Accidental Overexposure of Radiotherapy Patients in Białystok

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ACCIDENTAL OVEREXPOSURE OF RADIOTHERAPY PATIENTS IN BIAŁYSTOK

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FOREWORD

In February 2001, serious accidental overexposures involving patients who were undergoing post-operative radiotherapy occurred in Poland. The Government of Poland requested assistance from the IAEA under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency. The IAEA assembled and sent to Poland two teams of senior experts from France, Germany, Sweden, the United States of America and the IAEA.

The first team, composed of medical specialists, was charged with conducting an assessment of the lesions resulting from radiation for each individual patient, and consulting on the course of a future treatment plan.

The second team, composed of medical physics and radiation safety experts, was charged with evaluating the doses incurred by the affected patients, by, inter alia, reconstructing the fault conditions of the accelerator as far as was practicable, and by undertaking physical measurements and analysis of the treatment records. This report presents the assessment of the accidental overexposure made by the expert teams.

The IAEA is very grateful to the Government of Poland for giving it the opportunity to assist in the aftermath of the accidental overexposure described in this report, and, as a consequence, to draw valuable conclusions that can be shared with the international community and thereby contribute to the prevention of similar events in the future.

In particular, the IAEA wishes to express its gratitude to the Polish Ministry of Health; the National Atomic Energy Agency of Poland; the Sołtan Institute for Nuclear Research-Świerk; the M. Skłodowska-Curie Cancer Centre and Institute of Oncology, Warsaw; the Białystok Oncology Centre, Białystok; and the Radiotherapy Department of the General Hospital of the Łódź Vojevodship, Łódź.

The IAEA is very grateful to the experts comprising the two teams for making themselves available, for the dedication they showed in carrying out their tasks and for their contribution to the development and review of this report. The IAEA also wishes to acknowledge the Department of Radiology, School of Medicine of the University of New Mexico, Albuquerque, USA; the Department of Radiotherapy of the Institut Curie, Paris, France; the Department of Dermatology, University of Ulm, Ulm, Germany; and the Radiation Physics Department, Sahlgren Hospital, Göteborgs Sjukvård, Sweden. A complete list of the experts involved in the assessment of the accident is given at the end of this report.

The IAEA officers responsible for the preparation of this report were C. Nogueira de Oliveira, P. Ortiz-López and E. Buglova of the Department of Nuclear Safety and Security, and J. Iżewska and J.H. Hendry of the Department of Nuclear Sciences and Applications.

EDITORIAL NOTE

This report is based on information provided by or through the Polish authorities and the Institut Curie in Paris, France.

The report does not address questions of responsibility, legal or otherwise, for acts or omissions on the part of any person.

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EXECUTIVE SUMMARY

PART I. THE ACCIDENTAL OVEREXPOSURE

On 27 February 2001, a radiological accident occurred in the Białystok Oncology Centre (BOC) in Poland that affected five patients who were undergoing radiotherapy. The patients were given significantly higher doses than intended and, as a result, developed radiation induced injuries.

The accident resulted from a transitory loss of electrical power that caused an automatic shutdown of the Polish built linear accelerator, an accelerator of the NEPTUN 10P® type. The power cut occurred during the radiation treatment of a patient. Following the restoration of electrical power, the machine was restarted after its controls had been checked. The treatments were resumed and the patient receiving radiotherapy at the time of the power cut and four additional patients were treated.

Two patients experienced itching and burning sensations during their irradiation. This prompted the staff to halt the treatment. Subsequent dosimetry measurements revealed that the machine's output was significantly higher than expected. Further checks revealed that the dose monitoring system of the accelerator was not functioning properly, and that one of the electronic components of the safety interlock system was damaged. Subsequently, all five patients developed local radiation injuries of varying severity.

The International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources[1] establish the requirements for protection and safety, including those for the protection of patients. Recommendations on how to comply with these requirements have been published.[2]

[1] FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, INTERNATIONAL ATOMIC ENERGY AGENCY, INTERNATIONAL LABOUR ORGANISATION, OECD NUCLEAR ENERGY AGENCY, PAN AMERICAN HEALTH ORGANIZATION, WORLD HEALTH ORGANIZATION, International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources, Safety Series No. 115, IAEA, Vienna (1996).

[2] INTERNATIONAL ATOMIC ENERGY AGENCY, PAN AMERICAN HEALTH ORGANIZATION, WORLD HEALTH ORGANIZATION, Radiological Protection for Medical Exposure to Ionizing Radiation, Safety Standards Series No. RS-G-1.5, IAEA, Vienna (2002).

The requirements cover the investigation and reporting of accidental medical exposure.[3]

On 27 November 2001, the IAEA's Emergency Response Centre (ERC) received a request from the Polish Ministry of Health for assistance with the medical treatment of the patients and with the assessment of their doses under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency (Assistance Convention). The ERC, in response, arranged for an IAEA mission to be sent to Poland.

The objective of this mission was to assist the Government of Poland in response to its request for assistance. The mission was conducted by two teams of experts:

(1) A specialized medical team conducted an assessment of each individual patient for lesions arising from the irradiation, and was consulted on the course of a future treatment plan.
(2) A team comprising medical physics and radiation safety experts evaluated the doses received by the affected patients by reconstruction of the fault conditions of the accelerator, as far as was practicable, by physical measurement and by analysis of the treatment records.

PART II. MEDICAL ASSESSMENT

Medical examination revealed that the local injuries of all five patients were worsening significantly and required surgical treatment. Some patients had concomitant diseases, which complicated their condition. In 2002, three of the patients underwent surgery in the Oncological Surgery Ward of the Holy Cross Cancer Centre in Kielce, Poland. With the assistance of the IAEA, the two remaining patients were transferred to the Institut Curie in Paris, France, for treatment.

This report presents the results of the assessment covering the period prior to November 2002.

[3] See INTERNATIONAL ATOMIC ENERGY AGENCY, INTERNATIONAL LABOUR OFFICE, PAN AMERICAN HEALTH ORGANIZATION, WORLD HEALTH ORGANIZATION, Building Competence in Radiation Protection and the Safe Use of Radiation Sources, Safety Standards Series No. RS-G-1.4, IAEA, Vienna (2001).

PART III. DOSE ASSESSMENT

The approach adopted for the dose assessment was to test the NEPTUN 10P® radiotherapy accelerator of the BOC under normal conditions and to try to simulate the conditions of the event. To achieve this, a number of tests were performed that employed a wide spectrum of machine settings which included both the normal clinical mode and operation under simulation of the fault conditions.

The reconstruction of the fault conditions by the IAEA medical physics and radiation safety team showed this machine to be capable of producing a dose to water rate in reference conditions of the order of 100 Gy/min for an 8 MeV electron beam, if the limitation of the electron gun filament current is set at a high level, such as 1.4–1.5 A. Under these conditions, and with a treatment prescription of 150 monitor units, the machine may deliver doses in the order of 100 Gy or higher.

The IAEA medical physics and radiation safety team has validated the measurements made by the local physicists on the day of the accident under the fault conditions. The dose measured a few hours after the accident was very close to the measurements performed by the IAEA mission in December 2001, despite the fact that the machine had been repaired on the morning after the accident and then disassembled and left dismantled for several months. It was reassembled and put into operating condition at the request of the IAEA team, one day before their arrival at the BOC.

The doses derived from the biodosimetry measurements based on electron paramagnetic resonance (EPR) of the rib samples of three patients were as high as 60–80 Gy. They are generally lower than the doses reconstructed from the measurements made by the local physicists on the day of the accident. The differences are not significant and lie within the uncertainties of the EPR measurements and the uncertainties associated with the reconstruction of the fault conditions.

On the basis of the information gathered during the mission to Białystok, the IAEA medical physics and radiation safety team reconstructed the accidental exposures in sufficient detail as to be able to document the circumstances and disseminate the lessons learned from this event, taking into consideration the long delay between the accident and the conduct of the mission, and the ad hoc reassembly of the faulty NEPTUN 10P® accelerator by the local engineers. It should be noted that the reconstruction by the IAEA team of the doses that may have been delivered does not attempt to simulate exactly the conditions leading up to the accidental exposures, nor to put forward a full explanation for the doses received by the patients.

PART IV. STEPS TAKEN BY THE AUTHORITIES IN POLAND FOLLOWING THE EVENT IN BIAŁYSTOK

In March 2001, the Quality Assurance Section of the Polish Society for Radiation Oncology organized a conference and workshop for representatives of all the radiotherapy departments in Poland. On this occasion, those directives for QA procedures that are based on internationally sanctioned recommendations for external beam radiotherapy were presented. Protocols for radiological practices were delivered to all cancer centres.

According to a directive of the Ministry of Health, the National Consultant in Radiotherapy, an advisor to the Minister of Health, prepared the Report on the Status of Polish Radiotherapy and a development programme up to 2010 for radiotherapy infrastructure, equipment upgrading and replacement, cancer centre needs, and staff teaching and training. In 2002, the Minister of Health nominated a Committee of Experts that included members of the National Atomic Energy Agency (NAEA) to address the implementation of EURATOM Directive 97/43 on health protection of individuals against the dangers of ionizing radiation in relation to medical exposure.

The Committee prepared a Regulation on the conditions for the safe use of ionizing radiation for medical purposes and on the modalities for internally controlling compliance with the provisions of this Regulation. The Regulation was approved by the Minister of Health on 24 December and published in the Official Journal on 31 December (2002, NR. 241, Item 2098). This Regulation is mandatory for all organizations which use ionizing radiation for medical purposes.

The Regulation includes comprehensive provisions and requirements relating to radiation protection of nuclear installations and other radiation sources; authorization of activities involving the use of ionizing radiation by means of licences, permits and registration; and conduct of inspections. It covers in detail all the technical and administrative aspects of the application of ionizing radiation for medical purposes. Minimum requirements for equipment are detailed on the basis of the recommendations of the European Society of Therapeutic Radiation Oncology. Provision of QA procedures and internal and external audits are defined as obligatory. Regulation NR. 241 establishes clearly the responsibilities and competences of the NAEA, the sanitary inspection programme and the National Consultant in Radiotherapy.

PART V. CONCLUSIONS, RECOMMENDATIONS AND LESSONS TO BE LEARNED

Operating organization: Radiotherapy departments

The IAEA medical physics and radiation safety team concluded that a fault affecting the beam monitoring system of the NEPTUN 10P® accelerator led to a large increase in the dose rate, even though the display indicated a value lower than normal. This was due to a faulty diode preventing the safety interlock from functioning. In addition, the limitation on the filament current for the electron gun was set at a high level which meant that the dose rate due to the malfunction was many times higher than intended. The combination of these factors led to the substantially higher doses being delivered to the patients.

In order to help prevent other possible overexposures from occuring in similar circumstances, quality assurance (QA) programmes appropriate for accelerators that are used in the medical field need to include dosimetry checks of beam output prior to the resumption of patient therapy following power failures or any other unusual occurrence, such as an anomalous reading in the dose rate display.

National infrastructure for radiotherapy

In countries that have an unstable power grid, measures ought to be taken to ensure a uniform and stable AC power supply to institutions that use medical electrical equipment, in order to facilitate the safe operation of this equipment. These measures may be implemented by providing such institutions with independent power supply units, as appropriate.

A national QA programme for radiotherapy ought to include provision for ensuring rigorous implementation of comprehensive QA systems in the radiotherapy departments for both the physics and medical aspects, as well as review by an external audit system that uses experts in medical physics and radiation oncology, in accordance with the International Basic Safety Standards (paras 2.29, II.1, II.2, II.12, II.22, II.23). However, hospitals need to be equipped with adequate quality control tools to allow the implementation of such QA systems. Provision for conducting dosimetry checks of beam output after power failures needs to be included in the QA programme.

Increased awareness and understanding of any unusual situation ought to be promoted by inclusion in the training of all persons directly or indirectly involved in radiotherapy, and by dissemination of the lessons learned from

accidental exposures. However, this training should be appropriate to the function and professional needs of the individual concerned.

Equipment manufacturers and suppliers

The accidental overexposure in Białystok demonstrated that two faults in two circuits could occur at the same time and lead to machine operation with an ineffective beam monitoring system. Moreover, the probability of such a double fault occurring was increased by the fact that an inoperative interlock (the diode) went unnoticed until the second fault occurred in the beam monitoring system. In this situation, the interlock could allow the start sequence to progress, even if a second fault, a defective fuse in the power supply to the dose monitoring systems, rendered the system ineffective and led to the filament current being driven to its maximum.

The NEPTUN 10P® medical accelerator was designed prior to the publication of the standards of the International Electrotechnical Commission (IEC) that currently apply for accelerators of this kind. The dose monitoring system of the NEPTUN 10P® does not comply with the current IEC recommendations for the safe operation of accelerators used for medical purposes. In particular, Section 29.1.1.1 of IEC Standard 60601-2-1, issued in 1998, contains stricter criteria for the design of machine beam monitoring systems than those listed in the recommendations established by the IEC in 1981 (IEC-601-2-1).

The design for the new generation of NEPTUN accelerators, or for any other accelerator currently being developed, needs to apply the IEC 60601 standards, which are up to date. More specifically, with regard to dose rate monitoring systems and the safety interlocks, IEC 60601 provides for the following:

(a) *Design of the monitoring system.* If, under any fault conditions, the equipment can deliver an absorbed dose rate at normal treatment distance of more than ten times the maximum specified in the technical description, a radiation beam monitoring device, which shall use a circuit independent of the dose rate monitoring system, shall be incorporated on the patient side of the radiation beam distribution system. This shall limit the excess absorbed dose at any point in the radiation field to less than 4 Gy (Section 29.1.3). NOTE: In equipment capable of producing both X radiation and electron radiation, the termination of irradiation may need to be completed before the generation of the next pulse of radiation.

(b) *Design of safety interlocks.* Equipment shall be so designed and manufactured that, even in single fault condition, no safety hazard exists (Section 52).

(c) *Examination of safety interlocks.* The safety interlocks need to be examined to ensure fail-safe conditions, i.e. failure of any element which could affect the correct function of any interlock shall terminate irradiation. Section 29.1.3 further establishes that "…means to protect a possible overdose due to an absorbed dose rate more than twice the specified maximum, and limit the excess absorbed dose to less than 4 Gy … shall be tested between, or prior to, irradiations for their ability to function." In other words, the interlocks need to be tested before each new treatment. This would prevent an ineffective interlock from going unnoticed.

For existing equipment, particular emphasis needs to be given to:

(a) *Safety review and assessment.* As a general recommendation, when a new safety standard is issued, the safety of existing equipment needs to be reviewed and reassessed with regard to the need to increase safety to a level as close as practicable to that of the new standard. The relevant standards in this case are IEC 60601-1-4 and 60601-2-1. The improvements may be technological or procedural. The reassessment, however, needs to take into consideration all the implications of any change or modification. In relation to this event, issuing a warning notice with clear instructions requiring that verification of relevant interlocks be confirmed before each new irradiation and how to perform this verification may be necessary.

(b) *Warnings in instruction manuals.* The manufacturer needs to issue warning notes in the maintenance and service instructions covering the adjustment of limits to the filament current and of any other safety critical devices.

(c) *Restrictions on access.* As far as practicable, access to safety critical adjustments and components needs to be restricted to maintenance engineers instructed by the manufacturer specifically on the safety associated with these components. The restriction of access can be achieved by sealing certain potentiometers, by placing warning stickers on parts of the equipment or by taking administrative measures.

Certification of training for maintenance staff trained by the manufacturer needs to specify limitations or restrictions on the manipulation or adjustment of certain critical parts in the accelerator. Instructions need to put clear emphasis on safety elements and include warning notes.

Medical issues

The accidental overexposures of all five patients were serious. The conditions of some patients were complicated by the presence of concomitant diseases. Hyperbaric oxygen treatment improved the condition of the local injuries for some of the patients. All the patients underwent surgery.

It should be recalled that, following radiation injury, the evolution of vascular damage and the deterioration of the underlying blood supply occur after a significant delay, often one of months or years after the overexposure. At the time of writing, the damage that was manifested in these overexposed patients at the early stage was progressing with the development of complications.

The results of the surgical treatment that was performed are preliminary because of the short follow-up time and the incomplete healing of post-operative scars. However, the patients' conditions show significant improvement, in view of the severity of their injuries and the presence of concomitant diseases. The following recommendations, which derive from these cases, are also generally applicable to other accidental exposures that lead to the development of local radiation injuries:

(a) The injuries should not be treated in isolation without consideration of the individual patient's circumstances and the state of other medical issues.
(b) The type of surgery should depend on the degree of radionecrosis of the chest wall, such that:
    (i) If the chest wall can be preserved and if granulation of the deeper layers is effective, simple skin grafting can be undertaken.
    (ii) If the chest wall can be preserved but the granulation is inadequate or absent, then construction of myocutaneous flaps from dorsal or abdominal muscles will need to be considered.
    (iii) If the chest wall has to be partly removed owing to the extent of radionecrosis, the best treatment might be to use a flap of omentum brought through the diaphragm and covered by a skin graft.
(c) Surgical treatment of severe radiation injuries to radiotherapy patients can carry a significant risk of morbidity and mortality. Therefore, before any decision to undertake such major surgery is made, it needs to be clear that there is:
    (i) No apparent metastatic disease,
    (ii) Acceptable pulmonary reserve,
    (iii) Adequate myocardial perfusion and appropriate control of sepsis.

It is necessary to provide psychological support for patients with radiation induced injuries. Communication between a patient who has already successfully undergone surgery and one who is being prepared for it can be useful in encouraging the latter.

Regular and long term follow-up of patients is essential not only for oncological reasons but also to identify long term sequelae of cutaneous radiation syndrome.

1. INTRODUCTION

1.1. BACKGROUND

On 27 February 2001, an accidental overexposure occurred in the Białystok Oncology Centre (BOC) in Poland in which five patients undergoing post-operative radiotherapy were affected. The event resulted from the transitory loss of electrical power that caused an automatic shutdown of a NEPTUN 10P® type linear accelerator, a domestically manufactured machine. The power cut occurred during the radiation treatment of a patient. Following the restoration of electrical power, the machine was restarted after its controls had been checked. The treatments were resumed and the patient receiving radiotherapy at the time of the power cut and four additional patients were treated.

Two patients experienced itching and burning sensations during their irradiation, which prompted the staff of the BOC to halt further treatment. Subsequent dosimetry measurements revealed that the machine's output was significantly higher than expected. Further checks revealed that the dose monitoring system of the accelerator was not functioning properly, and that one of the electronic components of the safety interlock system was damaged. Subsequently, all five patients developed local skin reactions of varying severity. The International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources [1] establish the requirements for protection and safety, including those for the protection of patients. Recommendations on how to comply with these requirements are given in Ref. [2]. The requirements cover the investigation and reporting of accidental medical exposure (see Ref. [3]).

At the request of the Polish Ministry of Health, the IAEA assembled two teams of experts to conduct a medical assessment of each patient, to advise on future treatment and to assess the doses incurred in the overexposures by reconstructing the fault conditions that caused them, examining the treatment records and conducting physical measurements. This report contains the results of these assessments.

1.2. OBJECTIVE

At the request of Member States, the IAEA has, for a number of years, provided support and assistance and conducted follow-up investigations after serious accidents involving radiation sources. Reports have been published on

these investigations, which have covered radiological accidents involving workers, the public and patients undergoing radiotherapy. Examples of the latter were the accidental exposures in San José, Costa Rica [4] and Panama [5]. A report on the lessons to be learned from a review of a number of accidental exposures in radiotherapy has also been published [6].

The objectives of this report are to compile information about the causes and consequences of the accidental exposure, and to make recommendations about how such accidents can be avoided in future.

The information is intended for the use of national authorities such as regulatory bodies and health institutions, health administrators and a broad range of specialists, including radiation oncologists, radiotherapy technologists, medical physicists, manufacturers and maintenance organizations, and radiation protection specialists.

1.3. SCOPE

This report describes the circumstances and events surrounding the accidental exposure. It describes the health effects and provides conclusions relevant to national authorities, radiotherapy departments, and manufacturers of radiotherapy devices and treatment planning systems.

1.4. STRUCTURE

Section 2 provides background information on the Radiotherapy Department of the BOC, the accelerator involved in the overexposure, the radiation protection regulations and the cancer treatment infrastructure in Poland. Section 3 reviews the circumstances of the event. Section 4 deals with the actions taken in response to the event. Section 5 describes the assessment of the fault condition and details the doses incurred by the patients (along with the electron paramagnetic resonance (EPR) and biodosimetry findings). The clinical course of the overexposures is provided in Section 6, and Section 7 presents the conclusions, recommendations and lessons to be learned. Appendix I contains background information on radiation effects in humans in general and provides a commentary on the overexposures in Białystok. Appendix II presents haematological data for the five patients who were accidentally overexposed.

2. BACKGROUND

2.1. THE BOC

The BOC is one of 21 such facilities in Poland. It serves the northeastern part of Poland in the Podlaskie Voivodship, which has a population of about 1.3 million, and a part of the neighbouring Mazursko-Warmiskie Voivodship with an additional population of about 300 000. In 2001, the number of oncological consultations was 44 640 and 5894 patients were hospitalized.

The BOC is a typical regional centre in Poland, being reasonably well equipped and staffed. The number of patients it treats (radiotherapy patients per megavoltage unit) falls within the Polish average. The BOC has a Radiotherapy Department where over 1000 patients per year undergo teletherapy and over 200 patients receive gynaecological brachytherapy (Table 1). The centre has three teletherapy units:

(1) One COLINE® 4 MV photon accelerator (manufactured in Poland by IPJ-ZdAJ Świerk and installed in 1998);
(2) One NEPTUN 10P®, a 10 MV accelerator (manufactured in Poland by IPJ-ZdAJ Świerk and replacing the one involved in the radiation accident in 2001) which can deliver a 9 MV photon beam and 6, 8 and 10 MeV electron beams;
(3) One ^{60}Co THERATRON® 1000E unit (manufactured in Canada by Theratronics and installed in 1998).

The Radiotherapy Department is also equipped with a Polish made SIMAX simulator (also manufactured by IPJ-ZdAJ Świerk) which was acquired in 1998. The BOC does not have a CT scanner but has access to two scanners four days per week in two other hospitals in Białystok. The BOC also

TABLE 1. NUMBER OF RADIOTHERAPY PATIENTS TREATED ANNUALLY IN THE BOC

Year	Teletherapy	Brachytherapy
1999	907	276
2000	1242	205
2001	1124	207

operates two brachytherapy afterloaders: a SELECTRON® ^{137}Cs MDR unit and a recently installed GAMMAMED® 12i HDR unit.

The average number of patients per megavoltage treatment unit per year (taking into account the irradiation units that are in operation) is between 455 and 500; below the national average of 560. The number of patients treated on the NEPTUN 10P® accelerator was of the order of 40 per day. The ratio of curative treatments to palliative treatments is roughly 2:1.

There are currently 25 radiation oncologists at the BOC, 12 with a first degree of specialization and 13 with a second degree of specialization. The radiation oncologists work one shift of five hours. One radiation oncologist is always on duty, cover being provided 24 hours per day. Irradiation of the teletherapy patients is conducted in shifts, treatment being administered between 07:30 and 18:00.

There are always two radiographers (radiotherapy technicians) working at an irradiation unit. A radiation oncologist and a physicist are present during the adminstration of the first fraction of radiation treatment and also when the irradiation plan is changed during the course of treatment.

The Radiotherapy Department has a mould room where individual shielding blocks are prepared for the majority of radical (curative) treatments. The treatment protocols follow those of the Centre of Oncology in Warsaw (hereafter referred to as the Centre of Oncology (Warsaw)), the reference centre in Poland.

The Medical Physics Department at the BOC is reasonably well equipped, having three radiotherapy dosimeters:

(1) A Siemens unit acquired in 1970 (two ionization chambers), used only for relative measurements;
(2) An IONEX® 2500/3 unit (manufactured by Nuclear Enterprises Ltd) acquired in 1985 (six ionization chambers);
(3) A UNIDOS® unit (manufactured by PTW) acquired in 1999 (three ionization chambers).

The IONEX® and UNIDOS® electrometers and chambers have valid calibration certificates from the Polish Secondary Standard Dosimetry Laboratory (SSDL).

The Medical Physics Department has a water phantom WP 700 system that was acquired in 1998. The system was manufactured by Wellhofer Dosimetrie (Scanditronix) and is equipped with an IC-70 ionization chamber and two semiconductor detectors.

The BOC uses several treatment planning systems:

(a) MEVAPLAN® (by Siemens) acquired in 1989;
(b) THERAPLAN Plus® (by Theratronics, Canada) acquired in 1998;
(c) ALFRAD® (a 2-D system produced in Poland) acquired in 1998;
(d) ABACUS® (GAMMAMED) for brachytherapy treatment planning, acquired in 2000.

The staff of the Medical Physics Department comprises six medical physicists and two engineers who provide maintenance service for the radiotherapy units. Two of the physicists also act as radiation protection officers. They have certificates from the competent regulatory body, which in this case is the National Atomic Energy Agency of Poland (NAEA).

2.2. THE CLINICAL ACCELERATOR INVOLVED IN THIS EVENT

The NEPTUN 10P® involved in this event is a Polish version of the French accelerator NEPTUNE, manufactured under licence from the French designer and manufacturer (Fig. 1). Although the French NEPTUNE is no longer marketed, it is assumed that there are still accelerators of this type being

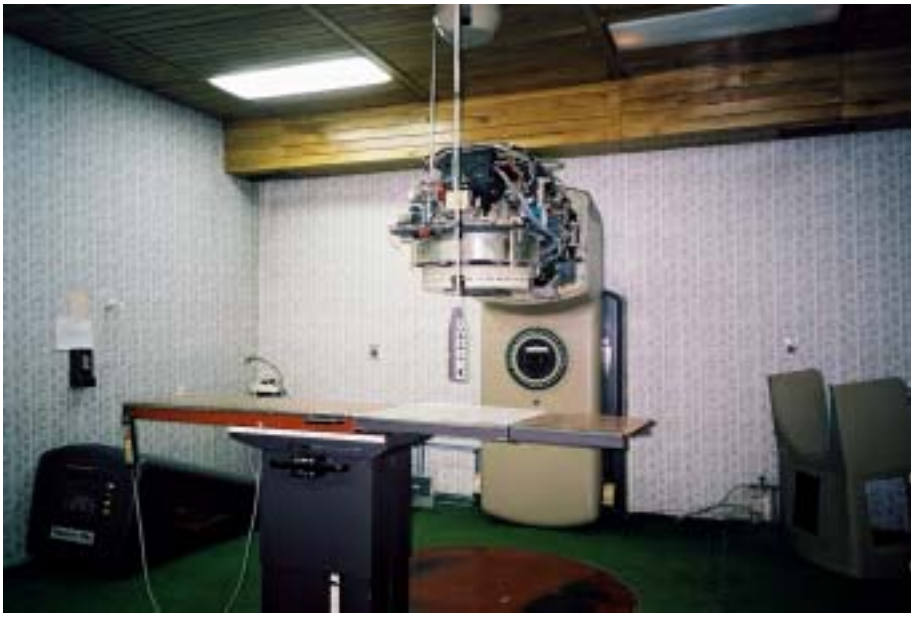

FIG. 1. The NEPTUN 10P® accelerator. The irradiation head was opened when measurements were being carried out during the IAEA mission.

used to provide treatment in a number of countries. The team was informed that the design and control and safety circuits described below were not modified in the Polish version except for the replacement of some components of similar characteristics. Moreover, the schematics used were actually the same. The NEPTUN 10P® is capable of delivering electron beams of 6, 8 and 10 MeV, as well as a photon beam of 9 MV.

It is not within the scope of this report to give a full description of the design and operation of medical electron accelerators used for therapeutic purposes. Reference should be made to the more specialized literature providing this information [7, 8]. Only a short description is given below of the parts relevant to this accidental overexposure.

2.2.1. The potential for higher electron current

Accelerators that are designed to deliver both electron beams and photon beams have the capability to produce a current in the acceleration guide tube which is much higher than that needed solely for the electron beam mode of operation. The reason for this is that in order to produce a photon beam, a large amount of the energy carried by the electron current impinging on the X ray target is lost in the process of producing X rays. The beam intensity is further reduced in the field flattening filter used to flatten the X ray beam profiles, and to compensate for these losses, that is, to obtain photon beams of a similar dose rate as electron beams, a much higher current of electrons (the current in the guide tube) is needed, one that may reach up to three orders of magnitude higher. Since the electrons are accelerated in pulses, an increase in the average current can be obtained by increasing the pulse frequency and the pulse current. In the case of the NEPTUN 10P®, the pulse frequency for the photon mode of operation is increased by a factor of three, i.e. to increase the average current by three orders of magnitude it is necessary to increase the pulse current by a factor of more than 300. In other words, the accelerator is designed to produce a pulse current in the order of 300 times higher than that needed to produce an electron beam of a similar dose rate.

2.2.2. The dose monitoring systems and their power supply

As is usual with electron accelerators, the beam in the NEPTUN 10P® is monitored by two transmission chambers, placed in the radiation head at the exit of the beam. Their purpose is to ensure an accurate and safe dose delivery. The monitor chambers deliver an electrical signal to the beam stabilization systems to control beam flatness and symmetry, as well as the dose rate. The electrical signal is proportional to the dose rate and, when integrated over time,

to the dose. The chambers are calibrated in the hospital against an external reference ionization chamber by establishing the ratio of monitor units (MU) of the transmission chambers to grays at the reference point, determined with the external chamber.

The dose rate signal is fed to a control circuit that ensures that the actual dose rate matches a preselected value (the nominal value). For the NEPTUN 10P®, five different values of dose rate can be selected. In addition, each of the two chambers is divided into two equal sectors, and by comparing their signals, the symmetry of the beam can be corrected and controlled. The high voltage required for both transmission chambers is provided by a single power supply (+300 V). The power supply receives its AC current through a fuse. This aspect played a central role in the development of this event.

2.2.3. International Electrotechnical Commission (IEC) requirements relevant to this event

The standards of the IEC [8] place safety requirements on accelerators; the most relevant to this event can be summarized as follows:

(a) *Dose monitoring systems.* Requirements on dose monitoring systems are as follows:
   (i) There shall be two systems arranged either in a primary/secondary combination or in a redundant combination[1];
   (ii) Malfunctioning of one dose monitoring system shall not affect the correct functioning of the other;
   (iii) Failure of any common element that could change the response of either system by more than 5% shall terminate radiation;
   (iv) When separate power supplies are used, failure of either supply shall terminate radiation.

(b) *Dose rate control.* If, under any fault conditions, the equipment can deliver an absorbed dose rate at normal treatment distance of more than ten times the maximum specified in the technical description, a radiation beam monitoring device, which shall use a circuit independent of the dose rate monitoring system, shall be incorporated on the patient side of the radiation beam distribution system. This shall limit the excess absorbed

[1] Redundant combination means that the selection of the MUs is set independently in each system; primary/secondary combination means that the selection of the MUs is done only on the primary system while the MU in the secondary system is automatically set at a value which is slightly higher (not more than 10%, according to the IEC standards).

dose at any point in the radiation field to less than 4 Gy. However, it should be noted that the IEC standards state that "…in equipment capable of producing both X radiation and electron radiation, the termination of irradiation may need to be completed before the generation of the next pulse of radiation." This is because, in fault conditions, the dose from one single pulse of radiation can be very high.

(c) *Controlling timer.* A controlling timer shall be provided and a means to limit the setting of the timer to a value which is not greater than 120% of the time to deliver the intended number of MU, or 0.1 min, whichever is greater, as calculated from the set dose and expected dose rate.

(d) *Design of safety interlocks.* Equipment shall be so designed and manufactured that, even in a single fault condition, no safety hazard exists.

It should be noted that these standards did not exist at the time the NEPTUNE and NEPTUN 10P® were designed.

2.2.4. The relevant interlock and the consequences of its failure

The NEPTUN 10P® requires a starting procedure to be followed in order to be able to initiate an irradiation process. The procedure requires the pressing of a series of keys in sequence, each of which initiates a check or control function. It is necessary to complete one series in order to be allowed to proceed to the next step. Satisfactory completion of each stage is indicated by a green light. Figure 2 illustrates the relevant series of keys on the control panel.

FIG. 2. Photograph of the control panel of the NEPTUN 10P® showing the series of keys relevant to this event.

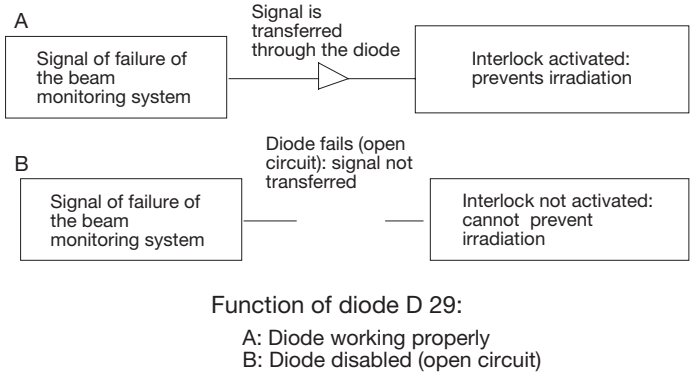

FIG. 3. Representation of the failure of the D29 diode.

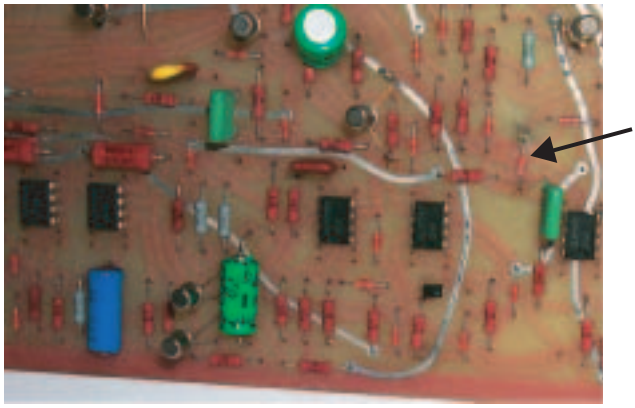

FIG. 4. Photograph of the electronic board and the D29 diode.

One of these keys initiates a check of the dose monitoring system. The test consists of supplying voltage to the electronic chain of the dose monitoring systems. If these keys fail to work properly, a signal is given to an interlock, which prevents the functioning of the modulator, the magnetron and the electron gun, thereby preventing initiation of the radiation beam. The signal is transferred to the interlock through a diode, designated D29 in the schematics of the electronic board (Figs 3, 4). When the dose monitoring system is working properly, the interlock is not triggered and the green light appears, thus allowing progression to the next step in the sequence. Since the voltage input to

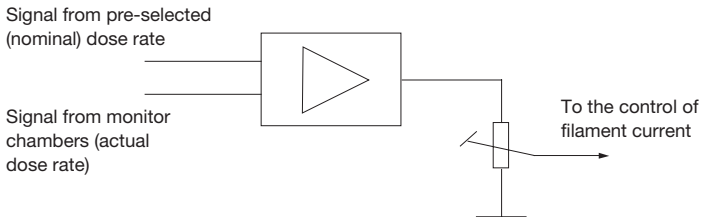

FIG. 5. Limitation of filament current by means of a potentiometer.

the dose monitoring system is taken from the power supply for the transmission chambers, the test also serves to verify that the high voltage is present (the +300 V from the power supply is reduced to one hundredth through a voltage divider and the 3 V are input to the dose monitoring system for the test). It is of interest to point out that, in the case of a 'break' of the D29 diode, the circuit becomes 'open' and the signal indicating failure of the beam monitoring system is not transferred to the interlock. A test of the dose monitoring system is ineffective for a break of the D29 diode, as the green light appears despite the break of this diode. Thus, the starting procedure can proceed to initiation of irradiation, even though the dose monitoring system is not working. This aspect was also crucial in this event.

2.2.5. Control and restriction of the current in the electron gun

The electron gun is controlled by the signal from the dose monitoring system by means of a comparison circuit (Fig. 5). The circuit compares this signal, which is proportional to the actual dose rate, with a constant voltage, which is itself proportional to the preselected dose rate, i.e. the nominal value.

When the dose rate is higher than the nominal value, the current to the electron gun filament is reduced and vice versa. This is achieved by controlling the AC in the primary of a transformer, the secondary of which is connected to the filament of the electron gun.

The current control circuit has an additional feature, one which is most relevant to this event; it sets a limit to the current of the filament of the electron gun. It does this by limiting the voltage of the signal that controls the current of the filament. As an example, when an electron beam of 8 MeV is used, for

which the normal value for the filament current may be of the order of 1.10 A[2], the limitation of the current can be set slightly above the normal value, for example at 1.12 A. This imposes a restriction on the electron gun current which, in the case of certain fault conditions occurring in the control system, could otherwise drive the current to a much higher value.

2.3. QUALITY ASSURANCE (QA) AND THE HISTORY OF RECENT DOSIMETRY AUDITS AT THE RADIOTHERAPY DEPARTMENT

The QA system of the radiotherapy units at the BOC follows the national recommendations for megavoltage machines [9] prepared and published by the SSDL which stipulates the need to undertake daily, weekly, monthly and quarterly checks of such units. These recommendations are consistent with international recommendations made by the IEC, ESTRO [10] and the IAEA [11]. The BOC is making every effort to follow the QA recommendations in radiotherapy at the national level.

The BOC has taken part in every national postal thermoluminescent dosimetry (TLD) audit organized by the External Audit Group of the SSDL since 1991. The SSDL is linked to the IAEA–WHO network of secondary standard dosimetry laboratories and its measurement methodology follows that of the IAEA. Table 2 shows the deviations between the doses stated by the BOC and those measured by the SSDL. In only one case was the deviation outside the acceptance limit of 5% and the reason for this was clarified.

The treatment planning procedure at the BOC was verified by the national External Audit Group in 2001 during on-site measurement with an anthropomorphic phantom. The results agreed to within 3% of the reference values.

2.4. REGULATORY CONTROL IN POLAND RELEVANT TO THIS EVENT

The NAEA is the Government agency empowered by the Atomic Energy Act of 10 April 1986 (AEA86) to establish detailed requirements related to the

[2] Although the AC values (in A) indicate the current in the primary of the transformer, the secondary of which provides power supply to the filament, this report refers to it as the 'filament current' for simplification.

TABLE 2. RESULTS OF TLD AUDITS ORGANIZED BY THE SSDL: DEVIATION BETWEEN THE DOSES GIVEN BY THE BOC AND THOSE MEASURED BY THE SSDL (%)

Year	Co-60	Linear accelerator photons	Linear accelerator electrons
1991	–0.7	–6.4	–2.1
1994	1.6	0.9	
1999	–1.3		
2000		–2.9	

radiation protection of nuclear installations and other radiation sources, to authorize activities by means of licences, permits, registration, etc., and to carry out inspections.

The President of the NAEA, in agreement with the Minister of Health, has the authority to set dose limits and indicators of radiation hazards and to set acceptable levels of ionizing radiation for consumer goods (AEA86–Art.13.2 and Rule dated 21 May 1988 governing the competences of the President of the NAEA).

For practices involving exposures to ionizing radiation, the President of the NAEA issues authorizations, stipulates the specific terms and conditions for the performance of these practices, and conducts inspections to ensure compliance (AEA86–Art. 22.1). The Ministry of Health is responsible for providing for the safe application of ionizing radiation for medical exposure by means of appropriate regulations (AEA86–Art. 13.1). X ray units with a power rating under 300 kV fall within the jurisdiction of the Ministry of Health and the State Sanitary Inspection (AEA86–Arts 22.2, 22.3, 33.4).

The Act of 1986 has been amended several times. The new Atomic Energy Act (AEA2000) was passed by Parliament on 29 November 2000 and has been in force since 1 January 2002. The new Act, as well as the old one, gives the necessary authority to the NAEA to fulfil its tasks as an independent national regulatory body in radiation protection and nuclear safety, which also includes regulatory control of the technical and administrative aspects of medical practices. Article 4 of AEA2000 in particular covers any practice involving exposures of the workforce or the public to ionizing radiation and:

(a) The manufacture, installation, use and maintenance of devices containing radioactive sources and the trade in such devices.

(b) The manufacture, purchase, commissioning and use of devices generating ionizing radiation.
(c) The commissioning of laboratories and rooms using ionizing radiation sources, including X ray rooms. These laboratories and rooms require a licence issued by, or notification made to, the President of the NAEA (Art. 5.2 of AEA2000) and are subject to inspections by NAEA inspectors. Exempted from this requirement are:
    (i) Facilities with X ray machines that are used for medical purposes and which have a power rating of less than 300 kV. These facilities are under the regulatory control of the Minister of Health and the State Sanitary Inspector of the Province.
    (ii) Organizational entities of the Ministry of Defence, which are under the control of the Military Sanitary Inspector, pursuant to Art. 5.3 of AEA2000.

AEA2000 (Art. 10) states that for a medical procedure (diagnosis or therapy) involving ionizing radiation, the benefits have to outweigh the possible harmful health effects.

2.4.1. Regulatory control of medical exposures

Regulatory control of medical exposure is the responsibility of the Ministry of Health. Article 15.3 of AEA2000 provides that the Minister of Health shall establish regulations governing the conditions for the safe application of ionizing radiation for medical purposes and the procedures for controlling compliance with these conditions. In issuing regulations, the Ministry of Health is obliged to take into account the principle of optimization and dose constraints for those persons who knowingly and willingly help, support and comfort patients undergoing medical procedures. Special rules apply for the medical exposure to ionizing radiation of children, pregnant women and breast-feeding women undergoing examinations and medical treatments. Special considerations govern accident prevention, namely, the QA system used in diagnostic X ray procedures, nuclear medicine and radiotherapy. Finally, there is a requirement to investigate patient doses that repeatedly and substantially exceed the guidance levels and it is also mandatory to investigate any accidental medical exposure.

2.4.2. Steps taken by the authorities in Poland following the event in Białystok

In March 2001, the Quality Assurance Section of the Polish Society for Radiation Oncology organized a conference and workshop for representatives

of all the radiotherapy departments in Poland. On this occasion, those directives for QA procedures that are based on internationally sanctioned recommendations for external beam radiotherapy were presented. Protocols for radiological practices were delivered to all cancer centres.

According to a directive of the Ministry of Health, the National Consultant in Radiotherapy, an advisor to the Minister of Health, prepared the Report on the Status of Polish Radiotherapy and a development programme up to 2010 for radiotherapy infrastructure, equipment upgrading and replacement, cancer centre needs, and staff teaching and training. In 2002, the Minister of Health nominated a Committee of Experts that included members of the NAEA to address the implementation of EURATOM Directive 97/43 on health protection of individuals against the dangers of ionizing radiation in relation to medical exposure.

The Committee prepared a Regulation on the conditions for the safe use of ionizing radiation for medical purposes and on the modalities for internally controlling compliance with the provisions of this Regulation. The Regulation was approved by the Minister of Health on 24 December and published in the Official Journal on 31 December (2002, NR. 241, Item 2098). This Regulation is mandatory for all organizations which use ionizing radiation for medical purposes.

The Regulation includes comprehensive provisions and requirements relating to radiation protection of nuclear installations and other radiation sources; authorization of activities involving the use of ionizing radiation by means of licences, permits and registration; and conduct of inspections. It covers in detail all the technical and administrative aspects of the application of ionizing radiation for medical purposes. Minimum requirements for equipment are detailed on the basis of the recommendations of the European Society of Therapeutic Radiation Oncology. Provision of QA procedures and internal and external audits are defined as obligatory. Regulation NR. 241 establishes clearly the responsibilities and competences of the NAEA, the sanitary inspection programme and the National Consultant in Radiotherapy.

3. THE ACCIDENTAL OVEREXPOSURE

3.1. DESCRIPTION OF THE EVENT

On 27 February 2001, a malfunction of the NEPTUN 10P® linear accelerator occurred following a sudden power cut. The machine was used for

radiation therapy at the BOC. Five patients, all of whom had been undergoing radiation treatment with an electron beam to the surgical wound following surgery for breast cancer, were overexposed. The prescribed doses were 2–2.5 Gy per fraction with an 8 MeV electron beam. The machine shut down during a mains power cut while a patient (subsequently designated as Patient 1) was on the treatment couch and had received only 5 MU of the prescribed 155 MU, which corresponded to 0.08 Gy of the prescribed 2.5 Gy.

The radiation technologist operating the machine contacted the chief physicist. The physicist restarted the machine, allowing the required 5 minute minimum warm-up time. He checked the machine controls, including the voltage levels of the power supply panel, and found that they were functioning as expected. The user's manual for the NEPTUN 10P® requires that detailed machine checks, including output measurements, be performed after emergency shut-offs of an accelerator caused by malfunction of any of the machine systems, but shut-off due to a power cut was not included in the list of emergency shut-offs in this manual. Machine shut-offs due to power cuts had happened many times in the past. The AC mains voltage in the hospital area was quite unstable and as many as two power cuts a day had occurred occasionally. The experience of the radiation technologist with previous power cuts indicated that, after resuming operation, the machine performed normally, i.e. without any change in its beam parameters. After the warm-up had been completed, the patient's treatment continued with the remaining 150 MU. The analogue dose rate indicator on the machine console fluctuated around 100 MU/min instead of showing the usual 290–300 MU/min. The MU counters worked slowly, which corresponded to the low dose rate indication at the machine console. The physicist adjusted the secondary timer on the console from 1.3 min to 1.5 min to allow completion of the treatment (150 MU/(100 MU/min) = 1.5 min).

Towards the end of the treatment of Patient 1, the radiation technologist noted a minor asymmetry of the radiation field indicated on the NEPTUN 10P® console and adjusted it. When the next patient (Patient 2) was being treated, the physicist was summoned to the mould room because of an emergency.

The next three patients treated (Patients 3, 4 and 5) reported an abnormal skin reaction. Patient 4 mentioned an unusual feeling during treatment and Patient 3 returned after treatment to complain of an itching and a burning sensation in the area of the irradiated field. After Patient 5 was treated, the radiation oncologist on duty examined all three patients. She noted a post-irradiation reaction for Patient 5 which could not be attributed to a dose of just a few grays that the patient ought to have received in the course of treatment.

The physicist discussed the problem with the chief radiation oncologist and further treatments with this machine were stopped.

3.2. THE DISCOVERY OF THE PROBLEM

As the machine seemed to be functioning abnormally, the physics team made dose output measurements of those radiation beams of the accelerator that were clinically used[3], i.e. the 8 and 10 MeV electrons and 9 MV photons. Initially, an old Siemens dosimeter used for regular quality control measurements was employed for output measurements. Its readings were off the scale for 300 MU, which is the usual number of MUs preset for output measurements in the water phantom under reference conditions. The local dosimetry standard, comprising an NE2581 ionization chamber and a 2500/3A IONEX® electrometer, was subsequently used. Again, the first readings for 300 MU were off the scale. On the low MU settings (100 MU for photons, 25 MU for 8 MeV, 50 MU for 10 MeV electron beams), the dose rate, without corrections applied for lower ion collection efficiency and non-linearity of monitor unit counter, was 37 times higher than the normal dose rate for an 8 MeV electron beam, 17 times higher for 10 MeV electrons and 3.5 times higher for 9 MV X rays. The individual measurements fluctuated within approximately 10% for each beam. The physicists noticed an increase in the current measured in the electron gun filament on the analogue display of the accelerator cabinet: 1.46 A instead of 1.20 A for 8 MeV electrons, 1.20 A instead of 1.00 A for 10 MeV electrons and 1.60 A instead of 1.50 A for the 9 MV photon beam. The chief physicist informed the manufacturer's service unit of the measured doses and requested assistance.

On the next day, 28 February, the local engineer examined the machine and discovered a broken fuse connecting the AC voltage supply to the DC power supply panel of the dose monitoring system of the accelerator and also a break in the D29 diode in a machine safety interlock system. After replacement of the faulty parts, the machine appeared to be 'back to normal'. The physicists performed the basic set of measurements of the characteristics of the photon and electron beams, such as percentage depth doses, beam profiles and dose outputs. The results for all beams were close to normal, although the energy of the 8 MeV electron beam was slightly lower.

[3] A 6 MeV electron beam generally available with NEPTUN machines was not used clinically at the BOC.

The chief physicist reported the abnormal machine output measured on the day of the accident (i.e. 27 February) to the director of the hospital and initiated the procedure for informing the emergency response unit of the regulatory body's Office for the Control of Radiation Sources (Applications Department).

According to the information provided to the IAEA team, the reliability of the dose measurements performed on 27 February in Białystok was questioned by the manufacturer which stated that the construction of the NEPTUN 10P® accelerator prevented the machine from generating a dose rate as high as that measured on the day of the accident.

4. THE RESPONSE TO THE ACCIDENTAL OVEREXPOSURE

4.1. LOCAL ACTIONS TAKEN ON DISCOVERY OF THE FAULT CONDITION

After being informed of the accident on 2 March 2001, the emergency response unit of the NAEA ordered an immediate cessation of operations with the NEPTUN 10P® at the BOC until the reasons for the accident could be explained, the consequences analysed, and the machine examined and repaired by the manufacturer's service unit. By coincidence, at about the same time, the planned reconstruction began of the hospital wing at the BOC where the NEPTUN 10P® accelerator was located. As this included moving the walls of some offices and the control room and replacing the floors, the accelerator parts in the bunker were covered with plastic. Its console, outside the bunker, was disconnected and moved to a 'safe' place. The modulator cabinet of the accelerator, which is normally located near the control console, was locked and the external cables disconnected. The machine remained in this condition until the reconstruction work was completed. It was not used or altered in any way during this time.

On 6 March, the first mission organized by the NAEA arrived at Białystok. It included two inspectors from the NAEA and the director of the manufacturering company. According to the information provided to the IAEA team, no measurements on, or alterations to, the machine were made; the inspectors interviewed the local staff and held a meeting with the director of the BOC. The NAEA inspectors made the recommendation that the

machine be carefully examined by the manufacturer as soon as the reconstruction of the hospital wing was finished.

In April, the BOC physicists sent the ionization chamber to the SSDL in Warsaw for recalibration, in order to confirm that the local dosimetry system had been working properly on the day of the accident. The SSDL verified the BOC system and certified that it was in good working order. The calibration certificate gave a calibration factor very close to that stated in the previous calibration certificate issued in 1999.

On 1 June, a mission organized by the Ministry of Health, in which ten experts took part, arrived at Białystok. They included representatives of the Ministry, medical physicists and engineers from the Warsaw and Poznan cancer centres, an NAEA regulatory control inspector and a physician. The subsequent report of the Ministry of Health estimated that a dose of approximately 8 Gy had been incurred by the affected patients. No explanations were given to the IAEA team as to how the figure of 8 Gy had been determined.

The reconstruction of the hospital wing was completed on 4 June. On 5 June, two service engineers from the manufacturer arrived to reconnect the machine, put it into operation and investigate the reasons for its malfunction. The machine was put back into working order, but neither were the beam characteristics determined nor dose measurements made.

On 6 June, two representatives of the manufacturer accompanied by two NAEA inspectors examined the machine and attempted to reproduce the accident conditions. They were assisted in this by the local staff. As a first step, the safety interlocks were checked and were all found to be in accordance with the machine specifications. Next, to reproduce the faulty conditions of a low dose rate displayed at the console and an actual high dose rate at the treatment distance, two experiments were performed: (i) detuning the accelerator and (ii) removing the fuse connecting the AC voltage to the DC power supply unit of the dose monitoring system and disabling the 'Interlock System I' by disconnecting the D29 diode.

Detuning of the accelerator brought the dose rate displayed on the machine console to a value of about 100 MU/min and, as was to be expected, the actual dose rate at the treatment distance was correspondingly low. Obviously, when being detuned, the machine was not capable of generating an increased dose rate. In addition, to maintain the 'beam on' condition, continuous operator intervention was required. The mission members concluded that an accidental detuning was not the reason for the malfunction of the machine.

The second experiment was then performed. A check of the machine failure by removing the fuse alone prevented the machine from starting; the machine could not progress to the 'beam on' condition because this was

prohibited by the 'absence dD' interlock. The function of the absence dD interlock is to stop the machine whenever the signal from the dose monitoring system is lower than a tolerance limit of 0.2 Gy/min, which is the case when the monitoring chambers are at a greatly reduced voltage. A simulation of the fuse failure with the simultaneous disconnection of the D29 diode resulted in a substantial increase of the current in the filament of the electron gun while the dose rate indicator on the machine console showed a low dose rate. An open circuit in the Interlock System I, caused by the absence of the D29 diode, prevented the normal functioning of the system in disabling the beam whenever the signal from the dose monitoring system fell outside the tolerance limit of 6.0 Gy/min. The current of the electron gun filament was manually adjusted to 1.4 A for the 8 MeV electron beam, which was close to the accident condition as remembered by the local staff. The subsequent output measurements conducted in a water phantom were made by the local physicists using the same geometry as that employed on the day of the accident. Again, the local physicists used the 2581 ionization chamber and the IONEX® 2500/3A electrometer for this purpose. The MU level was set at 150 (a setting similar to that for the five patients) and 15 subsequent dose measurements were taken. Time intervals between the measurements were close to those used for the patients, i.e. 5–6 min. With the D29 diode disconnected, the beam was turned on and the fuse taken out after a randomly selected time.[4] The scatter of the resulting measurements was high; the measured doses ranged from 5.4 Gy to 17.0 Gy, with two measurements off the scale; the mean was 11.4 Gy and the standard deviation 4.9 Gy.

The report produced by this mission team stated that it was not possible to determine precisely the doses given to the affected patients and emphasized that the doses to the individual patients ought not to have exceeded 25 Gy. The recommendation was made that the suspect circuit boards be taken back to the factory for closer inspection. The manufacturer removed four circuit boards of the machine interlocks and the power supply panel of the dose monitoring system. The Interlock System I (where the D29 diode is located) was sent to the Warsaw Technical University (WTU) for inspection. All boards sent for inspection were marked for identification. The inspection reports by the

[4] Removing the fuse after a random time had elapsed did not fully reproduce the measurement conditions prevailing on the day of the accident. After removal of the fuse, the voltage level on the monitoring chambers of the NEPTUN 10P® decreases from 300 V to about 5 V in approximately 5 min. On the day of the accident, the measurements were made a few hours after the patients had been overexposed and the monitoring chambers worked with a greatly reduced voltage. Therefore, on the day of the accident, the measurements made by the local physicists indicated much higher doses.

manufacturer and by the WTU indicated that the circuit boards were generally in good condition and met the original specifications. However, a few elements had been replaced locally, including the D29 diode. Further, both the manufacturer and the WTU stated that it was unlikely that the D29 diode would have been damaged in the power cut or during its restoration without the other electronic elements on the same board also suffering damage. The manufacturer speculated that the damage causing an open circuit in a diode could possibly be the result of accidental mechanical damage caused when soldering it on the board or by soldering it in inverse polarity. The damaged diode might go unnoticed for some time, but when the fuse also failed, it resulted in the machine operating with an uncontrolled dose rate. The electronic boards taken for examination on 6 June were not returned to the BOC until 5 December, and, according to the information provided to the IAEA team, the machine remained as it had been left after the replacements mentioned had been done.

4.2. THE IAEA RESPONSE AND THE EXPERT MISSION

The Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency (the 'Assistance Convention') and the Convention on Early Notification of a Nuclear Accident (the 'Early Notification Convention') are the prime legal instruments that establish an international framework to facilitate the prompt provision of assistance and exchange of information in the event of a nuclear or radiological emergency, with the aim of minimizing the consequences. Along with States party to these Conventions, the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Meteorological Organization (WMO) are full Parties.

The IAEA has specific functions under these Conventions, such as the responsibility to inform State Parties, Member States and other States of a nuclear or radiological emergency. It receives reports of an emergency from a designated competent authority in a State and verifies any unconfirmed reports of an emergency. It establishes primary functional links with the reporting State and any potentially affected States as appropriate, providing direct communication with the respective official national emergency response co-ordinating structures. It also establishes functional links with the FAO, UNOCHA[5], WHO, WMO and other organizations, as appropriate.

[5] United Nations Office for the Co-ordination of Humanitarian Affairs.

In order to meet its responsibilities under both the Assistance Convention and the Early Notification Convention, the IAEA established in 1986 a 24-hour warning point and operational focal point in its Secretariat, the Emergency Response Centre (ERC). This Centre is located at IAEA headquarters in Vienna, Austria, and at the time was administered by the Emergency Preparedness and Response Unit, Radiation Safety Section, Division of Radiation and Waste Safety of the Department of Nuclear Safety.

On 2 March 2001, the ERC was officially made aware of a radiotherapy overexposure in Poland by the President of the NAEA. At the same time, the President provided a summary of the overexposures that had occurred on 27 February at the BOC and indicated that it would be desirable that the ERC provide consultation assistance in connection with the incident.

On 22 June, the Polish authorities identified the official contact point for the assistance request as the Under-Secretary of State in the Ministry of Health. The ERC immediately contacted the Ministry of Health, as well as the Permanent Mission of Poland to the International Organizations in Vienna, and informed them that, on receipt of an official request, the IAEA was willing to send a specialist mission to Poland for consultative purposes.

The ERC received this official request on 27 November 2001 from the Ministry of Health. The request specifically asked for consultative expertise in:

(a) Assessment of the treatment of lesions arising from overexposure and provision of a treatment plan for the future for each individual overexposed patient,
(b) Assessment of the dose to each individual patient.

Discussions on the assistance to be provided took place between the IAEA's ERC and the Polish Ministry of Health and arrangements were settled concerning the availability, during the IAEA mission, of the overexposed patients, the personnel involved and the required data. The objective of this mission was to assist the Government of Poland with regard to its request for consultative assistance in responding to an accidental radiotherapy overexposure. The Polish Ministry of Health set 30 November as the appropriate date for the IAEA mission. The Polish authorities guaranteed to make available to the IAEA mission:

(a) All relevant records relating to the accident,
(b) All medical personnel involved,
(c) The maintenance engineer from the Warsaw Cancer Centre.

The IAEA mission to Poland consisted of two teams of experts:

(1) A specialized medical team that would conduct an assessment, for each individual patient, of the lesions arising from the overexposure, and advise on the course of a future treatment plan;
(2) A team, made up of medical physics and radiation safety experts, that would evaluate the doses incurred by the affected patients by, inter alia, reconstructing the fault conditions of the accelerator as far as practicable and by undertaking physical measurements and analysis of the treatment records.

The specialized medical team consisted of four experts: J.-M. Cosset, of the WHO's Radiation Emergency Medical Preparedness and Assistance Network (WHO/REMPAN) Centre in France; R.U. Peter, WHO/REMPAN Centre in Germany; F. Mettler, University of New Mexico School of Medicine; and I. Turai[6], of the IAEA. The medical physics and radiation safety team comprised three experts: G. Sernbö, Sahlgren Hospital, Sweden; J. Iżewska, IAEA and P. Ortiz-López, IAEA. The specialized medical team arrived in Poland on 30 November 2001 and the specialized dosimetry team arrived in Poland on 2 December.

On 14 December 2001, with the agreement of the Polish Ministry of Health, the IAEA sent out an 'Advisory Information' to all contact points identified under both the Early Notification Convention and the Assistance Convention in order to help prevent other possible overexposures if a similar situation occurred. This advisory information emphasized that particular attention needed to be given to:

(a) Quality control programmes of accelerators, which need to include relevant dosimetry checks after accelerator shutdowns due to power failures and any other unusual feature (e.g. accuracy of the dose rate display);
(b) Warning notes in the maintenance and service instructions concerning the setting for limiting the current to the electron gun filament and to any other safety critical devices.

[6] I. Turai currently works for the WHO.

5. DOSE ASSESSMENT

Until 5 December, the NEPTUN 10P® machine remained partially disassembled with the interlock boards removed to permit their examination. At the request of the IAEA medical physics and radiation safety team, it was put back into operation prior to the team's arrival at the BOC. The machine, made available to the team for inspection, was configured in its repaired state with all electronic boards in place and the systems functioning normally. The approach taken for the dose assessment was to test the machine under normal conditions and to try to simulate the conditions of the accident. To achieve this, a number of tests were performed using a wide spectrum of machine settings that included operation under normal clinical mode and operation under simulation of the fault conditions. Electronic engineers from the Warsaw Cancer Centre and from the manufacturer, who operated the machine, assisted the team.

5.1. NORMAL MACHINE CONDITIONS

Under the clinical mode of operation, the absorbed dose rate was measured at 4.46 Gy/min on 7 December 2001 under the conditions close to the treatment prescribed for the affected patients (source–skin distance (SSD) = 100 cm, field size 14 cm × 12 cm, depth of maximum dose (d_{max}) = 1.9 cm) measured for the 8 MeV electron beam at 300 MU/min. The corresponding beam output at 300 MU/min was 1.49×10^{-2} Gy/MU, which would result in a dose of 2.24 Gy at the prescribed 150 MU level. The dose rates and the corresponding beam outputs at 100 MU/min, 200 MU/min and 300 MU/min are given in Table 3. The measurements were performed in a water phantom with a plane parallel ionization chamber of the Roos type coupled with an UNIDOS® electrometer (PTW, Germany) and calibrated at the IAEA in terms of absorbed dose to water. The doses were calculated following the IAEA Code of Practice set forth in Technical Reports Series No. 398 [12].

The standard output of the 8 MeV electron beam measured by the local physicists before the accident was 1.61×10^{-2} Gy/MU at SSD = 100 cm, field size 10 cm × 10 cm, d_{max} = 1.6 cm, i.e. close to the output measured by the IAEA team in December 2001.

However, it is worth mentioning that the beam energy characteristics had changed since the measurements made by the local physicist on the day following the accident, i.e. the mean energy at the phantom surface increased from $\bar{E}_0$ = 6.6 MeV to $\bar{E}_0$ = 7.7 MeV, the depth of maximum dose increased from d_{max} = 1.6 cm to d_{max} = 1.9 cm and the practical range from R_p = 3.6 cm to

TABLE 3. DOSE RATES AND ACCELERATOR OUTPUT*

Selection (MU/min)	Dose rate (Gy/min)	Output (Gy/MU)
100	1.46	1.39×10^{-2}
200	2.93	1.45×10^{-2}
300	4.46	1.49×10^{-2}

* At 100 MU/min, 200 MU/min and 300 MU/min selected at the console of the NEPTUN 10P® for 8 MeV electron beam at SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm.

R_p = 4.1 cm. The beam parameters reconstructed in December during the IAEA mission are thus very close, but not identical, to those preceding the accident. This is understandable because the accelerator was disassembled for several months and put into operation only one day before the arrival of the IAEA medical physics and radiation safety team.

5.2. RECONSTRUCTION OF THE FAULT CONDITION

The dependence of the dose rate on the electron gun filament current for the same 8 MeV electron beam at the normal treatment distance was first tested (Fig. 6). The filament current was adjusted manually, with the internal dosimetry system of the machine and the corresponding interlock disabled, i.e. the D29 diode in the Interlock System I and the fuse connecting the AC voltage to the DC power supply unit of the dose monitoring system were removed. The absorbed dose rate increased from 4.46 Gy/min under normal working conditions (filament current of 1.10 A) to more than 100 Gy/min at the upper filament limitation of 1.50 A. It was concluded that, under the fault conditions, the machine was capable of producing a very high dose rate if the limitation to the filament current for the electron gun were set at a high level.

In order to reproduce the condition of the machine after the accident, the machine settings were based on notes of the dosimetry measurements made by the local medical physics staff at the time, i.e. preselected dose rate of 300 MU/min, filament current of the electron gun at 1.40–1.46 A and the dose rate indicator on the accelerator console at approximately 100 MU/min.

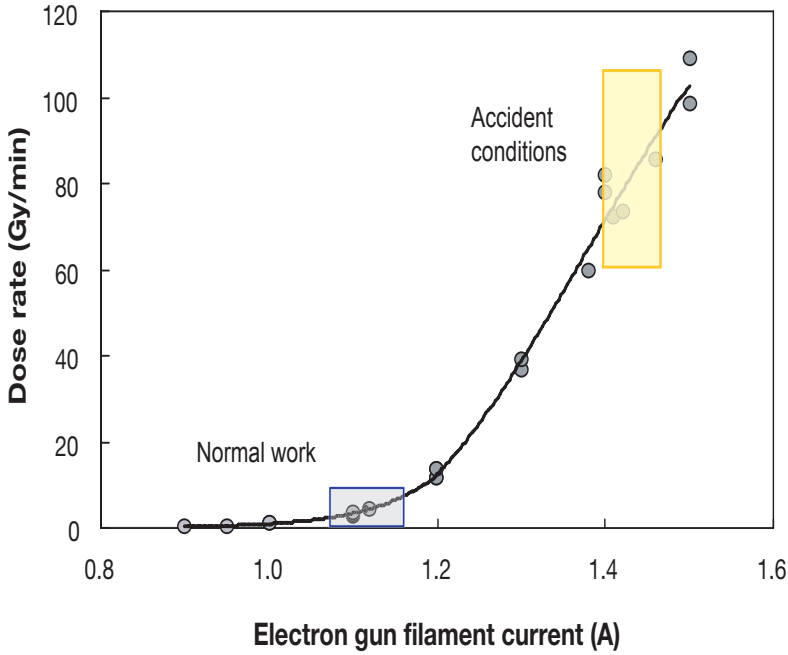

FIG. 6. The output of the 8 MeV electron beam of the NEPTUN 10P® in conditions close to the treatment prescription for the affected patients (SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm) as a function of the current in the primary of the transformer that provides AC to the filament of the electron gun.

5.2.1. Dose–response non-linearity of the MU counter in fault condition

Owing to the limited range of their dosimetry system, the measurements made by the local physicists were performed at 25 MU instead of 150 MU as was prescribed for the treatment of the affected patients. The dose values were then extrapolated from 25 MU to 150 MU. This value has a significant uncertainty owing to the errors in the NEPTUN 10P® MU counter. These errors were caused by an incorrect signal from the monitoring chambers system, which was operating with a greatly reduced polarization voltage. The tests of the MU counter were performed by the IAEA medical physics and radiation safety team using three different machines of the NEPTUN type located at the Oncology Hospital in Łódź, at the manufacturer's site in Świerk and at the BOC.

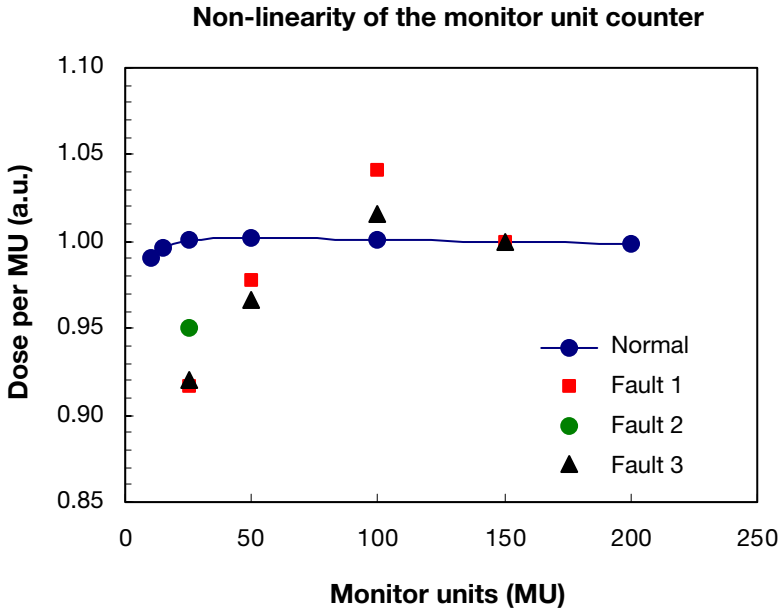

FIG. 7. The dose–response non-linearity of the NEPTUN 10P® MU counter caused by the incorrect signal from the monitoring system operating with a greatly reduced polarization voltage. The solid line corresponds to normal working conditions (the normal values were measured in Łódź), whereas the scattered data points correspond to the fault conditions (Fault 1 and Fault 2 were measured in Białystok and Fault 3 in Świerk). The measured doses per MU for the different MU numbers pre-set at the console are normalized to the dose per MU at 150 MU.

The measurements were performed at 300 MU/min in a phantom, at the normal treatment distance. The results are shown in Fig. 7. The 'normal' values were measured in Łódź. The measurements under fault conditions were performed with the fuse removed and the D29 diode disconnected. The filament limit was set at 1.48 A (for 'Fault 1') and at 1.46 A (for 'Fault 2') in Białystok, and at 1.10 A (for 'Fault 3') in Świerk. The value for Fault 3 was obtained on a NEPTUN 10P® accelerator of similar construction to that of the Białystok machine as regards the monitoring system and safety circuits, but with an electron gun of more recent design.

For each measurement series, the doses per MU for the different MU numbers that were pre-set at the console of the accelerator were normalized to the dose per MU at 150 MU. Under normal working conditions, the MU

counter shows insignificant dose–response non-linearity (less than 1%), in dose per MU, especially for low MU settings. Under fault conditions, the deviation from the linear response is significant and ranges from –8% at 25 MU to +5% at 100 MU. This means that the linear extrapolation of the doses measured at low MU to high MU would produce an underestimation of the doses at high MU by a factor that can be estimated from the data shown in Fig. 7.

The uncertainty in extrapolation of the dose measured at 25 MU to that at 150 MU under the fault conditions may be estimated from the data in Table 4, where the ratios of the dose measured at 150 MU to the dose measured at 25 MU and multiplied by 6 are given for normal and fault conditions. The average MU non-linearity correction for the fault condition is 1.08 ± 0.02, which corresponds to an uncertainty of 8% in the dose extrapolation.

5.2.2. Ion collection efficiency of the ionization chambers

Ionization chamber readings on the day of the accident had to be corrected to compensate for the decreased ion collection efficiency in the high intensity pulsed electron beam. As described by Boag [13], the collection efficiency of an ionization chamber irradiated by pulsed radiation from an accelerator depends on the mechanism of general recombination, which is a complex function of the chamber construction, the electrode separation, the polarization voltage and the ion density in the chamber cavity. For ion accelerator beams, the ion density depends on the dose per pulse. Under typical working conditions, the doses per pulse for clinical electron beams are lower than 2×10^{-3} Gy and the recombination effect is generally less than a few per cent for typical ionization chambers. At higher intensity beams, however, the free electron component and space charge effects become more significant and the theoretical model (based on general recombination) becomes less applicable. The dose per pulse in the fault conditions of the accelerator on the day of the accident was estimated to be 1.3×10^{-2} Gy ± 0.2×10^{-2} Gy. This figure was derived from the electron gun characteristics measured during the IAEA mission for a filament current of 1.43 A (Fig. 5), and taking account of the fact that the NEPTUN 10P® accelerator operates at 100 pulses per second in the 8 MeV electron beam mode.

The approach taken was to perform a series of measurements using a two-voltage technique: the convenient experimental method of determining the chamber recombination corrections as derived by Boag, and the check on their validity in the high intensity pulsed beam using theoretical calculations. A series of measurements for the different values of doses per pulse were

TABLE 4. RATIO OF THE DOSES AT THE TREATMENT DISTANCE MEASURED AT 150 MU TO THE DOSE MEASURED AT 25 MU AND MULTIPLIED BY 6

Test	Ratio of dose at 150 MU to dose at 25 MU × 6
Normal operation	1.00
Fault condition 1	1.09
Fault condition 2	1.05
Fault condition 3	1.09
Average 1–3	1.08

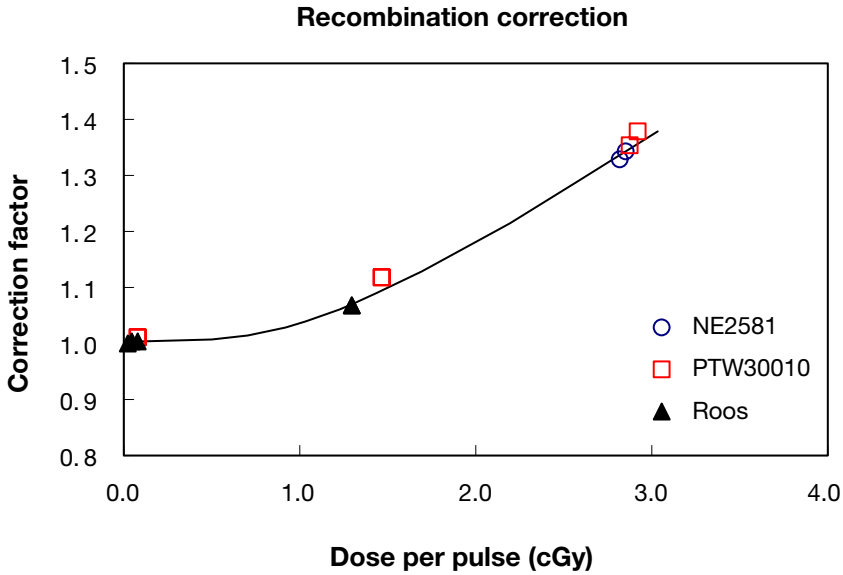

FIG. 8. Ionization chamber recombination corrections measured with a two-voltage technique for the different values of doses per pulse. Measurements performed on three NEPTUN 10P® machines in Łódź, Białystok and Świerk.

performed both with a Roos chamber and with two cylindrical 0.6 cm^3 chambers, NE2581 and PTW30010. The results are shown in Fig. 8.

For the Roos chamber, the measurements were verified against the IAEA Code of Practice [12] and compared with the theoretical calculations using the classic Boag formula for the ion collection efficiency, *f*, in a plane parallel chamber:

$$f = \frac{1}{u}\ln(1+u)$$

where $u = \mu m d^2/V$; μ is a constant depending on the ion recombination coefficient and ion mobility, m is dose per pulse, d is the plate separation and V is the polarization voltage.

The effect of the free electron component on ion collection efficiency was studied as well using the Boag formula modified by Hochhäuser [14]:

$$f = \frac{1}{u_0}\ln\left\{\left[\exp(pu_0 + p - 1)\right]/p\right\}$$

where p is the free electron fraction and u_0 is the 'exposure' variable.

The recombination correction factor $k_s = f^{-1}$ for the Roos type chamber is given in Table 5 where the results are compared for (i) the two-voltage technique, (ii) the Boag basic equation and (iii) the modified Boag formula accounting for the free electron component.

As can be seen from Table 5, the recombination corrections derived from the two-voltage technique are close to the theoretical values, which proves that the two-voltage technique is still applicable for a beam of 1.3×10^{-2} Gy/pulse.

A recombination correction of 1.08 ± 0.02 was estimated from Fig. 8 for the 2581 chamber, which is similar to the one used by the local physicist on the day of the accident.[7]

5.2.3. Verification of the dose measured on the day of the accident

The uncorrected dose measured by the local physicist on 27 February for the 8 MeV electron beam was 15.2 Gy at 25 MU, SSD = 100 cm, field size 10 cm × 10 cm, d_{max} = 1.6 cm in water, with 300 MU/min selected at the console of the accelerator. With the recombination correction of 1.08 ± 0.02 estimated for the NE2581 chamber with the two-voltage technique, the dose per 150 MU on the day of the accident becomes 99 Gy ± 9 Gy. The uncertainty in the dose measurement is a quadratic summation of the uncertainties originating from the non-linearity of the monitoring chamber working without voltage (8%), the calibration of the ion chamber at the standards laboratory (3%), uncertainties

[7] The original 2581 ionization chamber used on the day of the accident was not available to the IAEA team in December 2001, but this is not considered to have invalidated the results of the team's measurements.

TABLE 5. THE RECOMBINATION CORRECTION FACTOR K_S FOR A ROOS TYPE CHAMBER OPERATING AT 300 V AT 1.3×10^{-2} Gy/PULSE IN PULSED ELECTRON BEAM

Method used	Correction factor (k_s)
Interpolation of two-voltage technique (Boag)	1.078
Interpolation of two-voltage technique (IAEA[a])	1.078
Boag classical formula[b]	1.088
Boag (Hochhäuser) modified formula[c]	1.068

[a] Technical Reports Series No. 398 [12].
[b] $\mu = 10.7\ V\ mm^{-2}\ cGy^{-1}$[14], $m = 1.27$ cGy/pulse, $d = 2$ mm, $V = 300$ V.
[c] $p = 0.23$, other parameters as above.

intrinsic to the dosimetry protocol used (3%), and other factors associated with clinical dosimetry (>1%).[8]

The dose measured by the local physicists appears to be close to the dose of 115–127 Gy measured by the IAEA medical physics and radiation safety team on 7 December (see Table 5) using the reconstructed machine settings, i.e. for a filament current of 1.42–1.46 A. The irradiation time needed to deliver 150 MU was 1.5–1.8 min whereas, according to the information provided to the team by the local staff, the treatment time on the day of the accident was set to 1.5 min. The dose rate on the analogue indicator at the machine console was fluctuating around 100 MU/min. The team's ion chamber measurements were verified by measurements made with solid state dosimeters, such as alanine and GAFChromic film (Table 6).

Needless to say, a full reconstruction of the fault conditions of the accelerator prevailing on 27 February 2001 was virtually impossible after several months had elapsed, especially as the machine had been left partially disassembled since June 2001. Nonetheless, during the IAEA investigation, the machine was reconstructed so as to have the same configuration as it did during the accident. All indicators showed the reconstruction to represent closely the actual accident conditions, even though the beam energy was slightly higher compared with that measured on 28 February 2001 (Section 5.2.1 above). As can be seen from Table 5, the doses measured by the local physicists were

[8] Current codes of practice for dosimetry, such as those set forth in Technical Reports Series No. 398 [12], recommend the use of plane parallel chambers, such as the Roos chamber, which has lower energy electrons, rather than cylindrical chambers, such as the NE2581.

TABLE 6. ABSORBED DOSE TO WATER MEASURED UNDER THE SIMULATED FAULT CONDITIONS*

Machine settings	Dosimetry method	Dose per 150 MU (Gy)
MEASUREMENTS MADE BY IAEA TEAM (7–8 December 2001)		
Filament 1.45 A, 300 MU/min, irradiation time 1.5 min	Roos chamber	127 ± 4
Filament 1.46 A, 300 MU/min, irradiation time 1.7 min	Alanine	122 ± 4
Filament 1.45 A, 300 MU/min, irradiation time 1.8 min	GAFChromic film (MD-55-2)	115 ± 3
MEASUREMENTS MADE BY LOCAL PHYSICISTS (27 February 2001)		
Filament 1.40–1.45 A, pre-set 300 MU/min, irradiation time 1.5 min, chamber depth 1.6 cm	NE2581 0.6 cm^3	99 ± 9

* Measurement parameters: 8 MeV electron beam at 150 MU selected at the NEPTUN 10P® console, SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm in water with an ion chamber, alanine and GAFChromic films.

slightly lower than those measured by the IAEA team. The values measured by the IAEA team are to be understood as being estimates, rather than exact dose values actually delivered in the course of the accident. The team concluded that the local determination of the output of the accelerator after the accident was correct, within the uncertainty limits discussed earlier.

5.3. ASSESSMENT OF DOSES

The team performed simulations of the doses that would have been delivered to hypothetical patients with the 8 MeV electron beam under the fault conditions of the accelerator, as described above.

5.3.1. Simulation 1: Fuse break at the beginning of a treatment session

The first test consisted of simulating a fuse break at the beginning of a treatment session so that the voltage of the accelerator monitoring system decreased during the course of each treatment: each measurement started with the full voltage (300 V) being applied to the monitoring chambers and ended

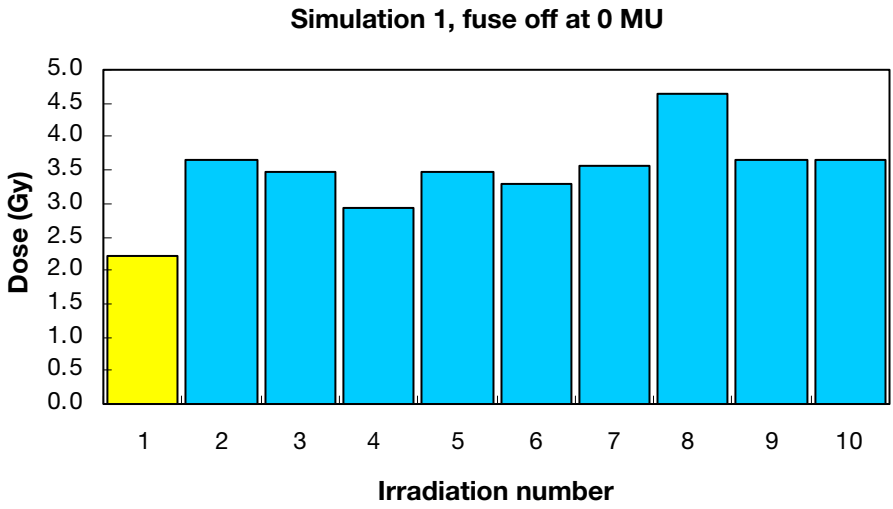

FIG. 9. Doses from 8 MeV electron beam to a hypothetical first 'patient' irradiated after shut-off of the accelerator; the fuse breaks at the beginning of the treatment session so that the voltage of the accelerator monitoring system is greatly reduced. The yellow bar indicates normal treatment conditions with an operational monitoring chamber. The absorbed dose to water was measured with a Roos chamber and a setting of 150 MU selected at the NEPTUN 10P® console (SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm in water). The filament current was set at different values that ranged between 1.10 A and 1.42 A.

with about 35–45 V being applied. The fuse was reinserted before the next treatment started and the exercise repeated for various settings of the electron gun filament. The purpose of this exercise was to simulate the doses to the first patient irradiated after restarting the accelerator after the power cut. The absorbed dose to water for each irradiation was measured with a Roos chamber, in a water phantom, and the salient parameters, SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm at 150 MU (as for the five patients), selected at the NEPTUN 10P® console. The filament currents were selected for each session in the range 1.10–1.42 A.

The doses for the subsequent treatment sessions are shown in Fig. 9. The yellow bar indicates normal treatment conditions (with the fuse in place) with a fully operational monitoring chamber system. The doses measured under the simulated fault conditions (blue bars) range from 3.3 Gy to 4.6 Gy with a mean of 3.6 Gy. A series of measurements performed with a GAFChromic film under the same conditions resulted in a cumulative dose of 15 Gy for five subsequent

irradiations. In this simulation, the fuse was removed at the start of each treatment session.

When the fuse was removed at a random point during the simulated treatment, that is, between 0 MU and 150 MU, the dose varied from 3.3–4.6 Gy for the fuse break at the start of the session (0 MU) to 2.3 Gy towards the end of the treatment (100 MU or more). This value of 2.3 Gy is close to that obtained under normal operating conditions with a high (though not maximum) voltage to the monitoring chambers.

5.3.2. Simulation 2: Fuse break at the beginning of a series of treatment sessions

The second test consisted of simulating the failure of the fuse with the simultaneous disconnection of the D29 diode. This simulation started with the removal of the fuse at the beginning of each measurement series. The MU number was set at 150 and a few dose measurements were taken. Time intervals between the measurements were close to those elapsing between the treatment of one patient and the next, i.e. 4 min. The limiting current of the electron gun filament was manually adjusted for different series from 1.22 A (normal) to 1.46–1.48 A (close to the accident conditions) as remembered by the local staff. The subsequent output measurements in a water phantom were in the same geometry as in the first simulation (see Section 5.2.1). The resulting doses are shown in Fig. 10. The first group of bars in Fig. 10 corresponds to the first treatment session, during which the fuse break was simulated. Each subsequent group, numbered from 2 to 6, corresponds to the subsequent treatments, which resumed successively following a 4 min break.

As mentioned, the doses in the first treatment were in the order of 3.3–4.6 Gy (Fig. 9), whereas the doses in treatments 2–6 varied from 58 Gy to 147 Gy, depending on the preselected limit for the filament current: the lower doses correspond to a 1.22 A limit and the higher doses to a limit of 1.46–1.48 A. The high doses in treatments 2–6 are due to the monitoring chamber having worked at a greatly reduced voltage, approximately 5 V. The irradiation times noted in this experiment varied from 0.5–0.8 min for the first treatment to 1.5–3.4 min for subsequent treatments.

If the machine timer was set at 1.5 min, as remembered by the local staff, and the irradiation stopped after 1.5 min and before completion of the preset 150 MU, the doses in treatments 2–6 would be reduced to approximately 25 Gy at the 1.22 A filament limit and to 100–110 Gy at the 1.46–1.48 A limit. The corresponding dose rates displayed on the machine console were 80–110 MU/min.

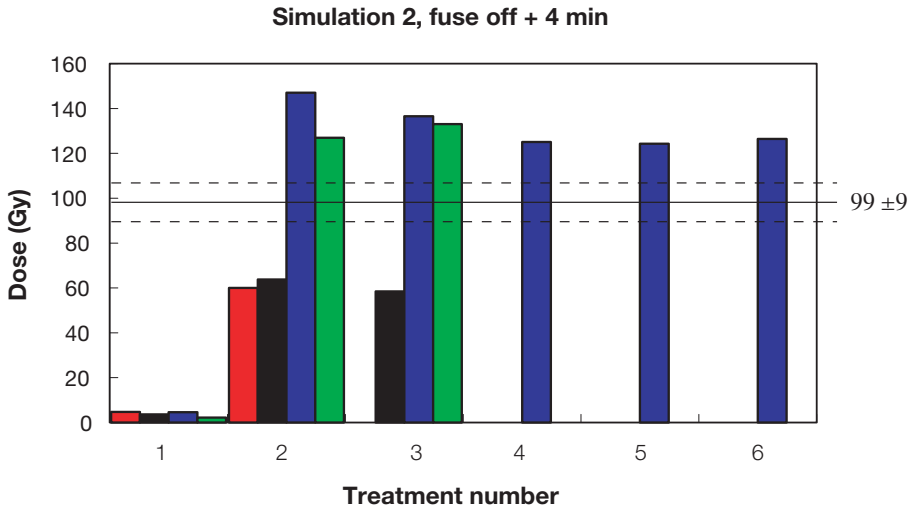

FIG. 10. Simulation of doses to patients after the fuse break. The groups numbered 1 to 6 represent consecutive patient treatments, each one resumed following a 4 min interval. Different colours correspond to different settings for limiting the filament current in the electron gun: 1.22 A (red and black bars), 1.46–1.48 A (blue and green bars). Absorbed dose to water was measured in a water phantom with a Roos chamber at 150 MU, SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm. The horizontal line indicates the dose measured by the local physicists on the day of the accident.

5.3.3. Simulation 3: Reverse dose reconstruction

Since dose levels below 25 Gy were reported by the previous missions that had examined the defective accelerator, such as the June mission of the NAEA, the team also performed a reverse reconstruction, by determining the machine settings for the irradiation conditions that would lead to doses lower than those described in Section 5.2.2. The limiting current of the electron gun filament was manually adjusted to 1.22 A (normal setting) and then decreased to 1.20 A, 1.18 A and 1.15 A. For each setting, measurements were taken at the fuse break and after a 4 min interval for the beginning of the subsequent treatment. The absorbed dose was measured in a water phantom with a Roos chamber at 150 MU, SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm.

While operating under the simulated fault conditions and within the selected range of parameter settings, the NEPTUN 10P® may deliver doses at the depth, d_{max}, of the order of 30–60 Gy per 150 MU (Fig. 11). These doses may result from resetting the limiting filament current from 1.15 A (just above

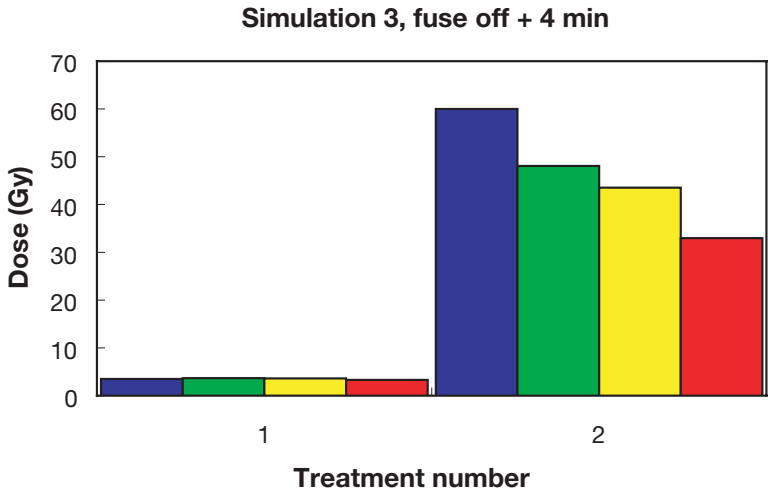

FIG. 11. Simulation of doses to patients after a fuse break. Measurements for group 1 were taken at the fuse break; group 2 corresponds to the subsequent treatment, started after a 4 min interval. The limiting current for the electron gun filament was manually set to 1.22 A (normal setting, blue bar), 1.20 A, 1.18 A and 1.15 A (green, yellow and red bars, respectively). The absorbed dose was measured in a water phantom with a Roos chamber at 150 MU, SSD = 100 cm, field size 14 cm × 12 cm, d_{max} = 1.9 cm.

the working level of 1.10 A) to 1.22 A (a typical limitation value for the 8 MeV beam). The corresponding dose rate on the machine console would vary from about 40 MU/min to 100 MU/min, and the irradiation time would be of the order of 2–4 min. These settings differ from the observations of the local staff that were reported to the team. However, if the machine timer was set at 1.5 min (according to the recollections of the local staff) and the irradiation stopped after 1.5 min without completing the preset 150 MU, the doses for treatment 2 decreased to levels of between 10 Gy and 45 Gy (red and blue bars in Fig. 11).

5.4. RETROSPECTIVE MEASUREMENTS OF THE PATIENT DOSES

5.4.1. Principles of retrospective biodosimetry with EPR

Retrospective EPR biodosimetry is a physical method of analysis that measures stable, radiation induced radicals in the calcified tissues of the human body, such as bones. It provides information on the doses received from exposure to ionizing radiation after the event, since the EPR signal is 'stored' in

the bone. This technique is of particular relevance to accident situations. The accident doses can best be reconstructed using samples taken from part of the exposed individual.

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) contained in bones is a suitable material for dose reconstruction because it contains stable, radiation induced radicals. The EPR signal induced by radiation in hydroxyapatite is proportional to the absorbed dose in the range up to a few hundred grays. The signal is stable over time and can be analysed long after the exposure occurred.

EPR retrospective biodosimetry has been used to estimate the doses received by three of the five patients involved in the accident. Bone samples were taken from the ribs during surgical procedures performed on Patients 3, 4 and 5 between May and October 2002.

A post-irradiation technique was used to determine the doses incurred by the three patients. The technique is based on a sequence of irradiations of the same bone sample with well-defined doses and seeks to establish the relationship between the dose and the EPR response, which is typically linear. The initial, unknown dose is determined by extrapolation of the line produced by linear regression.

As the EPR signal in hydroxyapatite exhibits beam quality dependence, electron beams were used for the post-irradiation of the samples that had similar energy and dose distributions as the 8 MeV beam of the NEPTUN 10P® accelerator in Białystok. The samples were irradiated in a plastic phantom, using a similar beam geometry to that used for the patients in Białystok. The irradiations were performed with clinical accelerators at the Institut Curie in Paris. The EPR measurements were performed by the Institut de Radioprotection et de Sûreté Nucléaire (IRSN) at Fontenay-aux-Roses.

5.4.2. Reconstruction of the patient doses from EPR measurements

The doses measured using EPR represent the cumulative dose received by the samples, that is, the sum of the doses from radiation treatment prior to the accident and the dose from the accidental exposure. The treatment prescription and the doses to the reference point are summarized in Table 7 for Patients 3, 4 and 5.

In order to correlate the treatment prescription with the actual dose received by the ribs, the exact positions in the patients that the bone samples were taken from need to be known. Knowing the depth of the samples is critical because the dose distribution along the electron beam axis falls off rapidly for the 8 MeV beam; that is, the dose at a depth in tissue of about 3 cm decreases by more that 30% compared with the dose at a depth of 1.9 cm, the depth of the dose maximum, d_{max}.

TABLE 7. DOSES TO THE REFERENCE POINT*

Patient	Field (cm)	Dose per fraction (Gy)	Calculated (MU)	No. fractions before the accident	Dose before the accident (Gy)
3	17 × 13	2.5	157	10	25
4	15 × 14	2.0	125	11 + 10 with bolus	22 + 20 with bolus
5	18 × 12	2.5	156	2	5

* d_{max} = 1.9 cm for the three patients, electron beam 8 MeV, SSD = 100 cm (the collimator and gantry angles are not relevant for this report).

Thin pieces of hard bone layers weighing 20–30 mg were used for the EPR measurements. Unfortunately, reconstruction of their position (depth under the skin) in the bodies of the patients was accompanied by an uncertainty of a few millimetres as the contour of each patient and the thickness of the tissue above the rib from which the sample was removed had changed in the several months that had elapsed since exposure.

The position (depth) of the ribs and their thickness were estimated individually for each patient on the basis of computer tomography scans taken in November 2001. Moreover, it is not clear whether the individual bone samples taken from each patient were taken from the frontal or the distal part of the rib in relation to the beam entry. An uncertainty of a few millimetres in the original position of the bone sample may result in an uncertainty in the dose reconstruction of about 20–30%, depending on the thickness of the rib and its position (depth under the skin) at the time of the patient's treatment.

The results of the EPR measurements of the bone samples are shown in Table 8, together with the estimated accident doses. They are compared with the doses derived from measurement of the treatment conditions of the individual patients taken by the local physics staff on the day of the accident. All doses are converted to the depth of the dose maximum, d_{max} = 1.9 cm.

An inhomogeneity correction was applied to the patient dose calculation from the EPR dose, because for the same electron fluence, the dose in the rib material is lower than the dose to the muscle, owing to the lower hydrogen content in bone [15]. The correction was determined from precise, three dimensional dose calculations performed by the Radiotherapy Department[9],

[9] Prof. B. Mijnheer and Dr. A. Blom are gratefully acknowledged for advising on the inhomogeneity correction for the doses in the rib for an electron beam of 8 MeV.

TABLE 8. PATIENT DOSES ESTIMATED FROM EPR MEASUREMENTS MADE BY IRSN COMPARED WITH THE DOSES DERIVED FROM MEASUREMENTS MADE BY THE PHYSICISTS IN BIAŁYSTOK ON 27 FEBRUARY 2001

Parameter	Patient 3	Patient 4	Patient 5
EPR dose to the sample by IRSN (Gy)	83 ± 7[a]	98 ± 10	75 ± 3
Depth of the sample (cm):			
Frontal position	1.9 ± 0.2	1.4 ± 0.2 2.4 ± 0.2 with bolus	1.9 ± 0.2
Distal position	2.3 ± 0.2	1.8 ± 0.2 2.8 ± 0.2 with bolus	2.3 ± 0.2
Cumulative dose before the accident, at the depth of sample (Gy):			
Frontal position	25 ± 0.3[b]	39 ± 1	5.0 ± 0.3
Distal position	23 ± 1	35 ± 1	5
Accident dose at the depth of sample (Gy):			
Frontal position	58 ± 0.2	59 ± 1	70 ± 0.3
Distal position	60 ± 1	63 ± 2	70 ± 0.1
Accident dose at d_{max} = 1.9 cm (Gy):			
Reconstruction for frontal position	59 ± 7	64 ± 11	71 ± 3
Reconstruction for distal position	67 ± 8	84 ± 19	78 ± 5
Dose measured after the accident and recalculated to MU settings for each patient	103 ± 9	83 ± 9	103 ± 9

[a] The uncertainty in the EPR dose corresponds to one standard deviation.
[b] The uncertainty in the dose is derived from the uncertainty in the original position of the sample and does not include the uncertainty in the clinical dosimetry under normal working conditions. For electron beams, the uncertainty in the clinical dosimetry is of the order of 3.5% [16].

Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, using the three dimensional treatment planning system developed by the University of Michigan (UM-Plan).

Table 8 shows that the doses derived from the EPR biodosimetry of the three patients are as high as 60–80 Gy. The uncertainties range from a few grays to almost 20 Gy. The highest uncertainty corresponds to a rapid decrease of dose with depth. In the case of Patient 4, a bolus was used which increased the depth from which the sample was taken, thereby increasing the uncertainty in the dose reconstruction. The dose to Patient 4, determined through EPR, agrees with that measured by the local physicists, but the doses to Patients 3 and 5 are generally lower, within the uncertainties of the reconstruction of the fault conditions.

5.5. SUMMARY OF FINDINGS MADE BY THE IAEA MEDICAL PHYSICS AND RADIATION SAFETY TEAM

The reconstruction of the fault conditions of the NEPTUN 10P® radiotherapy accelerator of the BOC by the IAEA medical physics and radiation safety team has shown this machine to be capable of producing a dose to water rate in reference conditions of the order of 100 Gy/min for an 8 MeV electron beam, if the limitation on the electron gun filament current is set at a high level, such as 1.40–1.50 A (Fig. 6). Under these conditions, with a treatment prescription of 150 MU, the machine may deliver doses in the order of 100 Gy or higher (Fig. 10).

The measurements taken on the day of the accident by the local physicists, under the fault conditions, have been validated by the IAEA medical physics and radiation safety team. The dose measured a few hours after the accident was very close to the values obtained by the IAEA mission in December 2001 (Table 6), despite the fact that the machine had been repaired on the morning following the accident and then disassembled and left dismantled for several months. It was reassembled and put into operating condition at the request of the IAEA team one day before its arrival at the BOC.

The doses derived from the EPR biodosimetry of the three patients are as high as 60–80 Gy. They are generally lower than the doses reconstructed from the measurements made by the local physicists on the day of the accident. Notwithstanding, the differences are not significant and lie within the uncertainties of the EPR measurements and the uncertainties associated with the reconstruction of the fault conditions.

On the basis of the information gathered during the mission to the BOC, the IAEA medical physics and radiation safety team has reconstructed the accidental exposures in sufficient detail as to be able to document the circumstances of this event and disseminate the lessons learned from it, bearing in mind the long delay between the accident and the conduct of the mission, and the ad hoc reassembly of the faulty NEPTUN 10P® accelerator by the local engineers. It should be noted that the reconstruction by the IAEA team of the doses delivered does not attempt to reproduce exactly the conditions leading up to the accidental exposures, nor to put forward a full explanation for the doses received by the patients.

6. CLINICAL COURSE OF THE OVEREXPOSURES

6.1. OVERVIEW

All five patients involved in the accident at the BOC developed local radiation injuries in the form of burns of differing severity. They have been treated at the BOC as well as at other centres. Individual descriptions of the evolution of the clinical course are described below.

Oncologists at the BOC consulted with their colleagues at the M. Skłodowska-Curie Memorial Institute, at the Centre of Oncology (Warsaw), at the Specialized Burn Centre in Siemianowice Slaskie, and at the Institute of Occupational Health in Łódź.

On the basis of the consultations, the prescribing of vitamins (orally and topically in the form of ointments) and Solcoseryl[10] (topically) was agreed for all of the patients who had been accidentally overexposed. In addition, Patients 2, 3 and 4 were treated with corticosteroids (Encortolon orally and Dexamethasone topically). In mid-May 2001, the overexposed patients were examined at the Burns Department of the Military Hospital in Warsaw. At that time surgery was not recommended. However, it was noted that, with the evolution of superficial ulcers, there might be a need for surgical intervention in the future.

On 4 June, the five patients were examined by specialists at the Centre of Oncology (Warsaw). It was concluded that the treatment adopted in the BOC was appropriate, and the following courses of treatment were recommended:

[10] Solcoseryl is a protein-free calf blood extract.

(a) To continue conservative treatment of all patients as long as possible, i.e. for about one year, to assess the progression of local complications;
(b) To continue hormonal steroid treatment of all patients except for Patient 1;
(c) To provide or restart rehabilitation of all patients in the Centre of Oncology (Warsaw);
(d) To re-evaluate, periodically, the protocol and the results of treatment.

In early August 2001, all five patients were administered systemic Pentoxifylline (a vasodilator) and Tocopherol (vitamin E). Topical treatment was continued using the enzymatic ointments Iruxol Mono and Fibrolan Salbe (collagenase with proteases, and plasmin deoxyribonuclease ointments).

Patients 1, 2 and 5 were admitted to the Department of Rehabilitation of the Centre of Oncology (Warsaw) and accommodated in the Centre's Hostel. During their outpatient treatment in Warsaw, they underwent rehabilitation that mainly consisted of exercises for the shoulder and massage of the arm.

These three patients were examined by a team of specialists and their local skin injuries tended daily. The specialists concluded that the treatment provided seemed to be effective and therefore decided to discharge all three patients at the end of August 2001.

Patients 3 and 4 were hospitalized in Białystok in response to an elevation in the count of cancer marker CA 125 and the presence of some pleural fluid detected by the CT scanner, as well as abnormal densities in their mediastina and lungs. After a month of treatment in Białystok they were admitted in September for rehabilitation to the Centre of Oncology (Warsaw), where they received treatment similar to that given to the other three patients.

While they were under examination in the BOC in September and October 2001, Patients 1 and 2 showed some improvement, but by the end of October their local injuries had worsened significantly and a necrotic process had developed.

On 31 October 2001, specialists at the Centre of Oncology (Warsaw) recommended that four of the five patients (all except Patient 4) begin hyperbaric oxygen (HBO) therapy the following week at the Institute of Marine and Tropical Medicine in Gdynia.

Haematological data of the patients gathered prior to their radiotherapy were available. Following the accidental exposures, blood samples were taken from the affected patients and analysed for the purpose of blood count comparison. The white blood cell counts for Patients 1 and 5 were within the normal levels. For Patients 2 and 4, a small decrease was detected within 1–2 weeks of their exposure. Patient 3 had leucopenia before the beginning of radiotherapy. Absolute lymphocytopenia was detected for all patients; for

Patients 2, 3 and 4 a stable decrease in blood counts was observed through to the end of 2001. Detailed blood counts for all patients covering the period prior to the overexposure and a nine-month follow-up period up until 12 December 2001 are given in Appendix II.

6.2. PATIENT 1

Patient 1 (date of birth: 9 June 1957) had a tumour resected from the right breast without mastectomy on 12 December 2000. The post-operative disease stage was T1N0 (15 nodes negative) M0, grade unknown. She received neither chemotherapy nor hormonal therapy.

Radiotherapy was started on 22 January 2001. Initially, a treatment consisting of 4 MV X rays in a total dose of 50 Gy (25 fractions of 2 Gy, 2 Gy fractions daily, five times per week) was delivered to the whole breast via two tangential fields. Then, a local boost with 8 MeV electrons in 2.5 Gy fractions was begun. The planned field size was 11 cm × 7 cm and exposure was set for 155 MU. The accidental exposure occurred on 27 February 2001 during delivery of the second fraction. The total dose to the chest wall was therefore 50 Gy with fractionated 4 MV X rays and one 2.5 Gy fraction of 8 MeV electrons plus that attributable to the accidental exposure.

A few hours after the accidental exposure, Patient 1 reported development of slight erythema in the exposed area. She was treated with the topical ointment Linomag (complex of linolic acid, linolenic acid and arachidonic acid) for three weeks (until 19 March). On 28 February topical treatment with Solcoseryl began. Erythema remained for six weeks and on 7 March an area of moist desquamation measuring 2 cm × 2 cm was noted. An X ray of the chest taken on 19 March revealed no pathological signs in the lung.

Tumour markers administered on 23 March were as follows: CA 125 - 12.31 mIU/ml, CEA - 1.88 mIU/ml, CA 15-3 - 4.58 mIU/ml. At the end of March, the patient noted some limitation of movement of the right shoulder. Systemic treatment with Panthenol (vitamin PP) and vitamin B1 began and topical Panthenol spray and ointment were used, which led to relief of the symptoms of pain, itching and limitation of movement of the right shoulder. On 27 March she was admitted to the BOC for treatment of an increasing area of desquamation in the irradiated field. She was discharged from the hospital on 6 April.

On 7 May, examination revealed superficial ulceration located at the surgical scar in the centre of the irradiated field and a 3 cm white border just inside the edges of the field. As the patient refused to be hospitalized, she was provided with a Neomycin spray and sterile gauze covered with Linomag for

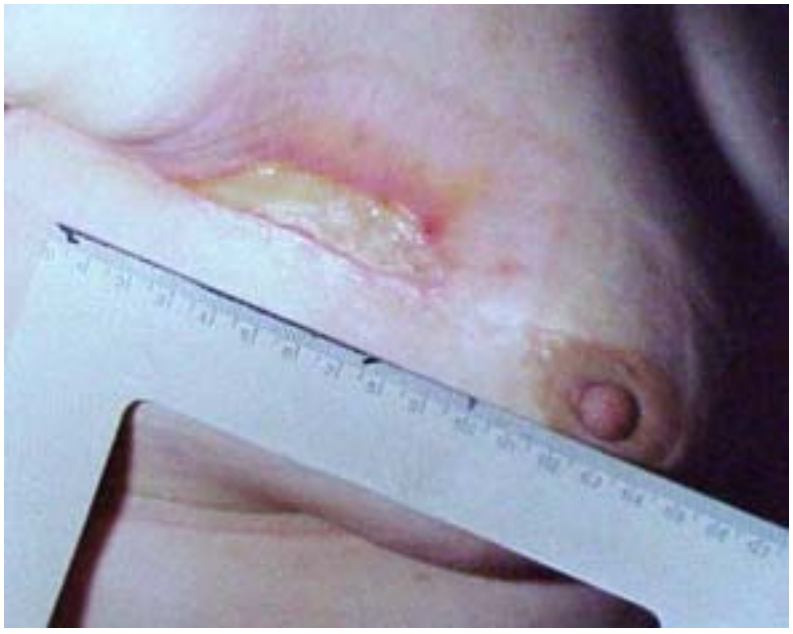

FIG. 12. Patient 1 on 4 June 2001: Ulcerated subaxillary area (4.5 mm ×18 mm).

topical treatment at home. An examination performed in June showed that the ulcerated area measured 4.5 mm × 18 mm (Fig. 12).

During topical treatment at home, the size of the ulcerated area remained unchanged up until July. Bacteriological culture taken from the ulcer on 11 July revealed Staphylococcus pyocyaneus +++, sensitive to Gentamycin, Amikacin, Vibramycin, Ciprofloxacin, Biseptol, Vancomycin and Netilmycin. On 1 August, Patient 1 was hospitalized in the Centre of Oncology (Warsaw), having been diagnosed as having cancer of the right breast, status post-tumorectomy, with right axillary lymph node dissection and post-radiotherapy lesion. She was admitted for rehabilitation, the treatment consisting of systemic Tocopherol and Pentoxyfylline, and local topical therapy with Argosulfan ointment. Staphylococcus aureus infection was present and was treated with topical Gentamycin. By 2 September small areas of necrosis had appeared in the irradiated field. Cancer markers were normal. HBO therapy was started on 6 November. After three weeks, the ulcerated area was reduced in size and severity.

Examination by the IAEA expert medical team on 30 November and 1 December revealed a 3.5 cm × 1.5 cm ulcerated lesion along the axis of the surgical scar (Fig. 13). The centre of the ulcer was 6 cm superior and lateral to

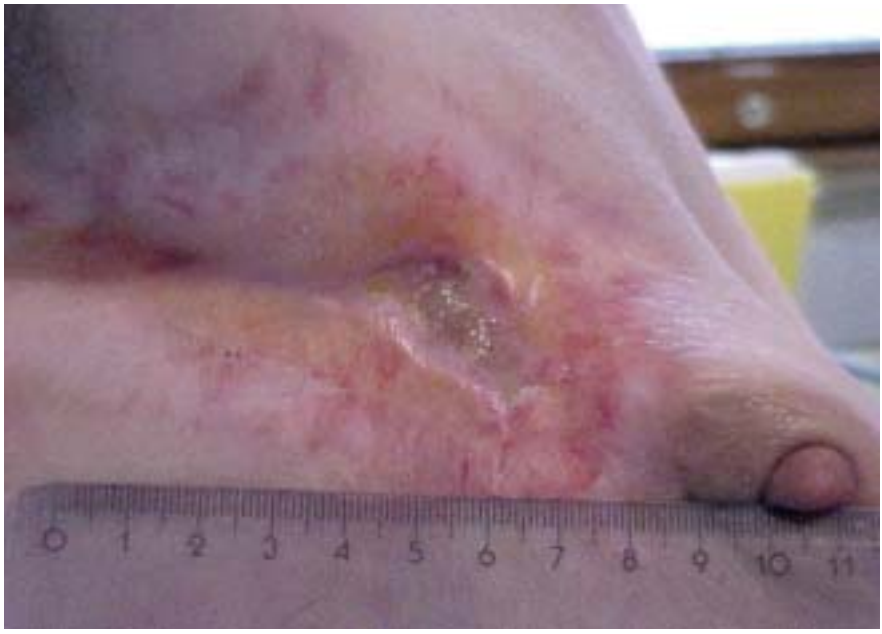

FIG. 13. Patient 1 in December 2001: Ulcerated lesion (3.5 cm × 1.5 cm) along the axis of the surgical scar.

the nipple. There was a 1 cm border of induration surrounding the ulcer and there were minor areas of telangiectasia in the axilla.

The IAEA expert medical team concluded that the condition of the patient did not appear to be serious at the time of examination and that surgery was not necessary. However, surgery may be required in the future. It was recommended that administration of Pentoxyfylline (800–1200 mg/d) and Tocopherol (400–500 mg/d) therapy be continued for a total treatment time of at least one year. On the basis of this regimen, the lesions of the patient could be expected to heal completely. Secondary cosmetic rehabilitation needs to be considered and made available at a later phase.

Patient 1 completed HBO therapy on 21 December 2001. In mid-January 2002, two small ulcerations with a diameter of about 1 cm were detected along the axis of her surgical scar. On 27 August 2002, the patient was admitted to the Oncological Surgery Ward in the Holy Cross Cancer Centre in Kielce. She was suffering from post-radiation fibrosis with superficial necrosis at the scar on her right breast. She underwent a one step operation on 30 August.[11] The operation

[11] Performed by Prof. A. Kułakowski.

involved making a wide excision of all the necrotic, prenecrotic and fibrotic tissues (distinctly identified by MRI and CT) and covering the wound with an omentum flap through a 'tunnel' prepared below the skin between the abdomen and the thoracic wall. The patient also underwent subcutaneous mastectomy of her right breast and skin grafts were positioned over the wound. The skin grafts were taken from the patient's thigh and thoracic wall at the right side. At the end of the operation a thin skin graft was positioned over the flap with skin that had been removed from the thigh.

At the end of October 2002, Patient 1 was still in the Oncological Surgery Ward of the Holy Cross Cancer Centre, as the healing of her post-operative wound, although satisfactory, was not complete.

6.3. PATIENT 2

Patient 2 (date of birth: 18 September 1955) had a right radical mastectomy on 15 May 2000. The disease stage was T3N0M0, Grade III. After surgery she received nine cycles of chemotherapy with Cyclophosphamide, Mitomycin C and 5-fluorouracil, these ending in December 2000. Radiotherapy began on 24 January 2001. She received 50 Gy (^{60}Co) to the supraclavicular, sternal and axillary regions. The chest wall was simultaneously treated with an 8 MeV electron beam. The field size was 14 cm × 14 cm and the dose administered in 25 fractions of 2 Gy. The accidental exposure occurred during delivery of the last (25th) fraction. The patient did not report any abnormal sensation or pain either during or immediately after the treatment.

The total dose to the area of interest from the electron beam only was 48 Gy (24 × 2 Gy fractions) plus that attributable to the accidental exposure. Erythema occurred within a day. This was quickly followed by dry desquamation. Moist desquamation appeared within one week of the accident occurring.

On 5 March, the patient began to experience pain at the site irradiated by the electron beam. She was admitted to the BOC on 12 March for one month. The irradiated site had a pale white appearance just inside the field margins. Therapy included administration of Linomag topical ointment; Solcoseryl; vitamin PP (nicotinic acid); vitamins B1, A and E; and topical corticosteroids. On 4 June, a 5 cm × 10 cm area of desquamation was detected in the central zone of the 10 cm × 14 cm depigmented area (Fig. 14).

By July, there was progression of the changes in the irradiated field with deeper ulceration centrally and a painful surrounding inflammation. A CT scan on 27 July was essentially negative with the exception of scarring in the lung apices. The patient went to Warsaw in August for rehabilitation treatment.

Enzymatic ointment, Tocopherol and Pentoxyfylline were provided and medication was required for pain relief.

In early October, examination revealed an area of necrosis of 1 cm × 3 cm in the centre of the irradiated field and the presence of small 'blisters' of a few millimetres each elsewhere in the field. The wound developed and by the end of October an 8 cm × 8 cm area of transient erythema was noted on the patient's back, overlying the right scapula. She became febrile and was treated with antibiotics.

HBO therapy began on 6 November and ended on 21 December 2001. Between 6 November and 19 November, the treatment was performed twice daily; from 20 November to 21 December it was performed once per day. The total number of exposition sessions was 46. Effective inhalation with 100% oxygen at a pressure of 2.5 bar resulted in a session lasting 75 minutes. It was concluded that HBO therapy led to local improvement in the three weeks following commencement of the treatment. Examination of the patient by the IAEA expert medical team on 30 November and 1 December 2001 revealed a 14 cm × 10 cm area that was pale, exhibited poor epithelialization and showed serous exudation and multiple punctate areas of bleeding. The superficial tissues appeared to be fixed to the chest wall. There were no obvious areas of necrosis or infection (Fig. 15).

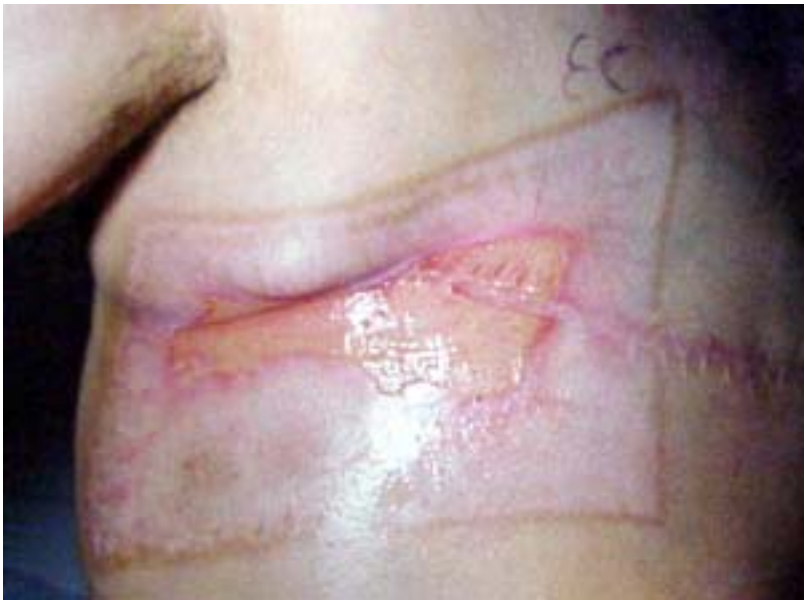

FIG. 14. Patient 2 on 4 June 2001: Moist desquamation area measuring 5 cm × 10 cm in the centre of a 10 cm × 14 cm depigmented field in the zone of the mastectomy.

The IAEA expert medical team concluded that at the time of the examination, surgery did not appear to be necessary; the patient's injury could possibly heal with conservative treatment or it might need reconstructive surgery based upon the future progression and expression of underlying vascular injury. It was recommended that administration of Pentoxyfylline (800–1200 mg/d) and Tocopherol (400–500 mg/d) be continued for a total treatment time of at least one year.

Patient 2 was discharged after completing the HBO therapy. In January 2002, her general condition was judged to be good. A small (1 mm × 2 mm) local ulcer was found in the irradiated area, where the patient experienced some itching. She felt well as a result of the conservative treatment administered and was being followed up at two week intervals in Białystok.

Patient 2 was admitted to the Oncological Surgery Ward of the Holy Cross Cancer Centre on 27 August 2002. She was suffering from post-radiation fibrosis with superficial necrosis at the scar of the mastectomy on the right hand side of her thorax. She underwent a one step operation on 6 September 2002.[12] The operation involved making a wide excision of all the necrotic, prenecrotic and fibrotic tissues (distinctly identified by MRI and CT) and covering the

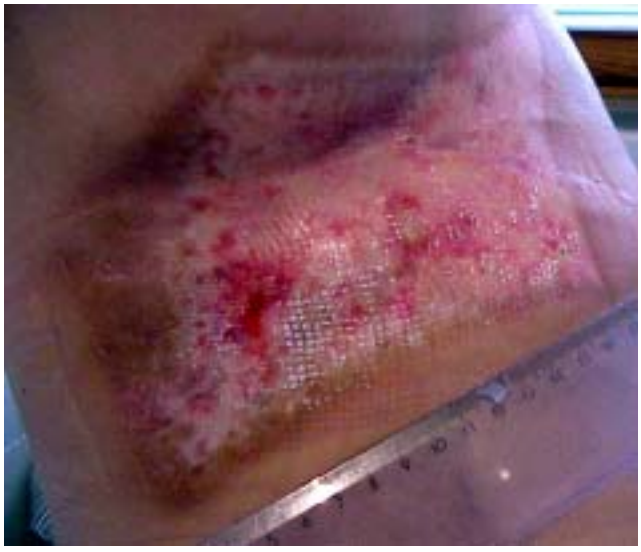

FIG. 15. Patient 2 on 1 December 2001: Depigmented area (14 cm × 10 cm) exhibiting poor epithelialization, marked exudation and multiple punctate areas of bleeding without obvious areas of necrosis or infection.

[12] Performed by Prof. A. Kułakowski.

wound with an omentum flap through a tunnel prepared below the skin between the abdomen and the thoracic wall. At the end of the operation a thin skin graft was positioned over the flap with skin that had been removed from the thigh.

At the end of October 2002, Patient 2 was still in the Oncological Surgery Ward of the Holy Cross Cancer Centre, as the healing of her post-operative wound, although satisfactory, was not complete.

6.4. PATIENT 3

Patient 3 (date of birth: 22 March 1941) had undergone a right radical mastectomy on 8 December 2000, staged as T2N2 (9 nodes +/21) M0. The tumour was Grade III. She received five cycles of chemotherapy before surgery and one cycle afterwards in January 2001. The chemotherapy consisted of treatment with Cyclophosphamide and Doxorubicin.

Radiation therapy was started on 13 February 2001. She received 25 Gy (^{60}Co) to the supraclavicular and axillary regions (10 × 2.5 Gy/fraction) and 20 Gy of radiation to the sternum in 10 fractions of 2 Gy each. The chest wall was simultaneously treated with an 8 MeV electron beam at 2.5 Gy/fraction. The field size was 17 cm × 13 cm and the exposure was 157 MU. The accidental exposure occurred during administration of the 11th fraction.

The total dose to the chest wall in the area of interest was 25 Gy of 8 MeV electrons plus that attributable to the accidental exposure. The patient stayed at the hospital when erythema was first observed. The erythema increased over the following two days and then regressed. On 12 March, moist desquamation began and the patient experienced moderate pain in the area where she had been treated with radiation. According to the physicians, the treatment field "looked as if the patient had received a full course of radiation therapy with X rays". There was some improvement and the patient was discharged from the hospital on 11 April.

On 23 April, Patient 3 was readmitted to hospital with a fever. She was given a systemic course of corticosteroids following which she developed steroid induced diabetes that required treatment with insulin. A CT scan on 2 May showed some pericardial fluid and a reaction in the antero-lateral right chest wall. Rehabilitation began in May. At this time the skin of the irradiated field showed a white 'frame' with a slight pinkness in the centre and this was accompanied by moderate pain. In June, ulceration was noted in the centre of the field at the surgical scar (Fig. 16).

On 23 May, the patient was hospitalized because of increasing pain in the irradiated field. At this time, examination revealed an area of deeper ulceration

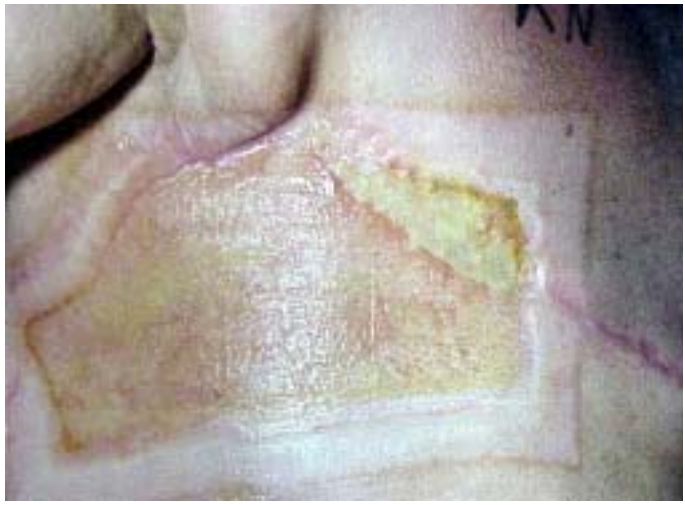

FIG. 16. Patient 3 on 4 June 2001: Superficial ulceration (3 cm × 7 cm) close to the medial edge of the irradiated field along the surgical scar.

(5 mm × 10 mm) in the centre of the field. At 160 mIU, the count of cancer marker CA 125 was elevated (the normal count is <35 mIU). The reason for this elevated CA 125 count was not clear, as the count had returned to normal by the end of October.

A CT scan done on 8 August showed evidence of chest wall thickening or oedema, and a moderate size effusion in the right pleural cavity. A chest X ray on that day showed a right mid-lung infiltrate or atalectasis and fluid in the right pleural cavity. The patient was then treated with systemic Pentoxyfylline and Tocopherol. Other treatments used over these months included Linomag topical ointment; Solcoseryl (I.V.); vitamins PP, B1, A and E; and insulin.

In September, Patient 3 went to the Centre of Oncology (Warsaw) for rehabilitation. Medication for pain relief was required during this time. She was discharged but was readmitted to a local hospital in October with a stomach ulcer diagnosed by endoscopy. The patient had a history of gastric ulceration dating back to 1992.[13] On 6 November, Patient 3 was referred for several weeks of HBO therapy, although this did not result in any obvious improvement.

[13] In 1995, Patient 3 underwent surgery at the hospital in Łomża because of bleeding from this gastric ulcer.

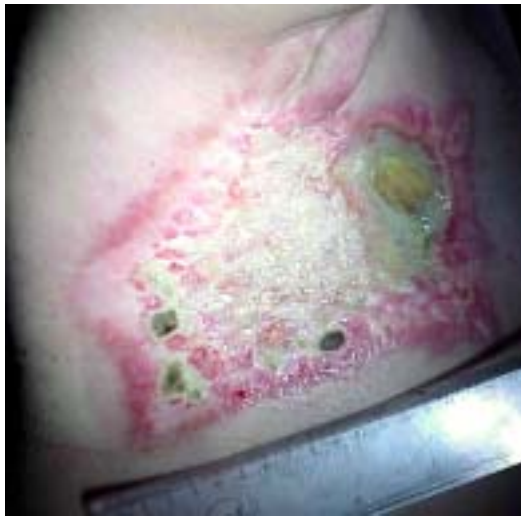

FIG. 17. Patient 3 on 1 December 2001: A 16 cm × 8 cm area which had islands of re-epithelialization and small (less than 1 cm × 1 cm), scattered areas of necrosis and ulceration.

Examination of the patient by the IAEA expert medical team on 30 November and 1 December revealed a 16 cm × 8 cm area which had islands of re-epithelialization and small (less than 1 cm × 1 cm), scattered areas of necrosis and ulceration. At the site of the surgical scar there was a 3 cm × 4 cm ulcer with a deeper central portion of 2 cm × 3 cm that extended to the underlying rib (Fig. 17).

The IAEA expert medical team obtained a new, non-contrasted chest CT scan on 1 December, which showed that the distance between the deep portion of the ulcer and the lung was only 1 cm. It also showed a moderate size fluid collection in the right pleural cavity (Fig. 18).

There was also a lesion in the dome of the right lobe of the liver. The measured density indicated that this was not a cyst. This lesion had not been visible on the previous contrasted CT scan. Specialists from the BOC concluded that it might represent a new metastasis or possibly a haemangioma.

The IAEA expert medical team concluded that at the time of examination the patient had very serious injuries that probably would not heal without intervention. The team observed glucosuria, which was considered as most probably of a transient nature and due to corticosteroids, but which could also have been of diabetic origin. The team recommended:

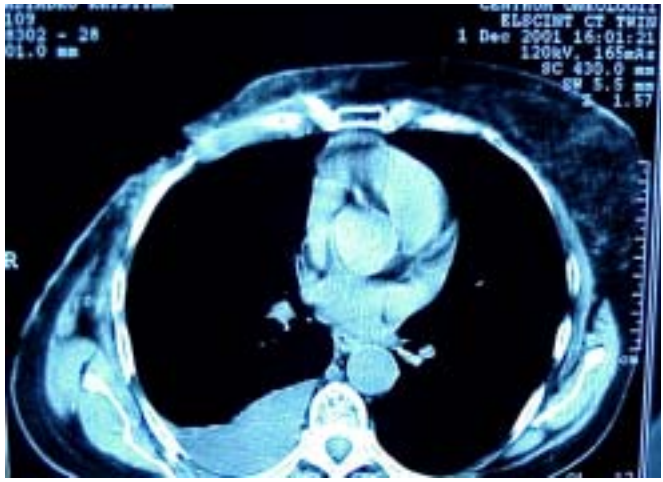

FIG. 18. CT scan of Patient 3 performed on 1 December 2001.

(a) Assessment of the extent of the radiation necrosis through the chest wall, with particular emphasis on the ribs, using NMR;
(b) Cessation of HBO therapy after completion of the protocol, as it did not significantly improve the clinical situation during the elapsed month;
(c) Continuation of Pentoxyfylline/Tocopherol therapy in order to reduce the extent of long term residual fibrosis;
(d) Consideration of surgical treatment at the earliest opportunity in order to avoid development of a catastrophic complication such as pneumothorax.

The team noted that the type of surgery would depend on the degree of radiation necrosis of the chest wall. Pending a decision on the kind of surgery to be performed, it was important that appropriate control of sepsis be achieved, as the patient ran a high risk of becoming septicemic if her glycosuria was diabetic in origin and not transient due to corticosteroids.

Patient 3 continued HBO treatment in January 2002 in Gdynia. In May and June 2002, she underwent chemotherapy treatment with Adriamycin in the BOC in response to the conclusion that had been reached at the BOC that liver metastases had been detected on a CT scan performed in December.

On 5 August, Patient 3 was admitted to the Oncological Surgery Ward of the Holy Cross Cancer Centre. She was in very poor condition, suffering mainly from deep radiation necrosis penetrating to the pleural cavity, with signs of pneumothorax at the scar of the mastectomy. No metastases were detected by the examination; therefore, the general conclusion reached was that the

previous supposition of the presence of liver metastases was questionable. The patient underwent a one step operation on 14 August.[14] The operation involved performing a wide excision of all the necrotic and prenecrotic tissues (distinctly identified by MRI and CT), the removal of four ribs, and finally, covering the wound with an omentum flap through a tunnel prepared below the skin between the abdomen and the thoracic wall. Patient 3 also underwent subcutaneous mastectomy of her left breast. At the end of the operation a skin graft from her left breast and her thigh was positioned over the wound and drainage of her right pleural cavity was established.

At the end of October 2002, Patient 3 was still in the Oncological Surgery Ward of the Holy Cross Cancer Centre, as the healing process of her post-operative wound, although satisfactory, was not complete. Ultrasound examinations repeated at monthly intervals from August to the end of October 2002 did not reveal any metastasis in this patient's liver.

6.5. PATIENT 4

Patient 4 (date of birth: 21 April 1956) underwent a left radical mastectomy on 9 July 2000. After surgery her disease was staged as T1N+ 18/18 (18 nodes positive for cancer of the 18 nodes sampled) M0. The tumour was Grade III. She received four cycles of chemotherapy (including Vinorubin and Doxorubicin). The last cycle was completed on 4 January 2001.

Radiotherapy was started on 29 January; she received 50 Gy (^{60}Co) to the supraclavicular and axillary regions in 20 × 2.5 Gy fractions and 42 Gy (^{60}Co) to the sternal region in 21 × 2 Gy fractions. The chest wall was simultaneously treated with the 8 MeV electron beam (2 Gy per fraction). Eleven fractions were done without a bolus and 10 fractions with a bolus. The accidental exposure occurred during administration of the 22nd fraction on 27 February. The intended exposure was 125 MU per treatment. After completion of the 22nd fraction, the patient reported to the technologist that she felt that "something was different". She left the department, but returned a few minutes later complaining of a burning or itching sensation. There was no visible change in the skin at that time. The patient was hospitalized and within a few hours post-exposure, she developed mild erythema and pain at the place where she had been irradiated. She was given an ointment, but by the second day a rash was visible on her body. The rash was presumed to be an allergic response and she was given steroids systemically and topically for six weeks. Moist

[14] Performed by Prof. A. Kułakowski.

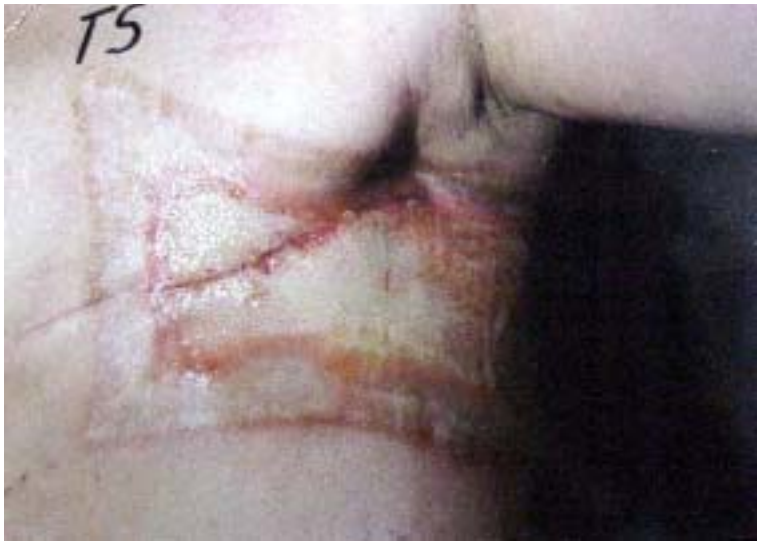

FIG. 19. Patient 4 on 4 June 2001: Moist desquamation in the irradiated area, following mastectomy to the left side.

desquamation was noted one month after exposure. After ten weeks she returned, complaining of worsening pain in the irradiated field. Physical examination revealed a white 3 cm border at the perimeter of the irradiated field with central fibrosis. The pain continued and this was aggravated by motion.

The patient was hospitalized at the Centre of Oncology (Warsaw) in May for rehabilitation and pain management. On 4 June, only moist desquamation with small erosions along the surgical scar was seen in the irradiated field (Fig. 19).

Patient 4 was then discharged. On 30 July, she returned to the BOC complaining of pain and weakness. A CT scan revealed a small pleural effusion. The count of the cancer marker CA 125 was 197. In August, there was an infection in the irradiated field that was treated with topical medications and Tocopherol and Pentoxyfylline systemically.

Patient 4 was readmitted to hospital in Warsaw in September for several days to obtain additional rehabilitation treatment. In October, the lesion became much worse. Debridement of a necrotic lesion was performed and staphylococcus aureus was cultured from the wound. The patient developed a large pleural effusion in October 2001 (Fig. 20) and a litre of fluid, which was negative for malignant cells, was removed from the lesion.

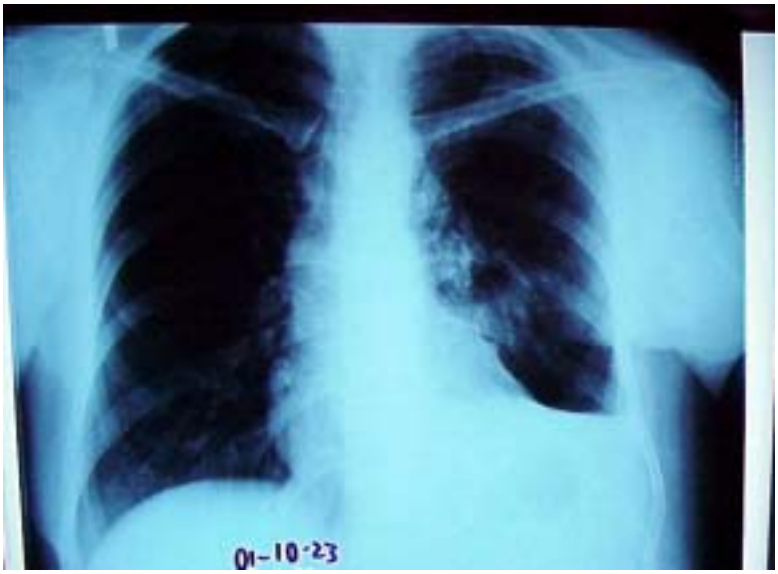

FIG. 20. Patient 4 on 23 October 2001: A large pleural effusion is visible on the left side of the chest X ray.

As Patient 4 showed clinical signs indicating progression of disease accompanied by poor general health, loss of weight, elevated cancer marker counts, and no signs of granulation in the area of the infected local injury, it was felt that she would not benefit from HBO treatment and as a consquence it was not offered to her.

Patient 4 was readmitted to the Department of Breast Cancer and Reconstructive Surgery of the Centre of Oncology (Warsaw) on 5 November. There was an anterior left lung mass which was suspected of being malignant. Biopsy analysis was performed on this mass four times, with negative results for cancer. A radionuclide bone scan showed increased activity in the left ribs in the area where the patient had been irradiated. A previous CT scan of the chest on 8 September had shown a small amount of pleural fluid on the left side and some reaction of the lung. A further CT scan of the chest on 6 November showed pleural fluid, a little pericardial fluid and probable mediastinal oedema, as well as fibrosis deep to the area of ulceration on the chest wall. A chest X ray also done on 6 November showed a large pleural effusion, which was drained. A subsequent chest X ray taken on the same day, post-thoracentesis, demonstrated that most of the fluid had been removed.

An MRI of the chest was also taken on 6 November and revealed a moderate amount of left pleural fluid and a little pericardial fluid. The ribs

were not clearly shown on the left side owing to fibrosis. The apex of the right ventricle of the heart was located just behind the necrotic lesion and there was an abnormal signal in the anterior and lateral left ventricular muscle. This was the area where the highest dose was to be delivered according to the computerized treatment plan. A chest X ray on 23 November showed reaccumulation of the large pleural fluid collection on the left side of the lungs. During November, treatment for the wound infected with pseudomonas aeruginosa included application of 10% saline and Metronidazole topically, then, from 26 November onwards, Nu-Gel absorbent dressing and biological ointment (based on sea algae); Tazocin (3 × 4.5 mg/d I.V. for a fever of <37.8 °C for three days); Ketonal analgesics (200 mg at night); Tramal (2 × 100 mg/d); Tamoxifen (20 mg/d); Ranitidine (200 mg at night, to treat the stomach ulcer); Tocopherol (reduced from 900 mg/d to 300 mg/d) and Pentoxyfylline (2 × 400 mg/d). The antidepressant therapy (Amitriptyline) was stopped on the admission of Patient 4 to the Centre of Oncology (Warsaw).

Examination of the patient by the IAEA expert medical team on 30 November and 1 December revealed that the general health status of the patient was fair. There was no dyspnoea, chest pain or cough. On palpation, the right breast was normal. The regional lymph nodes, liver and spleen were not enlarged. The function of the left arm was satisfactory, but the range of movement was slightly limited. Auscultation revealed dullness at the base of the left lung and a moderate to large pleural fluid collection in the left pleural cavity that had apparently reaccumulated (Fig. 21).

A radiation reaction of the skin and subcutaneous tissue ranging from Grades II to IV was noted in the irradiated field in the left area of the chest. The skin changes covered an area of 14 cm × 8 cm and in the centre of this area lay an ulcer of full thickness covering an area of 5 cm × 4 cm (Fig. 22).

The IAEA expert medical team concluded that at the time of examination the patient had very serious injuries that would not heal without intervention. The team recommended exploring for possible necrosis to the rib resulting from overexposure to radiation and myocardial damage using NMR. It was proposed that surgical treatment be considered at the earliest opportunity in order to avoid a catastrophic complication. Bearing in mind the decision to be taken regarding surgery, the team pointed out that as Patient 4 had deep necrotic lesions in the thin chest wall just above the heart she would be at additional risk from potential radiation induced cardiac injury.

Patient 4 was transferred to the Institut Curie in Paris for further treatment. On 23 May 2002, on her arrival in Paris, the following symptoms were observed: poor general condition, severe local pain, pyrexia between 38.0°C and 38.5°C (peaking at 39.5°C on 6 June), large necrotic destruction of

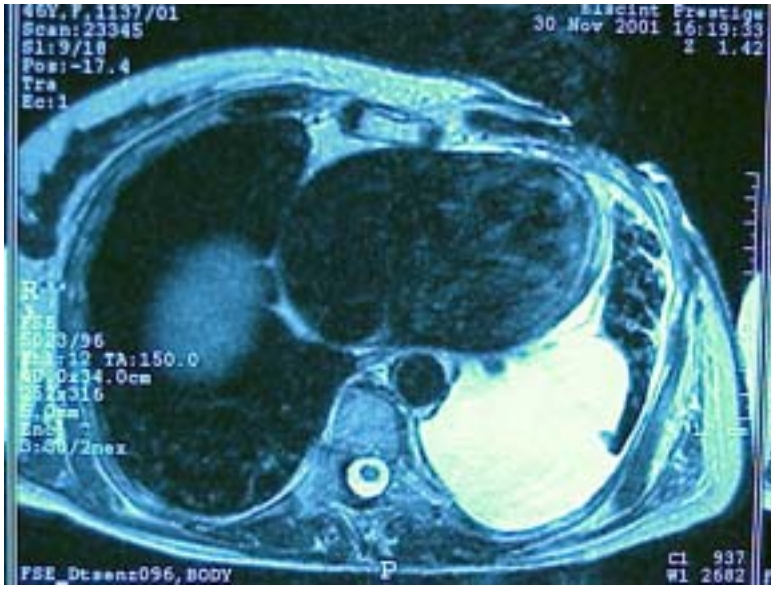

FIG. 21. Patient 4 on 30 November 2001: CT scan of thorax showing a large pleural effusion.

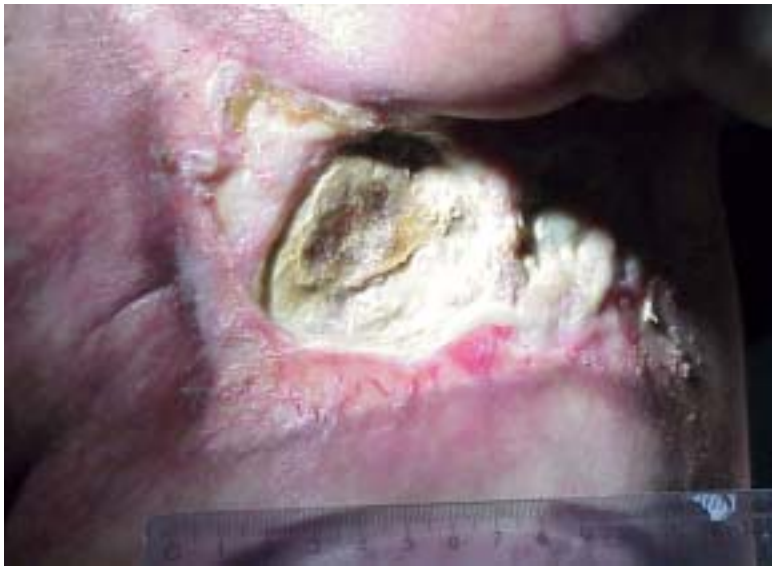

FIG. 22. Patient 4 on 1 December 2001: Severe skin changes following a radiation burn. The wound covers an area of 14 cm × 8 cm; in its centre lies an ulcer of full thickness covering an area of 5 cm × 4 cm.

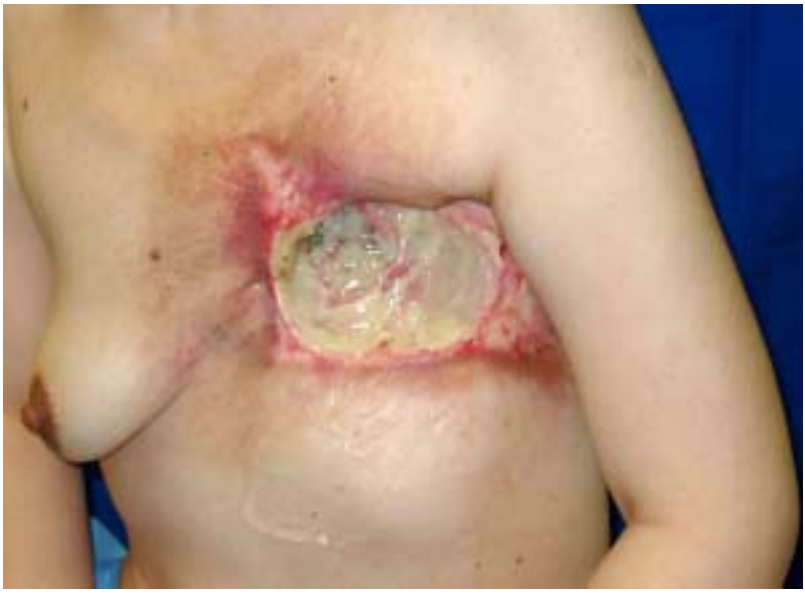

FIG. 23. Patient 4 in May 2002: Local injury before reparative surgery.

all the thickness of the left chest wall in the internal two thirds of the electron field, and severe superinfection by pseudomonas aeruginosa. The beating heart of Patient 4 was visible in the depth of the wound. The status of the local injury is shown in Fig. 23.

Patient 4 was first treated topically, using antibiotic therapy and pain relievers. The following analyses allowed the treatment to be focused further:

(a) Isotopic ventricular left ejection fraction examination (27 May): 60%, normal.
(b) MRI (28 May): pericardial and left pleural effusion, left ventricular anterior lesion (confirming previous Polish MRI data).
(c) Telethermography (6 June): all the irradiated volumes of the chest wall appeared to be 'cooler' and therefore were believed to be prenecrotic.
(d) Bacteriology: persistence of pseudomonas superinfection, despite treatment with antibiotics.

On 6 June, Patient 4 underwent her first surgical procedure after the overexposure.[15] This procedure consisted of several steps: exploration of the

[15] Performed by Dr. Clough, Dr. Couturaud and Prof. Chapelier.

abdomen, preparation of a large omentum flap, large ablation of all the necrotic and prenecrotic tissues of the left anterior chest wall, and positioning of the omentum flap brought from the abdomen through a subcutaneous tunnel. Histological analysis of large necrotic lesions showed no trace of tumour. Three stages of this surgery are illustrated in Figs 24–26.

In the early follow-up, it was observed that the omentum flap was accepted very well, with rapid cell proliferation and a 'filling in' of the wound. On 4 July, when the proliferation of the omentum flap was satisfactory, Patient 4 underwent her second reparative operation[16], which consisted of positioning a free skin graft (taken from the anterior part of the right thigh) on the omentum flap. Figure 27 presents the conditions of local injury after the treatment.

In the ongoing follow-up, a rapid 'take' of the graft was observed, along with an improvement in the general condition of Patient 4 and apyrexia. This patient returned to Poland on 15 July 2002 in a much improved general condition. After her return to Poland, the patient was admitted to the Radiotherapy Ward of the Holy Cross Cancer Centre on 2 August. She was subjected to routine laboratory tests and had X rays taken, which were within normal dose limits, and the dressing to her wound was changed frequently. The healing of her post-operative scars progressed well. The thoracic transplant was almost healed up and the epithelialization of her left thigh scar was very advanced.

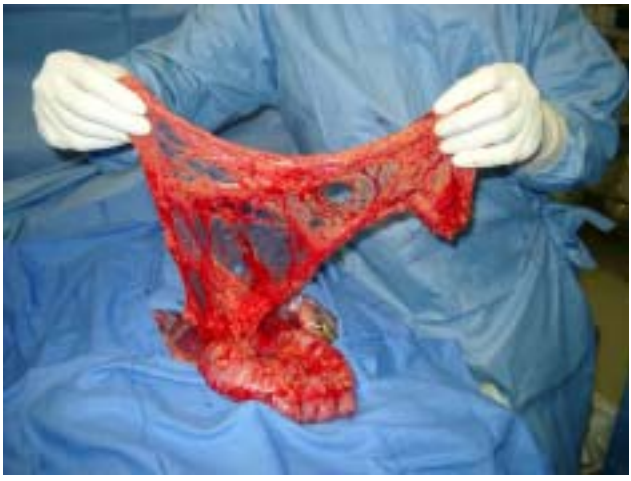

FIG. 24. Stages of surgery for Patient 4: Preparation of a large omentum flap.

[16] Performed by Dr. Couturaud and Dr. Thomas.

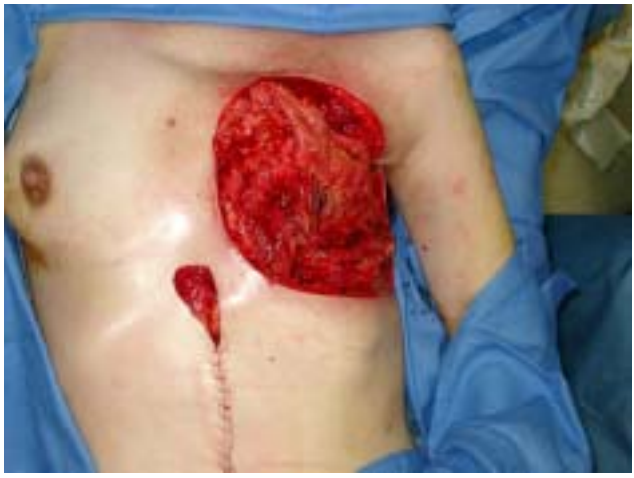

FIG. 25. Stages of surgery for Patient 4: Defect covered with an omentum flap.

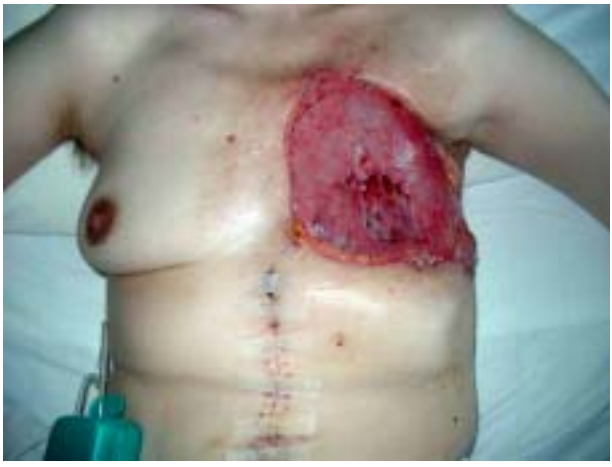

FIG. 26. Stages of surgery for Patient 4: End of operation.

During her stay in the Centre she used very few pain relievers, as her pain had decreased significantly after the operation. She was discharged on 16 August and given a prescription of Tamoxifen with instructions to change her dressing frequently. She was scheduled for follow-up one month after her release. The follow-up examination on 19 October revealed that her post-operative scar had healed up. The patient did not experience pain, and therefore the use of pain relievers was stopped.

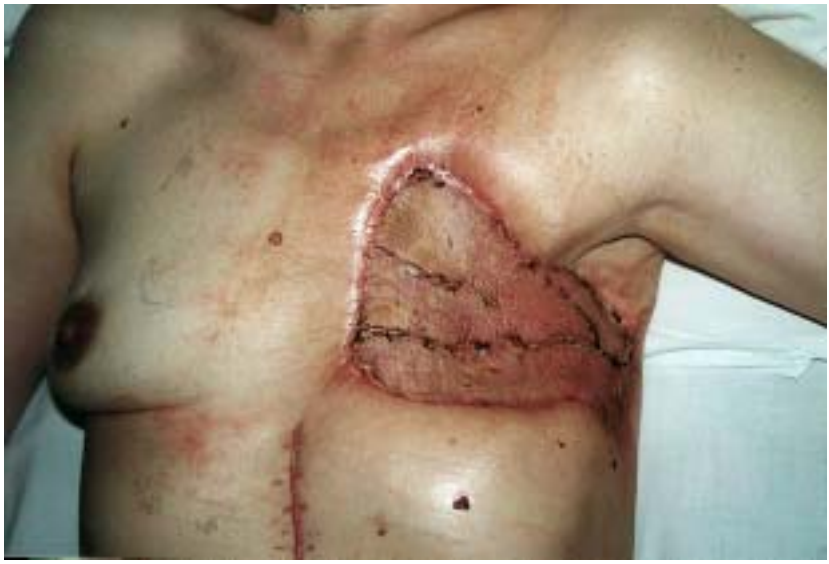

FIG. 27. Outcome of the two step surgery on Patient 4 at the Institut Curie, July 2000. The secondary defect has been covered by a free skin graft.

6.6. PATIENT 5

Patient 5 (date of birth: 5 September 1937) had a history of diabetes which had been successfully treated for 15 years with oral medication. Following a left sided radical mastectomy in November 2000, this patient's disease was staged as T2 N3 (5 nodes positive for cancer of 16 nodes sampled) M0. No tumour grade was available from the patient's history. The patient received two cycles of chemotherapy which were completed on 4 January 2001. Radiation therapy was started on 23 February. The patient received 5 Gy (^{60}Co) to the supraclavicular and axillary regions in 2 × 2.5 Gy fractions and 4 Gy (^{60}Co) to the sternal region in 2 × 2 Gy fractions. There was simultaneous treatment of the chest wall with 8 MeV electrons and the patient received 5 Gy in 2 × 2.5 Gy fractions. The field size was 18 cm × 11 cm and the planned exposure was 156 MU. Only two fractions were completed, as the accidental exposure occurred during administration of the third fraction. The total dose to the area of interest was 5 Gy of 8 MeV electrons plus that attributable to the accidental exposure. A faint erythema appeared after the third fraction on the day of the accident. The patient reported a "burning sensation" in the

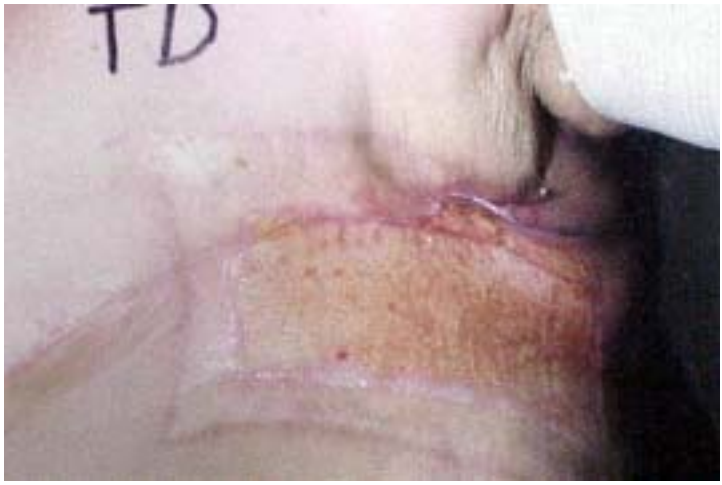

FIG. 28. Patient 5 on June 2001: The 7 cm × 14 cm central part of the 11 cm × 18 cm irradiated area became hardened, fibrotic in the centre and surrounded by a depigmented border.

irradiated field at the end of the treatment, and because of this report and the previous comments of Patient 4, the treatments were stopped.

Two weeks after the exposure, a slight erythema developed, turning to dry and moist desquamation during the following two weeks. Beginning in early April, epithelialization progressed, but Patient 5 felt a severe pain in the irradiated field, which seemed to be out of proportion to the clinically observed skin findings. In May, the irradiated area became fibrotic in the centre with a somewhat indistinct white border (Fig. 28).

The count of cancer marker CA 125 was slightly elevated. In July, the pain worsened but there was no change in the appearance of the irradiated field. In August, the patient went to the Centre of Oncology (Warsaw) for rehabilitation. Treatment in the Centre included administration of Linomag enzymatic ointment; systemic Tocopherol and Pentoxyfylline; Solcoseryl (I.V.); and vitamins PP, B1, A and E. A chest X ray on 31 October revealed a small infiltrate or atalectasis/fibrosis in the middle of the left lung.

Owing to her social conditions, Patient 5 stayed without interruption in hospitals between February and September 2001. The local injury in the irradiated field became infected in the middle of October and the infection spread quickly. A small area of necrosis (1.5 cm × 1.5 cm) appeared at the medial line of the wound (Fig. 29).

On 5 November, Patient 5 was admitted to the Institute of Marine and Tropical Medicine in Gdynia for HBO treatment. In spite of the HBO therapy,

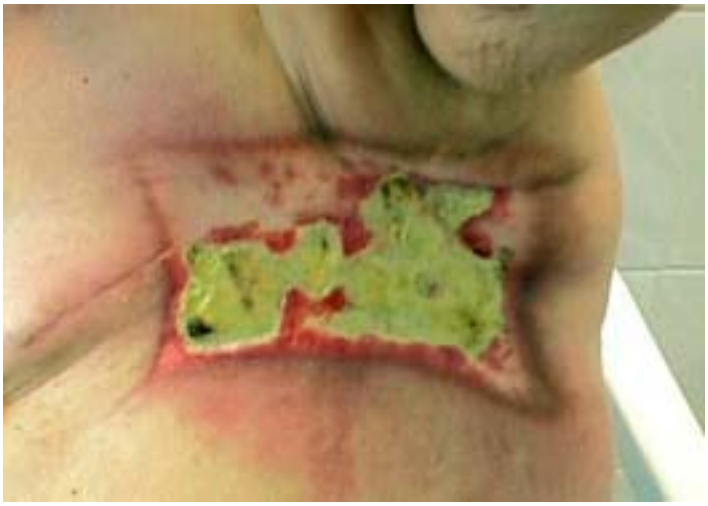

FIG. 29. Patient 5 on 6 November 2001: Highly infected local radiation burn (6 cm × 13 cm) in the area of the left mastectomy.

ulceration progressed over the ensuing month. The area of necrosis at the medial line increased to 5 cm × 5 cm. Other areas of necrosis (2–3 small necrotic foci) also appeared (Fig. 30).

Examination of the patient by the IAEA expert medical team on 30 November and 1 December revealed a large area (14 cm × 7 cm) of Grades III and IV radiation injury. In the area of the surgical scar there was a 5 cm × 5 cm necrotic lesion exhibiting a black colouration and of full thickness extending down to the ribs (Fig. 31).

A non-contrasted CT scan of the chest was requested by the team. The scan, which was performed on 1 December, revealed a small pericardial effusion. In addition, it showed that the apex of the left ventricle of the heart lay directly under the necrotic lesion and was slightly deformed by a focal bulge (Fig. 32).

The IAEA expert medical team concluded that at the time of examination the patient had very serious injuries. The conditions of treatment were complicated by the presence of concomitant diabetes mellitus. Surgical treatment was proposed as a matter of urgency. The team noted that the patient had a higher risk of becoming septicemic because of her diabetes. In addition, diabetes would make surgery and healing difficult, and a successful outcome uncertain. As with Patient 4, it was noted that Patient 5 presented deep necrotic lesions in the thin chest wall just above the heart, and therefore was at

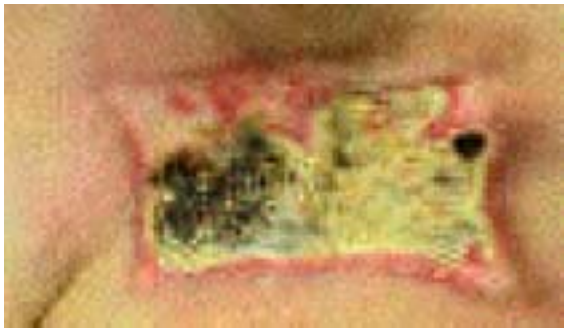

FIG. 30. Patient 5 on 20 November 2001: Superinfected necrotic radiation burn (7 cm × 13 cm) in the area of the left mastectomy.

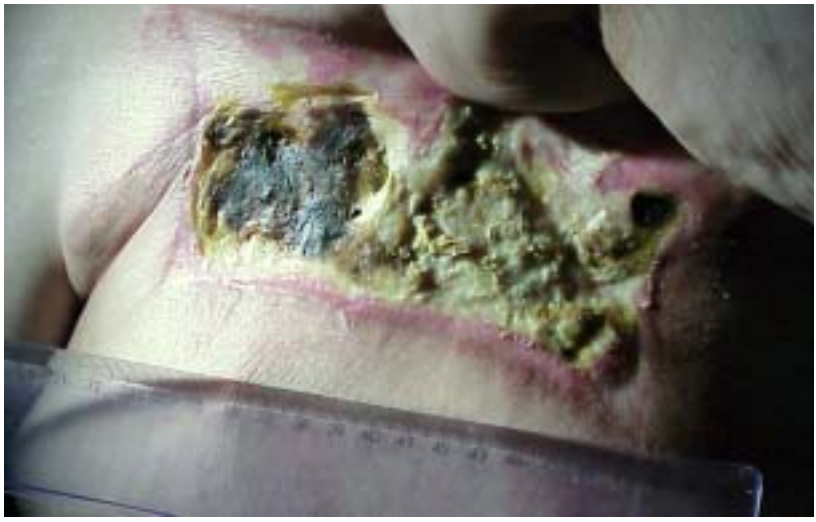

FIG. 31. Patient 5 on 1 December 2001: A large area (14 cm × 7 cm) of radiation injury of Grades III and IV.

additional risk owing to the potential cardiac damage induced by the over-exposure.

HBO therapy of the patient in Gdynia was interrupted over the Christmas period, but restarted in January 2002. On 8 February, the patient was admitted to the Radiotherapy Ward of the Holy Cross Cancer Centre. She suffered mainly from deep (2–3 cm) radiation necrosis located at the scar of the

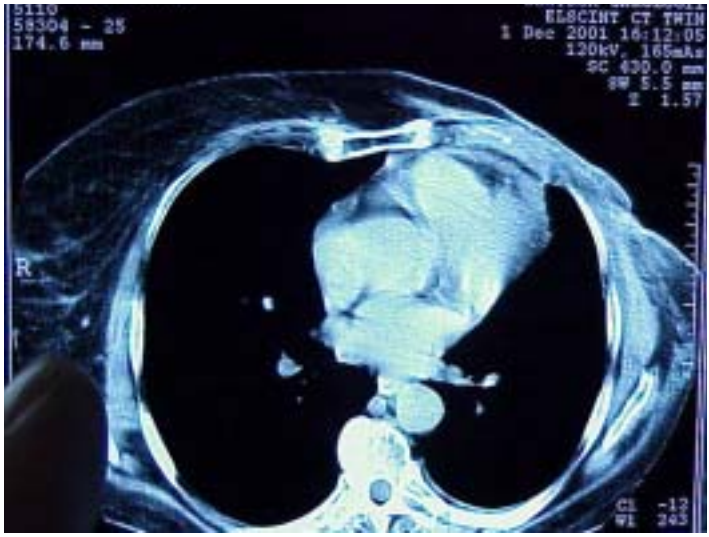

FIG. 32. Patient 5 on 1 December 2001: CT scan of the chest.

mastectomy on the left side of her thorax. The dimensions of the lesions were between 10 cm and 15 cm and the base of the ulceration was covered with a thick layer of necrotic tissue. On 3 August, excision of this necrotic matter was performed by a short procedure under general anaesthesia. Following this procedure, the dressing to her wound was changed frequently and Granuflex paste and colloidal Granuflex applied. The patient was discharged on 10 September and referred to the Institut Curie in Paris for further surgical treatment.

On admission to the Institut Curie on 10 September, Patient 5 was in an acceptable general condition. The large ulceration of the left anterior chest wall was almost stabilized. However, on the basis of the bacteriological samples taken on 11 September, there still existed a double superinfection with pseudomonas aeruginosa and staphylococcus, as well as a urinary superinfection. Treatment of infection was effected by local and systemic antibiotherapy. An isotopic ventricular left ejection fraction examination was performed on 11 September; it was normal at 55%.

On 13 September, a new CT scan was performed which showed the presence of a large ulceration with pleural reaction. However, there was no suspicion of a pericardial lesion. The ribs were slightly abnormal, but without obvious signs of radiation necrosis.

On 16 September, a first meeting[17] of medical experts convened to discuss the treatment course to be taken decided to forego the option of carrying out the omentum flap technique which had been successful for Patient 4, because:

(a) The patient had previously undergone abdominal surgery (cholecystectomy), and therefore the medical experts felt that the fibrosis that had been brought on by surgery might have rendered difficult the preparation of a sufficiently large omentum flap.
(b) The risk of contaminating the abdomen with pseudomonas was not to be discounted. An infection of this significance would have been extremely difficult to treat in a person of the age of Patient 5.
(c) The patient suffered from diabetes.

The decision was made to attempt a dorsal pedicled flap, after local preparation. The patient underwent a one step operation on 30 September 2002.[18] The operation consisted of making a wide excision of all the necrotic and prenecrotic tissues (precisely identified by MRI and CT). Samples of the excised tissues were taken for analysis at the laboratories of the Institut de Radioprotection et de Sûreté Nucléaire and of the Commissariat à l'Energie Atomique/Direction des Sciences du Vivant. Owing to the macroscopical aspect of the anterior parts of the 3rd, 4th, 5th and 6th ribs, they were completely resected. Removal of tissues stopped at the pleural and pericardial levels (which were not involved). A musculo-cutaneous flap (latissimus dorsi) was then prepared, along with its vascular pedicle. The flap adequately covered all the resected area. The immediate results of the surgery were satisfactory (Fig. 33).

Follow-up was relatively simple for Patient 5, who showed no marked infection, experienced good general health and recorded a rapid healing of the flap to 90–95%. An examination performed on 17 October showed that the process of healing was satisfactory except for a limited sector at the internal part of the flap, where there was an area of 1.5 cm × 1.5 cm that was not healing. However, it was expected that spontaneous healing of this area would be possible in the weeks following the examination and that complementary surgical treatment would not be necessary. Local treatment of the area was administered. Patient 5 was still in the Institut Curie at the end of October 2002 because the healing of her post-operative wound was not complete.

[17] Involving Dr. Clough, Dr. Couturaud and Prof. Chapelier.
[18] Performed by Dr. Clough, Dr. Couturaud and Prof. Chapelier.

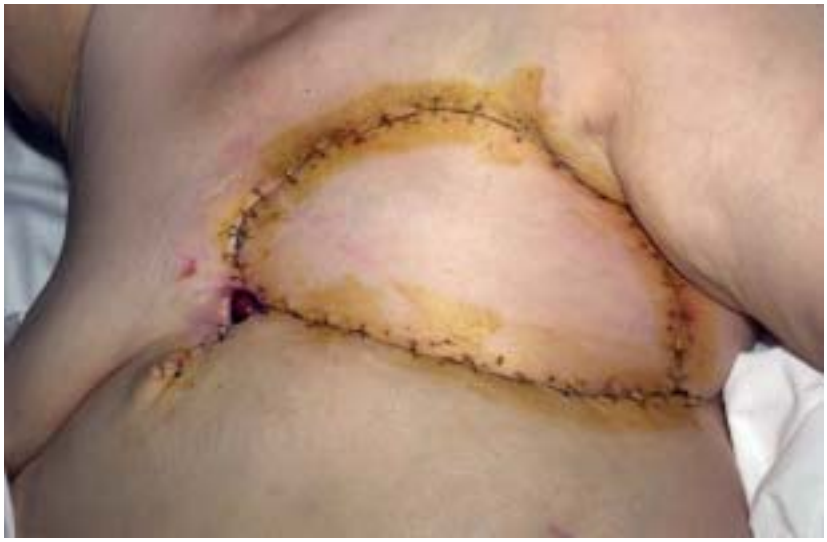

FIG. 33. Results of the one step surgery on Patient 5 at the Institut Curie, October 2002.

7. CONCLUSIONS, RECOMMENDATIONS AND LESSONS TO BE LEARNED

7.1. OPERATING ORGANIZATION: RADIOTHERAPY DEPARTMENTS

The IAEA medical physics and radiation safety expert team concluded that a fault affecting the beam monitoring system of the NEPTUN 10P® accelerator led to a large increase in the dose rate, even though the display indicated a value lower than normal. This was due to a faulty diode preventing the safety interlock from functioning. In addition, the limitation on the filament current for the electron gun was set at a high level which meant that the dose rate due to the malfunction was many times higher than intended. The combination of these factors led to substantially higher doses being delivered to the patients.

In order to help prevent other possible overexposures from occurring in similar circumstances, QA programmes appropriate for accelerators that are used in the medical field need to include dosimetry checks of beam output

prior to the resumption of patient therapy following power failures or any other unusual occurrence, such as an anomalous reading in the dose rate display.

7.2. NATIONAL INFRASTRUCTURE FOR RADIOTHERAPY

In countries that have an unstable power grid, measures ought to be taken to ensure a uniform and stable AC power supply to institutions that use medical electrical equipment, in order to facilitate the safe operation of this equipment. These measures may be implemented by providing such institutions with independent power supply units, as appropriate.

A national QA programme for radiotherapy ought to include provision for ensuring rigorous implementation of comprehensive QA systems in the radiotherapy departments for both the physics and medical aspects, as well as review by an external audit system that uses experts in medical physics and radiation oncology, in accordance with the International Basic Safety Standards (Ref. [1] paras 2.29, II.1, II.2, II.12, II.22, II.23). However, hospitals need to be equipped with adequate quality control tools to allow the implementation of such QA systems. Provision for conducting dosimetry checks of beam output after power failures needs to be included in the QA programme.

Increased awareness and understanding of any unusual situation ought to be promoted by including in the training all persons directly or indirectly involved in radiotherapy, and by disseminating the lessons learned from accidental exposures. However, this training should be appropriate to the function and professional needs of the individual concerned.

7.3. EQUIPMENT MANUFACTURERS AND SUPPLIERS

The accidental overexposure in Białystok demonstrated that two faults in two circuits could occur at the same time and lead to machine operation with an ineffective beam monitoring system. Moreover, the probability of such a double fault occurring was increased by the fact that an inoperative interlock (the diode) went unnoticed until the second fault occurred in the beam monitoring system. In this situation, the interlock could allow the start sequence to progress, even if a second fault, a defective fuse in the power supply to the dose monitoring systems, rendered the system ineffective and led to the filament current being driven to its maximum.

The NEPTUN 10P® medical accelerator was designed prior to the publication of the standards of the IEC that currently apply for accelerators of

this kind. The dose monitoring system of the NEPTUN 10P® does not comply with the current IEC recommendations for the safe operation of accelerators used for medical purposes. In particular, Section 29.1.1.1 of IEC Standard 60601-2-1, issued in 1998, contains stricter criteria for the design of machine beam monitoring systems than those listed in the recommendations established by the IEC in 1981 (IEC-601-2-1).

The design for the new generation of NEPTUN accelerators, or for any other accelerator currently being developed, needs to apply the IEC 60601 standards, which are up to date. More specifically, with regard to dose rate monitoring systems and the safety interlocks, IEC 60601 provides for the following:

(a) *Design of the monitoring system.* If, under any fault conditions, the equipment can deliver an absorbed dose rate at normal treatment distance of more than ten times the maximum specified in the technical description, a radiation beam monitoring device, which shall use a circuit independent of the dose rate monitoring system, shall be incorporated on the patient side of the radiation beam distribution system. This shall limit the excess absorbed dose at any point in the radiation field to less than 4 Gy (Section 29.1.3). NOTE: In equipment capable of producing both X radiation and electron radiation, the termination of irradiation may need to be completed before the generation of the next pulse of radiation.

(b) *Design of safety interlocks.* Equipment shall be so designed and manufactured that, even in single fault condition, no safety hazard exists (Section 52).

(c) *Examination of safety interlocks.* The safety interlocks need to be examined to ensure fail-safe conditions, i.e. failure of any element which could affect the correct function of any interlock shall terminate irradiation. Section 29.1.3 further establishes that "…means to protect a possible overdose due to an absorbed dose rate more than twice the specified maximum, and limit the excess absorbed dose to less than 4 Gy … shall be tested between, or prior to, irradiations for their ability to function." In other words, the interlocks need to be tested before each new treatment. This would prevent an ineffective interlock from going unnoticed.

For existing equipment, particular emphasis needs to be given to:

(a) *Safety review and assessment.* As a general recommendation, when a new safety standard is issued, the safety of existing equipment needs to be reviewed and reassessed with regard to the need to increase safety to a

level as close as practicable to that of the new standard. The relevant standards in this case are IEC 60601-1-4 and 60601-2-1. The improvements may be technological or procedural. The reassessment, however, needs to take into consideration all the implications of any change or modification. In relation to this event, issuing a warning notice with clear instructions requiring that verification of relevant interlocks be confirmed before each new irradiation and how to perform this verification may be necessary.

(b) *Warnings in instruction manuals.* The manufacturer needs to issue warning notes in the maintenance and service instructions covering the adjustment of limits to the filament current and of any other safety critical devices.

(c) *Restrictions on access.* As far as practicable, access to safety critical adjustments and components needs to be restricted to maintenance engineers instructed by the manufacturer specifically on the safety associated with these components. The restriction of access can be achieved by sealing certain potentiometers, by placing warning stickers on parts of the equipment or by taking administrative measures.

Certification of training for maintenance staff trained by the manufacturer needs to specify limitations or restrictions on the manipulation or adjustment of certain critical parts in the accelerator. Instructions need to place clear emphasis on safety elements and include warning notes.

7.4. MEDICAL ISSUES

The accidental overexposures of all five patients were serious. The conditions of some patients were complicated by the presence of concomitant diseases. HBO treatment improved the condition of the local injuries of some of the patients. All the patients underwent surgery.

It should be recalled that, following radiation injury, the evolution of vascular damage and the deterioration of the underlying blood supply occur after a significant delay, often one of months or years after the overexposure. At the time of writing, the damage that was manifested in these overexposed patients at the early stage was progressing with the development of complications.

The results of the surgical treatment that was performed are preliminary because of the short follow-up time and the incomplete healing of post-operative scars. However, the patients' conditions show significant improvement, in view of the severity of their injuries and the presence of

concomitant diseases. The following recommendations, which derive from these cases, are also generally applicable to other accidental exposures that lead to the development of local radiation injuries:

(a) The injuries should not be treated in isolation without consideration of the individual patient's circumstances and the state of other medical issues.
(b) The type of surgery should depend on the degree of radionecrosis of the chest wall, such that:
    (i) If the chest wall can be preserved and if granulation of the deeper layers is effective, simple skin grafting can be undertaken.
    (ii) If the chest wall can be preserved but the granulation is inadequate or absent, then construction of myocutaneous flaps from dorsal or abdominal muscles will need to be considered.
    (iii) If the chest wall has to be partly removed owing to the extent of radionecrosis, the best treatment might be to use a flap of omentum brought through the diaphragm and covered by a skin graft.
(c) Surgical treatment of severe radiation injuries to radiotherapy patients can carry a significant risk of morbidity and mortality. Therefore, before any decision to undertake such major surgery is made, it needs to be clear that there is:
    (i) No apparent metastatic disease,
    (ii) Acceptable pulmonary reserve,
    (iii) Adequate myocardial perfusion and appropriate control of sepsis.

It is necessary to provide psychological support for patients with radiation induced injuries. Communication between a patient who has already successfully undergone surgery and one who is being prepared for it can be useful in encouraging the latter.

Regular and long term follow-up of patients is essential not only for oncological reasons but also to identify long term sequelae of cutaneous radiation syndrome.

Appendix I

RADIATION EFFECTS IN HUMANS

I.1. BACKGROUND INFORMATION ON RADIATION EFFECTS IN HUMANS

Radiation effects in humans are caused by the deposition of energy in tissue. The energy produces ionizations which cause discrete molecular changes in cellular constituents, in particular in the genetic material composed of DNA. These molecular changes include breaks in the DNA strands which, if not properly repaired, can lead to the death of cells. The proportion of cells affected rises with increase inradiation dose. Individual cells can die by a process known as apoptosis before they divide, or they may fail to undergo successful division. Very high doses may cause cellular necrosis which generally leads to an inflammatory reaction. Cells vary in their sensitivity to radiation. Some types of lymphocytes and germ cells are very sensitive and undergo radiation-induced apoptosis. In contrast, many non-dividing cells in organs and body structures are unresponsive until they are induced to divide and express their latent injury. Renewing cell populations such as those in the epidermis, in the mucosal linings of the intestine and the mouth, and in the bone marrow, respond to irradiation at times depending on their normal renewal time.

The pathological changes identified after irradiation of a given organ depend not only on the physical parameters of the exposure, but also upon the radiosensitivity of the various organ components. In cases in which the functional or parenchymal cells of the organ are radiosensitive, loss of function of these cells will be the initial critical factor, although later, vascular compromise may become important. After substantial radiation exposure, failure of the organ system may result relatively quickly, e.g. in the gastrointestinal system. Marked abnormalities can be seen within several days of a moderate dose of radiation being received. When the organ irradiated has parenchymal cells that are part of a slow renewal system, the controlling factor resides in the more sensitive connective tissue cells, i.e. the microcirculation system that supplies blood to the parenchymal cells. An example of such an organ is the brain.

In renewing tissues, there is a threshold dose for the appearance of a reaction, and the reactions appear at a rate governed by the renewal rate of the tissue. The incidence of the reactions is dose dependent, but at high doses, when all regenerative cells are killed, the appearance rate then becomes independent of dose. These are the characteristics of early reactions in tissues, which occur in the first weeks following irradiation; late reactions appear after

months or years have elapsed. The time to expression of injury and the incidence of injury are both dependent on the dose. Late reactions include the so-called generic late reactions originating from direct damage in a given tissue, as well as the consequential late reactions in that tissue caused by injury in overlying renewing tissues. An example of the latter is late dermal injury after denudation of the epidermis caused by high doses.

Whether a tissue or organ actually survives in the short or long term depends not only on its radiosensitivity and the biologically effective total dose, but also on the volume of the organ irradiated. In general, small volumes will tolerate larger doses than will large volumes. If the radiation dose is high enough, the tolerance of the organ parenchyma will be exceeded. After moderate exposures, there may be some parenchymal damage, and the organ may recover either full or partial function. If the parenchymal cells of the organ are relatively resistant to radiation, no changes may be noted during the early period. However, this should not be construed as indicating that no clinical radiation damage will result. Vascular changes causing arteriolar narrowing may occur later with associated complications. Vascular changes are often responsible for the limiting dose that may be given to an otherwise radio-resistant organ.

In the first year after exposure, underlying radiation damage in parenchymal cells may become manifest in terms of clinically significant problems. These may also be complicated by vascular deterioration due to fibrosis, myointimal proliferation, and hyaline sclerosis of the subintimal and medial regions of small arteries and arterioles. Between one and around five years, an organ system may demonstrate further deterioration of vascularity and secondary degeneration of the parenchyma that can lead to decreased resistance to various additional types of trauma. In subsequent years, there is a slow progression of residual radiation damage and formation of dense fibrous tissue resulting from hypoperfusion and abnormal patterns of cellular matrix deposition. An increasing problem for survivors in this late period is radiation carcinogenesis.

At the time of the IAEA team's initial examination of the overexposed patients, they had already experienced the early reactions, but subsequent changes are still expected.

I.1.1. Basic aspects of radiotherapy

Radiotherapy is the use of ionizing radiation to kill cells in the body, commonly cancer cells. Usually, a radiation source outside the body is used to direct a beam of radiation to the volume of the tumour. The beam of radiation deposits energy in the tissues and kills cells exposed to the beam but not

elsewhere. Therefore, the effects of radiation are limited to tissues and organs exposed to the beam.

An external radiotherapy source can be either an electrical device, which emits radiation only when the electricity is turned on, or a shielded radioactive source which emits ionizing radiation when a shielded port is opened. The device in this accident, a linear accelerator, produces a radiation beam directed towards the patient. In this accident, electrons were used to irradiate the chest wall because they have a maximum penetration of only a few centimetres.

I.1.2. Dose–response relationships

Even the most accurately delivered radiotherapy cannot destroy a tumour without causing some damage to normal tissues. There is a very narrow range of dose and number of treatments that the radiation oncologist must work within. If the treating physician does not damage normal tissue to some extent, experience has shown that there will be very few tumours cured. In order to be able to cure tumours, radiation oncologists around the world use doses that will result in moderate to severe complications in only a very small percentage of the patients. This is regarded as acceptable practice in order to be able to cure cancers. On the other hand, even a small increase in dose above standard protocols will result in an increased complication rate.

From previous experience in radiotherapy, it has been found that there is a threshold dose for radiation-induced morbidity, and as the dose increases so the incidence rises steeply to the 50% level and then more gradually to the 100% level. The gradient is greater for late reactions than for early reactions in tissues, and is tissue dependent. Also, the gradient is much greater with large single doses than with fractionated doses (more details on fractionation effects are given below). In addition, with fractionated doses the gradient is slightly greater with increasing size of dose per fraction using the same number of fractions than with increasing numbers of fractions of constant size. For example, in one study of post-mastectomy breast radiotherapy using 22 fractions of photons, the incidence of late subcutaneous fibrosis was around 5% after 40 Gy, around 50% after 47.5 Gy, and near 100% after 55 Gy. Regarding severe late skin telangiectasia after electron irradiations delivered in the same schedule, the incidence was around 5% after 30 Gy, around 50% after 45 Gy, and near 100% after around 55 Gy. Electrons are less efficient (by about 10%) than photons in producing this type of late skin reaction.

In radiotherapy, it is the late reactions which usually provide a limit to the tolerated dose, in contrast to high overdosage situations where the early reactions cause the most morbidity. In this particular accident, the size of one of the fractions was markedly higher, estimated at 60–80 Gy (at d_{max}) in some of

the cases. The doses described above could be converted to single dose equivalents to obtain rough estimates of the incidence of morbidity after the total dose delivered. However, in the present case the dose in the overdosed fraction was itself very high. Calculations show that even the overdosed fraction on its own would cause severe morbidity in all cases. There would be near 100% morbidity for single doses above about 30 Gy regarding early skin desquamation and ulceration, and above about 15 Gy regarding pneumonitis (this applies to whole lung irradiation). Hence, in this accident, the doses in one part of the treatment were much too high and this resulted in much more cell killing and tissue damage than were necessary, leading to more complications and adverse effects than would have been expected from the prescription of the radiation oncologist.

I.1.3. Fractionation of radiation exposure

Fractionation of radiation exposure, or protraction of the dose over a period of time, almost always reduces the effect of the dose. Spreading a radiation dose out over days or weeks allows time for the cells to repair some of the radiation damage. As a radiation dose becomes increasingly protracted, there is even less effect, because not only is there repair but also growth of the cell population, as the result of cell divisions which are stimulated to heal the normal tissues. In tumours, cell population growth also results from the killing of tumour cells by the radiation, which allows the surviving malignant cells to repopulate. In radiotherapy, dose fractionation is used because quiescent cell populations in organs repair cellular injury to a greater extent than renewing epithelial tissues such as oral mucosa or epidermis, or tumours. Also, the protracted duration of radiotherapy allows the epithelial cells to repopulate and heal the tissues, but only as long as the duration is not so long as to allow some detrimental repopulation of tumour cells. Another aspect pertinent to this accident is that increases in the level of dosage per fraction are more damaging than increases in the number of 2 Gy fractions, for a given increase in total dose.

The increase in the probability of complications occurring in a given accident scenario can be estimated using previous knowledge of the gradient of the dose–response curve and the fractionation sensitivity of the tissues and organs irradiated in conventional radiotherapy schedules. This is done using a mathematical formula, expressing a linear quadratic function, which includes terms for the various parameters describing the probability of occurrence of a specific end point. This probability is an average for a large group of patients treated similarly. Hence, for the five overexposed patients, each of whom was treated differently, these calculations would usually only provide a very rough

estimate of the likely outcome for the average individual, unless the over-exposure is very high, as in the present case, and results in 100% incidence. Also, there is variation between patients in their degree of response, and so again individual predictions are difficult unless the dose is high and produces near 100% incidence of effect.

I.2. RADIATION EFFECTS ON THE TISSUES EXPOSED IN THE ACCIDENT

I.2.1. Effects on the skin

Changes in the skin that have been described in radiation therapy usually involve a course totalling 40–50 Gy (4000–5000 cGy) from an orthovoltage X ray source administered in 20–25 equal fractions over a 4–5 week time period. In such circumstances, patients may demonstrate a faint erythema resulting from capillary dilatation during the first week of treatment. Some epilation is then noted at 10–14 days. The main erythema usually appears in the third week of treatment, with the skin becoming red, warm and oedematous. Moist desquamation begins at the fourth week with exudation of serum.

In a normal course of radiotherapy, desquamation is usually healing by the time treatment is ended, the result of compensatory cellular regeneration in the basal layer of the skin. Dry desquamation is the maximum reaction that occurs if irradiation is halted during the third week at the 30 Gy (3000 cGy) level. In these circumstances, the skin may itch, and scaling and increased pigmentation may occur. The erythematous changes and desquamation are almost always confined to the treatment field, although occasionally they may extend beyond it. If doses exceed those discussed, induration and necrosis of the structures underlying the epidermis may occur.

Skin ulceration may occur early after high absorbed doses. These ulcers may heal but will ultimately recur. With more conventional doses such as those used in radiotherapy, painful, slow healing ulcers may occur and persist for years. The probable cause of these late ulcers is ischemia due to the arteriolar and small artery changes mentioned earlier.

With relatively large doses of radiation, such as a single dose greater than around 20 Gy, a bullous type, moist desquamation may occur in 3–4 weeks. In this situation, small blisters tend to coalesce and rupture. If the dose is high enough, blisters may be formed from beneath the basal cell layer. At this stage, the clinical lesion may appear very similar to a second or third degree thermal burn, but an important differentiating diagnostic point is that the patient will remember not having been burned. In such circumstances, the bullae may

become infected, and there may also be sloughing of the epidermis. A week or two after sloughing of the epidermis, the affected areas may become recovered with epidermis, although ulcers tend to recur with later arteriolar obliterative changes. In patients who have developed late radiation ulcers following fractionated radiotherapy with doses of 40–120 Gy (4000–12 000 cGy), there is a reduction in circulation that can be measured by radionuclide techniques. Venous and lymphatic vessel occlusion with swelling of an extremity have also been reported.

Skin tolerance to radiation depends significantly on the volume of tissue irradiated. As the volume of skin irradiated becomes smaller, the dose required to cause necrosis increases. For example, the skin tolerance dose for a circular field of 150 cm^2 is approximately 15 Gy (1500 cGy) in a single dose, whereas for a circular field of 50 cm^2 the tolerance dose is almost 20 Gy (2000 cGy). For fractionated radiotherapy situations, the skin tolerance dose is about 50 Gy for a skin area of 100 cm^2, 58 Gy for 16 cm^2 and 84 Gy for 4 cm^2.

Occasionally, there are rare atypical skin reactions to radiotherapy that resemble erythema multiforme, pemphigus and other diseases. Such reactions can begin in the irradiated area but then become more generalized. One of the confounding factors in the evaluation of overexposed persons is additional treatment which could change the reaction to radiation, such as prior or subsequent surgery or chemotherapy. All five patients in this accident had undergone prior surgery that had left a scar in the irradiated field. The adverse effects for these patients may thus have been much greater in the scar area. Radiation therapy can also exacerbate existing conditions such as psoriasis.

I.2.2. Effects on breast tissue

The effects of radiation on breast tissue following radiation therapy have been well described. In general, breast tissue is quite resistant to radiation, with the major changes occurring in the skin, although ultimately atrophy of the gland may occur. The changes that occur vary somewhat with the type of radiation used. With orthovoltage X radiation sources, the surface skin reactions are more prominent, whereas with megavoltage radiation and interstitial implants, deep induration is possible.

In terms of the adverse effects that might be expected following certain doses, there have been reports of late complications arising in patients who received 60 Gy over 8 weeks, followed by a boost raising the dose to between 70 Gy and 110 Gy. In this circumstance, somewhat more than 10% of the patients developed severe fibrosis. Other changes were also identified, including induration, atrophy, retraction of the nipple and telangiectasia. Ulceration was seen in less than 20% of the patients. Late histopathological

changes included dense fibrosis, non-specific vascular changes, fat necrosis, and the appearance of some atypical fibroblasts and arterioles that exhibit myointimal proliferation. Dysplastic changes and fat necrosis occurring after therapeutic irradiation can easily be confused with true neoplastic changes.

I.2.3. Effects on the lung

In this accident, the lung reaction was limited primarily to the penetrating ^{60}Co radiation therapy delivered to the sternal area. The effect of the 8 MeV electrons would be limited to the lung tissue and pleura immediately adjacent to the irradiated chest wall. The literature available relates predominantly to photon, rather than electron beam, radiation. The lung is a relatively radiosensitive organ. The radiosensitivity of the lung is a limiting factor in total body radiotherapy used for treatment of diffuse metastases and prior to bone marrow transplantation. In single dose treatment, 8 Gy of penetrating radiation is the accepted maximum because single doses of more than 7–8 Gy may produce radiation pneumonitis in some individuals.

The major changes which might occur following fractionated pulmonary radiation therapy are radiation pneumonitis and subsequent pulmonary fibrosis. The exact mechanism responsible for radiation pneumonitis is unclear, but it does involve loss of some of the epithelial cells, exudation of fluid in the alveolar space and subsequent thickening of the alveolar walls.

Radiation pneumonitis is very infrequent, but in those cases where it does occur it characteristically appears 1–4 months after the cessation of conventional radiotherapy. It is characterized by dry cough, râles, dyspnoea and fever. If both lungs are involved, severe respiratory distress, cyanosis, cor pulmonale, and even death from cardiorespiratory failure may occur. The diagnosis is usually made on the basis of radiographic findings of pneumonitis limited to the field of X ray therapy. Pleural effusions may occur, but they are uncommon. Time, dose and volume aspects are of particular importance in the development of clinical radiation pneumonitis. On the basis of several studies, a clinical threshold of 6–7 Gy for single doses has been suggested for the development of acute pneumonitis. A single dose of 8 Gy to both lungs will cause pneumonitis in about 30% of patients, rising to about 85% after 10 Gy. Five per cent of patients who receive a dose of 26 Gy in 20 fractions over 4 weeks to both lungs would be expected to develop pneumonitis. Similarly, 5% of patients receiving a total dose of 20 Gy in 10 fractions over 2–4 weeks are likely to develop pneumonitis. As the dose is increased to 30 Gy in 20 fractions over 4 weeks to both lungs, around 50% of patients will develop pneumonitis, and all patients receiving 30 Gy over 2 weeks in 10 fractions to one lung will develop pneumonitis. Clinical radiation pneumonitis is represented

pathologically by atypical epithelial cells and by congested capillaries and hyaline membrane formation lining the alveolar spaces. In addition, there are mononuclear infiltrates in the alveolar septa.

The radiological manifestation of radiation pneumonitis consists of a hazy alveolar infiltrate corresponding to the shape of the radiation port. As the later fibrotic stage progresses, atelectasis, pleural reaction, volume loss and even calcified plaques may be identified. Radiographic changes characteristic of pneumonitis are rare for a dose of less than 30 Gy in 3 weeks but are common when the dose exceeds 40 Gy in 4 weeks. Fibrotic changes are detectable if the dose exceeds 60 Gy delivered over 6 weeks.

In general, more changes are seen on CT images than on standard chest radiographs. Homogeneous or patchy areas of lung opacification and volume loss are the principal findings. The abnormalities are usually, but not always, confined to the radiation fields and are seen in about 80–90% of patients within 16 weeks of ending fractionated radiotherapy to the lung, although they may be seen as early as 2–4 weeks. At later times fibrosis may be detected.

I.2.4. Effects on the heart

The myocardium is composed of striated muscle fibres that essentially possess no regenerative capability. They are classified as fixed post-mitotic cells and are thus very resistant to the direct effects of radiation. The myocardium itself appears capable of withstanding fractionated radiotherapy doses as high as 100 Gy without obvious clinical or microscopic changes being identified. Late effects of radiotherapy on the cardiovascular system include cardiomyopathy, coronary artery disease, pericardial effusions and constrictive pericarditis. In one case of accidental exposure to an ^{192}Ir radiography source, there was localized myocardial damage. In that case, the absorbed dose to the myocardium was not calculated. However, the dose was high enough to cause necrosis of the overlying skin, soft tissue and rib.

Overall, data suggest that 40 Gy given in 2 Gy doses can be considered a threshold dose for clinical cardiomyopathy in both adults and children. Several commonly used drugs, including the anthracyclines (Doxorubicin and Daunomycin), not only induce cardiomyopathy by themselves but also enhance toxicity when combined with mediastinal irradiation.

Radiation-induced heart disease has been demonstrated in patients who have undergone mediastinal irradiation for treatment of Hodgkin's disease. The changes most commonly involve the pericardium rather than the heart muscle (myocardium). The changes seen in the pericardium include pericardial effusion, fibrosis and, possibly, subsequent constrictive pericarditis. Pericardial or myocardial disease has been observed in 6–7% of patients who have

received a mean fractionated total dose of 43 Gy to a large volume of the heart. Administration of 40 Gy in 16 fractions over 4 weeks has been reported to result in pericarditis in about 5% of patients. Patients being treated for Hodgkin's disease demonstrate a high incidence of complications when the total dose exceeds 60 Gy.

The acute form of presentation includes pleuritic chest pain, pericardial friction rub and fever. Pericardial effusion may cause tamponade in some cases. Recently, it has been noted that a large number of asymptomatic young patients having undergone mediastinal irradiation for treatment of Hodgkin's disease have developed pericardial effusions, decreased left ventricular reserve and decreased size of the left ventricular cavity. Long term clinical follow-up of these patients may show progression of the subclinical injury to a symptomatic stage. In another study, careful evaluation demonstrated occult or overt cardiac disease in nearly all patients treated for Hodgkin's disease with radiotherapy. The most common finding was constrictive pericarditis.

In patients that underwent mediastinal irradiation for treatment of Hodgkin's, after 10 years there was a 10% incidence of pericarditis and a 4% incidence of myocardial infarction. The incidence of pericarditis was significantly higher with total doses of 41 Gy or more. In the same group, examination of myocardial perfusion using nuclear medicine techniques 3–11 years after mediastinal irradiation for Hodgkin's disease revealed abnormalities in about 70% of asymptomatic patients treated. Fraction size was important, and 3 fractions of 3.3 Gy per week resulted in a 9% incidence of pericarditis compared with zero per cent when 4 fractions of 2.5 Gy per week were administered. Doses in excess of 35 Gy have induced a thickening of the pericardium and some interstitial myocardial fibrosis. There was epicardial coronary artery narrowing in almost half of the patients.

I.2.5. Effects on bone, cartilage and muscle

Adult bone is relatively resistant to the effects of irradiation, with any effects generally attributable to decreased blood flow. Actual necrosis of the bone is quite rare, and fractionated therapeutic doses up to 65 Gy given over 6–8 weeks normally do not cause bone necrosis. Bone is extremely dense and the absorbed radiation dose in bone varies markedly, depending upon the energy of the incident radiation. Thus, it is difficult to ascertain the precise bone dose necessary to produce necrosis since dose levels reported in the literature may be inaccurate.

The changes in adult bone demonstrated as being due to irradiation usually include a decreased capability to resist infection and an increased susceptibility to fracturing, with poor subsequent healing. The incidence of

spontaneous rib fracturing after post-mastectomy irradiation has been reported to be around 6% using a standard 2 Gy dose fraction, increasing to 20% with higher doses per fraction.

With mature bone, the direct effects of radiation are not apparent for some time. Some of the earliest changes following radiotherapy are detected as areas of decreased radioactivity measured on radionuclide bone scans. Such areas do not appear with a total fractionated dose of less than 20 Gy but they do appear in 60% of regions receiving more than 45 Gy. These changes appear 4–6 months after radiotherapy and may persist for up to 19 months. In the case of high doses, there is, pathologically, an absence of osteoblasts and osteocytes, with subsequent arteriolar intimal thickening. The bone is then subject to necrosis and fracture with minimal trauma. The bone becomes demineralized and exhibits an abnormal, coarse, trabecular pattern. The process often resembles Paget's disease. However, the appearance of fractures, lack of bone expansion, localized nature of the injury and clinical history generally exclude this diagnosis. It is sometimes difficult to exclude metastases and infection as causes of the radiographic changes identified.

Direct effects of radiation on muscle are uncommon. Acute radiation necrosis of skeletal muscle requires absorbed doses in excess of 500 Gy. At lower fractionated doses, from 22 Gy to 54 Gy, atrophy of muscle fibres may occur.

Appendix II

HAEMATOLOGICAL DATA FOR THE PATIENTS

TABLE 9. HAEMATOLOGICAL DATA FOR PATIENT 1

		Haematological parameters				
		Leucocytes ($10^3/\mu L$)	Lymphocytes		Erythrocytes ($10^6/\mu L$)	Platelets ($10^3/\mu L$)
			($10^3/\mu L$)	(%)		
Normal range		4.0–10.0	1.5–4.0	20–40	4.2–5.4	150–400
Before chemotherapy		ND*	ND	ND	ND	ND
After chemotherapy		ND	ND	ND	ND	ND
2001.01.17	Before radiotherapy	5.20	2.71	52.1	4.00	288
2001.02.27	Accident					
2001.03.03	4 d after	6.44	1.60	24.9	3.44	240
2001.03.26	3 weeks after	7.43	0.67	9.0	4.29	312
2001.04.03	5 weeks after	4.45	1.01	22.7	4.01	464
2001.06.26	4 months after	5.99	1.17	19.5	4.56	366
2001.09.04	6 months after	5.72	1.58	27.7	4.61	329
2001.10.31	8 months after	5.07	1.58	31.2	4.41	316
2001.12.12	During HBO in Gdynia	4.81	2.04	42.3	4.39	264

* ND = no data

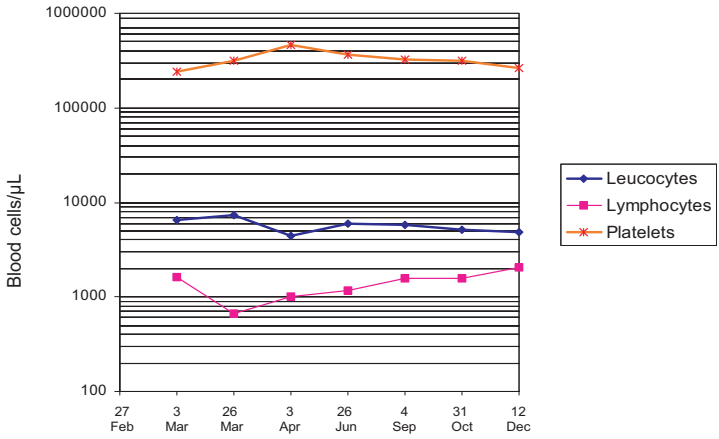

FIG. 34. Haematological chart of Patient 1 after the accident on 27 February 2001.

TABLE 10. HAEMATOLOGICAL DATA FOR PATIENT 2

		Haematological parameters				
		Leucocytes (10^3/μL)	Lymphocytes		Erythrocytes (10^6/μL)	Platelets (10^3/μL)
			(10^3/μL)	(%)		
Normal range		4.0–10.0	1.5–4.0	20–40	4.2–5.4	150–400
Before chemotherapy		ND	ND	ND	ND	ND
After chemotherapy		ND	ND	ND	ND	ND
2001.01.23	Before radiotherapy	5.32	1.31	24.6	3.90	241
2001.02.27	Accident					
2001.03.02	3 d after	3.74	0.35	9.5	4.35	200
2001.03.13	2 weeks after	3.77	0.63	16.7	4.11	164
2001.03.23	24 d after	5.37	1.01	18.7	4.43	249
2001.04.03	5 weeks after	5.73	0.93	16.2	4.49	224
2001.06.01	3 months after	7.24	0.91	12.6	4.32	385
2001.07.25	5 months after	8.21	0.81	9.9	4.51	310
2001.10.31	8 months after	6.02	0.64	10.6	4.50	332
2001.12.12	During HBO in Gdynia	4.95	1.16	23.5	4.43	308

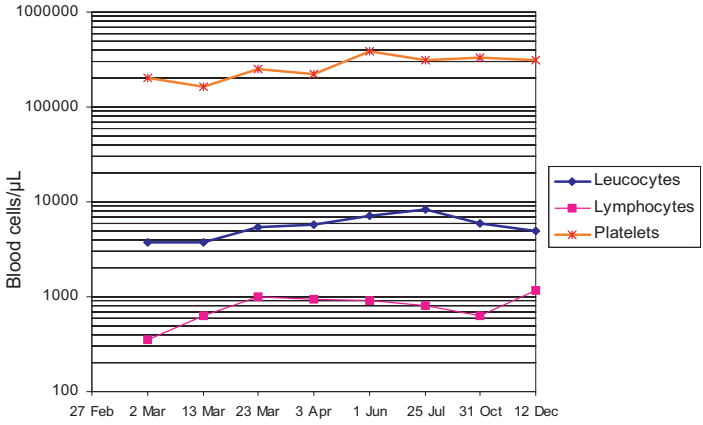

FIG. 35. Haematological chart of Patient 2 after the accident on 27 February 2001.

TABLE 11. HAEMATOLOGICAL DATA FOR PATIENT 3

		Haematological parameters				
		Leucocytes ($10^3/\mu L$)	Lymphocytes		Erythrocytes ($10^6/\mu L$)	Platelets ($10^3/\mu L$)
			($10^3/\mu L$)	(%)		
Normal range		4.0–10.0	1.5–4.0	20–40	4.2–5.4	150–400
Before chemotherapy		ND	ND	ND	ND	ND
After chemotherapy		ND	ND	ND	ND	ND
2001.02.13	Before radiotherapy	1.84	0.87	47.1	3.97	239
2001.02.27	Accident					
2001.03.01	2 d after	2.44	0.25	10.1	4.01	122
2001.03.06	1 week after	5.78	0.60	10.3	4.53	173
2001.03.08	10 d after	6.71	0.78	11.7	4.56	195
2001.03.12	2 weeks after	8.18	0.72	8.8	4.52	196
2001.03.14	16 d after	9.63	0.82	8.6	4.36	203
2001.03.23	24 d after	3.32	0.65	19.6	4.58	159
2001.04.04	5 weeks after	2.46	0.40	16.2	4.46	175
2001.05.07	2 months after	10.1	1.12	11.1	4.49	279
2001.07.23	5 months after	7.56	1.21	16.0	4.55	342
2001.09.07	During rehabilitation in Warsaw	8.10	ND	ND	3.83	302
2001.10.31	8 months after	3.62	0.67	18.6	3.62	334
2001.12.12	During HBO in Gdynia	4.05	1.16	28.6	4.18	344

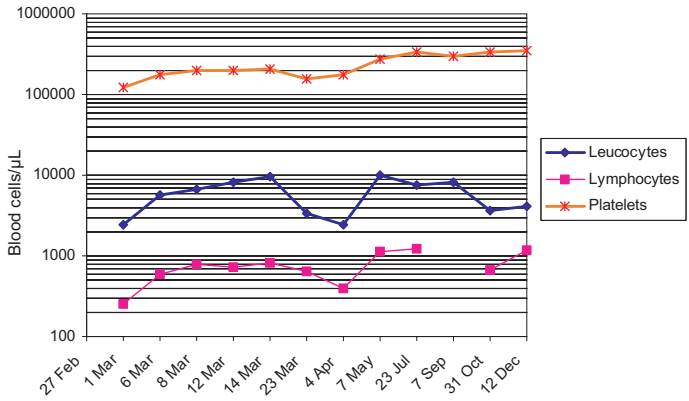

FIG. 36. Haematological chart of Patient 3 after the accident on 27 February 2001.

TABLE 12. HAEMATOLOGICAL DATA FOR PATIENT 4

		Haematological parameters				
		Leucocytes (10^3/μL)	Lymphocytes		Erythrocytes (10^6/μL)	Platelets (10^3/μL)
			(10^3/μL)	(%)		
Normal range		4.0–10.0	1.5–4.0	20–40	4.2–5.4	150–400
2001.10.04	Before chemotherapy	4.45	1.60	36.0	3.96	178
2001.01.04	After chemotherapy	5.58	1.68	30.0	4.42	221
2001.01.30	Before radiotherapy	4.86	1.34	27.5	4.15	170
2001.02.27	Accident					
2001.03.01	2 d after	6.43	0.29	4.5	4.18	113
2001.03.05	1 week after	3.86	0.51	13.1	4.12	133
2001.03.08	10 d after	6.36	0.60	9.5	4.01	166
2001.03.12	2 weeks after	8.19	0.60	7.3	4.00	147
2001.03.26	4 weeks after	4.34	0.60	13.8	3.72	129
2001.04.02	5 weeks after	4.29	0.76	17.7	3.69	165
2001.04.05	5.5 weeks after	4.49	0.68	15.0	3.91	172
2001.06.01	3 months after	7.19	1.03	14.4	4.36	253
2001.08.11	6 months after	4.30	0.75	17.4	4.17	192
2001.10.31	8 months after	6.55	1.20	18.3	4.06	351
2001.11.13	9 months after	10.40	ND	ND	4.68	359

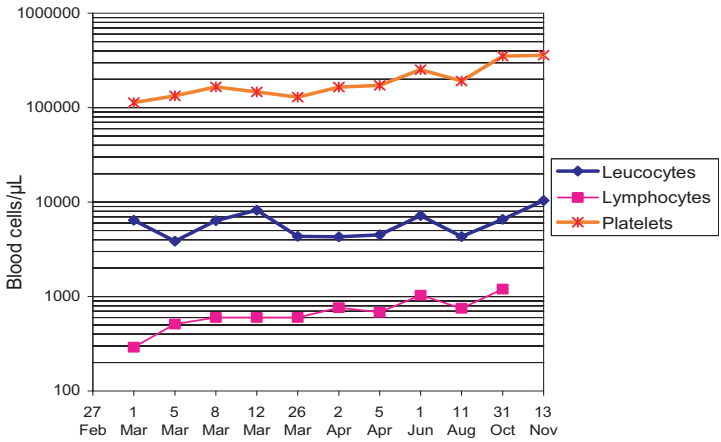

FIG. 37. Haematological chart of Patient 4 after the accident on 27 February 2001.

TABLE 13. HAEMATOLOGICAL DATA FOR PATIENT 5

		Haematological parameters				
		Leucocytes ($10^3/\mu L$)	Lymphocytes		Erythrocytes ($10^6/\mu L$)	Platelets ($10^3/\mu L$)
			($10^3/\mu L$)	(%)		
Normal range		4.0–10.0	1.5–4.0	20–40	4.2–5.4	150–400
2000.12.20	Before chemotherapy	7.05	3.37	47.7	4.99	173
After chemotherapy		ND	ND	ND	ND	ND
2001.02.23	Before radiotherapy	5.27	1.89	35.9	4.23	209
2001.02.27	Accident					
2001.03.03	4 d after	6.86	1.71	24.9	4.42	194
2001.03.06	1 week after	8.75	2.34	26.8	5.03	215
2001.03.12	2 weeks after	5.74	1.40	24.4	4.73	122
2001.03.23	4 weeks after	5.79	2.06	35.6	4.61	194
2001.04.04	6 weeks after	7.53	2.74	36.4	4.87	230
2001.06.01	3 months after	10.00	2.63	26.2	4.81	285
2001.07.24	5 months after	6.84	2.02	29.5	4.13	241
2001.10.31	8 months after	9.07	2.06	22.7	5.12	277
2001.12.12	During HBO in Gdynia	6.85	2.13	31.1	4.68	233

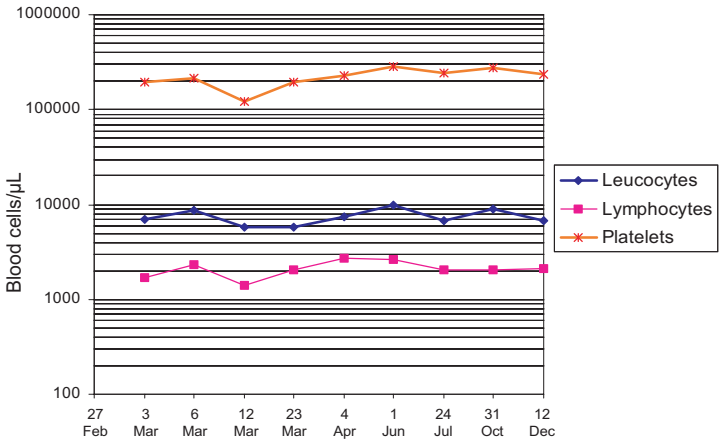

FIG. 38. Haematological chart of Patient 5 after the accident on 27 February 2001.

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