The radiological accident at the Bialystok Oncology Centre: cause, dose estimation and patient treatment

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Abstract

On February 27th 2001 five breast-cancer patients undergoing radiotherapy at the Bialystok Oncology Center, Poland, received a single, high dose of 8 MeV electrons generated by a Neptun 10p linear accelerator. The ultimate cause of the accident was a defective safety interlock and an obsolete safety system of the Neptun 10p accelerator which did not prevent its operation with the faulty interlock. The accident was caused by a damage to the beam monitoring system, leading to a large increase of the dose rate even though the display indicated a lower value than normal. The limitation of the filament current of the electron gun was set to a high level so that the dose rate was practically unrestricted. The combination of these factors led to the substantially higher doses to the patients. All patients experienced immediate pain and skin reddening, followed by moist desquamation and development of deep necroses by autumn 2001. In spring/summer of 2002 all patients underwent a surgical reconstruction of the chest wall with a subsequent skin transplantation. Two patients were treated in Paris, France and three in Kielce, Poland. In case of three patients pieces of rib bones were removed, allowing an estimation of the accident doses by electron paramagnetic resonance (EPR). EPR measurements were performed at the IRSN, France, and INCT, Poland. Irradiation of bone samples measured at the INCT was performed at the Oncology Center in Warsaw, Poland. In order to calibrate the EPR signal the samples were irradiated in the electron beam from the radiotherapy linear accelerator and in the gamma beam from radiotherapy Co-60 machine. In addition, the frequencies of chromosomal aberrations and micronuclei were analysed in peripheral lymphocytes of the patients and compared with the frequencies observed in patients undergoing a regular radiotherapy. It was found that the accident doses were heterogeneous and might have reached about 100 Gy. Presently, the health status of the patients is stable.

1. The accident

On February 27th 2001 five breast-cancer patients undergoing radiotherapy at the Bialystok Oncology Center, Poland, received a single, high dose of 8 MeV electrons generated by a Neptun 10p linear accelerator. Neptune 10p is a Polish version of the Neptune accelerator manufactured by the now non-existing company CGR and was designed before the IEC safety standards for accelerators of this kind were published. It is capable of delivering electron beams of 6, 8 and 10 MeV, as well as a photon beam of 9 MeV.

On the day of the accident the machine shut down due to a break in the mains power supply, while patient A1 was treated. After resuming operation the beam parameters appeared unchanged as judged by the readings of the console instruments. Following a warm up period the treatment was continued. The next four patients (A2-A5) reported itching and burning sensations during or shortly after treatment. Further treatments with the machine were stopped and dose output measurements of the beam were performed. They revealed that the doses were in the range of 99 ± 9 Gy per the prescribed 150 MU (monitoring units).
2. The cause of the accident

The Neptun 10p accelerator is designed to operate both in electron and photon modes. Photons are generated when electrons are slowed down in an X-ray target and this process is associated with a considerable energy loss. Therefore, in order to obtain an appropriate dose rate of the photon beam a high current of electrons must be generated. This current is about 300 times higher than needed to produce a therapeutic electron beam of a similar dose rate. The dose rate of the electron beam is monitored by two transmission chambers which deliver control signals to the central processing unit. In case of a discrepancy between the readings, a safety interlock system should shut down the machine.

Upon examination of the accelerator after the accident a broken fuse was discovered in the circuit of the power supply to the dose monitoring chambers. In addition, a diode controlling the signal transfer from the dose monitoring chambers to the safety interlock system was broken. Finally, the limitation of the filament current of the electron gun was set to a high level so that the dose rate of the electron beam was practically unrestricted. The outdated construction of the Neptun 10p allowed to operate the machine under those conditions without any warning signals displayed on the control panel. Although it is presently impossible to reconstruct the exact sequence of events leading to the accident, a combination of the described factors led to the substantially higher doses to the patients [1].

3. Dose reconstruction

Retrospective dosimetry was performed by two methods of biological dosimetry: electron paramagnetic resonance (EPR) and cytogenetic assay in peripheral blood lymphocytes. Based on the extent of radiation injuries it is certain that the doses received by patients A1 and A2 were lower than received by patients A3-A5. This indicates that the machine was progressively deteriorating during the accident.

3.1. EPR

EPR is a method allowing to measure the radiation doses absorbed by such tissues like bones and tooth enamel [2]. When these tissues, which are composed mainly of hydroxyapatite, are exposed to ionising radiation, stable CO$_2^-$ ions are formed in a quantity which is proportional to the dose. When an irradiated piece of a bone is placed in an EPR spectrometer equipped with a microwave generator and a gaussmeter the characteristic resonance signal of the CO$_2^-$ ion can be detected and quantified. Following the first measurement, the sample is irradiated several times in the laboratory with defined doses of ionising radiation and the signal is measured after each exposure. The initial dose is calculated by back-extrapolation of the fitted linear dose response curve.

In the course of surgical reconstruction of the chest wall of patients A3, A4 and A5, pieces of necrotic rib bones were removed. The doses received by the patients were assessed with the help of EPR. Additional irradiations were performed with 8 MeV electrons generated by a therapeutic linear accelerator. The values of the initial doses were composed of doses received by the samples during regular therapy before the accident and the dose from the accidental exposure. The former doses are known from the treatment histories and were subtracted from the obtained dose values.

Because the exact location of the analysed bone pieces and, consequently, the depth under the skin could not be reconstructed precisely, the doses were calculated assuming that the pieces were both in frontal and distal position [1]. The results are presented in table 1. They are in a fairly good agreement with those derived by the physicist on the day of the accident.

<table>
<thead>
<tr>
<th>Accidental dose at $d_{\text{max}} = 1.9$ cm, Gy</th>
<th>Patient A3</th>
<th>Patient A4</th>
<th>Patient A5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reconstruction for frontal position</td>
<td>59 ± 7</td>
<td>64 ± 11</td>
<td>71 ± 3</td>
</tr>
<tr>
<td>Reconstruction for distal position</td>
<td>67 ± 8</td>
<td>84 ± 19</td>
<td>78 ±5</td>
</tr>
</tbody>
</table>

Table 1. Doses received by patients A3, A4 and A5 as estimated by EPR.
3.2. Cytogenetic assay

Biological dosimetry by cytogenetic techniques is a well established method of dose reconstruction [3]. It is based on scoring chromosomal aberrations or micronuclei in peripheral blood lymphocytes of the exposed person. The dose is calculated by referring to a calibration curve generated previously by irradiating lymphocytes of healthy donors under in vitro conditions with defined doses. The method allows a precise dose estimation in cases of acute, whole body exposures. In cases of partial body exposure a certain fraction of the analysed lymphocytes will have been outside the irradiated field. During cytogenetic analysis these undamaged cells will "dilute" the yield of aberrations, leading to an underestimation of dose.

In order to assess whether the accidental exposure would be detectable in peripheral blood lymphocytes, chromosomal aberrations and micronuclei were analysed in lymphocytes of the accident patients [4]. It was shown that the dose response curve of aberrations in lymphocytes of patients undergoing radiotherapy has different characteristics than an in vitro dose response curve [5]. Due to this and to the fact that the exposed parts of the patient bodies were very small (between 77 and 221 cm$^2$) an estimation of the accident doses on the basis of a standard, in vitro calibration curve was not possible. Therefore, it was decided to compare the aberration and micronucleus frequencies observed in lymphocytes of the accident patients to those in breast cancer patients not involved in the accident, but who received similar radiotherapy treatments. The frequencies of aberrations and micronuclei were plotted against the equivalent whole body doses (EWBD) received during radiotherapy. The EWBD is the integral dose (total energy in jouls) absorbed by the patients divided by their body mass. In case of the accident patients, the EWBD values reflected the doses received prior to the accident. It could be expected, that an excess of aberration and micronucleus frequencies in lymphocytes of the accident patients over the plotted dose response curve of the control patients would be due to the accident dose. The results are shown in figure 1.

Although a good agreement between the frequencies of aberrations (dicentrics) and micronuclei was observed, there was a better cut-off between the accident and control patients for dicentrics than for micronuclei. The dicentric frequencies of patients A2, A3 and A4 are significantly higher than of the control patients (with one exception). In the case of patients A3 and A4 this result is in accord with the expectation, since both patients received high accident doses (table 1). However, this is not so for patient A2, who had the highest frequency of dicentrics but received a lower accident dose than patient A3 (as judged by the extent of late skin reactions). Also the frequency of dicentrics in lymphocytes of patient A5 did not match with the accident dose. We have reanalysed the frequencies of micronuclei in lymphocytes of patients A2 and A5 collected a second time in order to exclude the possibility, that the blood specimens have been mistaken. The second analysis revealed that no mistake occurred during the preparation of slides for the initial analysis.

Presently, we have no definite explanation for the missing correlation between the accident dose and the frequency of dicentrics and micronuclei in lymphocytes of patient A2 and A5. A factor which could be responsible for the low frequency of damage in lymphocytes of patient A5 could be, that she had a relatively large body mass (data not shown). 8 MeV electrons do not penetrate deeply into the tissue ($d_{max} = 1.9$ cm), hence fat tissue could act as a buffer shielding the blood flowing through the heart and lungs. The high frequency of damage in lymphocytes of patient A2 is difficult to explain. We have recently compared the in vitro sensitivity of lymphocytes of patients A2 and A5 to a dose of 2 Gy. Twice as many aberrations were observed in lymphocytes of patient A2 than A5 (unpublished results). It should be mentioned, that patient A2 was at the end of her therapy and received, among all accident patients, the highest cumulative dose of photons. It is, therefore, possible that the high level of cytogenetic damage is a result of a very high radiosensitivity of her lymphocytes. A higher than expected frequency of dicentrics and micronuclei was also observed in lymphocytes of one of the control patients. It has been observed by different authors that the frequencies of aberrations and micronuclei in lymphocytes of patients undergoing radiotherapy are strongly variably among individuals [6;7]. The reasons for this variability are not well understood. Apart from differences in individual, intrinsic radiosensitivity, they may result from differences in the proportion of lymphoid tissue in the exposed site [8], the kinetics of lymphocyte repopulation and the speed of blood flow through blood capillaries. Which of the factors may be responsible for the high level of cytogenetic
damage in lymphocytes of patients A2 and the control patient is not known. In any case, this variability precludes the unambiguous identification of the accident patients and may present a major problem in the application of biological dosimetry in accidents during radiotherapy.

FIG. 1. Frequencies of dicentric chromosomes (panel A) and micronuclei (panel B) in lymphocytes of accident patients (white squares) and control patients receiving regular radiotherapy (black squares). The EWBD of the accident patients represent doses received prior to the accident.

4. Patient treatment
All patients developed local radiation injuries in the form of burns, followed by dry and moist desquamation. They received vitamins and ointments. In August 2001 they received Pentoxifylline. By the end of October 2001 the injuries had worsened significantly and a necrotic process had developed. In November 2001 patients A1, A2, A3 and A5 underwent a hyperbaric oxygen therapy (HBO) with only a mild, temporary, palliative effect.

In Spring 2002 the injuries worsened progressively making surgical treatment necessary. Patients A4 and A5 were treated in the Institute Curie, Paris, patients A1, A2 and A3 in the Holy Cross Cancer Centre in Kielce. The surgical treatment of patients A1-A4 consisted of a wide excision of prenecrotic and necrotic tissues (identified by CT and MRI), covering the wound by an omentum flap through a "tunnel" prepared below the skin between the abdomen and the thoracic wall and skin transplantation from the thigh. In case of patients A3 and A4 pieces of ribs had to be removed. The same was true for patient A5 whose wound was subsequently covered with a musculo-cutaneous flap.

The surgical reconstruction of the chest wall was successful in all five patients. Their health status is stable at present. Possible late effects of the accident which may be anticipated are pulmonary fibrosis and cardiomyopathy.

References

