ovarian function in 88.6% of cases.

In a retrospective study conducted by Owens et al[47] 14 patients had a laparoscopic ovarian transposition of whom only one developed ovarian failure. No patients developed any complications or metastatic disease. Huang et al reported fourteen cases treated with laparoscopic ovarian transpositions.

Only one of the seven (14.29%) patients became ovarian failure and no intraoperative or immediate postoperative complication was observed[22]. Williams et al[37] study is a report of the outcome of 12 patients with Hodgkin disease. The young women underwent to transposition of the ovaries just prior to pelvic radiation. Two patients were excluded from the analysis and at follow-up five patients had evidence of ovarian function. Feneey et al[34] data suggest that the lateral ovarian transposition preserves the ovarian function in only 50% of patients undergoing pelvic radiotherapy following radical hysterectomy (Table I).

Ovarian transposition is the main approach to avoid ovarian damage in young woman to be exposed to pelvic irradiation[4]. The review show how ovarian transposition is related with significant preservation of ovarian function. It is now established as a simple and reliable method with reduced morbidity[30]. Laparoscopy avoid complications of laparotomy with well noted advantages technique related. The ovarian function is preserved in satisfactory percent of cases and complications are of poor entity.

Thev age is an important factor in maintaining ovarian function: it is reported that the rate of menopause after transposition and radiotherapy is high when age is more than 40 years[34,22,48]. Therefore bilateral ovarian transposition is recommended in patients who are <32 years of age. The progress in medically assisted reproductive techniques represents actually, with ovarian transposition, the best options for these young women for pregnancy outcomes.

Thibaud et al[38] concluded that ovarian transposition, performed before abdominopelvic irradiation during childhood and adolescence, can preserve the ovarian function. Longer follow-up is required to assess the risk of ovarian dystrophy because of vascular lesions or chemotherapy.

In other side, the ovarian function was highly preserved in those patients who had no adjuvant radiotherapy irrespective of the type of transposition or the position of transposed ovaries[40]. Further comparison between the ovarian transposition and non-ovarian transposition cancer groups is required to assess directly the efficacy of ovarian transposition on ovarian function preservation.

Concerning the risks of ovarian transposition, Hwang et al[23] show how the chance of ovarian metastasis on the transposed ovary is very negligible. Tabata et al[49,52] noted that metastasis are more frequent with adenocarcinoma and with bulky tumor. The risk of ovarian carcinoma affecting the transposed ovaries is extremely low. Several risk factors for ovarian involvement have been suggested[50]. It appears that non-squamous histology carries a higher risk than the squamous one. Sutton et al[51] reported an incidence of 0.5% in squamous cell carcinoma compared to 1.7% in adenocarcinoma. Therefore, ovarian metastasis in early cervical cancer occurs very rarely[52]. Moreover, the prevalence of port site metastasis is <1%, which would explain our results, as the majority of transpositions were performed laparoscopically[44].

Risk factors for cyst development include previous surgery, extensive ovarian mobilization albeit the mechanism is unknown and gynaecological pathology such as endometriosis or pelvic inflammatory disease[40]. Symptomatic cysts were identified by imaging and were treated either conservatively or surgically. The surgical treatment included needle puncture, cystectomy or oophorectomy. The conservative treatment included analgesics, hormonal or expectant management. The transposed ovary can also induce ovarian torsion[30,53].

Published data vary with regards to functional outcomes such as ovarian failure, ovarian cysts and metastases to the transposed ovaries but our systematic review of 32 studies confirms and generalizes the concept that the ovarian transposition is associated with a high preservation of the ovarian function, an acceptable rate of ovari-

Table I. Summary of the largest studies evaluating efficacy of ovarian transposition on ovarian preservation.

	Patients (n)	Ovarian preservation (%)
Gubbala et al	892	90%
Anderson et al	104	17%
Owens et al	14	93%
Thibaud et al	18	60%
Perri et al	30	50%
Pahisa et al	28	93%
Shou et al	27	69.2%
Williams et al	10	50%
Terenziani et al	11	60%
Morice et al	22	79%
Feeney et al	28	50%
Clough et al	20	85%
Hwang et al	53	95%
Huang et al	14	85.71%

an cysts and a low risk of metastases in the transposed ovaries.

Conclusions

The efficacy of ovarian transposition in patients undergoing radio-surgical treatment for gynaecological malignancies with high preservation of ovarian function and negligible risk of metastases to the transposed ovaries, despite rather common incidence of ovarian cysts, is well established. As quality of care remains an important issue in cancer care; careful expansion of patient selection could identify those premenopausal patients who would really benefit from this rather underutilized procedure. Laparoscopic ovarian transposition is a simple, safe, effective, but often forgotten, procedure for young premenopausal patients with cancer who are undergoing radiotherapy. Ovarian transposition should be offered and discussed at the time of cancer diagnosis in every young woman suffering from pelvic cancer.

However, further studies are still needed to evaluate the efficacy of ovarian transposition and for a careful follow-up.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Camphausen KA, Lawrence RC. Principles of Radiation Therapy. In: Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach. 11th ed. 2008.
2) Falk S. Principles of cancer treatment by radiotherapy. Surgery 2009; 27: 169-172.
3) Al-Fozan HM, Tulandi T. Fertility preservation in children young adults undergoing treatment for malignancy. Saudi Med J 2004; 25: 141-144.
4) Irtan S, Orbach D, Helfre S, Sarnacki S. Ovarian transposition in prepubescent and adolescent girls with cancer. Lancet Oncol 2013; 14: 601-608.
5) Wo JY, Viswanathan AN. Impact of radiotherapy on fertility, pregnancy, and neonatal outcomes in female cancer patients. Int J Radiat Oncol Biol Phys 2009; 73: 1304-1312.
6) Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in mid-life: Implications for forecasting menopause. Hum Reprod 1992; 7: 1342-1346.
7) Levy MJ, Stillman RJ. Reproductive potential in survivors of childhood malignancy. Pediatrician 1991; 18: 61-70.
8) Falcone T, Attaran M, Bedaiwy MA, Goldberg JM. Ovarian function preservation in the cancer patient. Fertil Steril 2004; 81: 243-257.
9) Barbera L. Effects of pelvic radiation therapy on fertility. J Gynecol Oncol 2003; 8: 101-106.
10) Perez C, Purdy J, Li Z, Hall E. Biologic and physical aspects of radiation oncology. In: Hoskins W, Perez C, Young R, Barakat R, Markman M, Mandall M, editors. Principles and Practice of Gynecologic Oncology. 4th edition. Philadelphia, Pa, USA: Lippincott Williams & Wilkins, 2005: pp. 375-459.
11) Kim SS. Fertility preservation in female cancer patients: current developments and future directions. Fertil Steril 2006; 85: 1-11.
12) Meirow D, Nugent D. The effects of radiotherapy and chemotherapy on female reproduction. Hum Reprod 2001; 7: 535-543.
13) Winarto H, Febia E, Purwoto G, Nuranna L. The need for laparoscopic ovarian transposition in young patients with cervical cancer undergoing radiotherapy. Int J Reprod Med 2013; 2013: 1-6.
14) Langer RD, Manson JE, Allison MA. Have we come full circle – or moved forward? The Women's Health Initiative 10 years on. Climacteric 2012; 15: 206-212.
15) Wo JY, Viswanathan AN. Impact of radiotherapy on fertility, pregnancy, and neonatal outcomes in female cancer patients. Int J Radiat Oncol Biol Phys 2009; 73: 1304-1312.
16) Gubbala K, Laios A, Gallos I, Pathiraja P, Haldar K, Ind T. Outcomes of ovarian transposition in gynaecological cancers; a systematic review and meta-analysis. J Ovarian Res 2014; 7: 69.
17) McCall ML, Keaty EC, Thompson JD. Conservation of ovarian tissue in the treatment of the carcinoma of the cervix with radical surgery. Am J Obstet Gynecol 1958; 75: 590-600.
18) Gunasheela D, Gunasheela S. Strategies for fertility preservation in young patients with cancer: A comprehensive approach. Indian J Surg Oncol 2014; 5: 17-29.
19) Pahisa J, Martínez-Román S, Martínez-Zamora MA, Torné A, Caparrós X, Sanjuán A, Lejárcegui JA. Laparoscopic ovarian transposition in patients with early cervical cancer. Int J Gynecol Cancer 2008; 18: 559-584.
20) Chuai Y, Xu X, Wang A. Preservation of fertility in females treated for cancer. Int J Biol Sci 2012; 8: 1005-1012.
21) Clough KB, Goffinet F, Labib A, Renolleau C, Campana F, de la Rochefordiere A, Durand JC. Laparoscopic unilateral ovarian transposition prior to irradiation: prospective study of 20 cases. Cancer 1996; 77: 2638-2645.
22) Huang KG, Lee CL, Tsai CS, Han CM, Hwang LL. A new approach for laparoscopic ovarian transposition before pelvic irradiation. Gynecol Oncol 2007; 105: 234-237.

23) Hwang JH, Yoo HJ, Park SH, Lim MC, Seo SS, Kang S, Kim JY, Park SY. Association between the location of transposed ovary and ovarian function in patients with uterine cervical cancer treated with (postoperative or primary) pelvic radiotherapy. Fertil Steril 2012; 97: 1387-1393.

24) Kwik M, O'Neill A, Hamani Y, Chapman M, Chou D. Laparoscopic ovarian transposition with potential preservation of natural fertility. J Minim Invasive Gynecol 2010; 17: 411-412.

25 Tulandi T, Al-Took S. Laparoscopic ovarian suspension before irradiation. Fertil Steril 1998; 70: 381-383.

26) Giacalone PL, Laffargue F, Bénos P, Dechaud H, Hédon B. Successful in vitro fertilization-surrogate pregnancy in a patient with ovarian transposition who had undergone chemotherapy and pelvic irradiation. Fertil Steril 2001; 76: 388-389.

27) Gizzo S, Ancona E, Patrelli TS, Saccardi C, Anis O,D'Antona D, Nardelli GB. Fertility preservation in young women with cervical cancer: an oncologic dilemma or a new conception of fertility sparing surgery? Cancer Invest 2013; 31: 189.

28) Scott SM, Schlaff W. Laparoscopic medial oophoropexy prior to radiation therapy in an adolescent with Hodgkin's disease. J Pediatr Adolesc Gynecol 2005; 18: 355-357.

29) Barbera L. Effects of pelvic radiation therapy on fertility. J Gynecol Oncol 2003; 8: 101-106.

30) Anderson B, LaPolla J, Turner D, Chapman G, Buller R. Ovarian transposition in cervical cancer. Gynecol Oncol 1993; 49: 206-214.

31) Maltaris T, Seufert R, Fischl F, Schaffrath M, Pollow K, Koelbl H, Dittrich R. The effect of cancer treatment on female fertility and strategies for preserving fertility. Eur J Obstet Gynecol Reprod Biol 2007; 130: 148-155.

32) Iavazzo C, Darlas FM, Gkegkes ID. The role of robotics in ovarian transposition. Acta Inform Med 2013; 21: 135-137.

33) Soda I, Ishiyama H, Ono S, Takenaka K, Arai M, Arai T, Iwase H, Sekiguchi A, Kawakami S, Komori S, Onda T, Hayakawa K. Assessment of transposed ovarian movement: how much of a safety margin should be added during pelvic radiotherapy? J Radiat Res 2015; 56: 354-359.

34) Feeney DD, Moore DH, Look KY, Stehman FB, Sutton GP. The fate of the ovaries after radical hysterectomy and ovarian transposition. Gynecol Oncol 1995; 56: 3-7.

35) Morice P, Juncker L, Rey A, El-Hassan J, Haie-Meder C, Castaigne D. Ovarian transposition for patients with cervical carcinoma treated by radiosurgical combination. Fertil Steril 2000; 74: 743-748.

36) Gareer W, Gad Z, Gareer H. Needle oophoropexy: a new simple technique for ovarian transposition prior to pelvic irradiation. Surg Endosc 2011; 25: 2241-2246.

37) Williams RS, Littell RD, Mendenhall NP. Laparoscopic oophoropexy and ovarian function in the treatment of Hodgkin disease. Cancer 1999; 86: 2138-2142.

38) Thibaud E, Ramirez M, Brauner R, Flamant F, Zucker JM, Fékété C, Rappaport R. Preservation of ovarian function by ovarian transposition performed before pelvic irradiation during childhood. J Pediatr 1992; 121: 880-884.

39) Terenziani M, Piva L, Meazza C, Gandola L, Cefalo G, Merola M. Oophoropexy: a relevant role in preservation of ovarian function after pelvic irradiation. Fertil Steril 2009; 91: 935-936.

40) Chambers SK, Chambers JT, Kier R, Peschel RE. Sequelae of lateral ovarian transposition in irradiated cervical cancer patients. Intern J Radiat Oncol Biol Phys 1991; 20: 1305-1308.

41) Shou H, Chen Y, Chen Z, Zhu T, Ni J. Laparoscopic ovarian transposition in young women with cervical squamous cell carcinoma treated by primary pelvic irradiation. Eur J Gynaecol Oncol 2015; 36: 25-29.

42) Morice P, Haie-Meder C, Pautier P, Lhomme C, Castaigne D. Ovarian metastasis on transposed ovary in patients treated for squamous cell carcinoma of the uterine cervix: report of two cases and surgical implications. Gynecol Oncol 2001; 83: 605-607.

43) Morice P, Castaigne D, Haie-Meder C, Pautier P, El Hassan J, Duvillard P, Gerbaulet A, Michel G. Laparoscopic ovarian transposition for pelvic malignancies: indications and functional outcomes. Fertil Steril 1998; 70: 956-960.

44) Picone O, Aucouturier JS, Louboutin A, Coscas Y, and Camus E. Abdominal wall metastasis of a cervical adenocarcinoma at the laparoscopic trocar insertion site after ovarian transposition: case report and review of the literature. Gynecol Oncol 2003; 90: 446-449.

45) Perri T, Ben-Baruch G, Davidson T, Beiner ME, Helpman L, Hoge L, Jakobson-Setton A, Meirow D, Ben Haim S, Korach J. Use of titanium spiral tacks for long-term oophoropexy before pelvic irradiation. Int J Gynecol Cancer 2014; 24: 1133-1136.

46) Bisharah M, Tulandi T. Laparoscopic preservation of ovarian function: an underused procedure. Am J Obstet Gynecol 2003; 188: 367-370.

47) Owens S, Roberts WS, Fiorica JV, Hoffman MS, LaPolla JP, Cavanagh D. Ovarian management at the time of radical hysterectomy for cancer of the cervix. Gynecol Oncol 1989; 35: 349-351.

48) Haie-Meder C, Mlika-Cabanne N, Michel G, Briot E, Gerbaulet A, Lhomme C, Cosset JM, Sarrazin D, Flamant F, Hayat M. Radiotherapy after ovarian transposition: ovarian function and fertility preservation. Intern J Radiation Oncol Biol Phys 1993; 25: 419-424.

49) Tabata M, Ichinoe K, Sakuragi N, Shiina Y, Yamaguchi T, Mabuchi Y. Incidence of ovarian metastasis in patients with cancer of the uterine cervix. Gynecol Oncol 1987; 28: 255-261.

50) Landoni F, Zanagnolo V, Lovato-Diaz L, Maneo A, Rossi R, Gadducci A, Cosio S, Maggino T, Sartori E,

Tisi C, Zola P, Marocco F, Botteri E, Ravanelli K, Cooperative Task Force. Ovarian metastases in early-stage cervical cancer (IA2-IIA): a multicenter retrospective study of 1965 patients. Int J Gynecol Cancer 2007; 17: 623-628.

51) Sutton GP, Bundy BN, Delgado G, Sevin BU, Creasman WT, Major FJ, Zaino R. Ovarian metastases in stage IB carcinoma of the cervix: a Gynecologic Oncology Group study. Am J Obstet Gynecol 1992; 166: 50-53.

52) Shimada M, Kigawa J, Nishimura R, Yamaguchi S, Kuzuya K, Nakanishi T, Suzuki M, Kita T, Iwasaka T, Terakawa N. Ovarian metastasis in carcinoma of the uterine cervix. Gynecol Oncol 2006; 101: 234-237.

53) Husseinzadeh N, Nahhas WA, Velkley DE, Whitney CW, Mortel R. The preservation of ovarian function in young women undergoing pelvic radiation therapy. Gynecol Oncol 1984; 18: 373-379.