PART II. FINDINGS OF THE EXPERT TEAM

4. ASSESSMENT OF DOSIMETRY, EQUIPMENT AND THE FACILITY

4.1. CALIBRATION OF THE BEAM

The absorbed dose to water from the beam of the Alcyon II Co-60 unit, was determined by the Expert Team, in accordance with IAEA Technical Report Series No. 277, Absorbed Dose Determination in Photon and Electron Beams – An International Code of Practice. Three different ionization chambers were used for these measurements. The values, obtained on 10 July 1997, were corrected for two factors:

1. There was a 10 month decay correction, back to 10 September 1996, in order to reconstruct doses delivered to patients over the period from the end of August to the end of September 1996 (correction factor of 1.115).
2. A distance correction was also made in order to reproduce the conditions of the actual treatments. The reason for this correction is that, according to Ms. Castellanos's report and the report of the early investigations following the accident, there had been an error of –2 cm with the optical distance indicator. This correction from SSD = 80 cm to SSD = 78 cm (e.g. 80.5 cm to 78.5 cm at maximum dose) is 1.053, which includes a small factor of about 0.2% for the increase in beam opening, i.e. the same field size of 10 cm x 10 cm, from a distance of 80 cm to 78 cm.

In addition, the IAEA/WHO TLD postal dose check service was used once more to verify the calibration measurements, which provided agreement within 1.5 % (see Table I.I of Appendix I). The detailed measurements and calculation spreadsheets are given in Table I.II of Appendix I.

Table II here summarizes the results of all the measurements made with the three different ionization chambers in Gy/min.

TABLE II. DOSE RATES FROM THE ALCYON II Co-60 UNIT (Gy/min)

	10 July 1997		Corrected back 10 months for decay		
Ion chamber	D_w(4.82,80,10x10)	D_{max}(0.5,80,10x10)	D_w(4 82,80,10x10)	D_{max}(0.5,80,10x10))	D_{max}(0.5,78,10x10)
PTW30001	1.344	1 687	1.578	1.881	1.980
PTW30002	1.334	1.674	1.566	1.867	1.966
Farmer	1.338	1 680	1.571	1.873	1 972

4.2. CONDITION OF THE ALCYON II CO-60 UNIT

The Alcyon II unit was in good condition, and the geometrical parameters were within acceptable tolerances for treatment of patients. The parameters controlled were (see Table I.III of Appendix I):

- Axial coincidence of the collimator
- Isocentre
- Optical distance indicator
- Coincidence between field size indicator on the collimator and light beam size
- Congruence of the light and/or radiation beam.

Deficiencies in the treatment couch were found in the expert review in July 1996. The couch was replaced at the beginning of 1997, and no deficiencies in the couch were found in the Expert Team's assessment in July 1997. However, the Team detected by touch a leakage of electrical current between the irradiation head and the couch. Electrical safety, e.g. electrical grounding, needs to be verified and ensured according to the International Electrotechnical Commission's standard IEC-601.

4.3. IRRADIATION ROOM

A visual inspection of facility interlocks and signals was performed during the mission. The findings were as follows:

- The red light signals at the entrance to the irradiation room for source on/off were working but the green light had failed. The signals should be larger and more clearly visible.
- The door switch worked when opening the door: the audio alarm switched on and the source returned to the shielded position. However, a signal interlocked with a radiation monitor placed at the end of the maze would be desirable.
- Emergency push buttons causing the source to be moved to the off position worked properly.

4.4. RADIATION SHIELDING

Dose rate measurements were made in different locations outside the irradiation room. From the results obtained, and on the assumption of a normal workload for this room of about 500 Gy/week and a use factor of 30% with the unattenuated beam directed to the ceiling, the radiation levels in

the room above would be 1 Sv/a. This room is occupied by patients staying for extended periods of time, visitors, and the attendant hospital staff. The shielding is not acceptable. In particular, the ceiling of this room was not designed for radiotherapy (see Figure I.1 of Appendix I).

Since the shielding cannot be increased, one solution that would merit a feasibility study would be to exchange the use of this room with the use of the shielded room for the Theratron 80, since the Theratron 80 has a beam stopper with an attenuation factor of about 1000.

4.5. DOSE MONITORING FOR PERSONNEL

Radiotherapy staff wear individual TLD dosimeters that are measured monthly by the Ministry of Health. These records were not reviewed by the Expert Team.

4.6. WRITTEN PROCEDURES

Working procedures for normal conditions were not available. Emergency procedures were not viewable at the time of the Expert Team's assessment.

4.7. PATIENTS' CHARTS AND CLINICAL DOSIMETRY

Status of the charts

A total of 113 patient therapy charts were reviewed, of which nine were from the Children's Hospital, 37 from the Calderón Guardia Hospital and the remaining 67 from the San Juan de Dios Hospital.

The therapy charts were reviewed at San Juan de Dios Hospital and at the law courts. None of those in charge at the time of the accident, including the dosimetrist, the radiation therapist from San Juan de Dios Hospital and the person who performed the initial calculation and calibration, were available for interview to help in reconstructing the charts

The treatment time is transcribed from a purpose written computer program. The name of the person who made the calculation was also on the computer sheets. There was no documentation of how the calculation of the treatment time had been made after the source had been changed: whether by

using a ratio or by using the new measured dose rate. There was also no indication that any review had been made of the treatment time calculation. The back page contained the daily record which had the fraction number, date, session dose and total dose. The doses entered there are the maximum dose per field and the total maximum dose per field. For most patients, single or parallel opposed fields are used and patients were treated at one field per day.

There was no running record of the tumour dose or the time used at each fraction, nor was there any indication of who treated the patient on a given day, or whether portal films[2] had been acquired and when. On a few of the charts, two treatment times were given on the front page: one for the Alcyon and one for the Theratron 80. Since there was no daily record of the time, it is not always possible to know which fractions were done on which machine. There was no indication that a chart review had been done in the course of the therapy. The charts for the Calderón Guardia patients were better documented, with diagrams showing the site of the fields and the blocking. The treatments also appeared more in keeping with better practice. Treatment at two fields per day was more common and many were isocentric.

Aim of the dose reconstruction and assumptions made

Since over 100 charts needed some form of dose reconstruction, it was not possible in the time allotted during the Expert Assessment to reconstruct the maximum and minimum doses to the planning target volume and to relevant points for all patients individually. Furthermore, calibration of the Alcyon by the Expert Team was in progress in the same week. A simplified dose reconstruction was therefore attempted. The prescribed dose, the number of fractions prior to the source change and the number of fractions following changing of the source were extracted from the charts, in addition to other important parameters. The number of fractions following the source change was counted from Monday 26 August 1996. For those charts where a Theratron 80 treatment time had been entered on the front page in addition to the Alcyon treatment time, it was assumed that the Alcyon was used for all treatments since there was no record of when the Theratron 80 had been used. In addition, a prior compilation of the doses after the source change by H. Marenco Zúñiga was also used to obtain other parameters.

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2 Portal films consist of pictures taken to verify the beam orientation to the patient's anatomy and are obtained with X rays (in the case of simulators) or with high energy photons (in the case of treatment machines).

The total tumour dose was reconstructed by adding the prescribed dose multiplied by the number of fractions administered prior to the source change to the estimated dose administered after the source change. The dose administered after the source change was estimated by multiplying the prescribed dose by a factor of 1.55 and by the number of fractions administered.

The factor of 1.55 was derived in the following way:

- a sample of patients was taken;
- the dose rate at d_{max}, for a 10 cm x 10 cm field at 78 cm source–skin distance (SSD) was taken from measurements made and corrected for decay to September 1996; the value was rounded to 2.0 Gy/min, and the distance of 78 cm corresponds to a nominal value of 80 cm in view of the error of 2 cm in the optical distance indicator at the time of the accident;
- the tumour dose was calculated by multiplying the dose rate d_{max} = 2.0 Gy/min by a field size factor and the percentage depth dose (PDD);
- the derived dose at the depth of the tumour was divided by the prescribed dose to obtain the overexposure factor;
- the result for the sample of patients was 1.55; this value was used for all patients to obtain Table I.IV in Appendix I;
- it was assumed that all patients were treated at a nominal SSD of 80 cm, unless otherwise indicated;
- the maximum entrance dose was also calculated in those cases where it was evident that it would pose an unusual problem, for example, if there was only one field, if the prescribed dose was deep inside the patient, if the prescribed dose per treatment was large, if the field size was large or if the patient's tissue reaction indicated it.

In addition to the approach of using a common factor, 1.55, for all patients, a specific calculation was made for a number of selected patients. This calculation, based on individual treatment times (where available) and the measured dose rate (1.97 Gy/min., see Table II), includes doses to organs at risk. These patients represent the greater part of the cases described in Section 5 on the medical effects. The values are presented in Table I.V of Appendix I.

In order to assess how the dose per fraction, being higher than normal, might influence the late (chronic) effects, the biologically effective dose (BED) [13–15] has been calculated for a small sample of patients (see Table I.VI of Appendix I) using the linear–quadratic (LQ) model for cell killing. The BED was then used to derive the dose that would be biologically equivalent had it been delivered in fractions of 2 Gy. As one example, for patient No. 54, who received approximately 52 Gy to the spinal cord in 15 fractions of 3.5 Gy each, this treatment is calculated to be biologically equivalent to a total dose of about 71 Gy, delivered in 36 fractions of about 2 Gy. This is especially relevant when comparing with tissue tolerance doses.

The following α/β ratios were used with the LQ model:

2 Gy for CNS

3 Gy for skin

5 Gy for bowel.

The key for the headings of Table I.IV, I.V and I.VI of Appendix I is as follows:

Dd	Deceased
FS	Field size
Pd	Prescribed dose per fraction
d	Dose per fraction
d<	Dose per fraction prior to source change
d>	Dose per fraction after source change
EqFS	Equivalent square of a field
FSF	Field size factor
D<	Total tumour dose before source change
D>	Total tumour dose after source change
D	Grand total dose
d_{max}	Dose per fraction at maximum dose depth
Dmax	Total dose at maximum dose depth (0.5 cm)
D(2.0)	Total dose given in fractions of 2.0 Gy that would be biologically equivalent to D.

5. MEDICAL EFFECTS OF RADIATION EXPOSURE OF THE PATIENTS

The Expert Assessment included the examination of 70 of the 73 surviving patients and a review of the information that was available on patients who had died over the previous nine months. The specific results of the examinations and review can be found in Appendix II. Each patient was examined by at least two and usually three physicians from the Expert Team, and a Costa Rican physician was present at each examination. The findings for all patients presented in this report represent a review and consensus conclusions by all the physicians. The conclusions were arrived at independently of the findings reached during investigations by PAHO, which were not made available to the Expert Team until after the assessment. Available autopsy results were also reviewed by all physicians.

On the basis of the temporal characterization of the physical effects of radiation exposure at the high levels used in radiotherapy as *acute* (first appearing within six months of exposure), *subacute* (first seen between six and 12 months following exposure) and *chronic* (first appearing 12 months or more after exposure), the effects observed in the surviving patients irradiated in the accident were predominantly subacute and chronic.

Many of the overexposed patients initially displayed reactions such as skin ulceration, severe mucositis, nausea, vomiting and diarrhoea. The nature of these acute effects initially manifested depended upon the part of the body irradiated. Many of these acute effects have healed, although some have persisted.

In general, the effects in the patients observed by the Team and those which are anticipated result from overexposure of specific sensitive tissues or a diminution in vascular blood supply. (Most chronic effects of radiation exposure are consequences of an irreversible narrowing of lumina of small blood vessels (arterioles): the thickness of the arteriolar walls is increased, thereby diminishing the size of the lumina and reducing vascular supply. As a result, tissues can become thin or atrophic and, if the diminution of blood supply is severe, the tissues become necrotic. The vascular changes may be progressive and may continue for years after the radiation exposure.) It should therefore be clear that effects will occur in these patients which are not yet apparent. However, future effects could be predicted to some extent if the conditions of exposure were better known.

The assessment of all the patients was complicated by a number of factors. One major task was differentiating adverse radiation effects from effects caused by malignant disease. Determining radiation effects can often be accomplished with the knowledge of the radiation sensitivity of tissues, the time course of expression of radiation effects and the known radiation dose, fractionation scheme, radiation location and field size. While chemotherapy can cause some potentiation of radiation effects, few of these patients were undergoing chemotherapy concurrently.

As stated in Section 1, the effect of radiotherapy treatment in killing normal cells can be minimized by the use of multiple radiation fields and fractionation of the radiation treatment in order to maintain the percentage of severe complications at a level considered acceptable. If the total dose is increased above the normal level, more cells will be killed. Also, if the number of fractions is reduced and the dose per fraction is increased correspondingly, even though the total dose stays the same, more cells will be killed. Both of these circumstances obtained in this accident. For many tissues, reducing the number of fractions and increasing the dose per fraction will cause a disproportionate increase in chronic effects in comparison with acute effects. Under these circumstances, relying on acute effects for the prediction of late effects will result in underestimation of the actual extent of the effects.

In the situation under consideration, the Expert Team noted differences in the radiation therapy practices and protocols for the same disease. Some of the protocols involved very large fields with treatment of each field every other day. More than half of the prescribed radiation therapy treatments had fewer than the normally accepted number of fractions. These practices undoubtedly aggravated some of the adverse radiation effects.

The current and critical physical problems due to the overexposure of these patients relate to several specific body systems: first, the central nervous system; second, the skin; third the gastrointestinal system; and fourth, the cardiovascular system. These systems are of critical importance in this accident both because of their tissue sensitivity to radiation and because the tumours being treated were generally head and neck, mediastinal or pelvic in origin. Even though the Expert Team singled out these categories for special attention, many other effects may develop in these patients in the future as a consequence of radiation exposure. Each patient involved in this accident had very different risk

factors and therefore needs to be evaluated individually using at least the data in the Appendices and their medical records presenting symptomatology and clinical evolution.

The Expert Team's examination represents an evaluation of the patient population at only one point in time. Any compensation and medical care should not be based solely upon this report since patients suffered acute effects and some died before this investigation. Similarly, many patients may develop adverse effects which are not yet apparent.

5.1. CENTRAL NERVOUS SYSTEM

Several patients already experienced difficulties, or may be expected to in the future, as a result of irradiation of the brain, spinal cord and peripheral nerves.

Generally, radiotherapy of the brain results in cortical atrophy in a large number of cases [16]. For children who have received 20–65 Gy (with fractions of less than 2 Gy per day), over half will develop cortical atrophy, 26% will have white matter changes (leukoencephalopathy) (Image 1) and 8% will have calcifications. Atrophy appears to be worse the younger the age of the child at irradiation. Some patients will also develop mineralizing microangiopathy (Image 2). Clinical findings after routine radiotherapy may relate to poor school performance and dysfunction of the pituitary gland and hypothalamus. If there is overexposure, adverse effects may be severe and can include lethargy, ataxia, spasticity and progressive dementia (Image 3). Radiation induced changes of the brain are potentiated by methotrexate and other chemotherapy administered before, during or after radiotherapy.

Cerebral necrosis is a serious and irreversible complication of radiation induced vascular disease. It is usually diagnosed one to five years after irradiation but can occur up to a decade later. Radiation induced necrosis occurs with a moderate probability when therapy schemes exceed 40 Gy in 10 fractions, 50 Gy in 20 fractions, 60 Gy in 30 fractions over a period of five weeks or when individual fractions exceed 3 Gy. There is a very high probability of necrosis when treatment schemes exceed 50 Gy in 15 fractions, 60 Gy in 20 fractions or 70 Gy in 30 fractions. Brain necrosis may be manifested by headache, increased intracranial pressure, seizures, sensory deficits and psychotic changes.

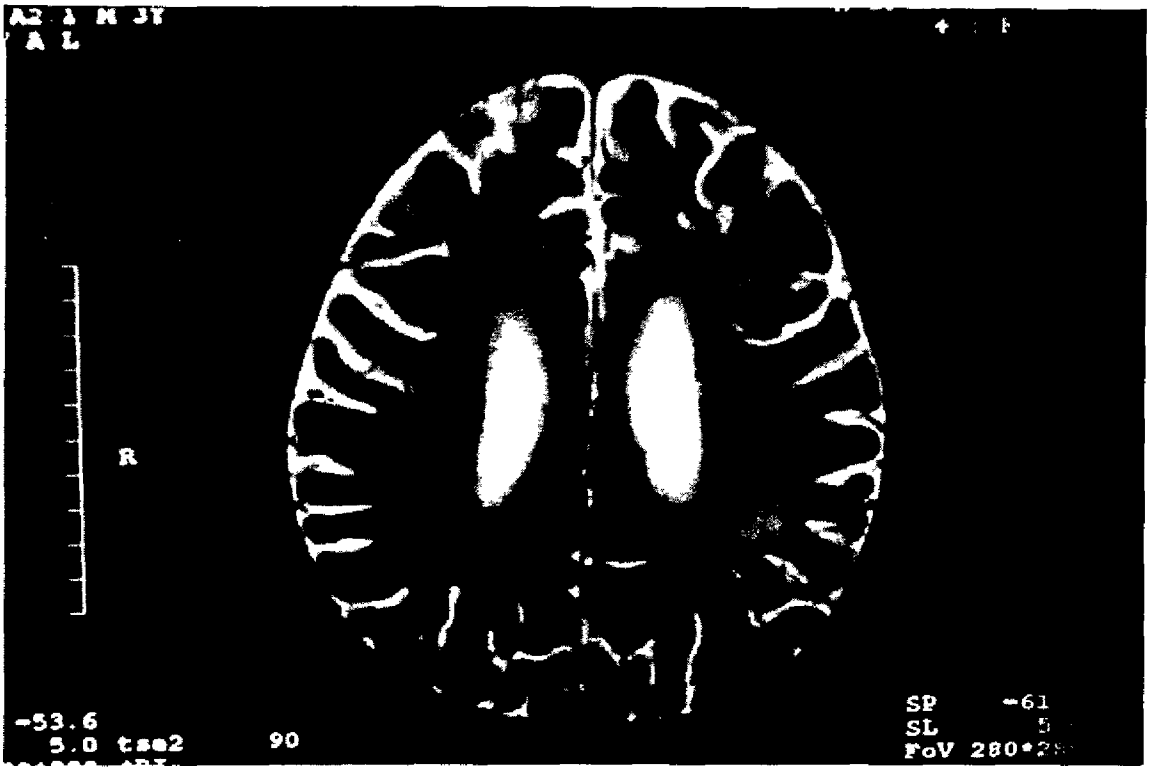

Image 1. A T_2 weighted nuclear magnetic resonance (NMR) scan of the brain shows characteristic white matter changes of leukoencephalopathy.

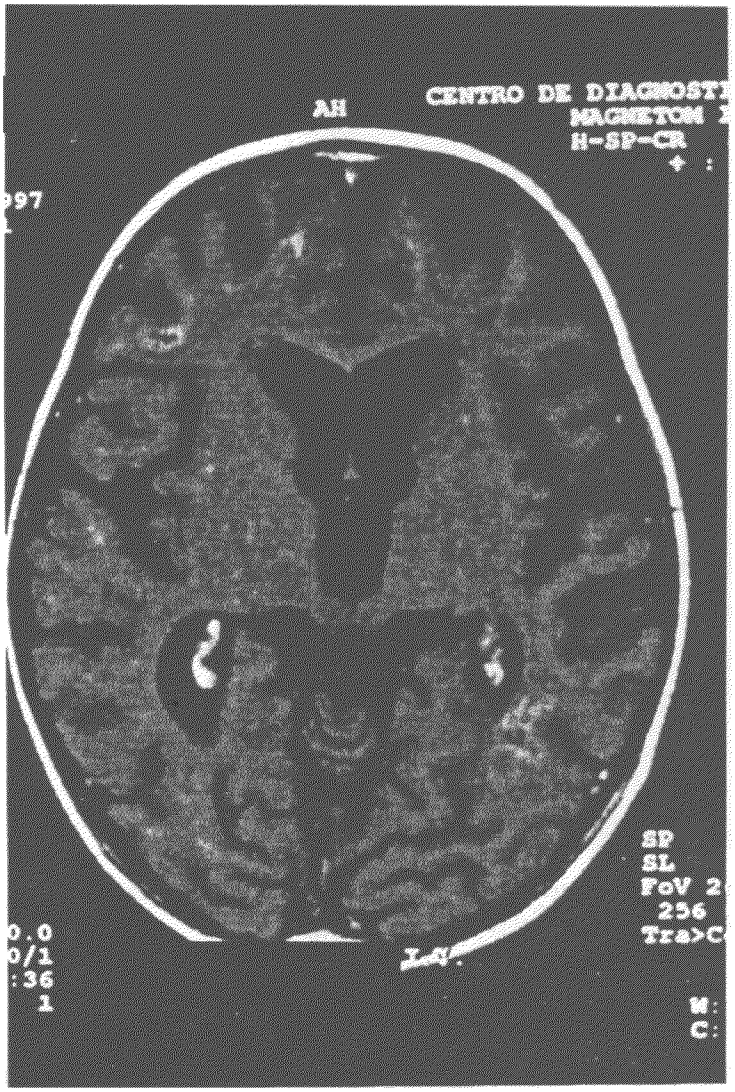

Image 2. A T_1 weighted NMR scan shows cortical changes of microangiopathy (white areas at top left and bottom right), cortical atrophy and ventricular enlargement.