Assessment of Sexual Function in Patients with Cancer Undergoing Radiotherapy – A Single Centre Prospective Study

DIMITRIOS VOMVAS[1], GREGORIS ICONOMOU[2], EVANTHIA SOUBASI[3], MICHAIL LEOTSINIDIS[4], HARALABOS P. KALOFONOS[2], STAVROULA BERATIS[3], DIMITRIOS KARDAMAKIS[1] and KONSTANTINOS ASSIMAKOPOULOS[3]

Departments of [1]Radiation Oncology, [2]Medical Oncology, [3]Psychiatry, [4]Public Health, University of Patras Medical School, Patras, Greece

Abstract. *Aim: The main objective was to delineate the rates and clinical course of sexual function and depression in cancer patients undergoing radiotherapy. Patients and Methods: Forty-eight male and 90 female radiotherapy-naive outpatients with breast or pelvic cancer completed the International Index of Erectile Function (IIEF) or the Female Sexual Function Index (FSFI), and the Hamilton Depression Scale (HDS) prior to (phase 1), at the end of (phase 2) and 12 months after radiotherapy (phase 3). Results: Overall, the majority of patients (93.8% of males and 80% of females) experienced intense sexual dysfunction. At presentation, males reported severe erectile dysfunction that was significantly associated with age. However, only in sexual desire was the difference between baseline and phase 3 significant. In females, an improvement was observed in all parameters of FSFI between phase 1 and 3. Females with stage III disease achieved lower scores in almost all parameters of FSFI than those with stage II. Finally, although a quarter of patients reported elevated depression scores, depression was not related to sexual function. Conclusion: A significant proportion of cancer patients experience intense levels of sexual dysfunction and depression throughout radiotherapy and the subsequent year. Pelvic radiotherapy affected sexual function to a higher degree than did breast radiotherapy.*

Quality of life (QoL) is now regarded important not only in oncology research, but also in the daily clinical practice. QoL is composed of many parameters, including sexuality (1, 2). Sexuality is a complex phenomenon with biological, interpersonal and psychological dimensions. The term 'sexual dysfunction' describes health problems interfering with sexual intercourse and reproduction, which in turn affect sexuality. Cancer patient groups have been studied regarding sexuality and sexual function in relation to their disease and impaired sexual function has been shown among those patients (3-5).

Radiotherapy (RT) has been shown to negatively affect sexual function, but the exact level of sexual impairment that patients can expect after RT remains uncertain (6-13). Most studies on post RT sexual dysfunction included patients with pelvic tumors (prostate cancer or uterine cancer). The most frequent sexual dysfunctions reported are loss of sexual desire (SD), erectile dysfunction (ED) and ejaculatory disorders in males, and loss of SD, decrease of lubrication, orgasm disorders and dyspareunia in females.

In the early 1980s, Goldstein *et al*. concluded that the main reason for the aggravation of erectile function post radiotherapy is vascular damage caused by the ionizing radiation (14). Additional factors include demyelination and fibrosis of the peripheral nerves and the radiation dose that the penile bulb and corpora cavernosa receive (15-21). The main causes of sexual dysfunction in females post radiotherapy include vaginal stenosis and fibrosis, decreased lubrication and vulvar fibrosis (22-25).

It has been reported that breast cancer patients who received adjuvant RT experience a certain degree of sexual dysfunction. In this group of patients, it has been shown that the type of surgery, chemotherapy and hormonal therapy, as well as psychological factors related to cancer diagnosis, are predominantly responsible for the differences observed in sexual function (26-31).

There are a number of both physician-administered and patient self-administered questionnaires available to evaluate sexual dysfunction. It is of paramount importance to obtain baseline pre-treatment data, as well as long-term follow-up data (32-35).

Thus, the first objective of the present study was to gain a better understanding of the frequency and clinical course of

Correspondence to: Dimitrios Kardamakis, Department of Radiation Oncology, University of Patras Medical School, 26504, Rion, Patras, Greece. Tel: +30 2610999540, Fax: +30 2610994475, e-mail: kardim@med.upatras.gr; d.kardamakis@yahoo.gr

Key Words: Sexual function, depression, radiotherapy.

sexual function and depression among Greek patients with either breast cancer or pelvic tumors who receive curative radiotherapy; the second objective was to examine the interrelations of those variables at three points in time.

Patients and Methods

Patients. The study was initiated in April 2006 and completed in September 2008. This is a prospective, single-centre clinical study approved by the Ethics Committee of the University Hospital (Protocol 105/3.4.06).

All patients had to meet the following eligibility criteria for inclusion in the study: histologically confirmed carcinoma of breast, prostate, urinary bladder, anus, uterus or rectum; no contraindication to external beam definitive RT (EBRT); ability to understand Greek; have a sexual partner during the period of the study; ability to attend the follow-up assessments.

Patients who had undergone RT in the past in the anatomic region of the thorax or pelvis, those with previous cancer (except basal cell carcinoma of the skin or *in situ* cervical carcinoma) and those with metastatic disease (stage IV) were excluded from the study. A radiation oncologist approached all patients fulfilling the inclusion criteria to assess their interest in participating in the study. After the initial consultation at the RT Department, all patients fulfilling the inclusion criteria were consecutively approached at random by a radiation oncologist and were informed in detail about the study. Prior to study participation, all patients signed an informed consent form.

Patients' sexual function and depression were evaluated prior to (phase 1), at the end of (phase 2), and 12 months after the completion of RT (phase 3). The evaluation included an interview and the completion of patients' self-reported questionnaires in the presence of two physicians, a radiation oncologist and a psychiatrist. Sociodemographic data were elicited from patients and disease-related information was obtained from the doctors or from the hospital charts.

Radiotherapy. All patients underwent EBRT daily, five times per week, which was administered by a linear accelerator. The dose per fraction to target volume ranged from 1.8 to 2.0 Gy and the total dose ranged from 50 to 70 Gy, depending on the histological type of the neoplasm. The dose was prescribed at the isocenter, according to the International Commission on Radiation Units and Measurements reference point (36).

Instruments (in order of administration). Depression severity was measured with the Greek 24-item version of the Hamilton Depression Rating Scale (HDRS24). This is a widely used observer rating scale, particularly thorough in the assessment of the somatic symptoms of depression. The HDRS includes 24 items rated on a scale of 0-2 or 0-4 (total score range: 0-76). Cut-off scores often applied are: 0-7 no depression, 8-13 mild, 14-18 moderate, 19-22 severe, 23 and above very severe (37).

Male sexual function was measured with the International Index of Erectile Function (IIEF) (34). The IIEF is a 15-item validated, multidimensional, self-administered questionnaire that includes five domains: erectile function (EF), orgasmic function (OF), sexual desire (SD), intercourse satisfaction (IS) and overall satisfaction (OS). The response to each question is given a numerical value of 0–5 or 1–5 and the sum of the values is the domain score. Higher scores indicate better sexual function. A score less than or equal to 25 characterizes erectile dysfunction (ED). In addition, severity of ED can be classified into five diagnostic categories: no ED (EF score=26-30); mild ED (EF score=22-25); mild to moderate (EF score=17-21); moderate (EF score=11-16); and severe (EF score=6-10).

The Female Sexual Function Index (FSFI) is a validated 19-item questionnaire designed to evaluate female sexual function. It includes six domains: desire, arousal, lubrication, orgasm, satisfaction and pain. Each domain is scored on a scale of 0 (or 1) to 5 (range for items 1, 2, 15 and 16=1-5), and was calculated as

Table I. *Patients' demographic and clinical characteristics*.

	All, n (%)	Females, n (%)	Males, n (%)
	138 (100)	90 (65.2)	48 (34.8)
Mean age, years	58.2 (29-84)	53.9 (29-81)	66.3 (31-84)
Cancer diagnosis			
Breast	72 (52.2)	72 (79.9)	-
Lung	3 (2.2)	-	3 (6.2)
Prostatic	18 (13)	-	18 (37.4)
Urinary bladder	3 (2.2)	-	3 (6.2)
Rectal	28 (20.3)	7 (7.7)	21 (43.7)
Chordoma	1 (0.7)	-	1 (2.0)
Anal	4 (2.9)	2 (2.2)	2 (4.1)
Uterine	9 (6.5)	9 (9.9)	-
Stage of disease			
I	32 (23.2)	30 (33.3)	2 (4.1)
II	60 (43.5)	30 (33.3)	30 (62.4)
III	46 (33.3)	30 (33.3)	16 (33.3)
Chemotherapy			
Yes	92 (66.7)	65 (72.2)	27 (56.2)
No	27 (19.6)	24 (26.6)	3 (6.2)
Hormonotherapy	19 (13.8)	1 (1.1)	18 (37.4)
Financial status			
>500 € per month	118 (85.5)	76 (84.4)	42 (87.4)
≤500 € per month	20 (14.5)	14 (15.5)	6 (12.4)
Residence			
Village	33 (23.9)	16 (17.7)	17 (35.4)
Town	105 (76.1)	74 (82.2)	31 (64.5)
Smoking (n/day)			
>10	38 (27.5)	22 (24.4)	16 (33.3)
≤10	2 (1.4)	2 (2.2)	-
No	98 (71)	66 (73.3)	32 (66.6)
Alcohol abuse			
Yes	20 (14.5)	4 (4.4)	16 (33.3)
No	118 (85.5)	86 (95.5)	32 (66.6)
Marital status			
Married	113 (81.9)	72 (79.9)	41 (85.4)
Unmarried	12 (8.7)	6 (6.6)	6 (12.4)
Divorced	3 (2.2)	3 (3.3)	-
Widowed	10 (7.2)	9 (9.9)	1 (2)
Type of surgery			
Biopsy	32 (23.2)	4 (4.4)	28 (58.3)
Conservative	53 (38.4)	53 (58.8)	-
Radical	53 (38.4)	33 (36.6)	20 (41.6)
Performance status			
0	91 (65.9)	70 (77.7)	21 (43.7)
1	44 (31.9)	20 (22.2)	24 (49.9)
2	3 (2.2)	-	3 (6.2)

Table II. *Severity of depression over the study period for both sexes.*

Depression severity	Males (%)			Females (%)			Overall (%)		
	Phase 1 n=48	Phase 2 n=45	Phase 3 n=41	Phase 1 n=90	Phase 2 n=87	Phase 3 n=88	Phase 1 n=138	Phase 2 n=132	Phase 3 n=129
None	54.2	37.8	58.5	43.3	46.0	58.0	47.1	43.2	58.1
Mild	18.8	22.2	22.0	30.0	26.4	23.9	26.1	25.0	23.3
Moderate	10.4	17.8	4.9	10.0	9.2	5.7	10.1	12.1	5.4
Severe	6.3	2.2	4.9	6.7	6.9	2.3	6.5	5.3	3.1
Very severe	10.4	20.0	9.8	10.0	11.5	10.2	10.1	14.4	10.1

previously described by Rosen *et al*. (35). The maximum score for each domain is 6, the maximum total score is 36 and the minimum 2. While higher scores indicate better sexual function, a domain score of zero indicates no sexual activity during the past month. A score less than 26.55 denotes sexual dysfunction.

Statistical analyses. All statistical analyses were performed using the statistical software SPSS version 17 (SPSS Inc. Chicago, IL, USA). Since the majority of our variables were not normally distributed, non-parametric statistics were applied. Medians and ranges were used for descriptive purposes as the data failed to meet the assumption of a normal distribution. The Friedman test was used to detect fluctuations at different time points. Post-hoc pair-wise comparisons were performed by applying the Wilcoxon sign-rank test after controlling for type 1 error using Holm's sequential Bonferroni method. The Spearman r correlation coefficient was calculated to assess the relationship between continuous variables (sexual function and depression). Univariate regression models were used to assess the effects of various factors on sexual function, while multivariate models were applied to study the simultaneous effect. The statistical significance level was set at α=0.05.

Results

Patients. Out of the 174 patients initially assessed, 138 agreed to participate in the study. Patients who refused to participate in the study believed that sexual function was either a taboo issue or less important than survival from cancer. Forty-eight men (34.8%) and 90 women (65.2%) were included (acceptance rate=79.3%). A total of 399 structured interviews were held and analyzed by the end of the study. The evaluation included an interview and the completion of patients' self-reported questionnaires in the presence of a radiation oncologist and a psychiatrist. The basic demographic and clinical patients' characteristics are given in Table I. Seven patients died, six developed metastatic disease and two refused to attend the follow-up.

Depression over time. The first part of our analysis focused on the rates and clinical course of depression over time. As shown in Table II, 53% of all patients reported some kind of depressive symptomatology at phase 1. There were no significant changes in the percentage of patients who experienced severe depression at the three time points, with the exception of male patients at phase 2 for whom data showed an increase in the percentage of 'very severe' depression. However, the overall percentage of non-depressive patients increased from phase 1 (47%) to phase 3 (58%), although insignificantly.

Sexual function in females. Overall, the analysis revealed that 80% of women experienced sexual dysfunction at phase I. For all women, an improvement was observed in all parameters of the FSFI, *i.e*., arousal, desire, lubrication, orgasm, pain, and satisfaction over the course of the study. FSFI total scores at phase 3 were higher compared to those at phase 1 and 2 ($p<0.05$, Table III).

Patient age was found to play a role in sexual function, that is, lower scores for all domains were observed for females older than 65 years of age compared to their younger counterparts. The differences were significant at all three study phases ($p<0.001$).

The disease stage influenced FSFI scores in certain domains. Women with stage III disease achieved lower scores compared to those with stage II disease. At phase 1, the differences were marginal for FSFI total ($p=0.073$), arousal ($p=0.056$), pain ($p=0.084$) and satisfaction ($p=0.056$). At phase 2, the differences of the above parameters along with desire and orgasm gained statistical significance ($p<0.05$), while at phase 3, all the scores were statistically different ($p<0.05$).

Neither chemotherapy nor type of surgery appear to affect sexual function. Married women achieved higher scores in all parameters of FSFI compared to unmarried ones ($p<0.05$). Patients with ECOG PS=0 presented higher total FSFI scores at phase 3 compared to those with PS=1 ($p<0.05$).

Sexual function in males. Although the incidence of severe ED in all three phases of the study was impressive (Table IV), it remained stable over time (severe ED=79.2% phase 1, 82.2% phase 3). However, only in SD was the difference statistically significant, particularly at phase 1 and 3 ($p<0.05$). The scores of IIEF domains are given in Table V.

Table III. *Median scores of Female Sexual Function (FSFI) domains in all females from baseline (prior to radiotherapy, phase 1) to end of follow-up (at 12 months postradiotherapy, phase 3).*

FSFI domain		Phase 1 n=90	Phase 2 n=86	Phase 3 n=88
Arousal	Median	0[a]	0[b]	2.4[a,b]
	Min	0	0	0
	Max	6	6	6
	25th	0	0	0
	75th	3.6	3.9	4.5
Desire	Median	1.2[a]	1.2[b]	2.4[a,b]
	Min	1.2	0.6	1.2
	Max	6	5.4	5.4
	25th	1.2	1.2	1.2
	75th	2.5	3	3.6
Lubrication	Median	0[a]	0[b]	2.7[a,b]
	Min	0	0	0
	Max	6	6	6
	25th	0	0	0
	75th	4.8	5.1	5.1
Orgasm	Median	0[a]	0[b]	3[a,b]
	Min	0	0	0
	Max	6	6	5.2
	25th	0	0	0
	75th	4	4	4.4
Pain	Median	0[a]	0[b]	4[a,b]
	Min	0	0	0
	Max	6	6	6
	25th	0	0	0
	75th	6	6	6
Satisfaction	Median	2.4[a]	2.4[b]	3.4[a,b]
	Min	0.8	0.8	0.8
	Max	6	6	6
	25th	1.2	1.6	2.4
	75th	4.8	4.8	5.2
Total	Median	3.6[a]	3.6[b]	18.8[a,b]
	Min	2	1.4	2
	Max	35.2	34.6	34.6
	25th	2.8	2.8	3.6
	75th	25.3	26.4	28.5

Values within a row with different superscript letters (a, b) are significantly different at $p<0.05$.

Table IV. *Incidence of erectile dysfunction in males from baseline (prior to radiotherapy, phase 1) to end of follow-up (at 12 months postradiotherapy, phase 3).*

	Phase 1		Phase 2		Phase 3	
	n	%	n	%	n	%
Dysfunction	45	93.8	86	91.1	44	97.8
Normal	3	6.3	4	8.9	1	2.2
Mild	2	4.2	1	2.2	2	4.4
Mild-moderate	2	4.2	-	-	2	4.4
Moderate	3	6.3	2	4.4	3	6.7
Severe	38	79.2	38	84.4	37	82.2
Total	48	100	45	100	45	100

Table V. *Scores of International Index of Erectile Function (IIEF) domains from phase 1 to phase 3.*

IIEF domain		Phase 1 n=48	Phase 2 n=45	Phase 3 n=42
EF	Median	1	1	1
	Min	1	1	1
	Max	29	30	30
	25th	1	1	1
	75th	6.5	4	2
OF	Median	0	0	0
	Min	0	0	0
	Max	10	10	10
	25th	0	0	0
	75th	2	0	0
SD	Median	4[a]	3	3[a]
	Min	2	1	2
	Max	10	10	10
	25th	2	2	2
	75th	7	6	6
IS	Median	0	0	0
	Min	0	0	0
	Max	13	15	15
	25th	0	0	0
	75th	0	0	0
OS	Median	6	7	6
	Min	2	2	2
	Max	9	10	10
	25th	5	5	5
	75th	7	7	7

EF, Erectile function; OF, orgasmic function; SD, sexual desire; IS, intercourse satisfaction; OS, overall satisfaction. [a]significant difference ($p<0.05$) between phase 1 and 3.

Patient age influenced sexual function in phase 2. The percentage of severe ED were slightly increased in males >65 years of age (severe ED: 57.8% >65 years, 26.7% <65 years). Better sexual function was reported in patients <65 years of age for almost all parameters apart from OS and IS in phase 3.

It was observed that PS=0 affected all parameters of IIEF positively, but only in EF was it statistically significant during phase 1 and 2 ($p<0.05$).

Unmarried patients scored higher in certain parameters of IIEF compared to married participants. In particular, they presented better scores at a statistically significant level in EF in phase 2 and 3, in OF in phase 2 and in OS during phase 1 and 2 ($p<0.05$). Finally, ED was unrelated to the primary lesion, other treatments (*i.e.*, chemotherapy or hormonal therapy) and stage of disease.

Relationships between sexual function and depression. The final stage of our analysis revealed almost no significant relationships between FSFI, IIEF and HDRS24 at the three points in time.

Discussion

To our knowledge, this is the first prospective examination in Greece and among the few prospective studies in the literature to evaluate sexual function using specific instruments in various subgroups of cancer patients treated with RT. The main findings to emerge were the high percentage of sexual dysfunction recorded in both sexes at baseline and at all follow-ups. Interestingly, in the pelvic tumor group, no difference was observed between patients who underwent RT compared to those who received concurrent chemo-RT. Similar results have been reported by Pietrzak *et al*. in a randomized phase III study with 316 patients. The authors observed no difference in the parameters of QoL and sexual function between preoperative RT and chemo-RT (38).

Our results indicate that age plays an important role in sexual function for both sexes. Higher incidence of sexual dysfunction was observed in patients >65 years old compared to their younger counterparts. This corresponds well with the literature, which documents that in the general population, aging has a negative effect on sexual function. Nevertheless, older adults consider sexual function an important element of their QoL (39-42).

In the present study, the analyses showed that married females and unmarried males reported overall better sexual function compared to unmarried females and married males. Several investigations have postulated that in the general population, the absence of a sexual partner, and not necessarily the marital status, is a risk factor for the appearance of sexual dysfunction (43). For example, a retrospective study by Shabsigh *et al*. investigated sexual activity in males with ED treated with tadalafil and found that the timing of sexual intercourse attempts were equal in married and unmarried patients (44).

The present study reports that 12 months after the initiation of RT, the incidence of severe ED in males was 82.2%. To our knowledge, this is among the highest that has been reported thus far in the literature. Incrocci *et al*. reported that the incidence of ED in prostate cancer patients post-RT range from 7% to 72% (19, 20). Our results contradict previous studies that have reported that hormonal therapy negatively influences EF (45-48), with the exception of a study by Chen *et al*., who reported no adverse effects of hormonal therapy on EF (49). There are three possible explanations for these different results: first, the small percentage of prostate cancer patients included in our study (13%); second, the median age of this subgroup of patients, which was 78.5 (range 56-80) years; and third, all of our patients commenced neoadjuvant hormonal therapy before the initiation of RT, so at the time of baseline assessment (phase 1) they had likely already suffered impaired sexual function as an adverse effect of hormonal treatment.

Regarding the possible effects of tamoxifen on the sexual function of women, a number of studies suggest a negative effect of antiestrogen treatment on sexual function in breast cancer patients, implying that this treatment disrupts sexual function by causing premature menopause, with estrogen loss leading to vaginal atrophy and androgen loss perhaps reducing sexual desire and arousability (50-52). In our study, only one patient out of the 72 breast cancer patients received hormonal therapy, making the drawing of meaningful conclusions impossible.

In general, we consider IIEF and FSFI useful tools for the estimation of sexual function in cancer patients treated with RT. A disadvantage of these questionnaires is that they record sexual function in the "last four weeks" (53). The time interval from diagnosis until a patient receives RT can be up to four weeks. During this period, the patient is overwhelmed by the symptoms of their disease and the adverse effects of prior treatment that may influence their sexual life to a great extent. We think that the high incidence of sexual dysfunction recorded prior to RT is probably due to this fact.

Finally, although no significant changes emerged in depression rates over time, almost a quarter of our patients experienced severe levels of depression at the beginning of treatment and continued to do so twelve months post-treatment. The symptomatology rates observed correspond well with an earlier study of our group (2) and are comparable to those reported in other countries (54, 55). Our findings are in line with the literature, which argues that once depression appears, it persists even after treatment is completed (56). In all likelihood, the limited correlations observed between depression and sexual function may in part be attributable to the fact that sexual function or dysfunction is multidimensional. That is, sexual dysfunction may be the result of the disease itself, age, adverse effects of medication, previous treatment modalities or even the interplay between cultural, environmental, neurophysiological, endocrine and relationship factors alongside mood (57).

Our study suffers from certain limitations. Firstly, the sample and subgroup sizes make comparisons among treatment groups difficult. Secondly, different surgeons operated on the patients with pelvic tumors, making the application of nerve-sparing techniques difficult in all patients. Thirdly, our analysis did not include medical co-morbidities, which in turn might have affected QoL and sexual function. The fourth limitation concerns the use of FSFI, which, albeit criticized as not being the most suitable instrument for sexually inactive participants, has thus far

been the sole validated instrument for assessing sexual function available in Greek.

It is now well documented that the majority of cancer patients welcome the provision of well-structured oral and written information about various aspects of their treatment and everyday life, including sexual issues (53, 58-61). It is still rather common among physicians to be reluctant to ask direct questions about a patient's sexual life, believing that this is either a violation of their personal life or that sexuality is not part of the presenting problem, or that they are not adequately trained to deal with sexual concerns (57, 62).

Although there is a tendency to consider sexual issues as taboo, our study found that cancer patients' opinions are different. Patients expressed a great desire to discuss and disclose information concerning their sexual life, as shown by the high percentage of study participants (*i.e.*, 79.3%). As has been shown in many studies, there are now effective interventions available for sexual dysfunction. The European Association of Urology recommends a treatment algorithm for ED in males. Treatment approaches include the use of medications (PDE5 inhibitors) and the use of devices (vacuum constriction device to the penis), or even penile prosthesis implantation as a third-line therapy (63). For females, local treatments with vaginal estrogen preparations have been used for the treatment of atrophic vaginitis (64, 65), as have dilators and self-stimulators that can be used on a regular basis with a lubricant for vaginal stenosis. Clitoral stimulators can be prescribed for females with a history of cervical, rectal and vaginal cancer. Schroder *et al*. studied females who received RT for cervical cancer and had therapy with a clitoral stimulator. They found that a few months after therapy, there was improvement in sexual desire, arousal, orgasm and satisfaction (66, 67). A significant number of patients who suffer from sexual dysfunction wish to receive treatment (19, 20, 68-70).

Conclusion

Overall, the current study showed that the majority of patients with cancer treated with RT experienced intense sexual dysfunction. We conclude that cancer patients undergoing RT experience an important degree of sexual dysfunction and depression which the radiation oncologist should not overlook. Evaluation and the treatment of these dysfunctions should be included in the standard routine approach to cancer patients, offering them holistic care. In modern Oncology, sexuality constitutes a promising field for further research with the aim of devising proper interventions to enhance patients' total function.

Conflict of Interest Notification

None.

References

1 Mousas B: Quality of life in oncology trials: a clinical guide. Semin Radiat Oncol *13*: 235-247, 2003.

2 Iconomou G, Mega V, Koutras A, Iconomou A and Kalofonos H: Prospective assessment of emotional distress, cognitive function, and quality of life in patients with cancer treated with chemotherapy. Cancer *101*: 404-411, 2004.

3 Mercandante S, Vitrano V and Catania V: Sexual issues in early and late stage cancer: a review. Support Care Cancer *18*: 659-665, 2010.

4 Sadovsky R, Basson R, Krychman M, Morales A, Schover L, Wang R and Incrocci L: Cancer and sexual problems. J Sex Med *7(1Pt2)*: 349-373, 2010.

5 Mendenhall W, Henderson R, Indelicato D, Keole S, Mendenhall N: Erectile dysfunction after radiotherapy for prostate cancer. Am J Clin Oncol *32(4)*: 443-447, 2009.

6 van der Wielen G, van Putten W and Incrocci L: Sexual function after three-dimensional conformal radiotherapy for prostate cancer: results from a dose-escalation trial. Int J Radiat Biol Phys *68(2)*: 479-484, 2007.

7 Little F and Howard G: Sexual function following radical radiotherapy for bladder cancer. Radiother Oncol *49*: 157-161, 1998.

8 Lilleby W, Fosså SD, Waehre HR and Olsen DR: Long-term morbidity and quality of life in patients with localized prostate cancer undergoing definitive radiotherapy or radical prostatectomy. Int J Radiat Biol Phys *43(4)*: 735-743, 1999.

9 Frumovitz M, Sun C, Schover L, Munsell M, Jhingran A, Wharton J, Eifel P, Bevers T, Levenback C, Gershenson D and Bodurka DC: Quality of life and sexual functioning in cervical cancer survivors. J Clin Oncol *23*: 7428-7436, 2005.

10 Wei JT, Dunn RL, Sandler HM, McLaughlin PW, Montie JE, Litwin MS, Nyquist L and Sanda MG: Comprehensive comparison of helth-related quality of life after contemporary therapies for localized prostate cancer. J Clin Oncol *20*: 557-566, 2002.

11 Turner SL, Adams K, Bull CA and Berry MP: Sexual dysfunction after radical radiation therapy for prostate cancer: a prospective evaluation. Urology *54*: 124-129, 1999.

12 Hassan I and Cima RR: Quality of life after rectal resection and multimodality therapy. J Surg Oncol *96*: 684-692, 2007.

13 Heriot AG, Tekkis PP, Fazio VW, Neary P and Lavery IC: Adjuvant radiotherapy is associated with increased sexual dysfunction in male patients undergoing resection for rectal cancer: a predictive model. Ann Surg *242*: 502-510, 2005.

14 Goldstein I, Feldman MI, Deckers PJ, Babayan RK and Krane RJ: Radiation associated impotence. A clinical study of its mechanism JAMA *251(7)*: 903-910, 1984.

15 Fish B, Picket V, Weinberg V and Roach M: Dose of radiation received by the bulb of the penis correlates with risk of impotence after tree-dimensional conformal radiotherapy for prostate cancer. Urology *57*: 955-959, 2001.

16 Van der Wielen G, Mulhall JP and Incrocci L: Erectile dysfunction after radiotherapy for prostate cancer and radiation dose to the penile structures: a critical review. Radiother Oncol *84*: 107-113, 2007.

17 Mulhall JP, Ahmed A, Parker M and Mohideen N: The hemodynamics of erectile dysfunction following external beam radiation for prostate cancer. J Sex Med *2*: 432-437, 2005.

18 Zelefsky MJ and Eid JF: Elucidating the etiology of erectile dysfunction after definitive therapy for prostate cancer. Int J Radiat Biol Phys *40(1)*: 129-133, 1998.
19 Incrocci L: Sexual function after external-beam radiotherapy for prostate cancer. What do we know? Crit Rev Oncol Hematol *57(2)*: 165-173, 2006.
20 Incrocci L and Slob AK: Incidence, etiology, and therapy for erectile dysfunction after external beam radiotherapy for prostate cancer. Urology *60(1)*: 1-7, 2002.
21 Mangar SA, Sydes MR, Tucker HL, Coffey J, Sohaib SA, Gianolini S, Webb S, Khoo VS, MRC RT01 Trial Management Group and Dearnaley DP: Evaluating the relationship between erectile dysfunction and dose by the penile bulb: using data from a randomized controlled trial of conformal radiotherapy in prostate cancer (MRC RT01, ISRCTN4772397). Radiother Oncol *80(3)*: 355-362, 2006.
22 Grigsby PW, Russell A, Bruner D, Eifel P, Koh WJ, Spanos W, Stetz J, Stitt JA and Sullivan J: Late injury of cancer therapy on the female reproductive tract. Int J Radiat Oncol Biol Phys *31(5)*: 1281-1299, 1995.
23 Jensen PT, Groevold M, Klee MC, Thranov I, Petersen MA and Machin D: Longitudinal study of sexual function and vaginal changes after radiotherapy for cervical cancer. Int J Radiat Oncol Biol Phys *56*: 937-949, 2003.
24 Amsterdam A, Krychman M: Sexual function in gynaecologic cancer survivors. Expert Rev Obstet Gynecol *3(3)*: 331-337, 2008.
25 Andersen BL and van der Does J: Surviving gynecologic cancer and coping with sexual morbidity: an international problem. Int J Gynecol Cancer *4*: 225-240, 1994.
26 Takahashi M, Kai I, Hisata M and Higashi Y: Attitudes and practice of breast cancer consultations regarding sexual issues: a nationwide survey of Japanese surgeons. J Clin Oncol *24*: 5763-5768, 2006.
27 Burwell SR, Case LD, Kaelin C and Avis N: Sexual problems in younger females after breast cancer syrgery. J Clin Oncol *24(18)*: 2815-2821, 2006.
28 Maguire P: Breast conservation *versus* mastectomy: psychological considerations. Semin Surg Oncol *5(2)*: 137-144, 1989.
29 Hannoun-Levi JM: Treatment of breast and uterus cancer: physiological and psychological impact on sexual function. Cancer Radiother *9(3)*: 175-182, 2005.
30 D. Bukovic, Fajdic J, Hrgovic Z, Kaufmann M, Hojsak I and Stancerić T: Sexual dysfunction in breast cancer survivors. Onkologie *28(1)*: 29-34, 2005.
31 Schrover LR: The impact of breast cancer on sexuality, body image, and intimate relationships. CA Cancer J Clin *41*: 112-120, 1991.
32 Jones LR: The use of validated questionnaires to assess female sexual dysfunction. World J Urol *20*: 89-92, 2002.
33 Rosen RC: Assessment of female sexual dysfunction: review of validated methods. Fertil Steril *77(4)*: 89-93, 2002.
34 Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J and Mishra A: The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology *49(6)*: 822-830, 1997.
35 Rosen RC, Brown C, Heinman J, Leiblum S, Meston C, Shabsigh R, Ferguson D and D'Agostino R Jr.: The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for assessment of female sexual function. J Sex Marital Ther *26*: 191-208, 2000.
36 Report No. 50: Prescribing, recording and reporting photon beam therapy. Bethesda: International Commission on Radiation Units and Measurements (ICRU), 1993.
37 Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry *23*: 56-62, 1960.
38 Pietrzak L, Bujko K, Nowaski MP, Kepka L, Oledzki J, Rutkowski A, Szmeja J, Kladny J, Dymecki D, Wieczorek A, Pawlak M, Lesniak T, Kowalska T and Richter P; Polish Colorectal Study Group: Quality of life, anorectal and sexual functions after preoperative radiotherapy for rectal cancer: report of a randomized trial. Radioth Oncol *84(3)*: 217-225, 2007.
39 Moreira ED, Kim SC, Glasser D and Gingell C: Sexual activity, prevalence of sexual problems, and associated help-seeking patterns in men and women aged 40-80 years in Korea: data from the Global Study of Sexual Attitudes and Behaviors (GSSAB). J Sex Med *3(2)*: 201-211, 2006.
40 Derogatis LR and Burnett AL: The epidemiology of sexual dysfunctions. J Sex Med *5(2)*: 289-300, 2008.
41 DeLamater J and Karraker A: Sexual functioning in older adults. Curr Psychiatry Rep *11(1)*: 6-11, 2009.
42 Korfage IJ, Pluijm S, Roobol M, Dohle GR, Schröder FH and Essink-Bot ML: Erectile dysfunction and mental health in a general population of older men. J Sex Med *6(2)*: 505-512, 2009.
43 Valadares ALR, Pinto-Neto AM, Osis MJ, Sousa MH, Costa-Paiva L and Conde DM: Prevalence of sexual dysfunction and its associated factors in women aged 40-65 years with 11 years or more of formal education: a population-based household survey. Clinics *63(6)*: 775-782, 2008.
44 Shabsigh R, Broderick GA, Althof S, Natanegara F and Wong DG: Daily patterns of sexual intercourse attempts by men with erectile dysfunction treated with tadalafil: influence of age and marital status. Int J Impot Res *21(5)*: 285-291, 2009.
45 Zelefsky MJ, Cowen D, Fuks Z, Shike M, Burman C, Jackson A, Venkatramen ES and Leibel SA: Long term tolerance of high-dose three-dimensional conformal radiotherapy in patients with localized prostate carcinoma. Cancer *85*: 2460-2468, 1999.
46 Pinkawa M, Piroth MD, Asadpour D, Gagel B, Fischedick K, Siluschek J, Kehl M, Krenkel B and Eble MJ: Neoadjuvant hormonal therapy and external-beam radiotherapy *versus* external-beam irradiation alone for prostate cancer. A quality of life analysis. Strahlenther Onkol *185(2)*: 101-108, 2009.
47 Stephens RJ, Dearnaley DP, Cowan R, Sydes M, Naylor S, Fallowfield L, RT01 collaborators: The quality of life of men with locally advanced prostate cancer during neoadjuvant hormone therapy: data from the Medical Research Council RT01 trial (ISRCTN47772397). BJU Int *99(2)*: 301-310, 2007.
48 Traish AM and Guay AT: Are androgens critical for penile erections in humans? Examining the clinical and preclinical evidence. J Sex Med *3(3)*: 382-404, 2006.
49 Chen CT, Valicenti RK, Lu J, Derose T, Dicker AP, Strup SE, Mulholland SG, Hirsch IH, McGinnis DE and Gomella LG: Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer? Int J Radiat Oncol Biol Phys *50(3)*: 591-595, 2001.
50 Mortimer J, Boucher L, Baty J, Knapp DL, Ryan E and Rowland JH: Effect of tamoxifen on sexual functioning in patients with breast cancer. Am J Clin Oncol *17(5)*: 1488-1492, 1999.

51 Mourits MJ, Bockermann I, de Vries GE, van der Zee AG, ten Hoor KA, van der Graaf WT, Sluiter WJ and Willemse PH: Tamoxifen effects on subjective and phychosexual well-being, in a randomised breast cancer study comparing high-dose chemotherapy. Br J Cancer *86*: 1546-1550, 2002.

52 Kwan KW and Chlebowski RT: Sexual dysfunction and aromatase inhibitor use in survivors of breast cancer. Clin Breast Cancer *9(4)*: 219-24, 2009.

53 Hendren S, O'Connor BI, Liu M, Asano T, Cohen Z, Swallow CJ, Macrae HM, Gryfe R and McLeod RS: Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. Ann Surg *242(2)*: 212-223, 2005.

54 Trask PC, Paterson AG, Hayasaka S, Dunn RL, Riba M and Johnson T: Psychosocial characteristics of individuals with non-stage IV melanoma. J Clin Oncol *19*: 2844-2850, 2001.

55 Dolbeault S, Szporn A and Holland JC: Psycho-oncology: Where have we been? Where are we going? Eur J Cancer *35*: 1554-1558, 1999.

56 Patrick DL, Ferketich SL, Frame PS, Harris JJ, Hendricks CB, Levin B, Link MP, Lustig C, McLaughlin J, Ried LD, Turrisi AT 3rd, Unützer J, Vernon SW, National Institutes of Health State-of-the-Science Panel: Pain, depression, and fatigue. J Natl Cancer Inst *95*: 1110-1117, 2003.

57 Katz A: The sounds of silence: Sexuality information for cancer patients. J Clin Oncol *23(1)*: 238-241, 2005.

58 Kirby R, Watson A and Newling D: Prostate cancer and sexual functioning. Prostate Cancer Prostatic Dis *1*: 179-184, 1998.

59 Bourgeois-Law G and Lotocki R: Sexuality and gynecological cancer: A needs assessment. Can J Hum Sex *8(4)*: 231-240, 1999.

60 da Silva GM, Hull T, Roberts PL, Ruiz DE, Wexner SD, Weiss EG, Nogueras JJ, Daniel N, Bast J, Hammel J and Sands D: The effect of colorectal surgery in female sexual function, body image, self-esteem and general health: a prospective study. Ann Surg *248*: 266-272, 2008.

61 Iconomou G, Viha A, Koutras A, Koukourikou I, Mega V, Makatsoris T, Onyenadum A, Assimakopoulos K, Vagenakis AG and Kalofonos HP: Impact of providing booklets about chemotherapy to newly presenting patients with cancer: a randomized controlled trial. Ann Oncol *17(3)*: 515-520, 2006.

62 Merrill J, Laux LF and Thornby J: Why doctors have difficulty with sexual histories. South Med J *83*: 613-617, 1990.

63 Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, Vardi Y, Wespes E, European Association of Urology: Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation. Eur Urol *57*: 804-814, 2010.

64 Vagifem (package insert). Novo Nordisk A/S, 2003.

65 Rioux JE, Devlin C, Gelfand MM, Steinberg WM and Hepburn DS: 17-Estradiol vaginal tablet *versus* conjugated equine estrogen vaginal cream to relieve menopausal atrophic vaginitis. Menopause *7*: 156-161, 2000.

66 Hoffman MS, Wakeley KE, Cardosi RJ: Risk of rigid dilation for a radiated vaginal cuff: related rectovaginal fistulas. Obstet Gynecol *101(5)*: 1125-1126, 2003.

67 Schroder M, Mell L, Hurteau J, Collins Y, Rotmensch J, Waggoner S, Yamada S, Small W Jr. and Mundt A: Clitoral therapy device for treatment of sexual dysfunction in irradiated cervical cancer. Int J Radiat Oncol Biol Phys *61(4)*: 1078-1086, 2005.

68 Incrocci L, Slagter C, Slob K and Hop W: A randomized, double-blind, placebo-controlled, cross-over study to assess the efficacy of tadalafil (cialis®) in the treatment of erectile dysfunction following three-dimensional onformal external-beam radiotherapy for prostatic carcinoma. Int J Radiat Oncol Biol Phys *66(2)*: 439-444, 2006.

69 Miller D, Wei J, Dunn R, Montie J, Pimentel H, Sandler H, McLaughlin P and Sanda M: Use of medications or devices for erectile dysfunction among long-term prostate cancer treatment survivors: potential influence of sexual motivation and/or indifference. Urology *68*: 166-177, 2006.

70 Reese J, Keefe F, Somers T and Abernethy A: Coping with sexual concerns after cancer: the use of flexible coping. Support Care Cancer *18*: 785-800, 2010.

Received November 7, 2011
Revised December 13, 2011
Accepted December 14, 2011