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Options for Fertility Preservation in Cancer Patients

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Options for Fertility Preservation in Cancer Patients

R. Dittrich, L. Lotz, J. Hackl, S. Nichols-Burns, T. Hildebrandt, H. Schneider, I. Hoffmann, M. W. Beckmann

Little attention was given to fertility loss as a potential consequence of radio-/chemotherapy in the past. In recent years, interest in fertility preserving measures for cytotoxic therapy has risen sharply and includes the establishment of the network FertiPROTEKT. Cryoconservation of sperm is an established method of fertility preservation for males. Options for females include transposition of the gonads prior to radiotherapy, protection of the gonads using gonadotropin-releasing hormone (GnRH) analogues, and cryoconservation of embryos, oocytes, and ovarian tissue. Although most of the aforementioned methods are currently regarded as experimental, they make it possible for affected women to have children after recovering from disease. Fertility-preserving procedures should therefore be offered to all patients facing fertility loss before cytotoxic treatment is administered. Rapid and simultaneous collaboration with a specialized fertility center and provision of correct and detailed information for the patient are of extreme importance. This article discusses the importance of fertility-preserving methods for the specialty of gynecology and outlines the currently available techniques. **J Reproduktionsmed Endokrinol 2014; 11 (5–6): 274–9.**

Key words: fertility preservation, family planning, cancer, ovary

■ Introduction

Increasing survival rates for cancer patients and an increasing awareness of the quality of life after chemo-/radiotherapy have focused attention on the preservation of fertility after cancer treatment. Due to great progress in reproductive medicine, measures that make it possible for affected women to have children after recovering from the disease can now be offered.

The effects of malignant disease on gonadal function are caused in most cases indirectly by the influence of cytotoxic therapy. Chemotherapy and/or radiotherapy very often lead to partial or complete impairment of the ovaries and spermatozoa, severely reducing or eliminating fertility. The gonadotoxic effects are strongly dependent on the patient's age (older age correlating to higher risk), the type, dose and duration of chemotherapy and radiation therapy (Table 1, 2).

The aim of the present article is to provide basic information on fertility-preserving measures and to enhance awareness among medical staff treating affected patients that such measures are available. Our main focus is on fertility preservation for women, but options for men are also mentioned.

■ Options for Fertility Preservation in Women

In general, diseases that require treatment that is gonadotoxic represent an in-

Table 1. Infertility after Treatment with Different Cytotoxic Drugs

	Toxic effect on spermatozoa	Initiation of ovarian dysfunction
High risk	– Chlorambucil – Cyclophosphamid – Nitrosoharnstoff – Busulfan – Fludarabin – Procarbazine – CCNU	– Chlorambucil – Cyclophosphamid – Busulfan – CCNU – Mitomycin C
Moderate risk	– Doxorubicin – Vinblastin – Cytarabin – Cisplatin – Topoisomerase-I-Hemmstoffe	– Doxorubicin – Vinblastin – Cisplatin – Topoisomerase-I-Hemmstoffe
Low risk	– Methotrexat – 5-Fluorouracil – 6-Mercaptopurin – Vincristin	– Methotrexat – 5-Fluorouracil – 6-Mercaptopurin – Vincristin
Unknown risk	– Bleomycin – Etoposid – Gemcitabin – Taxane – Oxaliplatin – Irinotecan – Antibody – Small molecules	– Etoposid – Nitrosoharnstoffe – Gemcitabin – Taxane – Oxaliplatin – Irinotecan – Antibody – Small molecules

Table 2. Radiotoxicity and Ovarian Insufficiency. Adapted from [Demewood MD 1986]

Risk of Sterility	Ovarian radiation dosage (Gy) (Patient age in years [y])
No effect	0.6
Some risk	1.5
60%	2.5–5 (15–40y)
70%	5–8 (15–40y)
100%	> 8 (15–40y)
100%	2.5–5 (> 40y)

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dication for measures to protect the ovary. Fertility-preserving measures have to be customized to match the patient's individual clinical situation. Aspects to be taken into account include the time available before the start of oncological therapy, patient's age, relationship status, potential ovarian involvement in the cancer, and gonadotoxic measures that are to be used (Fig. 1). If possible, it should be ensured that operations are carried out as fertility-conserving surgeries. In terms of radiotherapy, attention must be paid to sufficient gonad protection by the choice of treatment fields and lead aprons.

Transposition of the Ovaries (Ovariopexy)

In patients with Hodgkin or non-Hodgkin lymphomas, cervical carcinoma, colorectal carcinoma, or other solid malignancies which require radiotherapy to the pelvis, the ovaries can be surgically repositioned away from the radiotherapy field before starting treatment. The ovaries are laparoscopically mobilized after transection of the ovarian ligaments or by opening the retroperitoneum via bilateral division of the peritoneum along the infundibulo-pelvic ligament, so that a transection of the fallopian tube is not necessary in most cases. Subsequently, the mobilized ovary is fixed cranio-laterally to the peritoneum of each paracolic gutter. Ovaries can be marked with radio-paque metal clips, so their location can be checked during treatment. The proportion of patients < 40 years of age who recover regular ovulatory cycles after radiotherapy with this technique is up to 85% [2]. The success rate with this method depends on applied radiation dosage and scattered radiation. Rare complications include pain during ovulation, cyst formation, thrombosis, and ischemia [3].

GnRH Analogues

Gonadotropin-releasing hormone (GnRH) agonists may be utilized to inhibit the release of follicle-stimulating hormone in postpubertal women, inducing transient hypogonadotropic hypogonadism and placing the ovaries in a "resting" state. Hereby, it is anticipated that follicles can be protected and fertility be preserved. The latest meta-analysis including only randomized controlled studies ($n = 6$) reported a reduced rate of premature ovarian failure with GnRH agonist administration, with an odds ratio of 3.5 [4]. Preliminary results of the most recent study

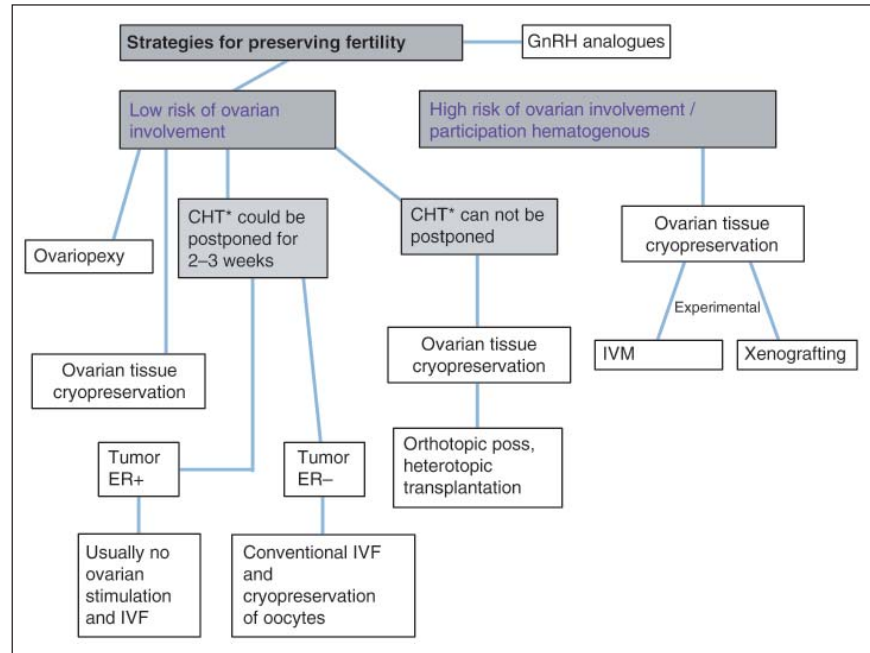


Figure 1. Planned Approach at German University Reproductive Centers. Mod. from [1]. * CHT = Chemotherapy treatment

of LHRH analog during chemotherapy to reduce ovarian failure in early stage, hormone receptor-negative breast cancer (Prevention of Early Menopause Study-[POEMS-] SWOG S0230) show a reduced rate of premature ovarian failure by using LHRH analogue (OR = 0.3; 95%-CI: 0.10–0.87; $p = 0.3$ [unadjusted analyses]) [5]. On the other hand, other studies on administration of GnRH agonists in adjuvant chemotherapy for breast cancer and lymphoma did not demonstrate a significant benefit [6, 7]. When used, GnRH analogues should be administered at least 1 week before starting chemotherapy due to the initial increase in the release of gonadotropins (known as the "flare-up" effect), and administration should continue for at least 1–2 weeks after the last chemotherapy cycle. If the time window before the start of chemotherapy is less than a week, it is possible to combine GnRH agonists with GnRH antagonists in order to reduce flare-up [8]. Side effects of GnRH analogues can include menopausal symptoms (although this is also possible with chemotherapy alone) and a reduction in bone mass if the drug exposure is longer than 6 months. It should also be noted that possible negative effects of GnRH analogues on the prognosis for patients with estrogen receptor-positive diseases (e.g., breast carcinoma) have not yet been clarified. This method is currently regarded as safe, noninvasive, and easy

to administer [9] and may be considered on an individual basis in combination with other fertility-protecting measures if possible. Statements regarding the chance of pregnancy cannot be made at the present time and must be discussed in detail during the information talk with the patient. Further randomized prospective studies are lacking.

Cryopreservation of Unfertilized and Fertilized Oocytes

Prophylactic cryopreservation of unfertilized and fertilized oocytes is a well-established assisted reproductive technique (ART) and is especially applicable in the frame of fertility preservation prior to gonadotoxic therapy. Ovarian stimulation to harvest oocytes can be carried out with most postmenarchal women aged ≤ 40 years. With the development of new protocols, stimulation can begin at any point during the menstrual cycle of the patient, so that the working time frame requires only 2 weeks prior to start of cytotoxic therapy. Use of GnRH-antagonists and ovulation induction with a GnRH-agonist prevents ovarian hyperstimulation syndrome, which would require postponement of chemotherapy. Cytotoxic therapy can begin 1–2 days after follicle puncture [10].

Freezing pronuclear stage zygotes using traditional slow cryopreservation has been well established, especially in

countries like Germany where planned cryopreservation of human embryos by nuclear fusion is prohibited by law. Survival rates after conventional slow freezing of zygotes are between 70 and 80%. Clinical pregnancy rates amount to 18% with an implantation rate of 10% per transferred embryo [11, 12]. Survival rate for vitrified zygotes is > 90% with a cleavage rate of 80% on day 2 and blastocyst formation rate on day 5 > 30% [13]. Al Hasani et al have published clinical pregnancy and implantation rates of 30% and 17% [11].

Another ART is the cryopreservation of unfertilized oocytes. Despite publication of the first birth after cryopreservation of unfertilized oocytes with a slow freezing protocol in humans 1986 [14], this technique was considered controversial due to the low survival rates of the cells. Based on improved survival rates due to slight modifications of slow freezing and vitrification protocols, the cryopreservation of unfertilized oocytes now represents an effective ART. Pregnancy rates can be achieved comparable to those resulting from IVF treatment using fresh eggs [15]. In a randomized controlled trial, pregnancy rate was compared with surplus slow freeze and vitrified oocytes. Results demonstrated that vitrification leads to a better survival of oocytes (81% vs. 67%; $p < 0.001$), higher rate of fertilization (77% vs 67%; $p = 0.03$), and higher pregnancy rate per thawed oocytes compared to slow freeze oocytes (5.2% vs 1.7%; $p = 0.03$) [16]. However, other clinics report equivalent success of the two freezing methods in observational studies [17], and it is likely that clinic-specific success rates vary with different cryopreservation protocols. Today, over 1000 children worldwide have been born through cryopreservation of unfertilized oocytes. Based on available data, no increased risk of congenital anomalies has been observed [18]. The malformation rate of children born by cryopreserved oocytes does not differ from those after spontaneous concep-

tion. Due to these advances, the American Society for Reproductive Medicine no longer considers cryopreservation of unfertilized oocytes experimental, but an established method for retaining fertility [19].

Risks associated with ovarian stimulation are low. In the complication register of the FertiPROTEKT network no shift of chemotherapy due to complication was required in 205 stimulations. In patients with hormone-dependent tumors, such as hormone receptor-positive breast cancer or hormone-dependent genital tumors, ovarian stimulation should be critically discussed because of increased estradiol levels. In consultation with the oncologist, gonadotropins, antiestrogens (e.g., tamoxifen) or aromatase inhibitors (e.g., letrozole) could be administered during ovarian stimulation to reduce the unwanted rise of estradiol and to carry out an antiestrogenic effect on the tumor cells with a reduced risk of cancer progression [10].

One point against cryopreservation of zygotes or unfertilized oocytes as an option for fertility preservation in cancer patients is the need of hormonal stimulation to achieve more than 1 oocyte. Stimulation is accompanied with a delay of the chemotherapy because normally the start of the stimulation procedure, which already needs at least 10 days, is at the beginning of the follicular phase. When the patient is in the luteal phase, it is necessary to wait until bleeding occurs. An alternative is already to initiate the ovarian stimulation in the luteal phase together with the administration of Gonadotropin-Releasing Hormone antagonist (GnRH-antagonist), which is administered to induce immediate luteolysis. The success of this application was already shown by von Wolff et al in 2009 [20] and recently at the Meeting of the European Society of Human Reproduction and Embryology in 2014, where the results of 674 cases of luteal phase stimulation were presented [21].

In-vitro maturation

In-vitro maturation (IVM) involves obtaining immature oocytes, maturing them, and then fertilizing them. Immature oocytes from small antral follicles are obtained by transvaginal aspiration after short stimulation with follicle-stimulating hormone (FSH) and/or human chorionic gonadotropin (HCG), if necessary. Harvested oocytes are matured in-vitro into fertilizable metaphase II oocytes and can then be cryopreserved. It is unnecessary to expose patients to high-dose gonadotropin therapy with this method, and the time required before follicular puncture is shorter than with conventional stimulation, making it easier to avoid a delay in the start of chemotherapy. Immature oocytes can also be obtained during processing of biopsied ovarian tissue. IVM of oocytes during cryopreservation of ovarian tissue offers an additional option of fertility preservation without additional risk and expense for the patient [22]. However, with the exception of results from a few research groups, data on pregnancy rates with this procedure are still very limited and the reported rates are lower than those with conventional in-vitro fertilization (IVF) [23, 24].

Cryopreservation of Ovarian Tissue

Cryopreservation of ovarian tissue has been investigated as a method of fertility preservation for more than a decade and has recently achieved considerable success. Over 25 live births have been reported following transplantation of cryopreserved ovarian tissue ([25] and personal communication). Technically, ovarian extraction is a simple procedure. Ovarian tissue can be obtained using minimally invasive techniques during laparoscopy, with unilateral ovariectomy or partial ovariectomy. Cryopreservation of ovarian tissue can be carried out independent of menstrual phase and, therefore, does not lead to any delay in oncological therapy (Table 3). In centers that offer cryopreservation of ovarian tissue,

Table 3. Comparison of the Fertility Preservation Options in Women

	Characteristics	Time required	Pregnancy rate
Cryopreservation of ovarian tissue	Laparoscopy, retransplantation	Immediately	Over 25 live births worldwide
Cryopreservation of unfertilized oocytes	Stimulation	10–14 d	20–30%
Cryopreservation of fertilized oocytes	Partner, stimulation	10–14 d	20–35%

Table 4. Comparison of the Fertility Preservation Options in Women

	Advantages	Disadvantages
Cryopreservation of ovarian tissue	– No treatment delay – Only way to preserve fertility in prepubertal girls – Treatment of women without a partner – No unwanted estrogen peak – Can be used in chemo- and radiotherapy – Restoration of fertility and endocrine function	– Risk that tumor cells may be reimplanted – Limited experience
Cryopreservation of unfertilized oocytes	– Can be used in chemo- and radiotherapy – Treatment of women without a partner	– Treatment delay – Not for prepubertal girls – Unwanted estrogen peak
Cryopreservation of fertilized oocytes	– Established method with high pregnancy rate – Can be used in chemo- and radiotherapy	– Partner – Treatment delay – Not for prepubertal girls – Unwanted estrogen peak

the procedure can be performed 1 day after the patient's first visit. After the tissue has been removed, it can be processed immediately or transferred in specific transportation containers to a center that is specialized in the cryopreservation of ovarian tissue with an associated cryobank.

A transport duration of 4–5 hours before cryopreservation is possible without any problems [26]. In addition, the viability of the tissue appears also to be preserved for longer periods of time (overnight transport), as the first live birth in Germany after re-transplantation of cryopreserved ovarian tissue has demonstrated [27].

In general, cryopreservation of ovarian tissue involves similar cryogenic processes as those utilized for cryopreservation of oocytes or embryos. "Slow freezing" is currently recommended for freezing ovarian tissue due to current higher efficiency with this method. In all previously published births following retransplantation of cryopreserved ovarian tissue, the tissue underwent slow freezing [22]. Of note, however, experimental tests demonstrate increasingly better results for vitrification [28]. The main purpose of cryopreservation of ovarian tissue is to preserve viable ovarian tissue for potential reimplantation if ovarian function fails following cancer treatment. Ovarian tissue is usually reimplanted at the natural site (orthotopically), in a peritoneal pocket, or in the residual ovarian bed, in order to allow spontaneous conception. The first reimplantation of ovarian tissue in Germany was performed in 2007 at the Department of Gynecology at Erlangen University Hospital [29]. Resumption of hormonal function in reimplanted tissue

has now been documented on many occasions, and there have been over 25 recently reported births following orthotopic reimplantation of cryoconserved ovarian tissue. The first birth after reimplantation of cryoconserved ovarian tissue in Germany occurred on October 10, 2011 [30]. The first international surveys of birth rate per ovarian tissue transplantation report a success rate of approximately 15%, which is likely to increase in the future.

The possibility that tumor cells may be concurrently reimplanted is a problem that must be discussed with the patient. To date, there have been no cases in which this has been confirmed, although considerable caution is advised regarding cryopreserved tissue from patients with leukemia, borderline ovarian tumor, or with a high risk of ovarian metastases (e.g., in adenocarcinoma of the cervix or stage III–IV breast cancer) [31, 32]. An option for these patients could be the maturation of follicles in vitro without transplantation. The ability of primordial follicles of ovarian tissue to fully mature in vitro and produce fertilizable, viable ova has only been demonstrated in a few animal model reports. Total in-vitro maturation of human oocytes from cryopreserved ovarian tissue is not yet possible [33]. However, it is quite conceivable that in the next few years this technique will be successful in humans [34].

Another option is ovarian tissue xenotransplantation. Ovarian tissue is transplanted into a surrogate host, such as immunodeficient mice (e.g., SCID mice), which do not have rejection reactions against foreign tissue. Follicles that mature can be punctured to obtain oocytes. This method has been used experimentally to test the vitality of frozen ovarian

tissue and to assess any malignant contamination [32] (Table 4).

Combination of Different Techniques

To increase the effectiveness of individual measures, a combination of the described fertility preservation strategies could be considered. For example, when 2 weeks are left before starting chemotherapy, ovarian stimulation could be performed and on the day of oocyte retrieval, ovarian tissue could also be harvested for cryopreservation at the same time [35]. Removing ovarian tissue first and starting ovarian stimulation approximately 1–2 days later is an alternative approach. The partial removal of ovarian tissue does not substantially affect the average number or quality of oocytes retrieved after ovarian stimulation [36]. Moreover, GnRH analogues could also be administered simultaneously with the induction of ovulation in these patients, thereby protecting remaining follicles.

Options for Fertility Preservation in Men

In men, cryopreservation of ejaculate or testicular tissue are established means of creating a fertility reserve. A therapeutically effective method that protects testicular function from gonadotoxic effects of chemotherapy or radiotherapy has to be developed [37]. Hormonal suppression of spermatogenesis in cytostatic chemotherapy (e.g. using GnRH analogues) has been attempted, but does not provide sufficient gonadal protection [38]. In radiotherapy, shielding of the testes from radiation or removal from the radiation field offers an effective measure to prevent unwanted damage and is widely practiced.

Cryopreservation of Sperm

Cryopreservation of an ejaculate is the established method of choice. Multiple sperm donations can be provided and a frozen depot created and maintained in reproductive medical centers, prior to the start of gonadotoxic treatment. This reserve could be used for ART-measures at a later date. Spermatozoa are relatively cryoresistant and post-thaw survival rate is high. Many pregnancies have been achieved using this method [39].

For prepubertal boys, cryopreservation of sperm is inappropriate because provision of an ejaculate is not yet possible. For adolescent boys undergoing puberty, germ cells can be obtained for cryopreservation through extraction from testicular biopsies or by electroejaculation. However, both methods are invasive procedures [40].

Cryopreservation of Sperm from Testicular Tissue (TESE)

A testicular biopsy could be performed to isolate spermatozoa from testicular tissue when no spermatozoa are found in the ejaculate. With this method, sperm cells are present in up to 75% of cases. TESE is an established process and is combined with intracytoplasmic sperm injection (ICSI) for later fertility. However, the success rate depends on the amount of viable spermatozoa present in testicular tissue at the time of cryopreservation [41].

The so-called Onco-TESE is particularly useful in patients with unilateral or bilateral testicular tumors, as well as patients with azoospermia before or after gonadotoxic therapy. Even for long-term survivors of oncological diseases with azoospermia, Onco-TESE can be offered as an opportunity for future fatherhood [42].

Experimental Approaches

Recovery of testicular tissue via biopsy provides a method for recovery of germ-line stem cells before the start of treatment which can be maintained through cryopreservation. This is currently the only conceivable method to preserve fertility for prepubertal boys and, therefore, the cryopreservation of immature testicular tissue should be considered for these patients. After a successful treatment, the tissue or the germ line stem cells contained therein could be used for process-

es which initiate the differentiation of germ cells. The intact tissue could be transplanted ectopically or orthotopically (autografts or ectopic xenografting). Future studies should elucidate the most appropriate method for clinical application [35].

Conclusion

In view of the good treatment options recently available for oncological diseases, it is now virtually essential to provide patients of reproductive age with counselling regarding fertility preservation. Fertility preservation is of great importance to many young women and men diagnosed with cancer, and in general the quality of counselling performance regarding fertility preservation is highly valued by patients [43]. Today, there is a large range of potential fertility preservation techniques available. For men, sperm cryopreservation remains the gold standard; by combination of cryopreservation with TESE/MESA or TESE/ICSI there is a good chance to realize a desire to have children. In women, transposition of the gonads before radiotherapy, the use of GnRH analogues, and cryopreservation of embryos, oocytes and ovarian tissue are available. The decision as to which treatment is most suitable in the patient's individual situation has to be made during a personal discussion with her and requires intensive interdisciplinary communication, among oncologists, radiotherapists, and reproductive medicine specialists. The individual approach is determined above all by the patient's age, the nature of the tumor entity, the remaining time before oncological treatment, the planned treatment measures, and the urgency of the patient's wish to have children. Support and advice are available in German-speaking countries from centers affiliated with the FertiPROTEKT network, as well as from the present authors. Details are available on the network's website,

www.fertiprotekt.eu

Conflict of Interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

References

1. Sonmez M, Oktay K. Fertility preservation in female patients. *Hum Reprod Update* 2004; 10: 251–66.
2. Bisharah M, Tulandi T. Laparoscopic preservation of ovarian function: an underused procedure. *Am J Obstet Gynecol* 2003; 188: 367–70.
3. Han SS, Kim YH, Lee SH, Kim GJ, Kim HJ, et al. Underuse of ovarian transposition in reproductive-aged cancer patients treated by primary or adjuvant pelvic irradiation. *J Obstet Gynecol Res* 2011; 37: 825–9.
4. Bedaiwy MA, Abou-Setta AM, Desai N, Hurd W, Starks D, et al. Gonadotropin-releasing hormone analog cotreatment for preservation of ovarian function during gonadotoxic chemotherapy: a systematic review and meta-analysis. *Fertil Steril* 2011; 95: 906–14.
5. Halle CF, Moore JMU, Phillips KA, Boyle FM, Hitre E, et al. Phase III trial (Prevention of Early Menopause Study [POEMS]-SWOG S0230) of LHRH analog during chemotherapy (CT) to reduce ovarian failure in early-stage, hormone receptor-negative breast cancer: An international Intergroup trial of SWOG, IBCSG, EOCG, and CALGB (Alliance). *J Clin Oncol* 2014; 32 (Suppl): LBA 505.
6. Munster PN, Moore AP, Ismail-Khan R, Cox CE, Lacey M, et al. Randomized trial using gonadotropin-releasing hormone agonist triptorelin for the preservation of ovarian function during (neo)adjuvant chemotherapy for breast cancer. *J Clin Oncol* 2012; 30: 533–8.
7. Demeestere I, Brice P, Peccatori FA, Kentos A, Gaillard I, et al. Gonadotropin-releasing hormone agonist for the prevention of chemotherapy-induced ovarian failure in patients with lymphoma: 1-year follow-up of a prospective randomized trial. *J Clin Oncol* 2013; 31: 903–9.
8. von Wolff M, Kammerer U, Kollmann Z, Santi A, Dietl J, Frambach T. Combination of gonadotropin-releasing hormone (GnRH) agonists with GnRH antagonists before chemotherapy reduce but does not completely prevent a follicle-stimulating hormone flare-up. *Fertil Steril* 2011; 95: 452–4.
9. Behringer K, Thienen I, Mueller H, Goergen H, Eibl AD, et al. Fertility and gonadal function in female survivors after treatment of early unfavorable Hodgkin lymphoma (HL) within the German Hodgkin Study Group HD14 trial. *Ann Oncol* 2012; 23: 1818–25.
10. Chung K, Donnez J, Ginsburg E, Meirou D. Emergency IVF versus ovarian tissue cryopreservation: decision making in fertility preservation for female cancer patients. *Fertil Steril* 2013; 99: 1534–42.
11. Horne G, Critchlow JD, Newman MC, Edozien L, Matson PL, Lieberman BA. A prospective evaluation of cryopreservation strategies in a two-embryo transfer programme. *Hum Reprod* 1997; 12: 542–7.
12. Al-Hasani S, Ozmen B, Koutlaki N, Schoepper B, Diedrich K, Schultze-Mosgau A. Three years of routine vitrification of human zygotes: is it still fair to advocate slow-rate freezing? *Reprod Biomed Online* 2007; 14: 288–93.
13. Liebermann J, Tucker MJ, Graham JR, Han T, Davis A, Levy MJ. Blastocyst development after vitrification of multipronuclear zygotes using the Flexipet denuding pipette. *Reprod Biomed Online* 2002; 4: 146–50.
14. Chen C. Pregnancy after human oocyte cryopreservation. *Lancet* 1986; 1: 884–6.
15. Cil AP, Seli E. Current trends and progress in clinical applications of oocyte cryopreservation. *Current Opin Obstet Gynecol* 2013; 25: 247–54.
16. Smith GD, Serafini PC, Fioravanti J, Yadiid I, Coslovsky M, et al. Prospective randomized comparison of human oocyte cryopreservation with slow-rate freezing or vitrification. *Fertil Steril* 2010; 94: 2088–95.
17. Grifo JA, Noyes N. Delivery rate using cryopreserved oocytes is comparable to conventional in vitro fertilization using fresh oocytes: potential fertility preservation for female cancer patients. *Fertil Steril* 2010; 93: 391–6.
18. Noyes N, Porcu E, Borini A. Over 900 oocyte cryopreservation babies born with no apparent increase in congenital anomalies. *Reprod Biomed Online* 2009; 18: 769–76.
19. Mature oocyte cryopreservation: a guideline. *Fertil Steril* 2013; 99: 37–43.
20. von Wolff M, Thaler CJ, Frambach T, Zeeb C, Lawrenz B, et al. Ovarian stimulation to cryopreserve fertilized oocytes in cancer patients can be started in the luteal phase. *Fertil Steril* 2009; 92: 1360–5.
21. Germeyer A CE, Jauckus J, Strowitzki T, von Wolff M. Timing of ovarian stimulation in patients prior to chemo- or radiotherapy – an analysis of 674 stimulations [P-505]. Poster at the ESHRE-meeting in Munich, 2014. <http://www.posters2view.eu/eshre-2014/view.php?nu=505> (last accessed: September 8, 2014).

22. Huang JY, Tulandi T, Holzer H, Tan SL, Chian RC. Combining ovarian tissue cryobanking with retrieval of immature oocytes followed by in vitro maturation and vitrification: an additional strategy of fertility preservation. *Fertil Steril* 2008; 89: 567–72.
23. Chian RC, Uzelac PS, Nargund G. In vitro maturation of human immature oocytes for fertility preservation. *Fertil Steril* 2013; 99: 1173–81.
24. Roesner S, von Wolff M, Eberhardt I, Beuter-Winkler P, Toth B, Strowitzki T. In vitro maturation: a five-year experience. *Acta Obstet Gynecol Scand* 2012; 91: 22–7.
25. Donnez J, Dolmans MM, Pellicer A, Diaz-Garcia C, Sanchez Serrano M, et al. Restoration of ovarian activity and pregnancy after transplantation of cryopreserved ovarian tissue: a review of 60 cases of reimplantation. *Fertil Steril* 2013; 99: 1503–13.
26. Rosendahl M, Schmidt KT, Ernst E, Rasmussen PE, Loft A, et al. Cryopreservation of ovarian tissue for a decade in Denmark: a view of the technique. *Reprod Biomed Online* 2011; 22: 162–71.
27. Dittrich R, Lotz L, Keck G, Hoffmann I, Mueller A, et al. Live birth after ovarian tissue autotransplantation following overnight transportation before cryopreservation. *Fertil Steril* 2012; 97: 387–90.
28. Amorim CA, Curaba M, Van Langendonck A, Dolmans MM, Donnez J. Vitrification as an alternative means of cryopreserving ovarian tissue. *Reprod Biomed Online* 2011; 23: 160–86.
29. Dittrich R, Mueller A, Binder H, Oppelt PG, Renner SP, et al. First retransplantation of cryopreserved ovarian tissue following cancer therapy in Germany. *Dtsch Arzteblatt Intern* 2008; 105: 274–8.
30. Muller A, Keller K, Wacker J, Dittrich R, Keck G, et al. Re-transplantation of cryopreserved ovarian tissue: the first live birth in Germany. *Dtsch Arzteblatt Intern* 2012; 109: 8–13.
31. Dolmans MM, Marinescu C, Saussoy P, Van Langendonck A, Amorim C, Donnez J. Reimplantation of cryopreserved ovarian tissue from patients with acute lymphoblastic leukemia is potentially unsafe. *Blood* 2010; 116: 2908–14.
32. Lotz L, Montag M, van der Ven H, von Wolff M, Mueller A, et al. Xenotransplantation of cryopreserved ovarian tissue from patients with ovarian tumors into SCID mice – no evidence of malignant cell contamination. *Fertil Steril* 2011; 95: 2612–4.
33. Liebenthron J, Koster M, Drengner C, Reinsberg J, van der Ven H, Montag M. The impact of culture conditions on early follicle recruitment and growth from human ovarian cortex biopsies in vitro. *Fertil Steril* 2013; 100: 483–91.
34. Telfer EE, McLaughlin M. In vitro development of ovarian follicles. *Semin Reprod Med* 2011; 29: 15–23.
35. Dittrich R, Lotz L, Mueller A, Hoffmann I, Wachter DL, et al. Oncofertility: combination of ovarian stimulation with subsequent ovarian tissue extraction on the day of oocyte retrieval. *Reprod Biol Endocrinol* 2013; 11: 19.
36. Huober-Zeeb C, Lawrenz B, Popovici RM, Strowitzki T, Germeyer A, et al. Improving fertility preservation in cancer: ovarian tissue cryobanking followed by ovarian stimulation can be efficiently combined. *Fertil Steril* 2011; 95: 342–4.
37. Jahnukainen K, Ehmcke J, Hou M, Schlatt S. Testicular function and fertility preservation in male cancer patients. *Metabol* 2011; 25: 287–302.
38. Shetty G, Meistrich ML. Hormonal approaches to preservation and restoration of male fertility after cancer treatment. *J Natl Cancer Inst Monogr* 2005; 34: 36–9.
39. Schlatt SKS. Fertilitätsprotektion bei Männern. *Gyn Endocrinol* 2012; 10: 91–7.
40. Meseguer M, Garrido N, Remohi J, Pellicer A, Simon C, et al. Testicular sperm extraction (TESE) and ICSI in patients with permanent azoospermia after chemotherapy. *Hum Reprod* 2003; 18: 1281–5.
41. Ramasamy R, Lin K, Gosden LV, Rosenwaks Z, Palermo GD, Schlegel PN. High serum FSH levels in men with nonobstructive azoospermia does not affect success of microdissection testicular sperm extraction. *Fertil Steril* 2009; 92: 590–3.
42. Hsiao W, Stahl PJ, Osterberg EC, Nejat E, Palermo GD, et al. Successful treatment of postchemotherapy azoospermia with microsurgical testicular sperm extraction: the Weill Cornell experience. *J Clin Oncol* 2011; 29: 1607–11.
43. Denschlag D, Germeyer A, Nawroth F, Lawrenz B, Henes M, et al. Counselling performance about fertility preservation in young women facing cancer: a prospective multicentric evaluation of patient's concerns and experiences in 146 women. Selected oral communication session at the ESHRE-meeting in Munich, June 2–July 2, 2014.

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