Sexual rehabilitation after treatment for gynaecological cancer

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A controlled study on vaginal blood flow during sexual arousal among early stage cervical cancer survivors treated with conventional radical or nerve-sparing surgery with or without radiotherapy

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International Journal of Gynecolgical Cancer (2017); in press.

Abstract

Objectives

Sexual problems among cervical cancer survivors may in part be caused by reduced vaginal blood flow due to damaged hypogastric nerves during radical hysterectomy with pelvic lymphadenectomy, and/or by radiation-induced vaginal changes after pelvic radiotherapy. A nerve-sparing modification of radical hysterectomy (NSRH) may preserve vaginal blood flow. Vaginal blood flow during sexual arousal was compared between different treatment modalities.

Methods

We investigated pre-menopausal women treated for early-stage cervical cancer with radical hysterectomy (*n* = 29), NSRH (*n* = 28), NSRH with radiotherapy (*n* = 14), and controls (*n* = 31). Genital and subjective sexual arousal in response to sexual stimuli were measured using vaginal photoplethysmography, and a questionnaire. Results were compared by using a between (treatment groups) by within (stimulus) study-design.

Results

Participants were 29-51 (mean: 42) years old and included 1-14 (mean: 5) years after treatment. Measured vaginal blood flow in women treated with NSRH was similar to controls. Women treated with radical hysterectomy had a significantly lower vaginal blood flow compared to controls overall and lower compared to the NSRH group during sexual stimulation. Women treated with radiotherapy had a vaginal blood flow intermediate between the other groups without significant differences. The erotic films were equally effective in enhancing subjective sexual arousal among treatment groups.

Conclusions

Sexual dysfunctions are often distressing. Many patients and partners experience psychosexual healthcare needs, but the provided information and care is generally limited. Psychosexual support should go beyond physical sexual functioning, and should take aspects such as sexual distress, relationship satisfaction, and the partner perspective into account. Additionally, offering more practical and reassuring information about sexuality after cervical cancer would be valuable for both CCSs and their partners.

Introduction

In the Netherlands early-stage (FIGO IA2 – IIA) cervical cancer patients are primarily treated with radical hysterectomy with pelvic lymphadenectomy (RH). The conventional surgical RH procedure for stage IB and IIA cervical cancer is a modified Wertheim operation with adaptations by Meigs and/or Okabayashi.[124] Since 2000, nerve-sparing modifications of the RH (NSRH) have been developed in Leiden.[59,60] This modification aims to prevent damage to the pelvic autonomic nerves and reduce the risk of sexual problems.[18,22,31,59,125] For approximately one third of women surgery is followed by adjuvant radiotherapy if lymph node metastases and/or other risk factors are found.[7]

Although RH for early stage cervical cancer leads to good survival, sexual morbidity due to treatment is still a matter of concern. Frequently reported sexual problems are diminished lubrication, dyspareunia, vaginal shortening and/or tightening, and subsequent sexual distress. Cervical cancer survivors (CCS) reported significantly more sexual problems, both compared to their situation prior to treatment, and to healthy controls.[13,18,31]

The vaginal blood flow response to sexual stimuli, and subsequent vaginal lubrication, is a reflex innervated by the hypogastric nerve.[126-129] During RH the pelvic autonomic hypogastric plexus may become damaged, leading to reduced vaginal blood response and subsequent vaginal dryness during sexual arousal.[34,35,126,130] This mechanism possibly causes various sexual problems experienced by CCS.[13,18,31] Maas et al. (2004) found that the vaginal blood flow response to sexual stimuli to be lower in CCS after RH, both compared to women who had undergone a simple hysterectomy and to healthy controls.[125]

In a previous pilot study we explored whether conducting a NSRH prevents the reduction in vaginal blood flow response. We compared ten women after NSRH to 13 women after RH and 14 healthy controls. According to the results there was a trend for a lower vaginal blood flow response after RH compared to NSRH.[131] Vaginal blood flow in women treated with NSRH was similar to healthy controls.[131] A larger study was needed before conclusions as to the efficacy of NSRH could be drawn.

Pelvic radiotherapy (RT) may lead to vaginal fibrosis, stenosis and mucosal atrophy with vaginal dryness, and can induce sexual morbidity.[30,49] Women who were treated with RT more often reported vaginal shortening and/or tightening, decreased lubrication, and dyspareunia compared to women treated with RH alone.[30,49] A small study indicated that the vaginal blood flow response was reduced after RT as well.[132] Therefore, it should be evaluated whether treatment with postoperative RT counteracts the expected preserved vaginal blood flow response after NSRH.

This psychophysiological, controlled study is an extension of our pilot study.[131] It was investigated whether women treated with NSRH have a less disrupted vaginal blood flow response during sexual stimulation than women treated with RH, and whether it

is similar compared to age-matched healthy controls. Also, it was explored whether treatment with postoperative RT is associated with a decreased vaginal blood flow response after NSRH.

Methods

Participant recruitment

For this study we recruited women to enlarge the groups of our original pilot study using an identical procedure. We enlarged the groups who had undergone RH, NSRH, and the healthy controls that were recruited by Pieterse et al. before 2008.[131] The effect of postoperative RT was investigated by including a fourth treatment group of women treated with NSRH and RT (NSRH/RT).

CCS were selected from medical files at Academic Medical Centre Amsterdam (AMC) and Leiden University Medical Centre (LUMC). The age-matched control women were recruited through advertisements in diverse media. Eligible women received information about the study by mail. Women that were interested to participate were subsequently screened on in- and exclusion criteria by telephone.

Eligible CCS were treated for early stage cervical cancer (FIGO IA2 – IIA); treated with RH using the Okabayashi method at AMC, or NSRH-Swift procedure, with or without RT, at LUMC. All eligible women had to be between 18 and 51 years of age and at least 12 months after treatment.

Exclusion criteria for CCS were signs of recurrent or metastatic cervical cancer; removed ovaries during surgery; and treatment with neoadjuvant chemotherapy and/or postoperative chemoradiation. Control women were excluded if they had a history of cancer; a history of abdominal or pelvic surgery; were pregnant; or had participated in research regarding sexual arousal during the past year. Women were excluded from all treatment groups if they were not able to understand Dutch; or had undergone other perineal, pelvic or abdominal surgery. Furthermore, as our pilot study and previous literature demonstrated that post-menopausal women had a lower vaginal blood flow response compared to premenopausal women, women older than 51 years and/or with post-menopausal status were excluded from all treatment groups to control for confounding.[131,133] When eligible women between 40 to 51 years of age reported menopausal complaints, a blood sample was taken to measure their follicle stimulation hormone (FSH) and estradiol levels. Women were considered postmenopausal when serum-FSH > 40 IU/l and/or estradiol ≤ 20 pg/ml.[134] In case of doubt, women were classified as postmenopausal and excluded. Since pelvic RT induces menopausal changes, and as in none of the current participants an ovary had been transposed, these exclusion criteria were not applied to the women treated with NSRH/RT.[16]

Participants received a financial compensation of 45 euros and compensation for travel expenses. This study was approved by the LUMC Medical Ethics Committee.

Measurements

Genital arousal

Vaginal pulse amplitude (VPA) in response to sexual stimuli was measured by a vaginal photoplethysmograph: a menstrual tampon-sized device containing an orange-red light source and a photocell. The light source illuminates the capillary bed of the vaginal wall and the phototransistor responds to the light backscattered by the vaginal wall and the blood circulating within it. When the signal is connected to an alternating current (AC) amplifier, vaginal pulse amplitude (VPA) is measured, which reflects the phasic changes in vaginal engorgement accompanying each heartbeat, with larger amplitudes reflecting higher levels of vaginal vasocongestion.[135–138] VPA is a sensitive, specific, and reliable measure of vaginal vasocongestion, and has been used in earlier studies that observed diminished vaginal blood flow in women with neurological damage and in women after RH. VPA was recorded continuously during the experimental session.

The procedure and stimulus material was identical to our previous study. After a 5-minute baseline period, during which a neutral film (a non-erotic documentary film excerpt) was shown and baseline measurements of genital response were collected, the first 5-minute erotic film was shown. Subsequently, again a 5-minute neutral film was shown followed by the second 5.5-minute erotic film. The two erotic film excerpts (consisting of videos depicting cunnilingus and intercourse) were taken from women-made, female-centred erotic videotapes.[139]

Subjective arousal

Subjective sexual arousal was assessed after each neutral and each erotic film by one item asking participants to indicate their feelings of sexual arousal on a 7-point Likert scale (ranging from 1 “not at all” to 7 “very strong”).[140]

Participant characteristics

Items measuring socio-demographic characteristics that were included were age (in years), having a partner (yes/no), educational level (primary/secondary/tertiary), negative sexual experience (yes/no) and being sexually active (yes/no). Treatment data, time since treatment (months) and hormone use (as part of hormone replacement therapy after RT, or oral or hormonal intrauterine contraception in control participants) (yes/no) were gathered from CCS’ medical records. Sexual functioning was assessed using the 19-item *Female Sexual Function Index* (FSFI) (Cronbach’s α = .97 within the current sample).[91] Higher scores indicate better sexual functioning. Furthermore, sexually related personal distress was assessed with the 12-item *Female Sexual Distress Scale* (FSDS) (Cronbach’s α = .92 within the current sample).[91,141] Higher scores indicate higher levels of sexual distress.

Experimental procedure

Participants were asked to complete the questionnaires prior to their visit. During the first part of the participants’ visit they were instructed about the genital device and their informed consent and questionnaires were obtained. Participants privately

inserted the vaginal device and further instructions were presented on a monitor in the participant room. It was emphasized that the participant could stop the experiment at any time without having to provide a reason. One trained female researcher (RB), not blinded to the treatment group, tested all participants.

Statistical analysis

A software program (VSRRP98; developed by the Technical Support Department of Psychology, University of Amsterdam) was used to analyse the genital data. VPA was sampled at 20 Hz across baseline and subsequent trails. A two-pass algorithm for automatic artefact removal (©Molenkamp Technical Support Group University of Amsterdam) was used to analyse the VPA data. After artefact deletion the peak-to-trough amplitude was calculated for each remaining pulse and averaged over 60 seconds epochs.

Prior to analysis, all dependent variables were examined for fit between their distributions and the assumptions using univariate analyses. In order to reduce positive skewness of the VPA data, all VPA data were logarithmically transformed ($\log_{10}$). For each stimulus (two neutral stimuli and two erotic stimuli), a $\log_{10}$ VPA mean score were calculated by averaging all epochs of the specific stimulus. To analyse differences in the $\log_{10}$ VPA mean scores between four groups for the four stimuli, the $\log_{10}$ VPA mean scores were submitted to a 4 (treatment group) X 4 (stimulus) repeated measurements ANOVA. Furthermore, to control for baseline differences in VPA, the $\log_{10}$ VPA mean scores were also submitted to a 4 (group) x 2 (erotic stimulus) repeated ANCOVA, using each individual's $\log_{10}$ mean baseline score of the first neutral stimulus as covariate.

To analyse differences in the subjective sexual arousal between the four groups for the four stimuli the mean subjective arousal scores were submitted to a 4 (treatment group) x 4 (stimulus) repeated measures ANOVA. To assess differences in participant's characteristics and dependent variables between the four groups one-way ANOVA's or chi-squared tests were used. The outcomes of the subjective measurements and the objective measurement were compared and used to describe the subject populations in detail. In case of significant differences in participant characteristics between groups, their influence on genital arousal was evaluated by conducting covariance analysis.

All data was analysed using IBM SPSS version 20 (Armonk, NY, USA) and a significance level of 5%. Effect sizes were reported as d, ηp^2 and V, and classified as small ($d = 0.2$; $\eta p^2 = .01$; $V = .10$), medium ($d = 0.5$; $\eta p^2 = .06$; $V = .30$), or large ($d \geq 0.8$; $\eta p^2 = .14$; $V = .50$).[142] With an alpha value of 0.05, a power of 80% and an effect size of $d = 0.8$, a minimum of 26 women for each treatment group was needed.[142]

Results

Participant population

The RH group (n = 29) consisted of 12 women who were recruited before 2008 by Pieterse et al. (2008) and 17 women recruited at the AMC in the current extended phase of the study.[131] One woman treated with RH recruited before 2008 was 52 years old at the time of measurement and excluded from further analyses. The NSRH group (n = 28) consisted of 10 women who were recruited before 2008 and 18 women after 2008. Furthermore, in this phase of the study we recruited 14 women treated with NSRH/RT. In total, 327 out of 429 (76%) eligible CCS did not participate, due to lack of time (n = 48), no interest because of a lack of sexual problems (n = 36), intrusive nature of the experiment (n = 70), a negative association with the cancer (n = 17), travel distance to the hospital (n = 7), or unstated reasons (n = 149).[131] Lastly, the healthy control group (n = 31) consisted of 12 women who were recruited before 2008 and 19 women that were willing to participate after 2008. Two controls who were recruited before 2008 were 52 years old and excluded.

Participant characteristics

Women in the RH group were treated about twice as long ago in comparison to women treated with NSRH with and without RT (see Table 1, page 56). Furthermore, women treated with NSRH were educated at secondary level relatively more often compared to the other three groups. As expected, the moment of participant inclusion (before or after 2008) differed between treatment groups, since none of the women treated with RT were recruited before 2008. Due to the inclusion criteria, women treated with NSRH/RT reported to use hormone replacement therapy more often, compared to the other three participant groups.

Univariate results indicated that, among sexually active participants, there was a non-significant trend for different levels of sexual dysfunction between groups, while explorative post-hoc analyses showed no significant differences between groups (F(3, 87) = 2.19, p = .096, ηp^2 = .07, post-hoc p = .426 to 1.000). However, women in the NSRH/RT group reported higher levels of sexual distress compared to the other three groups (F(3, 97) = 5.85, p = .001, ηp^2 = .16). No significant differences between groups were found with regard to age as intended, having a partner, having had negative sexual experiences or sexual activity.

Since treatment groups differed with regard to several characteristics, the influence of these characteristics on our primary outcome, vaginal blood flow, were analysed. The VPA mean scores throughout the experimental session were not influenced by the moment of inclusion of participants (F(1, 100) = 2.38, p = .126, ηp^2 = .02), hormone use (F(1, 96) = 0.36, p = .552, ηp^2 = .004), time since treatment while controlling for treatment group (β = -.11, t(1, 70) = -.70, p = .486), or sexual distress (β = -.003, t(1, 96) = -.73, p = .468). Therefore, the following analyses were not controlled for participant characteristics.

Genital arousal

Figure 1 shows the VPA responses of the treatment groups throughout the experimental session. The overall VPA mean scores were significantly different between the four treatment groups ($F(3, 102) = 6.55$, $p = .001$, $\eta p^2 = .17$); the RH group had an overall lower VPA mean score than the NSRH group ($p = .005$) and control group ($p < .001$), but not compared to the NSRH/RT group ($p = .115$). The NSRH groups with and without RT, and control group did not significantly differ from each other ($p = 1.000$). Also, the VPA mean scores were significantly different between the four stimuli (film fragments) ($F(3, 102) = 147.22$, $p < .001$, $\eta p^2 = .60$). The VPA mean scores during the two erotic stimuli were significantly higher than the VPA mean scores during the two neutral stimuli. Also, the VPA mean scores during the second neutral and erotic films were significantly higher than during the first neutral, and erotic films ($p <.001$). See Table 2, page 57.

An interaction effect was found and the treatment groups showed significantly different VPA responses to the four film fragments ($F(9, 294) = 2.91$, $p = .003$, $\eta p^2 = .08$). During the first neutral film fragment, at baseline, the four groups significantly differed ($F(3, 102) = 4.02$, $p = .010$, $\eta p^2 = .11$); the RH group had a lower VPA mean score (3.34 ± 0.41) compared to the controls (3.68 ± 0.41) ($p = .009$, $d = 0.84$), but a non-significant trend compared to the NSRH group (3.60 ± 0.36) ($p = .100$, $d = 0.69$) and no difference compared to the NSRH/RT group (3.63 ± 0.45) ($p = .176$, $d = 0.66$). The NSRH groups with and without RT,

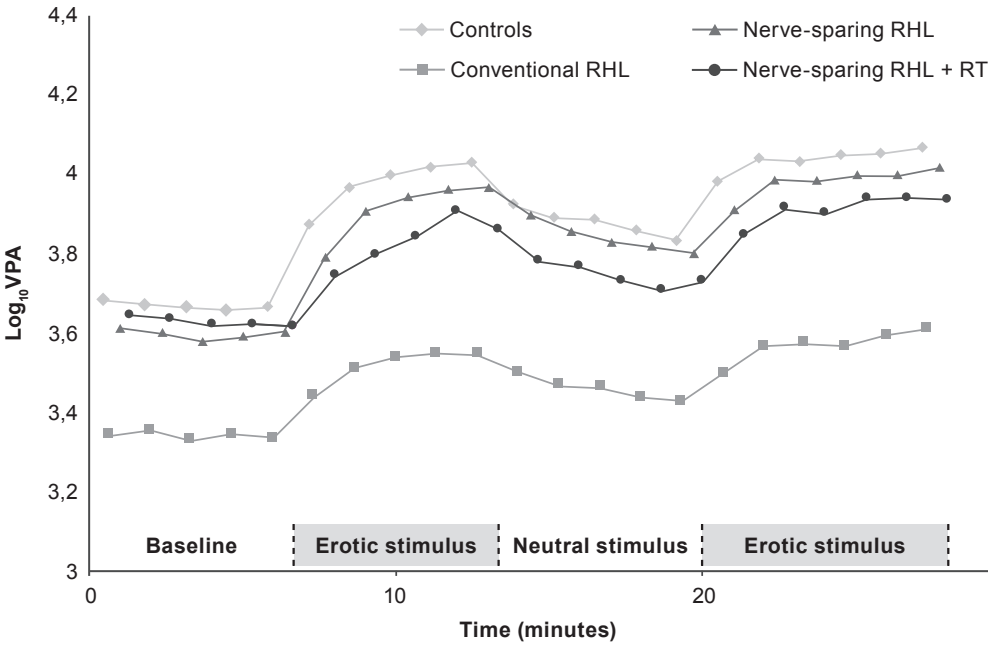

Figure 1. Change in logarithmically transformed mean vaginal pulse amplitude (log_{10} VPA) during the experimental session: Neutral stimulus 1 (baseline assessment) (1-5 min), Erotic stimulus 1 (6-10 min), Neutral stimulus 2 (11-15 min), Erotic stimulus 2 (16-21 min). Controls $n = 31$; Conventional RHL $n = 29$; Nerve-sparing RHL $n = 28$; Nerve-sparing RHL + RT $n = 14$. RHL = radical hysterectomy with pelvic lymphadenectomy; RT = postoperative radiotherapy.

Table 1
Descriptive characteristics of all participants.

		Controls	Conventional RHL	Nerve-sparing RHL	Nerve-sparing RHL with EBRT	F / χ^2	Effect-size[4]
		n = 31	*n* = 29	*n* = 28	*n* = 14		
Socio-demographic							
Treatment centre	LUMC	N/A	12 (41)	28 (100)	14 (100)	32.37***	.68
	AMC	N/A	17 (59)	N/A	N/A		
Time of inclusion	<2008[1]	12 (39)	12 (41)	10 (36)	N/A	8.32*	.29
	>2008	19 (61)	17 (59)	18 (64)	14 (100)		
Age (years)		41.42 ± 5.54	43.62 ± 6.15	40.68 ± 4.71	43.07 ± 5.15	1.69	.05
Time since treatment (months) (*n* = 75)		N/A	88.55 ± 43.06 [a]	30.68 ± 16.02 [b]	37.08 ± 19.76 [b]	28.16***	.45
Educational level	Secondary	15 (48)	17 (59)	23 (82)	7 (50)	8.10*	.28
	Tertiary	16 (52)	12 (41)	5 (19)	7 (50)		
Partner (yes)		23 (74)	20 (69)	22 (79)	11 (79)	0.84	.09
Hormone use (yes) (n = 98)		5 (16)	2 (7)	0 (0)	11 (79)	41.89***	.65
Negative sexual experience (yes) (*n* = 97)		4 (15)	6 (21)	4 (14)	2 (14)	0.54	.08
Sexually active		28 (90)	27 (93)	22 (79)	11 (79)	3.68	.19
Questionnaires							
Sexual functioning (FSFI)[2]		29.71 ± 4.83	29.76 ± 4.88	27.13 ± 5.01	26.30 ± 6.56	2.19	.07
Sexual distress (FSDS)[3]		6.94 ± 6.46 [a]	8.34 ± 8.09 [a]	9.92 ± 9.97 [a]	18.62 ± 11.58 [b]	5.85**	.16

LUMC: Leiden University Medical Centre; AMC: Amsterdam Medical Centre Amsterdam; RHL: radical hysterectomy with pelvic lymphadenectomy; RT: postoperative radiotherapy. Data are displayed as: Average ± standard deviation; Number and percentage of participants to which characteristic is applicable. Due to rounding percentages may not add to one hundred. [1] Recruited by Pieterse et al. (2008). [2] FSFI: *Female Sexual Function Index*; results among sexually active participants. [3] FSDS: *Female Sexual Distress Scale*. [4] Effect-sizes V for χ^2-tests and ηp^2 for F-tests; classified as small (ηp^2 = .01; V = .10), medium (ηp^2 = .06; V = .30), or large (ηp^2 = .14; V = .50) (Cohen 1988). *p < .05, **p < .01, ***p < .001. [a b c] Significantly different from other group(s) with p < .05.

and healthy controls did not significantly differ from each other (p = 1.000).

While controlling for the VPA differences at baseline, the VPA mean scores were significantly different between the four treatment groups during the first erotic film (F(3, 102) = 4.87, p = .003, ηp^2 = .13) and during the second erotic film (F(3, 102) = 4.53, p = .005, ηp^2 = .12). The RH group showed a lower VPA mean score both compared to the NSRH group (p = .009 and p = .007 respectively) and the controls (p = .017 and p = .020 respectively), but not compared to the NSRH/RT group (p = 1.000 and p = .802 respectively). The NSRH groups with and without RT, and healthy controls did not significantly differ from each other during both erotic films (p = .316 to 1.000).

Subjective arousal

The four treatment groups reported comparable levels of subjective sexual arousal throughout the experiment (F(3, 102) = 0.78, p = .510, ηp^2 = .02). Furthermore, participants reported significantly higher levels of subjective sexual arousal erotic film 1 and 2 compared to during neutral film 1 and 2 (F(3, 102) = 332.05, p < .001, ηp^2 = .77). These results indicated that the erotic films were equally effective in enhancing subjective sexual arousal among the treatment groups. See Table 2.

Table 2
The untransformed vaginal pulse amplitude mean scores and subjective arousal scores during the four stimuli for the four groups.

	Controls	**Conventional RHL**	**Nerve-sparing RHL**	**Nerve-sparing RHL with EBRT**
	***n* = 31**	***n* = 29**	***n* = 28**	***n* = 14**
Objective report: VPA (mV) [1]				
Neutral stimulus 1	1.96 ± 1.34	1.00 ± 0.76	1.70 ± 1.37	2.07 ± 1.95
Erotic stimulus 1	4.13 ± 2.37	1.69 ± 1.56	3.53 ± 2.33	3.22 ± 3.03
Neutral stimulus 2	3.35 ± 1.98	1.24 ± 0.87	2.99 ± 2.14	2.61 ± 2.19
Erotic stimulus 2	4.73 ± 2.62	1.84 ± 1.64	4.07 ± 2.81	3.87 ± 3.67
Subjective report: sexual arousal (Likert scale)				
Neutral stimulus 1	1.19 ± 0.40	1.34 ± 0.72	1.50 ± 1.00	1.14 ± 0.36
Erotic stimulus 1	3.77 ± 1.43	3.66 ± 1.37	3.61 ± 1.17	3.57 ± 0.85
Neutral stimulus 2	1.26 ± 0.63	1.34 ± 0.61	1.14 ± 0.36	1.07 ± 0.27
Erotic stimulus 2	4.74 ± 1.46	4.41 ± 1.27	3.82 ± 1.31	4.00 ± 0.68

Data are displayed as: Average ± standard deviation. [1] VPA: Vaginal Pulse Amplitude; mV: millivolt.

Discussion

In this extended study we have enlarged the NSRH, RH, and control groups of our pilot study, and also added a fourth treatment group of cervix cancer survivors treated with NSRH and postoperative RT.[131] It was found that premenopausal women treated with NSRH showed a vaginal blood flow that was comparable to healthy controls, both at rest and in response to sexual stimulation. Women treated with conventional RH, however, showed a significantly lower vaginal blood flow compared to control women, both at rest and during sexual stimulation. Compared to women who had undergone NSRH, those treated with RH had a significantly lower response during sexual stimuli. The vaginal blood flow of women treated with postoperative RT did not differ from the other three groups. The erotic films that were used were equally effective in enhancing subjective sexual arousal among groups.

The results were in line with previous VPA research conducted by Maas et al. (2004), showing that RH was associated with a lower vaginal blood flow response in comparison to healthy controls.[125,131] Furthermore, our preliminary indications that the vaginal perfusion response among women treated with NSRH was better preserved than after RH, and similar to the response of the control women, were also confirmed.[131] These results support the hypotheses that the nerve-sparing modification of RH may better preserve the vaginal blood flow by reducing the denervation of the vaginal wall. The vaginal perfusion response differences between the treatment groups were also found after controlling for the individual baseline differences and, thus, not critically dependent on the baseline vaginal blood flow at rest.[131]

RT-induced fibrotic changes and damage to the micro-vascularity in the vaginal wall was expected reduce the vaginal blood flow among women treated with NSRH/RT.[44,132] However, in our small sample of NSRH/RT participants we could not confirm the previous hypothesis of Pras et al. (2003) that RT induces would reduce vaginal blood flow.[132] Moreover, the autonomic nerves, innervating the reproductive organs, are responsive to circulating steroids such as oestrogen. Both a change in the number of autonomic nerves due to RH, and lower levels of oestrogen due to radiation-induced menopause, may reduce vaginal blood flow.[143,144] However, the majority of our NSRH/RT sample used hormone replacement therapy.[145] Therefore, in order to draw conclusions regarding the impact of RT on vaginal blood flow and its subsequent impact on sexual functioning among survivors, further investigation is needed.

Despite their vaginal blood flow differences, the surgery groups did not differ with regard to their levels of sexual dysfunction or subjective sexual arousal throughout the experiment. This is in line with other studies reporting an absence of differences in sexual functioning between women treated with respectively without nerve-sparing intention.[13,131,146] The research results from Brotto et al. (2012) also showed that vaginal blood flow and sexual functioning are not necessarily associated.[103] Their mindfulness-based intervention for sexual concerns improved gynaecological cancer survivors' sexual functioning, and increased subjective sexual arousal during erotic film, while their physiological genital arousal remained unchanged.[103] Taken

together, the results indicated that the vaginal blood flow response after treatment is not the most important determinant of experienced sexual concerns among CCS. Sexuality after cancer treatment is a biopsychosocial phenomenon associated with both physical factors, such as fibrosis, anatomical changes and vaginal denervation, but also psychological and interpersonal factors, such as worry about pain or relationship dissatisfaction.[51,147] Therefore, it remains unknown to what extent conducting a nerve-sparing modification contributes to the prevention of patient-reported postoperative sexual morbidities in comparison to psychological or interpersonal interventions.

Several limitations of this study should be taken into account. While analysing the differences between the women treated with surgery and control groups with regard to our outcome measurements, the power to detect large effects was sufficient (84-86%).[142] However, due to the sample sizes of these groups, the power to find medium or small effects was lower (46-48% and 12% respectively). This may have been a reason that only a non-significant trend was found for a lower vaginal blood flow at rest in the RH group compared to the NSRH group. Furthermore, since the NSRH/RT group was relatively small, the power to detect large (66-68%), medium (32-33%) or small effects (0.09%) when comparing this group to the others was even smaller. Therefore, the inability to find differences in the vaginal blood flow response between women treated with or without RT may be due to the limited power of the analyses. Furthermore, the difficulty we found when recruiting women for our study may be due to the invasive and possibly confronting nature of the experiment. This may have introduced bias as women who had more negative experiences during (sexual rehabilitation after) treatment may have declined participation more often.

In conclusion, our study confirms for the first time that the reduction of vaginal blood flow caused by conventional RH for early-stage cervical cancer, can be avoided by conducting a nerve-sparing modification of RH. The current study has clarified the impact of surgery for early-stage cervical cancer on the physical aspects of sexuality through objective assessment of the vaginal blood flow response during arousal. In view of the similar oncological outcomes, conducting NSRH may be preferred over RH. It is also important to stress that support for early-stage CCS should not only depend on the type of treatment, but rather on the patients' and partners' experience with their sexual recovery, and that addressing sexuality during rehabilitation after cancer treatment may reduce the risk of sexual dysfunction. The findings may enable further development of tailored patient information and support, and health care providers should support patients in the rehabilitation phase after treatment to prevent or reduce sexual distress among CCS.