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Technical Innovations and Notes

TESTICULAR DOSES IN DEFINITIVE RADIATION THERAPY FOR LOCALIZED PROSTATE CANCER

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Purpose: To measure the dose received by the unshielded testes during a conventional course of 18 MV photon radiotherapy for localized prostate cancer and to identify the factors influencing it.

Methods and Materials: For each of four patients, a wax block containing thermoluminescent chips was attached to the posterior aspect of the scrotum in close proximity to the testes on each day of treatment during a full course of radical radiotherapy, and dose measurements were obtained. The distances between the thermoluminescent chips and the beam edge were verified by measurement from port films. The accuracy of the in vivo measurements and the factors influencing the testis dose were studied using a phantom arrangement. Six factors were considered: (a) the relative contributions from primary and scattered radiation, (b) the amount of buildup required for the thermoluminescent chips that monitored testis dose, (c) the position of the testes within the scrotum, (d) field size, (e) distance from the field lower border, and (f)

Results: Median daily doses to the testes in four patients ranged from 5 to 7 cGy. Daily doses for the four patients ranged from 4 to 14 cGy. The total dose to the testes over the full course of therapy ranged from 1.8 to 2.4 Gy. The daily dose depended primarily on the distance from the field lower border. This was increased by approximately 2.5 cGy when a 6 MV port film was taken. The relative contributions from primary and scattered radiation were found to be similar. Dose measurements at the posterior aspect of the scrotum overestimated the testis dose by approximately 15%.

Conclusion: The most important factors influencing the dose received by the testis are the distance from the testes to the field lower border and the occasion of a port film. A knowledge of the number of port films and the average distance from the field lower border to the testes allows a reasonable prediction of testes dose without daily measurement.

In vivo dosimetry, Prostate cancer, Testis dose, TLD, Scatter dose.

INTRODUCTION

When prostate cancer is treated by radiation it is inevitable that the unshielded testes receive some of the dose. Sources contributing to this unwanted dosing include scatter from the machine head and treatment volume; primary transmission through the collimators; scatter from the floor, walls and ceiling of the room; and, at higher energies, neutrons and neutron-induced gamma radiation generated mainly from materials in the machine head. This dose is usually considered to be low and inconsequential (9). It is assumed not to influence testosterone secretion from the testes, although it will usually be sufficient to abolish spermatogenesis (8).

Prostate cancer is under endocrine control (6). Specifically, lower levels of testosterone may cause tumour regression (6).

If the possibility exists that radiation received by the testes causes inhibition of testosterone secretion from the testes, which, in turn, causes decrease of serum levels of testosterone, which, in turn, causes regression of tumor in the prostate, it may be possible to exploit this when treating prostate cancer. At the very least, it may mean that some benefit might be obtained by not shielding the testes. It is our intention to perform studies that investigate aspects of this sequence of events. One of these aspects is the quantification of the dose received by the testes during a conventional course of radiotherapy for localized

Chapman for assistance in TLD quality control and for preparation of the figures.

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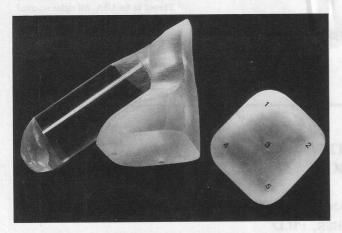


Fig. 1. A photograph of the acrylic scrotum and penis with the labeled TLD positions. Positions 4 and 5 are on the anteroinferior aspect.

prostate cancer. It is this quantification that is the subject of this article.

A number of measurements (1, 5) and calculations (3, 4) have been made of the radiation dose outside the treatment area but few have been concerned with 18 MV photons (7, 11) and none have looked specifically at the dose received by unshielded testes during treatment of prostate cancer. However, discussion in the literature on the effects of radiation on the testes from radiation treatment for Hodgkin's disease (2) suggests that the testes should be shielded. This is in conflict with a recent study (9).

The specific aims of the present study are to (a) measure the dose of radiation received by the testes during a conventional course of radiotherapy for localized prostate cancer and (b) examine which factors influence this dose.

METHODS AND MATERIALS

The experiments performed in this study were of two main types: (a) measurements on block phantoms, a water phantom and an anthropomorphic phantom, and associated equipment to identify dose modifying factors and (b) measurements on patients undergoing radiation therapy.

Equipment

The dosimeters used for the phantom study to determine the testis dose were LiF thermoluminescent dosimetry (TLD) chips: TLD square chips $(3.1 \times 3.1 \times 0.9 \text{ mm})^1$ and round chips (diameter 4.5 mm, thickness 0.9 mm). Analysis was performed in a dedicated TLD labo-

ratory with controlled environment. Equipment included an automated TLD reader³ and a TLD oven.⁴

Chips were kept in sets of 30. Chip sets underwent regular 'uniformity' measurements to monitor reproducibility and estimate each chip's sensitivity, relative to the others in the set. The annealing protocol relied on programmed heating at 400°C for 1 h followed by 2 h heating at 100°C. Chip sensitivity was determined by irradiation of each set to 1.0 Gy on a rotating phantom designed to ensure that each chip was separated from its nearest neighbor. Preannealing of the chips before reading involved heating at 100°C for 15 min. The chips were read using the automated reader and then reannealed before reuse. The error between uniformity irradiations associated with this protocol was 1.25% (1 standard deviation).

Ion chamber measurements were performed using a 0.6 cc chamber and electrometer. A selection of polystyrene and solid water phantoms was used. The water tank measurements were performed using a commercial dosimetry system.⁵

Measurement of the dose due only to neutrons was not done in this study, as the literature (11) indicated that this dose is typically 0.04% of the treatment dose.

Phantom measurements

An acrylic phantom scrotum and penis (Fig. 1) were constructed and attached to a commercial anthropomorphic phantom.⁶ This system was used to assess the accuracy of the method of patient dose measurement and the factors that modify testis dose.

Patient measurements were performed using a wax holder containing four TLD chips (this device will be referred to as the *testis dose monitor*). The design of this device is illustrated in Fig. 2.

Six experiments were conducted to determine (a) the relative contributions from primary and scattered radiation, (b) the amount of buildup required for the testis dose monitor, (c) the effect of position of the testes within the scrotum, (d) the effect of field size, (e) the effect of distance from the field lower border, and (f) the dose to the testes from the taking of port films. Each experiment was performed three times.

A reference treatment geometry (Fig. 3) was defined for the 4-field box technique used for this treatment to normalize the phantom measurements. The anterior and posterior (AP/PA) fields were 12×8 cm and the lateral (LAT) fields 12×8 cm. The field dimensions were chosen as representative (within 2 cm) of a typical treatment. The distance from the testis dose monitor to the field

¹ Harshaw/Filtrol, 6801 Cochran Road, Solon, OH 44139.

² Alnor Oy, P.O. Box 506, SF-20101 Turku, Finland.

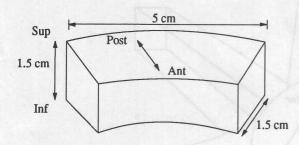
³ Harshaw 2000D/2080.

⁴ PTW-Freiburg, Lorracher Strasse 7, D-7800, Freiburg, Germany.

⁵ Wellhofer Dosimetrie, Bahnhofstrasse 5, D-90592, Schwarzenbruck, Germany.

⁶ Rando-Alderson anthropomorphic phantom.

PERSPECTIVE VIEW



SUPERIOR VIEW

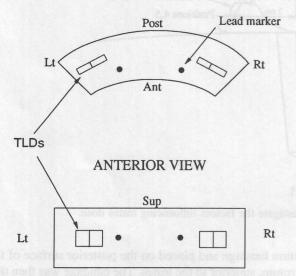


Fig. 2. A diagram of the testis dose monitor showing three views.

lower border was 5 cm. The distance to the center of the scrotum was 7 cm.

The relative contributions of primary and scatter radiation. To investigate the nature of the radiation incident on the testes, water phantom measurements were performed along the central axis of a 12×8 cm beam and along a parallel axis 7 cm outside the field edge.

Integrated ionization measurements were also performed in air for a 12×8 cm field with the ion chamber placed at the isocenter and 7 cm from the field edge. The measurements were performed for 5 acrylic buildup cap thicknesses from 0 to 3 cm.

An attempt to estimate the contributions from primary and scatter radiation was made using the block phantom arrangement in Fig. 4. A $30 \times 30 \times 30$ cm acrylic block was used to simulate the pelvis and a 5.2 cm diameter acrylic buildup cap the scrotum with testes. Measurements were performed with and without a 9 cm Pb shield

above the phantom for separate irradiations. An attempt to measure the primary contribution alone was made by placing a 9 cm Pb shield between the field lower border and the ion chamber with buildup cap.

Testis dose monitor thickness. The amount of buildup required for the testis dose monitor was determined by irradiating four testis dose monitors using the standard treatment geometry with thicknesses ranging from 0.5 to 5 cm.

Position of testes. The effect of different positions of the testes within the scrotum was determined by placing TLDs at five positions (Fig. 1) within the phantom scrotum and irradiating using the standard treatment geometry. A large dose (20 Gy) was delivered to the pelvis to give a sufficient dose to the scrotum TLDs to obtain a reasonable signal for analysis.

Field size. The effect of field size was determined using the rando phantom and standard treatment geometry. The treatment and testis doses were monitored during repeated irradiation of the phantom. Measurements of the testis dose relative to the dose at isocenter were recorded for 8 \times 8 cm, 12 \times 8 cm, 17 \times 8 cm, and 17 \times 18 cm fields while maintaining a constant distance of 7 cm from the lower border to the centre of the scrotum.

Distance from field lower border. The effect of distance of the testis from the field lower border was determined using the rando phantom and reference treatment geometry. The distance from the centre of the scrotum to the field lower border ranged from 3 cm to 11 cm in 2 cm increments. TLD measurements were made with the phantom scrotum for each distance from the field lower border.

Port films. The contribution from AP and LAT port films was recorded by repeated treatment of the phantom with and without a 25×25 cm 6 MV photon beam. Measurements were made with the TLDs placed inside the phantom scrotum.

Patients

To be eligible for the study patients had to be prescribed and treated with conventional radiotherapy for localized prostate cancer. Informed consent was required. Because of the large number of measurements required for daily assessment it was decided to study four such patients.

Treatment

Conventional radiotherapy consisted of treatment in the prone position using a 4-field box isocentric technique on a 18 MV linear accelerator.⁷ Patients were prescribed 60 to 66 Gy in 2 Gy fractions and treated five times per week. The field sizes (as equivalent squares), used for each patient, were 9.1, 9.3, 8.8, and 9.8 cm, respectively.

⁷ Varian Clinac 1800.

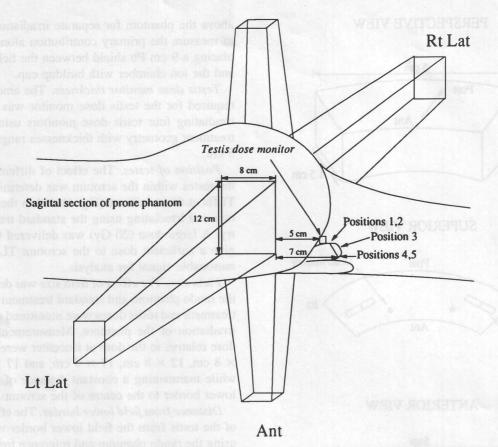


Fig. 3. The reference treatment geometry used to investigate the factors influencing testes dose.

For each patient, on average, two 6MV port films were taken during each week of treatment. The distance from the field lower border to the testis dose monitor was determined on each occasion and compared with that measured from the simulator film.

TLD positioning

Patient measurements were performed using the testis dose monitor. The testis dose monitor was held within a

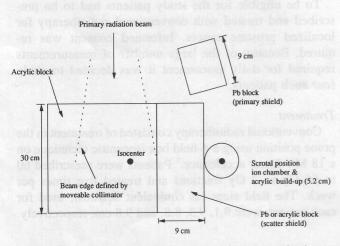


Fig. 4. Block phantom arrangement for estimation of primary and scatter components at testis outside the field edge.

cotton bandage and placed on the posterior surface of the scrotum, superior to the testes. The bandage was then tied up and around the scrotum. The testis dose monitors had two small lead shot balls placed laterally, near two TLD chips, to enable their location to be determined from port films (Fig. 2).

A separate testis dose monitor was placed on each patient for every treatment fraction. The dose received was determined by normalizing the TLD readings from the chips in the testis dose monitor to the readings obtained from four chips, from the same set, exposed to a dose of 0.2 Gy in the primary beam and adjusting for their relative sensitivities determined from uniformity measurements.

RESULTS

Phantom Measurements

The relative contribution of primary and scatter radiation. The depth dose in the central axis was typical of a 18 MV beam with low surface dose and depth dose maximum at 2.6 cm of water. The depth dose 7 cm from the field edge had the characteristic high dose at the surface caused by electron contamination, with photon attenuation dominating after 0.5 cm. The leakage through the collimators was measured to be 0.6%.

Figure 5 shows the effect of acrylic buildup thickness

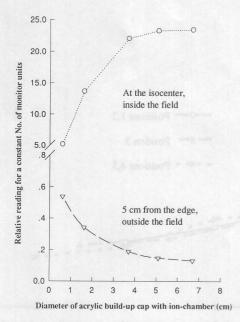


Fig. 5. Relative ionization in air recorded for a constant number of monitor units for five buildup cap diameters at isocenter (inside the field) and 5 cm outside the field.

for an ion chamber placed at the isocenter in air and an ion chamber placed adjacent to a block phantom in the primary beam. The maximum reading in the scatter beam was obtained with no buildup, while a 5.2 cm diameter cap was required to obtain a maximum reading in the primary beam.

The change in ionization with increasing buildup cap thickness is in keeping with that expected for a high energy photon beam. The result is the inverse outside the field, indicating that electron contamination is almost completely attenuated by the smallest cap. Change in ionization above 0.7 cm is in keeping with that expected for a low energy photon beam.

The measurements with and without shielding to determine the contribution from primary and scattered radiation are presented in Table 1. As expected, approximately 50% of the scrotal dose was received from each source.

Testis dose monitor thickness. The dose received inside the testis dose monitors of different thicknesses is presented in Table 2. The maximum dose occurs when the thickness was between 0.5 cm and 2.5 cm. The 0.5 cm and 1.5 cm thick testis dose monitors record a dose 19% greater than the mean dose in the phantom scrotum when

Table 1. The percentage dose measured with and without primary and scatter radiation shielding using the block phantom and build-up cap of 5.2 cm shown in Fig. 4

9 cm Pb shielding used (refer Fig. 4)	Percent ionization at scrotal position relative to ionization at isocenter						
None	1.90						
Primary	1.07						
Scatter	0.97						

the field lower border was 7 cm from the scrotum center. The corresponding mean dose received inside at the center of the acrylic scrotum is presented in the same table.

Position of testes within the scrotum. The relative dose distribution within the acrylic phantom for the standard treatment geometry is presented in Fig. 6. The dose varied across the testes, but was primarily a function of the distance from the field lower border, which varied with chip position (Fig. 3).

Field size. The influence of field size on testis dose is shown in Fig. 7 for three distances from the field lower border. The dose to the testes increases by about 1% in absolute terms, or almost a doubling in relative terms, for the range of field sizes used for this treatment.

Distance from the field lower border. Figure 6 shows the fall off in dose at the testis with increasing distance from the field lower border. Positions 1 and 2 and 4 and 5 have been averaged because they were at the same distance from the field lower border.

Port films. Treatment of the phantom with and without port film indicated that each 6 MV port film that included the scrotum in the primary (large field) beam delivered an additional 2 or 3 cGy (depending on whether an A/P or LAT film was taken). We assume in later calculations that, on average, a dose of 2.5 cGy is delivered from a port film.

Patient measurements

Data from the daily dose measurements for the four patients are reported in Table 3.

The distance between the lead marker and the field lower border, as determined from the patient's port film, is recorded in Table 4 for treatments when port films were taken. The distances ranged from a minimum of 2.2 cm to a maximum of 7.3 cm.

A predicted dose (as a percentage of the isocenter dose) to the testes, based on the measured distance to the field lower border and the data in Fig. 6, is also reported in

Table 2. The dose (as a percentage of the dose at the isocenter) to the testes and testis dose monitor (TDM) on the anthropomorphic phantom for different monitor build-up thicknesses

Thickness of TDM* (cm)	Dose at the TDM [†] (% ± SD)	Dose inside testes [‡] (% ± SD)			
0.5	1.71	1.43			
1.5	1.92	1.61			
2.5	1.89	1.87			
5.0	1.62	1.63			

Accuracy of the measurement is \pm 0.05.

SD = standard deviation.

^{*} AP and S/I dimension.

[†] Percent dose relative to the dose at the isocenter (distance from lower border is 5 cm).

[‡] Percent dose inside acrylic scrotum relative to the dose at the isocenter (distance from lower border is 7 cm).

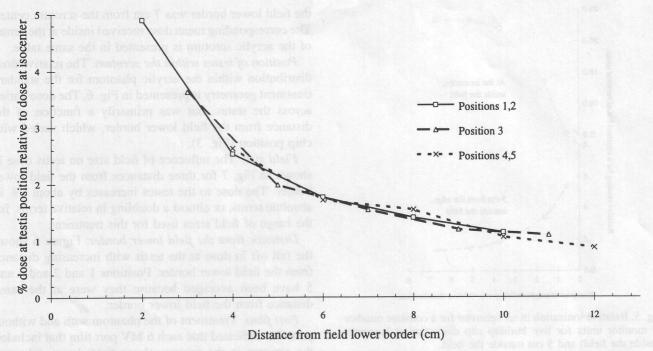


Fig. 6. Percentage dose in the testis relative to dose at the isocenter for the phantom arrangement in Fig. 3, as a function of distance from the field lower border. The three lines correspond to positions within the scrotal phantom.

Table 4. Using the mean predicted dose for each patient the expected doses per 2 Gy fraction without port film were 5.6, 4.4, 4.8, and 6.6 cGy, respectively.

DISCUSSION

The measurements of primary and scatter components are in keeping with similar reports on low energy beams (1). The peak reading inside the testis dose monitor is the result of competing buildup of primary transmission and attenuation of low energy scatter. This limits the maximum dose that can be realized at the testis. A reasonable measurement of testis dose outside the field edge using TLDs, requires only 1 cm tissue equivalent buildup in place at the same distance as the testis from the field lower border.

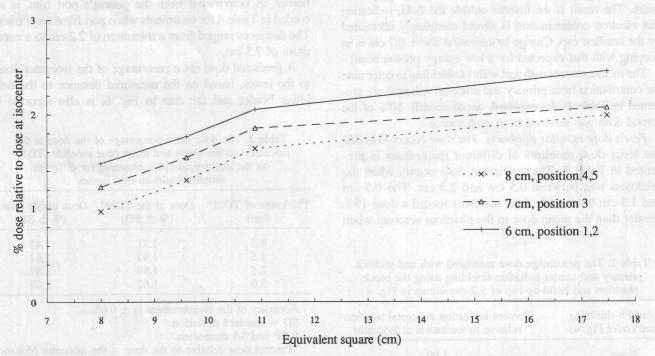


Fig. 7. Percentage dose in the testis relative to dose at the isocenter for the phantom arrangement in Fig. 3, as a function of field size. The three lines correspond to positions within the scrotal phantom at three distances from the field lower border.

Table 3. The testis dose data for four patients who had daily measurements

Patient	No. fractions		Po	ort film dos	e included	Port film dose removed				
		No. port films	Range (cGy)	Mean (cGy)	SD (cGy)	Total (cGy)	Range (cGy)	Mean (cGy)	SD (cGy)	Total (cGy)
1	33	8	3.4-10.2	6.0	1.9	198.9	3.4-7.8	5.4	1.2	178.8
2	33	10	3.0-10.2	6.2	1.8	204.8	3.0-8.1	5.4	1.5	179.8
3	30	8	3.0-8.9	5.3	1.8	160.3	3.0-6.4	4.7	1.4	154.3
4	33	10	4.7-14.9	7.3	2.3	241.8	4.7-14.9	6.6	1.9	216.8

The data without port film dose assumes 2.5 cGGy per port film.

The predominant factors influencing the dose received by the testis were the occasion of a port film and the distance of the testis from the lower border of the field.

For the patient measurements, the distance from the field lower border to the testis dose monitor varied considerably because of alignment of the testis dose monitor on the patient, treatment setup, and daily anatomical variation. This, however, did not greatly affect the estimate of testis dose from the phantom data, provided a good estimate of the mean distance of the field lower border to testis dose monitor was obtained. The differences between the measured testis dose with port film dose removed (from Table 3) and the predicted dose (from Table 4) are -0.2, +1.0, -0.1, and 0.0 cGy. The larger difference for patient 2 may be explained by a significant change in the field lower border late in treatment, which resulted in an inaccurate estimate of the mean distance to the testis.

Table 2 illustrates the perturbing influence of the testis dose monitor on the dose at the center of the acrylic scrotum. It also provides a simple relationship between dose determined by the testis dose monitor and the dose at the center of the acrylic scrotum when the monitor is ≤ 1.5 cm. The data in Table 2 suggest that a testis dose monitor that is about 1.5 cm thick allows full contribution from the high energy component to the testis dose. The choice of a 1.5 cm thickness testis dose monitor ensures adequate buildup to the TLDs in the testis dose monitor. The data for the 0.5 cm testis dose monitor suggest that a reliable relationship exists between the dose to the testis dose monitor and the mean dose within the acrylic scrotum. We chose a 1.5 cm thick monitor because it gave the maximum value for a constant number of monitor units with a constant relationship between dose in the phantom scrotum.

From the results from the four patients studied, it is reasonable to assume that an estimate of the dose to the testis can be made accurately, provided a record of the number of port films is taken and a method, using the port films, for measuring the distance of the testes from the field lower border is available.

For the purpose of our proposed study to monitor testicular function using testosterone levels during, and for 1 year after, a course of radiotherapy, it is of no benefit to

Table 4. Distances (cm) between the field lower border and the testes as measured from port films in four patients

Patient	Port film												
	1	2	3	4	5	6	7	8	9	10	Mean	Range	2SD
1													
(cm)	4.0	3.5	3.9	4.3	3.3	3.1	4.8	3.9			3.8	1.7	1.1
(%)	2.6	3.2	2.5	2.4	3.4	3.6	2.2	2.5			2.8		1.1
2											2.0		
(cm)	6.9	*	7.3	4.9	5.4	3.5	3.8	3.8	2.7	6.4	4.9	4.6	3.3
(%)	1.6	*	1.5	2.0	1.8	3.2	2.7	2.7	4.1	1.7	2.2	1.0	3.3
3													
(cm)	4.6	4.9	7.1	4.4	5.4	3.7	2.7	4.9			4.7	4.4	2.6
(%)	2.3	2.0	1.6	2.4	1.9	2.8	4.1	2.0			2.4	•	2.0
4													
(cm)	4.0	3.8	3.0	2.2	3.1	3.7	4.0	3.0	3.2	3.4	3.3	1.9	1.1
(%)	2.6	2.7	3.7	4.8	3.6	2.8	2.6	3.7	3.5	3.4	3.3		

The predicted relative dose (%) to the testes, for each distance, is given in italics.

²SD = two standard deviations.

^{*} In this case the port film was incorrectly positioned. As the TLD markers were not on the film, the % dose value could not be predicted.

perform more accurate dose measurements than done in this study, as the dose used in conventional treatment will be insufficient to detect a significant alteration in testosterone level (10). The predicted estimate will suffice to report the approximate range of doses received by patients in the study.

REFERENCES

- 1. Fraass, B. A.; van de Geijn, J. Peripheral dose from megavolt beams. Med. Phys. 10:809–818; 1983.
- Fraass, B. A.; Kinsella, T. J.; Harrington, F. S.; Glatstein, E. Peripheral dose to the testes: The design and clinical use of a practical and effective gonadal shield. Int. J. Radiat. Oncol. Biol. Phys. 11:609–615; 1985.
- Francois, P.; Beurtheret, C.; Dutreix, A. Calculation of the dose delivered to organs outside the radiation beams. Med. Phys. 15(6):Nov-Dec; 1988.
- 4. Glickstein, S. S. Analytical modeling of thermoluminescent albedo detectors for neutron dosimetry. Health Phys. 44(2):103–114; 1983.
- 5. Green, G.; Chu, L.; Thomas, D. Dose level outside radio-therapy beams. Br. J. Radiol. 56:543; 1983.
- 6. Huggins, C.; Hodges, C. V. The effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. Cancer Res. 1:293–297: 1941

- 7. McGinley, P. H.; Wood, M.; Mills, M.; Rodriquez, R. Dose levels due to neutrons in the vicinity of high-energy medical accelerators. Med. Phys. 3(6):297–402; 1976.
- 8. Shalet, S. M.; Tsatsoulis, A.; Whitehead, E.; Read, G. Vulnerability of the human Leydig cell to radiation damage is dependent upon age. J. Endocrinol. 120:161–165; 1989.
- Shalet, S. M. Effect of irradiation treatment on gonadal function in men treated for germ cell cancer. Eur. Urol. 23:148-151; 1993.
- Shapiro, E.; Kinsella, T. J.; Makuch, R. W.; Fraass, B. A.; Glatstein, E.; Rosenberg, S. A.; Sherins, R. J. Effects of fractionated irradiation on endocrine aspects of testicular function. J. Clin. Oncol. 3:1232–1239; 1985.
- 11. Tosi, G.; Torresin, A.; Agosteo, S.; Foglio Para, A.; Sangiust, V.; Zeni, L.; Silari, M. Neutron measurements around medical electron accelerators by active and passive detection techniques. Med. Phys. 18(1):54–60; 1991.