THE INSTITUTE OF ONCOLOGY, LJUBLJANA[1]
UNIVERSITY CLINIC OF GYNECOLOGY,
DEPARTMENT OF REPRODUCTION, LJUBLJANA[2]

THE INFLUENCE OF RADIOTHERAPY ON SPERMATOGENESIS IN PATIENTS WITH TESTICULAR SEMINOMA IN RELATION TO PROTECTION FROM SCATTERED RADIATION

Kovač V[1], Umek B[1], Marolt F[1], Škrk J[1], Reš P[2], Kuhelj J[1]

Abstract – In 40 patients with testicular seminoma that had been treated with unilateral orchiectomy and prophilactic irradiation of retroperitoneal lymph nodes, there was established the extent of impaired spermatogenesis and measured the gonadal dose during irradiation by means of TLD dosemeters. Before radiotherapy (RT) only 11 patients had adequate results of semen analysis. After RT in most cases the quality of semen deteriorated. In patients, whose testes were shielded from scattered radiation, the impairment of semen after RT was smaller than in patients that were not shielded, yet the difference was not statistically significant because of the small number of the patients studied. A comparison of the measured gonadal dose in 4 unprotected and 8 protected patients showed that by the use of shielding the gonadal dose was lower for about two thirds.

UDC: 616.681-006.2:615.849.2.06:612.616.2

Key words: testicular neoplasms, seminoma, radiotherapy–adverse effects, semen–analysis, spermatogenesis

Orig sci paper

Radiol Iugosl 1990; 24: 191-4

Introduction – Contemporary methods of treatment allow a longer disease-free survival or complete recovery for an increasing number of patients. Radiotherapy (RT) (in addition to chemotherapy and some surgical treatment) influences the functions of many organic systems, which may result in an impaired quality of life after a successful treatment (1).

Negative influence of ionizing radiation upon spermatogenesis in animals and humans has been reported by numerous authors (2, 3, 4). After irradiation there can be seen a decreased state of fertility, which is shown in an altered quality of ejaculate. The impairment depends on the applied dose, the manner of fractionation and upon the primary fertility of the patients (5, 6).

After RT has been completed, the function of testic: *(a)* completely recovers, *(b)* partially recovers, or *(c)* patients remain sterile. The speed and the extent of recovery is influenced by the above factors, therefore it cannot easily be foreseen. Hence semen cryopreservation before RT is of special importance (7, 8).

In clinical practice there are also treated young patients (in reproductive age) with seminoma who want to have children after their recovery. Therefore we were interested in finding out to which extent and for how long RT impaired the spermatogenesis of the remaining testis with respect to the gonadal dose of scattered radiation (9).

It was tried to improve the treatment by shielding the testes from scattered radiation, which was evaluated by measuring the gonadal dose and performing the controlling of semen quality.

Materials and methods – 40 patients with an average age 30 years (from 18 to 48 years) were treated with unilateral orchiectomy and prophilactic irradiation of retroperitoneal lymph nodes. All patients had a histologically confirmed diagnosis of testicular seminoma.

In the period 1981–1983 29 patients were treated without shielding the remaining testis from scattered radiation *(Group I)*. In 14 of these patients semen analysis was performed before *and* after RT, whereas in 15 patients it was performed either before *or* after RT. The gonadal dose was measured in 4 patients.

Later, in the years 1988–1989, a special lead shield was constructed to protect the testis from scattered radiation during treatment in supine position (Fig. 1). In prone position the testis was

Received: March 29, 1990 – Accepted: April 5, 1990

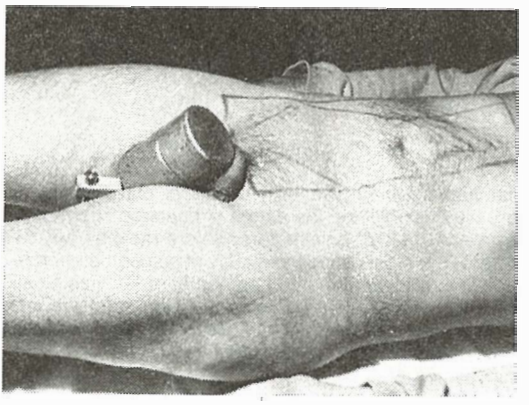

Fig. 1: Patient with contact gonadal shield during treatment with external beam irradiation

still unshielded. In this manner 11 patinets *(Group II)* were treated. In all patients the semen analysis before RT was made, whereas in 6 patients the semen analysis after RT was performed as well. The gonadal dose was measured in 8 patients.

The impairment of spermatogenesis in relation to the gonadal dose was statistically evaluated with Fisher's exact test and Chi-square test.

Both groups of patients were treated with two opposite fields, with 8 MeV X-rays from linear accelerator MEL SL 75/20, the tumour dose being 3000 cGy (20x150 cGy, in four weeks). The dose was measured by TLD dosemeters (LiF rods) that were attachet to the patient's testis. The dosemeters were thermally treated and read out in a TLD reader Toledo 654 (D. A. Pitman Inst.) (10).

Semen specimens were collected and analyzed before and after RT at the University Clinic of Gynecology in Ljubljana according to conventional methods (11). When the patients had their sperm analysed several times, the spermatogram showing the greatest impairment was taken into account except when the analyses were made in the course of the same month.

If the ejaculate before RT was adequate, semen cryoconservation was performed for possible artifical insemination. Thus, 11 patinets from Group I and 10 patients from Group II gave sperm for cryoconservation at the University Clinic of Gynecology in Ljubljana.

Results – The results of measuring the gonadal dose in patients with shielded and unshielded testis are shown in Table 1. It is evident therefrom that by the use of shielding the gonadal dose was decreased approximately by two thirds. Thereby there was achieved a gonadal dose of 1.5% of the applied tumour dose.

Table 1 – Gonadal dose at the end of the treatment

	Number of patients	Median dose (cGy)	Range (cGy)	% of tumour dose
Group I unshielded testis	4	127	124-156	4.2
Group II shielded testis	8	45	26-120	1.5

Table 2 – Results of semen analyses before and after RT in patients *without* gonadal shield during treatment *(Group I)*.

Before RT		After RT (in 0-38 months, median 10.5 months)				
		OAT II	OAT III	AZOO	NECRO	WSA
NORMAL	7	1	1	2		3
OATI	6		1	2		3
OAT II	4	*1**		2		1
OAT III	5		*2**	1		2
NECRO	2				*1**	1
WSA	5**		2	3		
TOTAL	29	2	6	10	1	10***

* No evidence of increased impairment
** Semen analysis was only made after RT, the fertility before RT was proven by the partner's pregnancy.
*** Semen analysis was made only before RT, patients declined further analysis or were lost from the follow-up

NORMAL normal spermatogram
OAT I oligoastenoteratozoospermia grade I
OAT II oligoastenoteratozoospermia grade II
OAT III oligoastenoteratozoospermia grade III
AZOO azoospermia
NECRO necrozoospermia
WSA without semen analysis

A semen analysis was made before and after RT. The analysis results in unshielded and shielded patients are shown in Tables 2 and 3. It is evident therefrom that the patients of Group II (with the shield) had lesser impairments of spermatogenesis than the patients of Group I (without the shield).

In order to exactly compare the effect of different doses upon spermatogenesis only patients with spermatograms before and after RT were considered, i. e. 14 patients from Group I and 6 patients from Group II (Table 4). In Group I, i.e.

those with unshielded testis, 10 patients had worse results of spermatoanalysis after RT and 4 patients had equal results, whereas in Group II, where the special gonadal shield was used, this ratio was 2:4. Because of the small sample we used Fisher's exact test, which shows $p = 0.16$, which means that the difference between the groups is not statistically significant though such conclusions are suggested.

As we wanted to have a more representative sample, Group I was supplemented by 5 patients who had children before RT, i.e. who were primarily fertile though this fertility was not established by a previous spermatogram. Chi-square (with Yates correction) shows $p = 0.11$, which is not statistically significant either.

Table 3 – Results of semen analyses before and after RT in patients with gonadal shield during treatment *(Group II)*

	Before RT	After RT (in 0-12 months, median 4 months) NORMAL	OAT II	WSA
NORMAL	4		1	3
OZ I	1	*1**		
ASZ I	1		1	
ATZ I	1			1
OAT II	3		*3**	
OAT III	1			1
TOTAL	11	1	5	5**

* No evidence of increased impairment.
** Semen analysis was made only before RT, patients have not been motivated for further analysis.

NORMAL normal spermatogram
OZI oligozoospermia grade I
ASZ I astenozoospermia grade I
ATZ I astenoteratozoospermia grade I
OAT II oligoastenoteratozoospermia grade II
OAT III oligoastenoteratozoospermia grade III
WSA without semen analysis

Table 4 – Comparison of semen analysis results of patients of both groups after RT (patients lacking an analysis either before or after RT have been eliminated)

	Number of patients with increased impairment	without increased impairment	Total
Group I unshielded testis	10	4	14
Group II shielded testis	2	4	6
Total	12	8	20

Discussion – It is evident from Table 1 that the range of the measured gonadal doses was very broad. This can be attributed mostly to the different distances between the testis and the edge of the treatment field, and also to the size of the treatment field.

Our results are close to other results in the literature. Smithers et al achieved by their protection that the gonadal dose amounted 1.5 to 2.5% of the nodal dose (12), Schlappack et al achieved 2.0% of the nodal dose (13), Fossa et al achieved 1 to 3% of the target dose (5) and Fraass et al reached the gonadal dose of less than 1% of the dose aplied (14).

The majority of seminoma patients already had impaired spermatogenesis before RT. This could be explained (a) by testicular histologic abnormalities that give rise to process of malignisation, (b) by surgical stress at orchiectomy, and (c) by anxiety about infertility and the success of the treatment.

Our semen analyses and measurements of the gonadal dose confirm the finding that in patients with testicular seminoma scattered radiation *additionaly* impairs spermatogenesis (2, 3, 5, 15).

By the contact shield of the testis during exposure to X-rays the gonadal dose was reduced from 4.2% to 1.5% of the applied tumour dose, which less impairs the spermatogenesis. A statistically more significant difference has been expected, the number of the patients, however, seems to have been too small for more significant results.

A detailed analysis of Tables 2 and 3 shows that the impairments of spermatogenesis in Group I were not only more frequent but also more intensive.

Most patients had spermatograms made several times after RT and it has been possible to establish the reversibility of the impairment in most cases. The exception were the patients who had severely impaired spermatogenesis even before RT.

In spite of the reversibility of the impairment, the state after RT cannot be anticipated with certainty, which is due to the above-mentioned different states of spermatogenesis before RT and to different intensiveness of the repair mechanism. Since scattered radiation during RT cannot be completely avoided, semen cryoconservation before the beginning of the treatment is still indicated.

It is the aim of our further research to achieve a higher degree of protection than we have reached so far. We also intend to follow up the

children of our patients that should be born after RT in order to establish any possible effects of scattered radiation upon the offspring and to be able to give advice to patients in the reproductive age. So far our results have been quite encouraging.

Povzetek

VPLIV RADIOTERAPIJE NA SPERMATOGENEZO PRI BOLNIKIH S SEMINOMOM TESTISA Z OZIROM NA ZAŠČITO PRED SIPANIM ŽARČENJEM

40 bolnikom s seminomom testisa, ki so bili zdravljeni z enostransko orhiektomijo in profilaktičnim obsevanjem retroperitonealnih bezgavk, smo ugotavljali stopnjo okvare spermatogeneze in med obsevanjem merili gondadno dozo s TLD dozimetri. Samo 11 bolnikov je imelo pred radioterapijo (RT) normalen spermatogram. Po RT smo ugotovili v večini primerov poslabšanje rezultatov semenske analize. Pri bolnikih, ki smo jim ščitili testise pred sipanim žarčenjem, je bila okvara speramatogeneze manjša kot pri tistih, kjer posebne zaščite še nismo uporabljali. Zaradi majhnega števila bolnikov razlika med skupinama ni bila statistično signifikantna, ampak se je le nakazovala. Merjenje gonadne doze 4 bolnikom, ki jim preostalega testisa nismo ščitili in 8 bolnikom z zaščitenim testisom je pokazalo, da smo z uporabo zaščite gonadno dozo zmanjšali za približno dve tretjini.

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Author's address: Viljem Kovač, MD, The Institute of Oncology, Zaloška 2, 61000 Ljubljana