TOTAL BODY IRRADIATION

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Topics

- *Clinical indications*
- *Irradiation techniques*
- *Basic dosimetry*
- *In vivo dosimetry*
- *Trieste experience*

Clinical indications

The scope of the haematopoietic stem cells transplant

- The transplant replaces the patient's diseased bone marrow with stem cells from a healthy donor (***allogenic transplant***) or from the patient himself (***autologous transplant***);
- Donor stem cells reconstitute the recipient's haematopoietic and immune systems ;
- The ***pre-transplant protocol*** or ***conditioning regimen*** aims at eradicating the patient's hematopoietic pluripotent stem cells by combining different chemotherapy agents or chemo and radio-therapy in a regimen that includes Total Body Irradiation (TBI) or High Total Body Irradiation (HTBI).

Clinical indications

The role of TBI in the pre-transplant protocol :

- ***Cyto-ablative scope***: residual neoplastic eradication;

- ***Immunosuppressive scope***: induction of immuno-suppression to reduce the GVDH (Graft-versus-host disease), a complication that can occur after a stem cell or bone marrow transplant in which the newly transplanted donor cells attack the transplant recipient's body;

- ***Myelo-ablative scope:*** eradicate the patient's hematopoietic system to allow repopulation.

Clinical indications

Certain indications: ***Leukaemias in adults and childhood***

- ✓ Acute lymphoblastic leukaemia (ALL),
- ✓ Acute myeloid leukaemia (AML),
- ✓ Chronic myeloid leukaemia (CML),
- ✓ Myelodysplastic syndrom (MDS).

Optional indications: ***Solid tumors in childhood***

- ✓ Neuroblastomas,
- ✓ Ewing sarcomas,
- ✓ Plasmocytomas / multiple myelomas.

In clinical test:

- ✓ Morbus Hodgkin's disease (MHD)
- ✓ Non-Hodgkin's lymphomas (NHL).

Clinical indications

TBI applications in haematology and oncology :

a) myeloablative TBI :

supra-lethal doses of RT (7-15.75 Gy) is administered in association with one or more chemotherapy drugs to condition patients with haematological malignancies to autologous or allogeneic bone marrow or peripheral blood stem cell transplant ;

b) non-myeloablative TBI:

low-dose TBI (≤2 Gy) is administered in one session, in conditioning regimens for allogeneic transplants in elderly patients (> 55 yrs) or in patients who had already received transplants without supra-lethal radiotherapy in the conditioning regimen ;

c) *low dose cytoablative TBI*:

low-dose (1-1.5 Gy) TBI, fractionated into 10-15 cGy/day, is administered 2-3 times weekly to control low-grade non-Hodgkin's lymphoma or chronic lymphoid leukemia

Clinical indications

Scheduling:

One fraction

- *Non - myeloablative TBI*
- Myeloablative TBI (8Gy) for allogenic HCT

More fractions:

- *2Gy x 2/die x 3 days (Seattle protocol)*
- *3.3 Gy x 3 days*
- *3.8 Gy x 3 days*
- *others*

Clinical indications

Recording and reporting

For TBI therapy, as for all radiation treatment, the patient's clinical details and case history must be recorded, together with early and late adverse side effects.

Clinical chart

Demographic data;

Clinical history, diagnosis and disease stage;

Purpose of the radiation treatment:

- myeloablative TBI
- non-myeloablative TBI
- low-dose cytoablative TBI

Type of transplant;

Associated chemotherapy;

Acute toxicity.

Clinical indications

Dosimetric chart

Type of treatment Unit:

- beam energy
- nominal dose rate
- source-skin distance or source-axis distance

Patient's position:

- supports for supine, prone, seated, half seated, standing positions
- limb positions (raised, flexed, etc.)
- position in relation to beam incidence (antero-posterior; postero-anterio; latero-lateral)

Patient's data (thickness):

- head
- neck
- Chest
- abdomen

Clinical indications

Dosimetric chart

Dose:

- Dose point prescrition and Total Dose
- Fractionation; Dose per fraction
- Actual Dose Rate in TBI position

Dose Homogeneity at:

- chest
- abdomen
- lower limbs

Dose to organs at risk (OAR):

- lungs
- lens of the eyes (recommended)
- kidneys (recommended)
- gonads (recommended)

In vivo dosimetry:

- systems and uncertainty.

Clinical indications

Sub-acute and late toxicity: evaluation criteria

As more and more patients survive for longer after allogeneic or autologous transplantation clinical interest is starting to focus on mid- (sub-acute) and long-term (chronic) complications.
Factors in the onset of **sub-acute** and **chronic toxicity** after hematopoietic stem cell transplantation are:

Pre-transplant factors:

- ✓ age of recipient
- ✓ previous or concomitant disease
- ✓ brain or lung radiotherapy
- ✓ intrathecal metotrexate

Transplant factors:

- ✓ **TBI**
- ✓ chemotherapy
- ✓ number of infused hemopoietic stem cells

Post-transplant factors:

- ✓ immunosuppressive therapy
- ✓ infections (cytomegalovirus, aspergillosis, etc.)
- ✓ GvHD
- ✓ steroid therapy
- ✓ antibiotic therapy

Clinical indications

most frequent side effects of myeloablative conditioning with TBI in transplant patients

Table 2. Most frequent sub-acute and late side effects after myeloablative TBI-based conditioning: incidence and tests

Effect	Incidence	Tests
Renal failure (hemolytic/uremic syndrome, acute tubular necrosis, acute nephropathy)	5-15%	renal function tests
Interstitial pneumonia	5-15%	Chest diagnostic tests
Cataract	4-22%	Ophthalmologic examination
Impaired Growth	40-90%	Growth hormone (GH)
Delayed puberty	40-60%	Testosterone-estradiol
Permanent amenorrhoea	90%	FSH-LH-gonad function
Male sterility	95%	Testosterone/spermiogram
Veno-occlusive disease of the liver	< 5%	Liver function
Cognitive deficits	< 20%	Neuropsychological tests
Neurological toxicity	< 5%	MRI/CT
Hypothyroidism		TSH-T3-T4
Covert	25-43%	
Overt	3-13%	

Clinical indications

Final consideration:

- Experience over the last twenty years has demonstrated that ***fractionated and hyperfractioned TBI*** are associated with a lower incidence of side effects than STBI (8-10 Gy) at a high dose rate.
- The ***probability of severe radiotherapy-induced toxicity and fatality*** is reduced after TBI fractioned into one or more sessions a day.
- ***The use of compensators*** for the lung, brain, and eyeballs is also a parameter to control the apparition of some collateral effects like interstitial pneumonia, cognitive functions deterioration and cataract.
- ***A total dose of TBI above 10 Gy*** has been correlated with a higher incidence of secondary tumors (*relative risk of second tumors*: 0.9 with dose <10 Gy *vs* 1.9 with dose >12 Gy and 4.1 with dose >13 Gy)

Clinical indications

Bibliography

The British Journal of Radiology, 70 (1997), 1204–1207

Review article

The radiobiological basis of total body irradiation

T E WHELDON

Departments of Radiation Oncology and Clinical Physics, CRC Beatson Laboratories and Beatson Oncology Centre, Glasgow G61 1BD, UK

StrahlentherOnkol. 2006 Nov;182(11):672-9.

Biologically effective dose in total-body irradiation and hematopoietic stem cell transplantation.

Kal HB, Loes van Kempen-HarteveldM, Heijenbrok-Kal MH, Struikmans H.

Irradiation techniques

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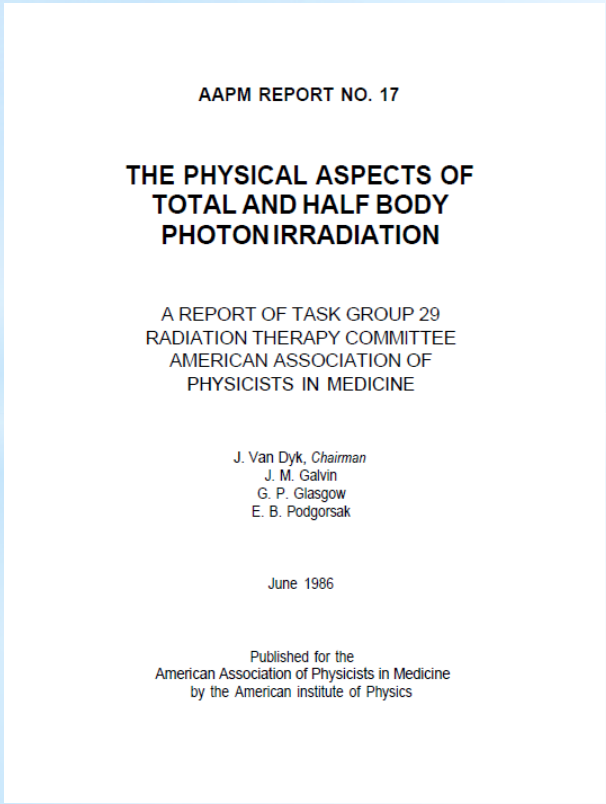

AAPM REPORT NO. 17

THE PHYSICAL ASPECTS OF TOTAL AND HALF BODY PHOTON IRRADIATION

A REPORT OF TASK GROUP 29
RADIATION THERAPY COMMITTEE
AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE

J. Van Dyk, *Chairman*
J. M. Galvin
G. P. Glasgow
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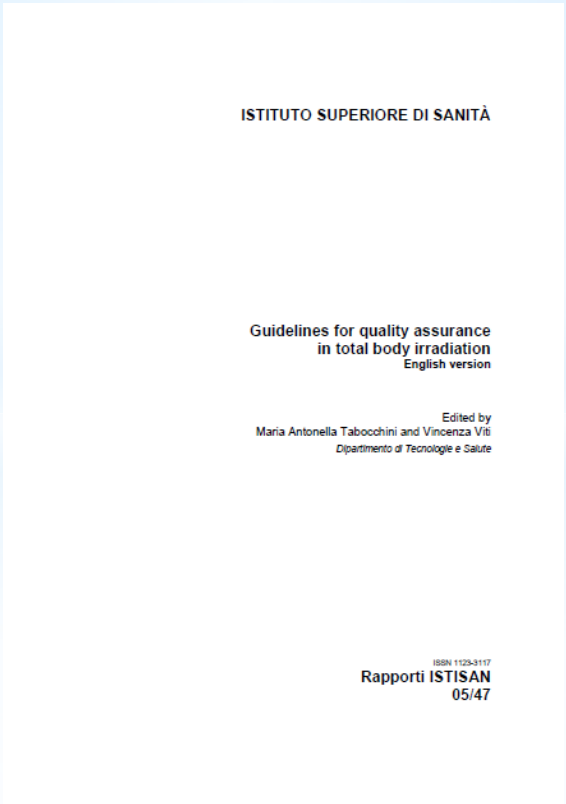

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Guidelines for quality assurance in total body irradiation
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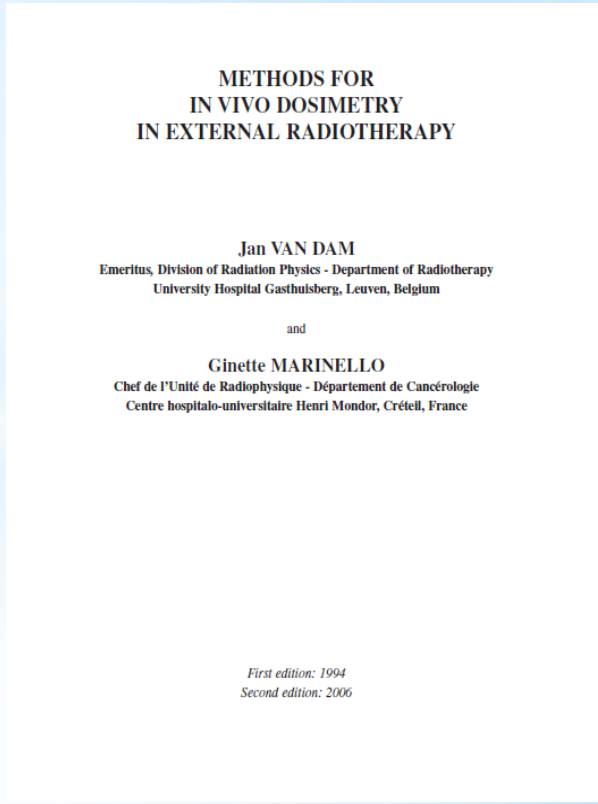

METHODS FOR
IN VIVO DOSIMETRY
IN EXTERNAL RADIOTHERAPY

Jan VAN DAM
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University Hospital Gasthuisberg, Leuven, Belgium

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Centre hospitalo-universitaire Henri Mondor, Créteil, France

First edition: 1994
Second edition: 2006

Irradiation techniques

Technical aspects: **Set-Up**

It should be as simple, reproducible and comfortable for the patient as possible in order to:

- ***guarantee delivery*** of every single fraction of treatment without interruption;
- ***reduce the time*** for patient positioning particularly when TBI is part of the daily routine work;
- ***standardize procedures*** of medical, physical, technical and nursing staff;
- ***guarantee accuracy of dose distribution***.

Irradiation techniques

Technical aspects:

- Radiotherapy Unit and Bunker size
- Beam incidence
- Patient supports
- Partial transmission shield placement
- Check system for shield placement
- *In vivo* dosimetry
- Check system for *In vivo* dosimetry

J Med Phys. 2006 Jan;31(1):5-12.

Whole body radiotherapy: A TBI-guideline. Quast U.

Irradiation techniques

Technical aspects: Radiotherapy Unit and Bunker size

General considerations (AAPM REPORT NO. 17)

1) the higher the energy, the lower the dose variation (excluding the the effects of the build-up region and tissue inhomogeneities).

2) the larger the treatment distance, the lower the dose variation.

3) the larger the patient diameter, the larger the dose variation.

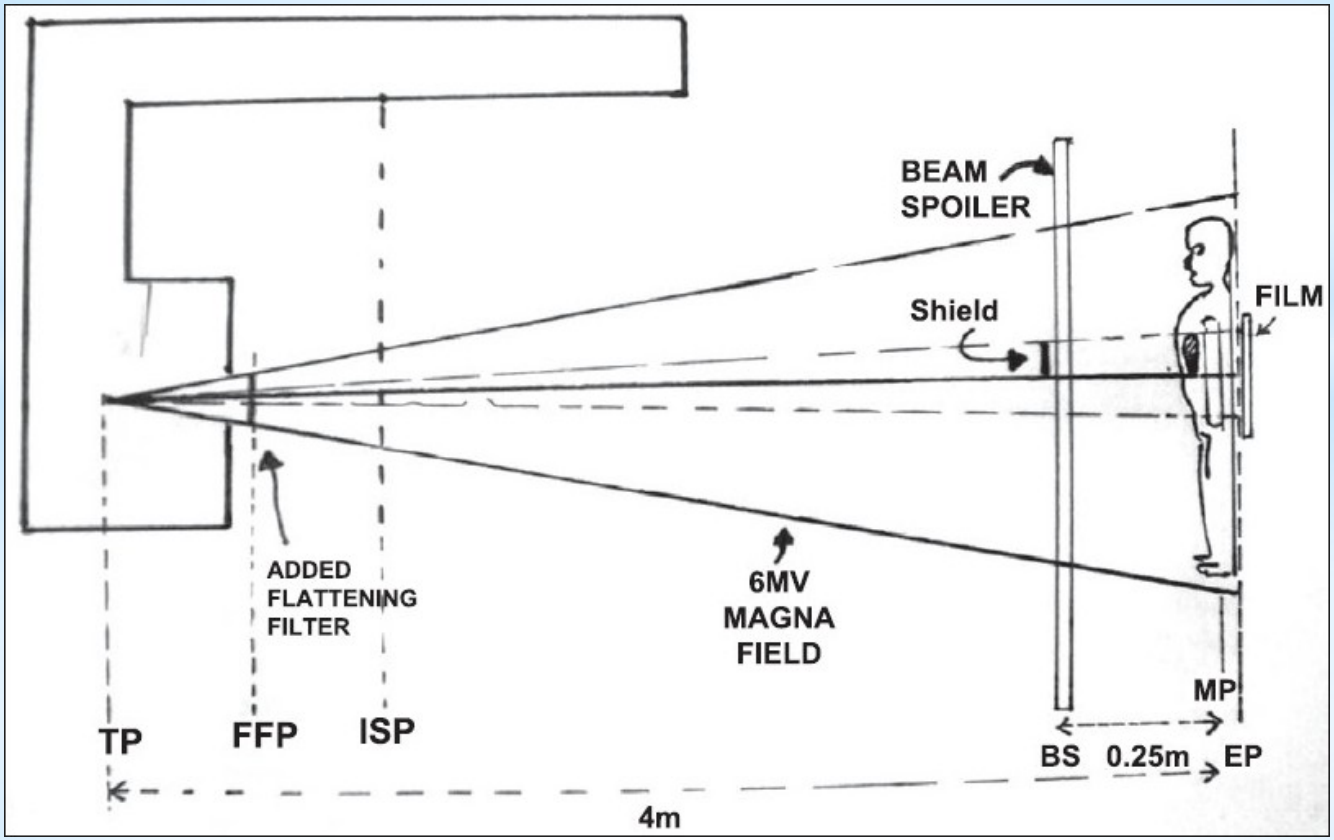
4) AP/PA treatments will yield a variation not larger than 15% for most megavoltage energies and distances.

5) Lateral opposed beams will usually give a greater dose variation compared to AP/PA treatments especially for adult patients.

For pediatric cases or higher energy x-ray beams, a ±15% uniformity might be achievable with bilateral fields.

Irradiation techniques

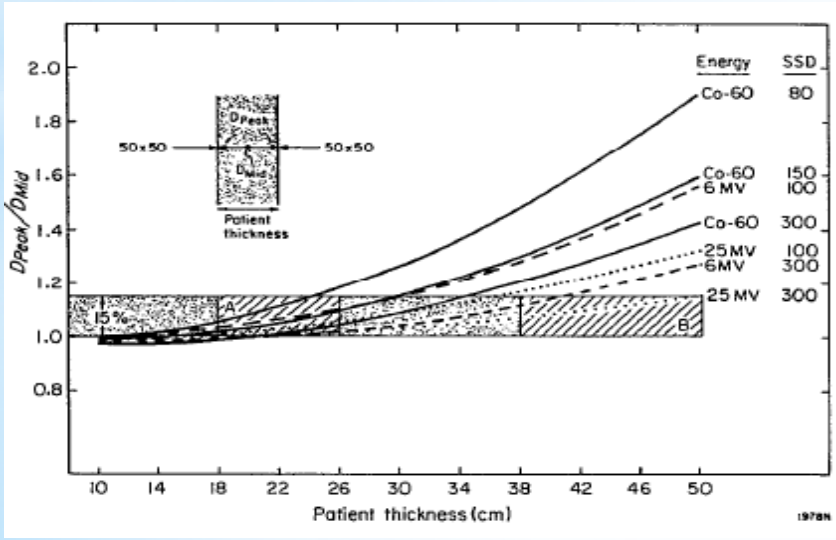
Technical aspects: Radiotherapy Unit and Bunker size



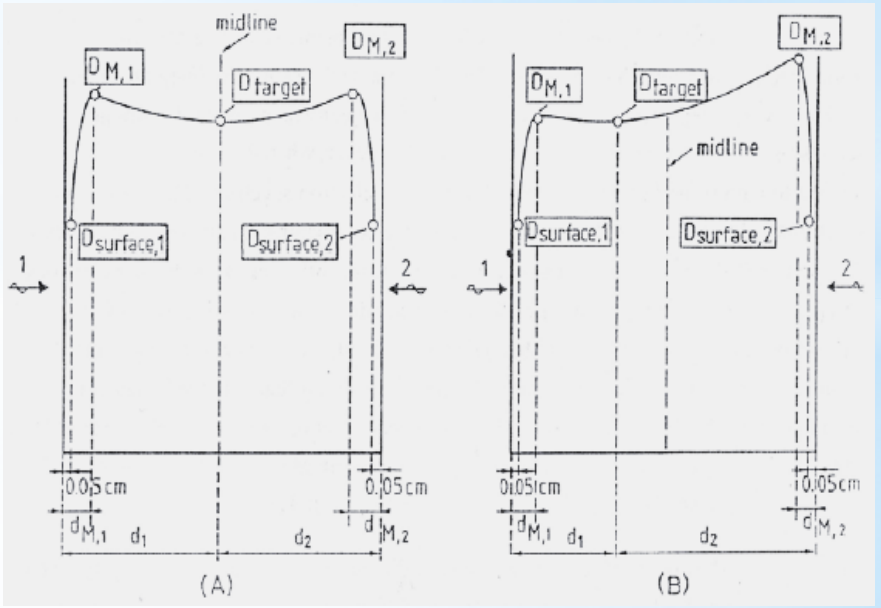
Irradiation techniques

Technical aspects: Radiotherapy Unit and Bunker size

- 4-15 MV photon beams is recommended:
  good homogeneity in the absorbed dose distribution for the different geometries of radiation



Ratio of peak dose to midplane dose on the central ray versus patient thickness. AAPM REPORT NO. 17

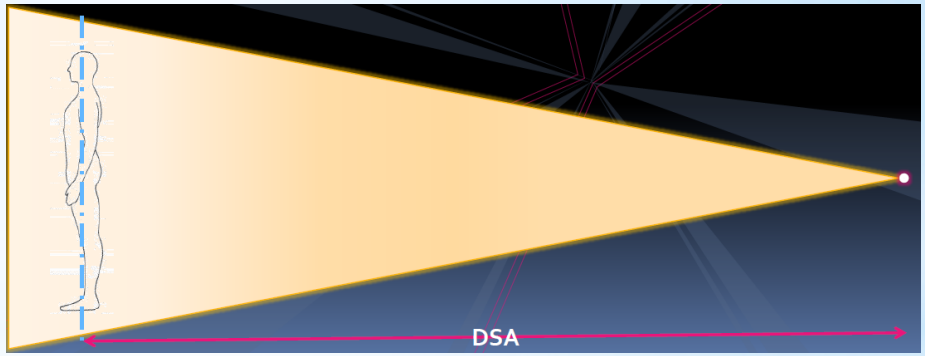


Schematic representation of the different doses involved in in vivo dosimetry for 2 parallel opposed photon beams. **METHODS FOR IN VIVO DOSIMETRY IN EXTERNAL RADIOTHERAPY, booklet 1 ESTRO 2006**

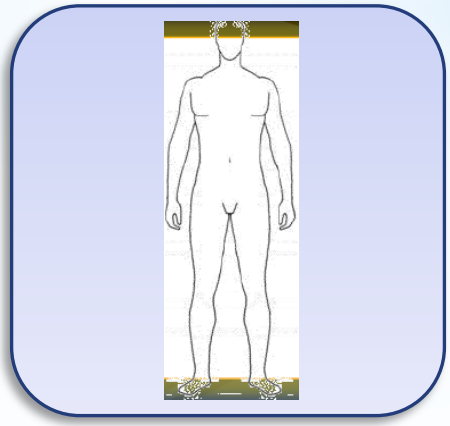
Irradiation techniques

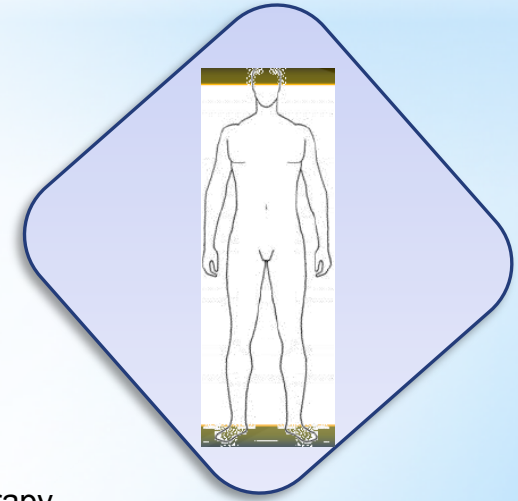
Technical aspects: Radiotherapy Unit and Bunker size

- **Large distance:**
  more then 3 - 4 m



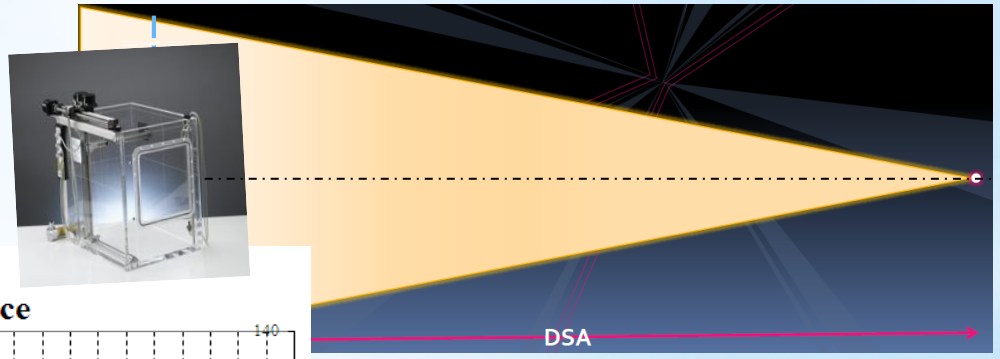
- **Large field :**
  40x40 cm² at 0° or 45° collimator angle

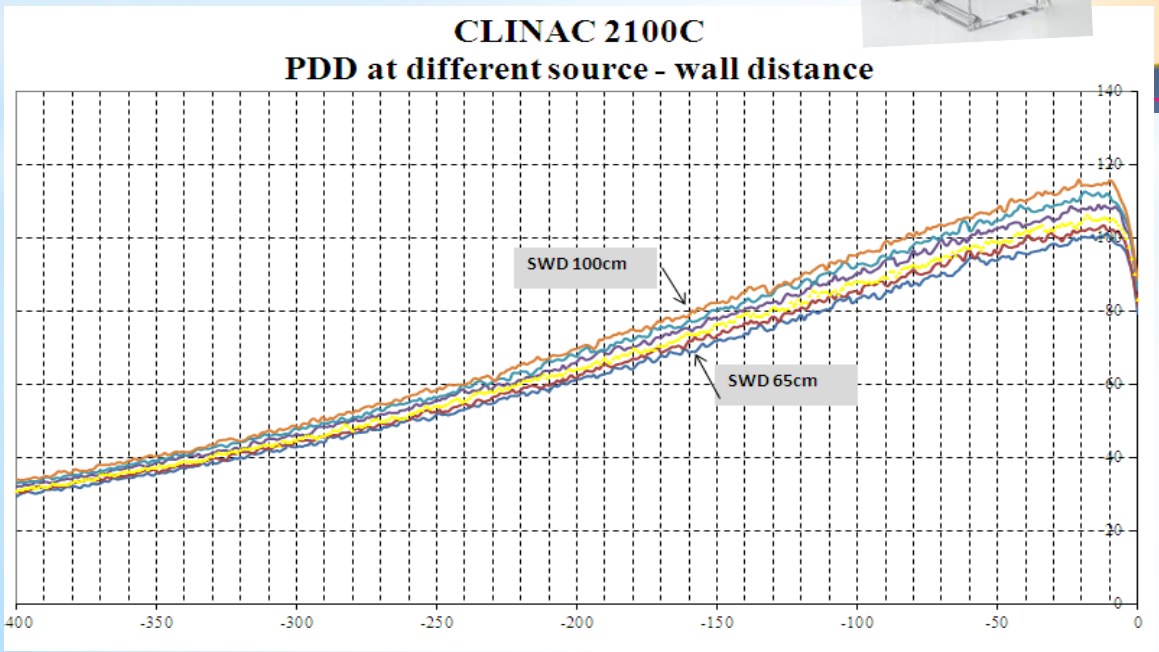




Irradiation techniques

Technical aspects: Radiotherapy Unit and Bunker size



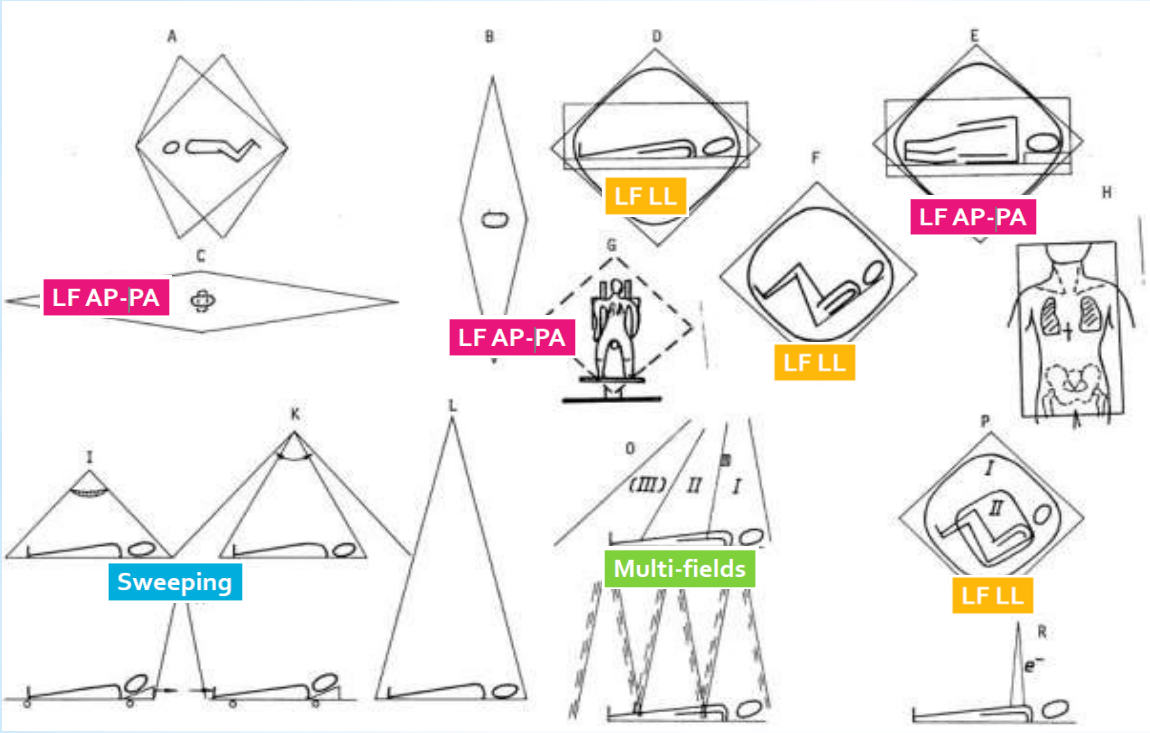


Measurements:

need to measure the PDD curve and profile curves for TBI special conditions: large field, large SSD, etc…

Irradiation techniques

Technical aspects: Beam Incidence



LF AP-PA

antero-posterior (AP) and postero-anterior (PA)

LF LL

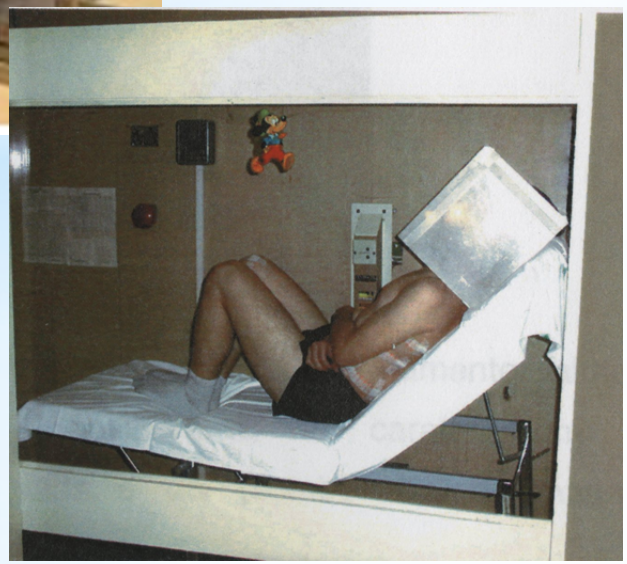
Latero-lateral (LL)

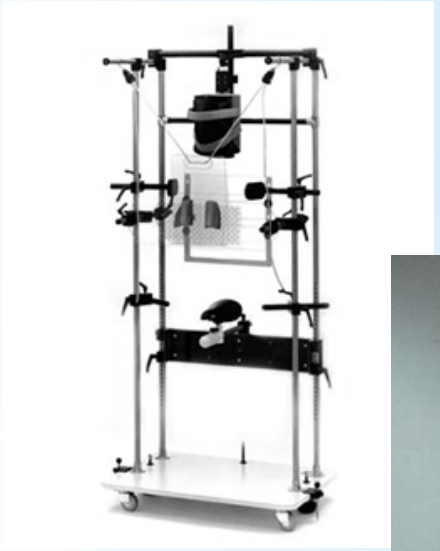
Multi-fields

Sweeping

Irradiation techniques

Technical aspects: ***supports*** **(bed, support for irradiation while standing);**





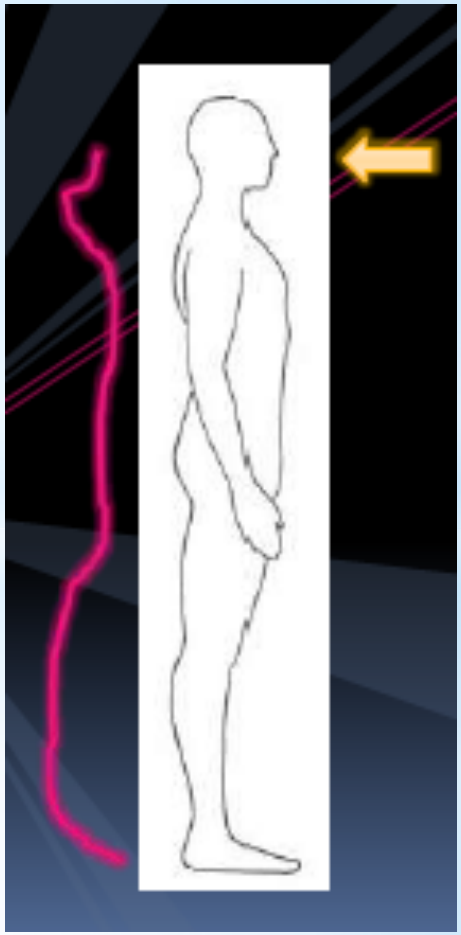
Irradiation techniques

Table 1. The commonest TBI techniques

Patient's Position	Beam alignment	Advantages and Indications	Disadvantages
Supine/fetal	Horizontal	Comfortable and reproducibile. Indicated for pediatric patients	Lateral incidence; difficulty in shield and compensator placement
Supine/Prone	Vertical	Indicated for children under 1 metre in height who require sedation	Height limit
Standing	Horizontal	Anterior and posterior incidence; easy shield and compensator placement; indicated in fractionated dose schedules.	Position cannot be maintained for long
Lateral decubitus	Horizontal	Anterior and posterior incidence; shields and compensators can be used; indicated in single dose therapy schedules because the position can be maintained for a long time.	Accurate shield placement verification is essential

Irradiation techniques

AP-PA irradiation



Advantages:

- *Opposing horizontal beams 40x40 cm*
- *DSA ≥ 4m*
- *body* thickness less and more homogeneous in various districts (head, neck, thorax, abdomen, ..)
- Simple set-up and easy shielding (good lung shielding)

Disadvantages:

- placement of uncomfortable treatment

Irradiation techniques

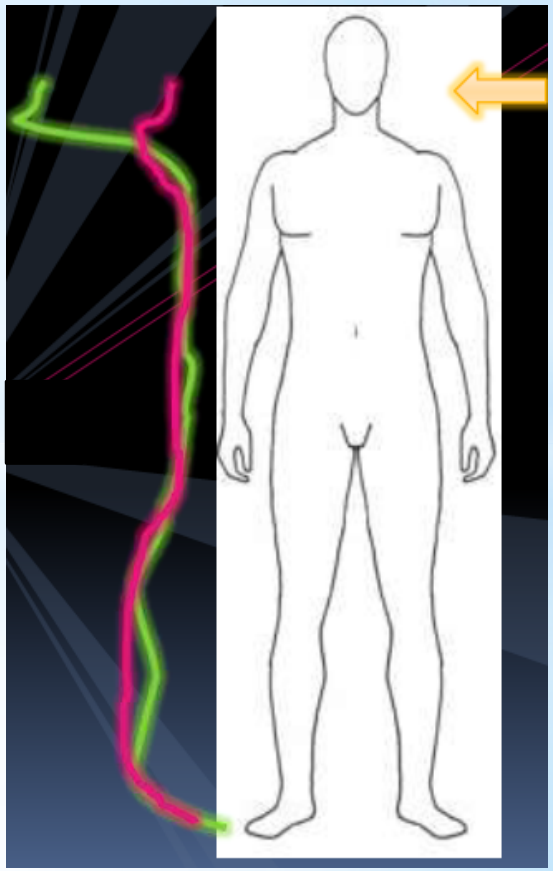
LL irradiation

Advantages:

- *Opposing horizontal beams 40x40 cm*
- *DSA ≥ 4m*
- *Confortable displacement*

Disadvantages:

- Greater body thickness and less homogeneous in various districts (head and neck overdose)
- Hard shielding
- not recommended for adult treatment but possible for children



Irradiation techniques

Dose Rate effect

"A higher TBI dose rate has been shown to be an adverse prognostic factor for developing IP (Interstitial pneumonia)…. The use of fractionated TBI at a dose rate of 7.5 cGy/min or less rather than 15 cGy/min is recommended…"

Br J Cancer. 2004 Jun 1;90(11):2080-4. Carruthers SA, Wallington MM.
Total body irradiation and pneumonitis risk: a review of outcomes.

"The last twenty years has demonstrated that fractionated and hyperfractioned TBI are associated with a lower incidence of side effects than STBI (8-10 Gy) at a high dose rate."

«Guidelines for quality assurance in total body irradiation»
Report ISTISAN 05/47

Irradiation techniques

Recommendations for the doserate

- ***Fractionated Dose*** ≥10-12 Gy
  ⇒ **dose-rate < 15-16 cGy/min**

- ***Single Dose*** (10 Gy low dose-rate)
  ⇒ **dose-rate <5 cGy/min**

- ***Mini-TBI:*** 2 Gy in one fraction
  ⇒ **dose-rate < 10 cGy/min**

«Guidelines for quality assurance in total body irradiation» Report ISTISAN 05/47

Irradiation techniques

Dose Rate effect

The actual dose-rate in patient is determined by:

- ***SAD***
- ***Repetion Rate (MU/min) or Doserate (Gy/min)***
- ***Presence of attenuators/compensators***
- ***Patient size***

The reduction of dose rate can be obtained by increasing the treatment distance or lowering the dose-rate of the accelerator.

Irradiation techniques

Technical aspects: Beam Spoiler

"In TBI it's desiderable to ensure that the *skin surface receives close to the fully prescribed dose*."
High energy beams needs the use of a ***PMMA plate*** of such a thickness as to absorb the build-up region of the depth dose curve.

Table 1 Central Axis % Depth Doses at different measurement geometries.

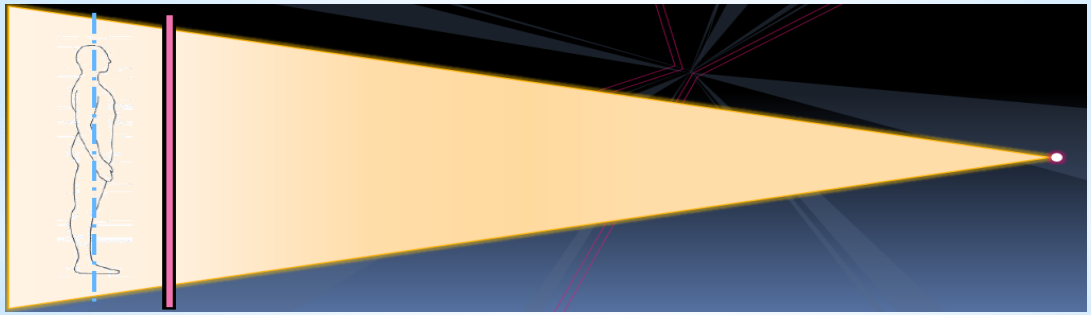
No	Depth cm	% Depth doses measured present work						Podgorsak Montreal Canada 1985 4.0m	Bhat Adelaide Australia 2001 3.4m	Gliwice Poland 3.75m
		No beam spoiler 4.0m	No beam spoiler 4.3m	With 1.0 cm beam spoiler 4.0m		With 1.5 cm beam spoiler 4.0m				
				100% at skin	100% at 1.5 cm	100% at skin	100% at 1.5 cm			
1	0	79.3	–	100.0	103.9	100.0	104.9	–	–	–
2	1.5	100.0	100.0	96.3	100.0	95.5	100.0	100.0	100.0	100.0
3	5.0	93.0	93.0	87.9	91.3	87.4	91.6	93.0	92.5	92.1
4	10.0	80.5	80.8	74.9	77.8	75.0	78.6	80.8	82.0	79.5
5	15.0	68.3	68.8	62.7	65.2	63.2	66.3	69.6	70.8	67.9
6	20.0	57.2	57.5	52.0	54.0	52.6	55.1	58.3	59.6	57.6
7	25.0	47.4	47.8	42.7	44.4	43.6	45.7	–	49.8	48.2

Ravichandran R, et al., Beam configuration and physical parameters of clinical high energy photon beam for total body irradiation (TBI), **Physica Medica (2010)**

Irradiation techniques

Technical aspects: Beam Spoiler Effect

The PMMA spoiler must be placed close to the patient (10-30 cm)



The build-up region is minimized, infact additional scatter component increases the input dose.

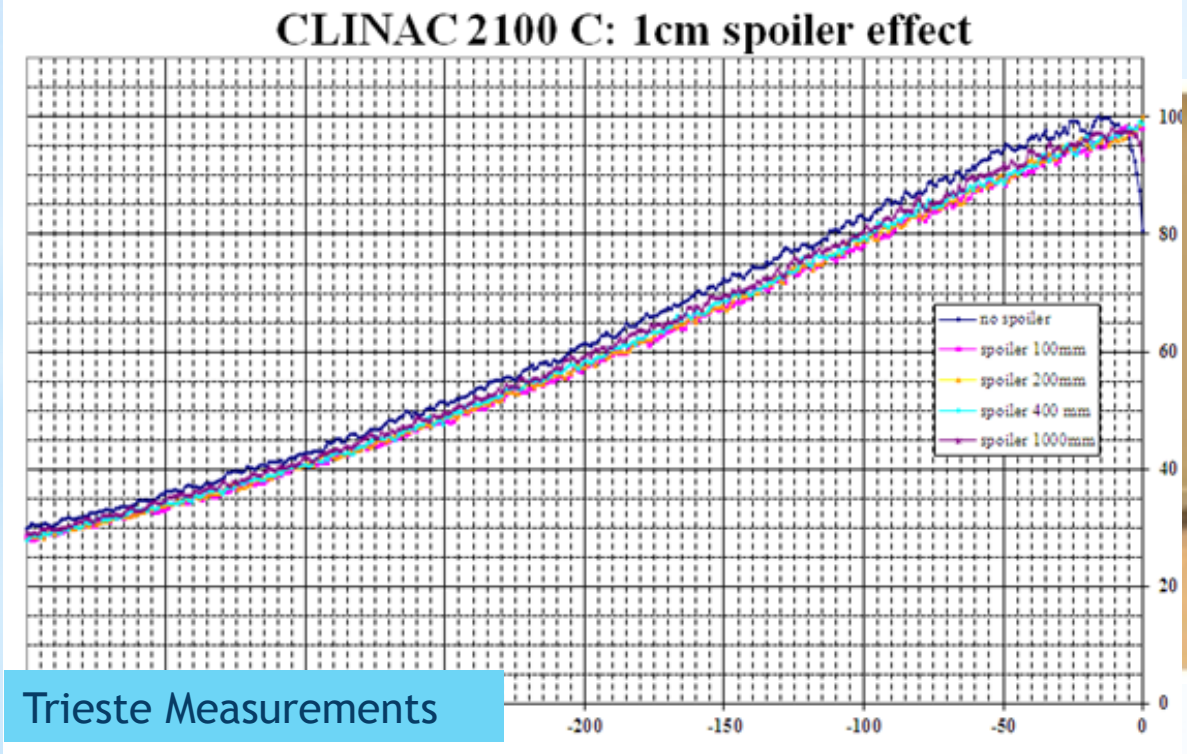
You must evaluate the attenuation (typically on the order of 5%) and the influence on beam quality

Table 3 Beam quality variations with treatment distance.

No.	Source axis Distance(SAD) d (cm)	Intensity ratios 20/15	Intensity ratios 25/15
1	200.0	0.8495	0.7160
2	227.5	0.8484	0.7148
3	259.4	0.8478	0.7133
4	300.0	0.8471	0.7122
5	350.0	0.8472	0.7112
6	400.0	0.8467	0.7110
7	400.0(1.0BS)	0.8544	0.7591
8	400.0(1.5BS)	0.8491	0.7150

Irradiation techniques

Technical aspects: Beam Spoiler Effect



Trieste Measurements

Irradiation techniques

Technical aspects: Target Volume

The ***target volume*** of myeloablative TBI is all malignant cells including those circulating as well as the whole cellular immune system

It means that the Whole Body including the Skin.

Organs with a high risk of recurrence ("homing phenomenon") and meninges, testes, may required additional local radiotherapy

Irradiation techniques

Technical aspects: Organ at risks

The dose of HTBI can exceed the tolerance of organs at risk, particularly for the lung or the lens of the eyes.

Lungs are at particularly high risk

Interstitial pneumonia has been one of the main fatal complications of TBI in conditioning regimens for allogeneic transplant.

Irradiation techniques

Technical aspects: Dose Prescription

The TBI dose is normally prescribed at the ***abdominal and lung midplanes***

In order to take account of the density and geometry of the beam central section and to at least three pulmonary sections (upper, middle and lower parenchyma), **CT scan is recommended for treatment planning.**

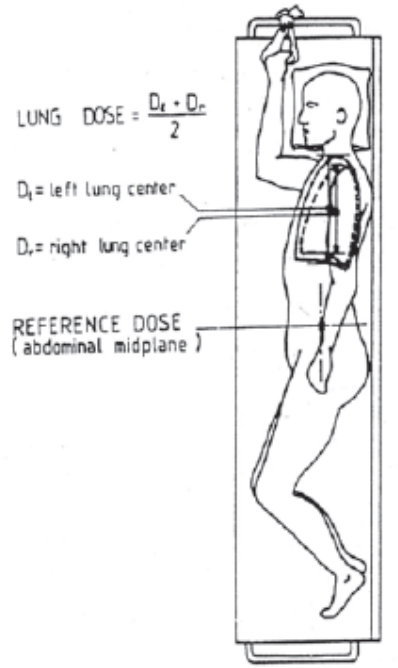


Figure II.8: Reference points usually used in total body irradiation

Irradiation techniques

Technical aspects: Dose Prescription

The dose delivered to other critical organs such us **gonads, lens of the eyes**, or **kidneys** must be recorded in the reporting, together with longitudinal and cross-section irregularities at different reference points (**head, neck, mediastinum, pelvis, lower limbs**).

The dose variation at the different reference points should be between ± 10%.

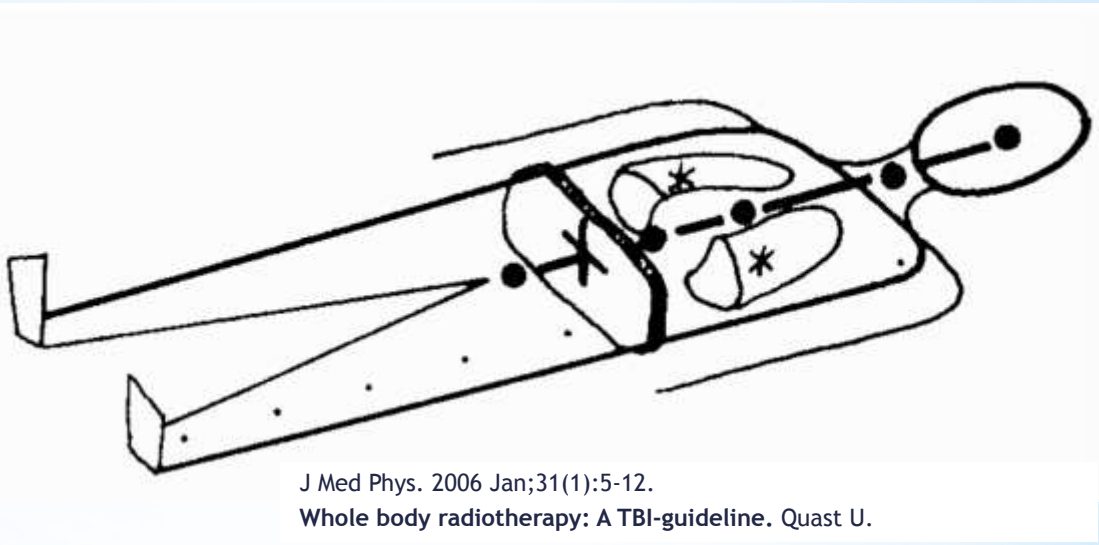
If, because of irregular thickness, the dose is not within this range, **compensators** may need to be applied around areas of lesser thickness.

Irradiation techniques

Technical aspects: Dose Prescrition

*The dose reference point (+) **for dose specification to the target is defined** at **mid abdomen at the height of the umbilicus**.*

***The** dose reference points (*) for lung dose specification are defined as mid points of both lungs…*



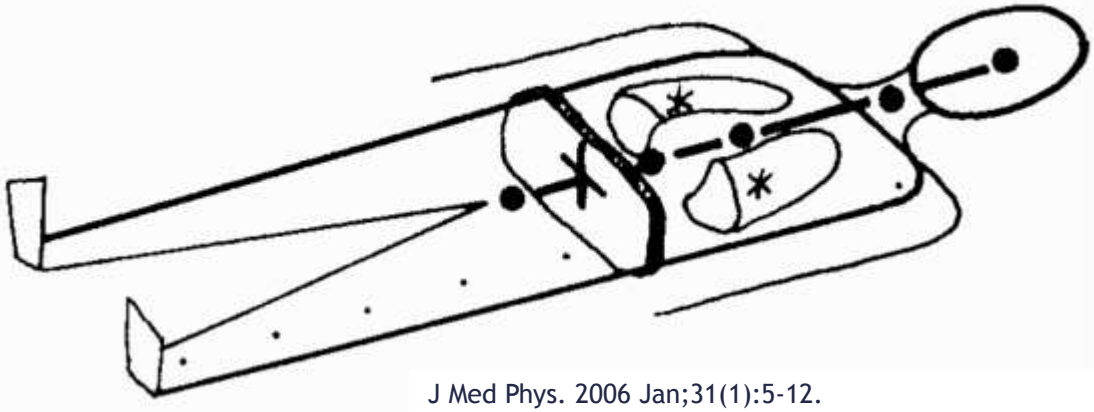
J Med Phys. 2006 Jan;31(1):5-12.
Whole body radiotherapy: A TBI-guideline. Quast U.

Irradiation techniques

Technical aspects: Spatial Dose Distribution

The spatial distribution of dose in the target can be characterized by the DVH or…by determining the dose at the specification point and the dose variation in the target (D_{Ref}, D_{min}, D_{max}).

*This triplet of values can be derived from the longitudinal homogeneity of dose (at **selected points (•) along the midline**)*



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Irradiation techniques

Technical aspects: tissue compensators

Simple tissue compensators that extend completely across the patient can be used to decrease the dose to thinner body sections like the necks or ankles.

If room geometry forces the use of lateral fields, **much more** extensive compensation will be needed.

Irradiation techniques

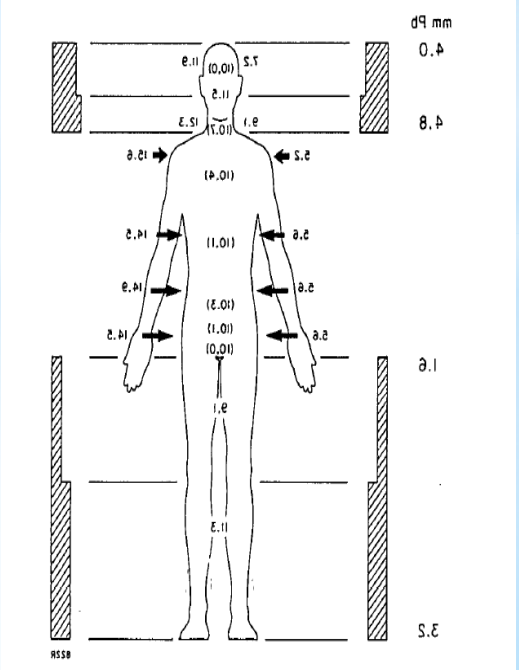
Technical aspects: Shielding critical structures

The **lungs** are an example of an organ system that is particularly sensitive to radiation, easily effected by other therapy regimes.

Two methods for reducing the dose to critical structures:

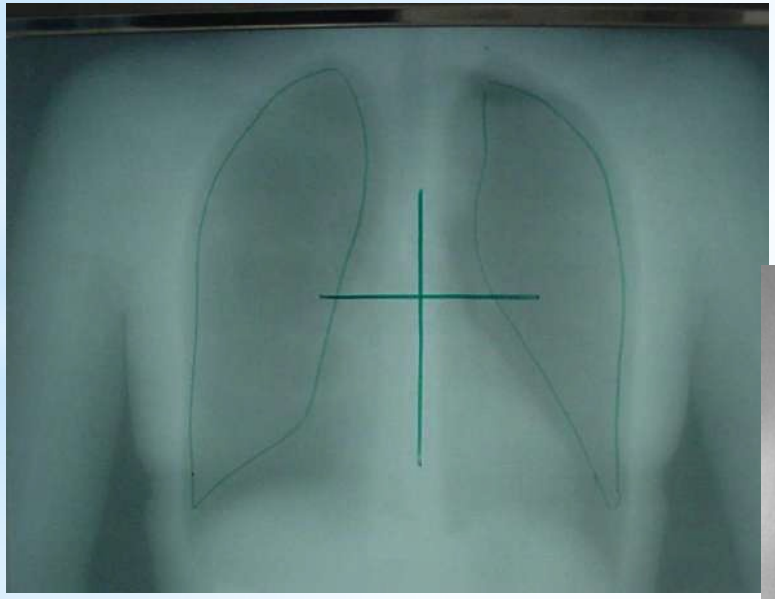
1) it is possible to place strips of absorbing material completely across the patient to shield these regions. The compensator can be placed on the treatment unit head using the block tray.
   Port film is used to check the positioning of the compensator.

2) more shielding for the lungs by placing ***cerrobend blocks*** between the source of radiation and the patient.
   These alloy blocks conforms more tightly to the lung shadow as seen on a radiograph.

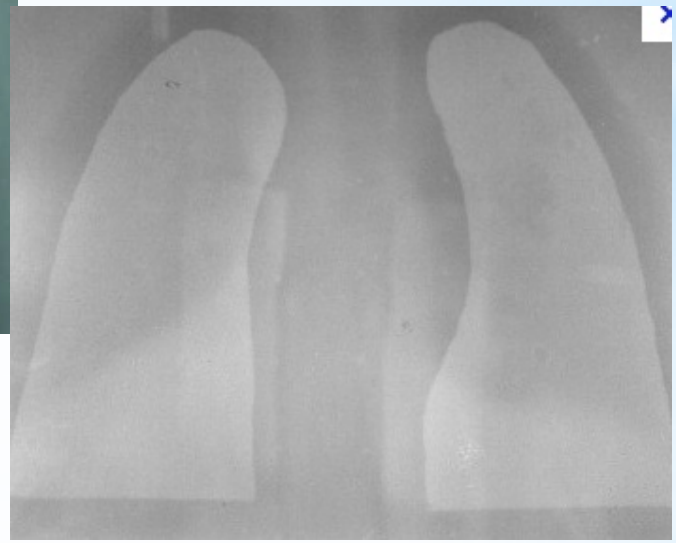


Irradiation techniques

Lungs Lead Shielding



- *X-Ray film and shielding design*
- *Portal film Verification*



Irradiation techniques

Lungs and kodney Lead Shielding

- *X-Ray film and shielding design and Portal film Verification*

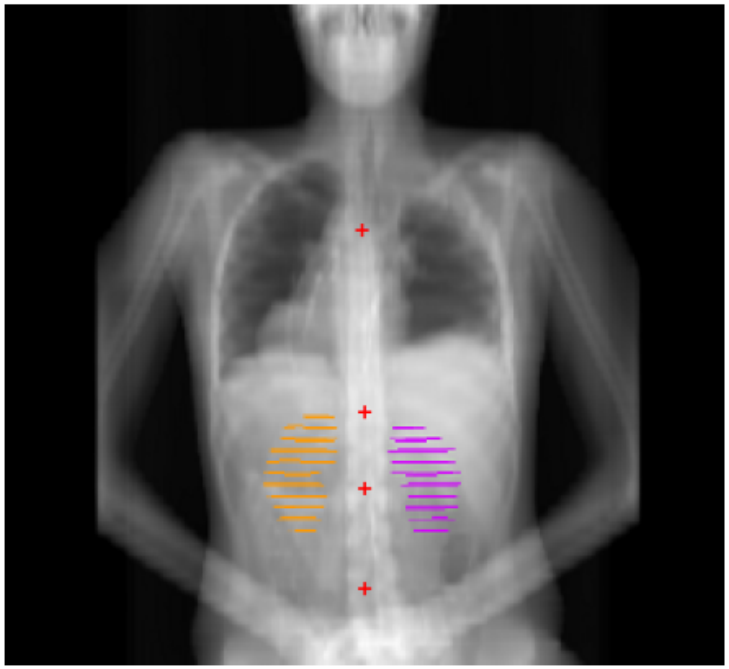


Figure1: DRR with segmented kidneys and external markers

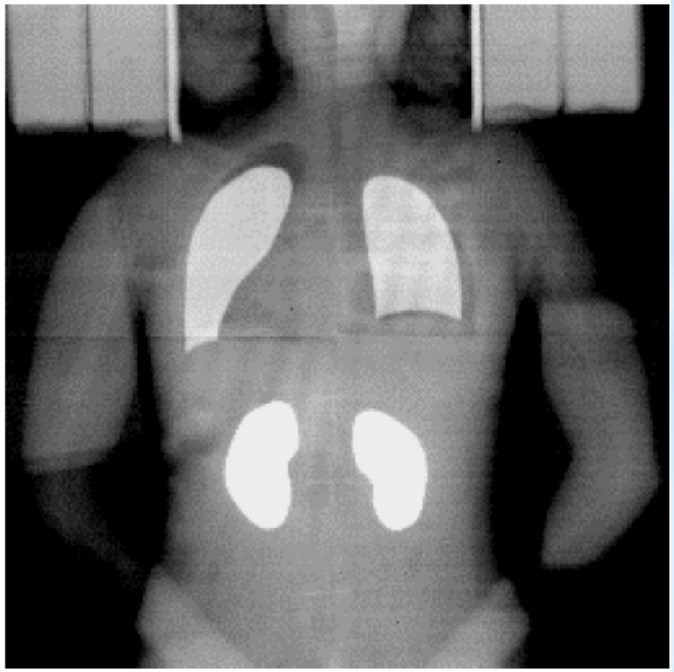


Figure 2: PortalVision XL image with lung and kidney shielding blocks

Irradiation techniques

Lungs Shielding /Compensation

LL : lungs "compensated" by arms
AP-PA : Shaped Lead shielding

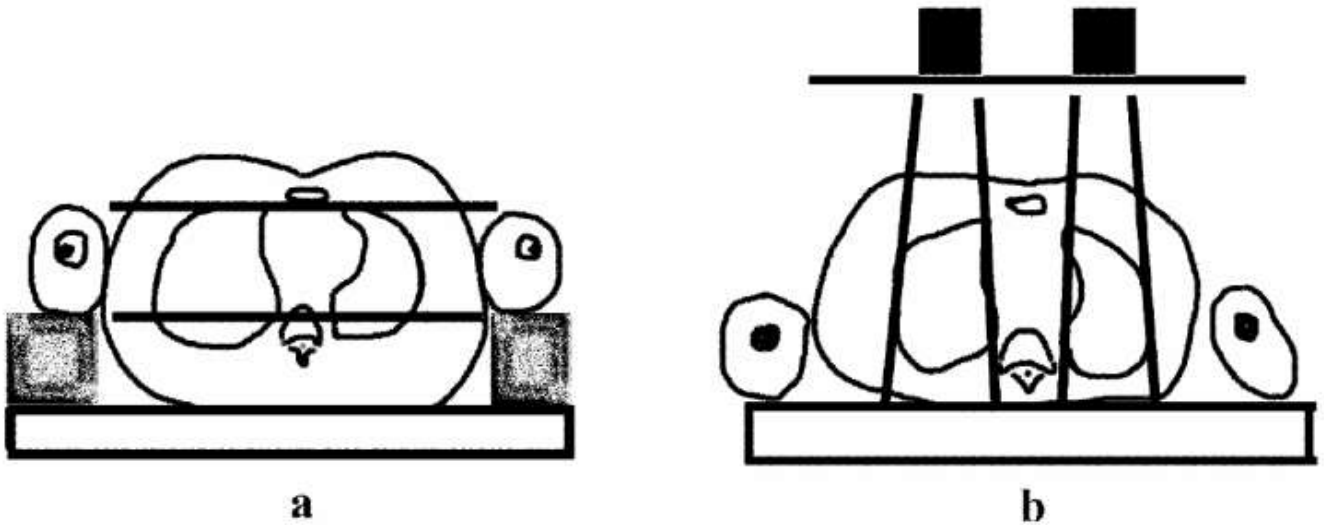


Fig. 5. Shielding of the lungs. a: Bilateral TBI. b: Anterior-posterior TBI.

Basic Dosimetry

New approach at TBI SAD

Step 1. Determine an absolute calibration of the radiation beam using the large field geometry and the largest phantom available.

Step 2. Correct this dose such that it represents both:

(a) the dose that would be obtained for a phantom that covers the entire beam

(b) the dose that would be obtained for a deep phantom i.e. full scattering conditions.

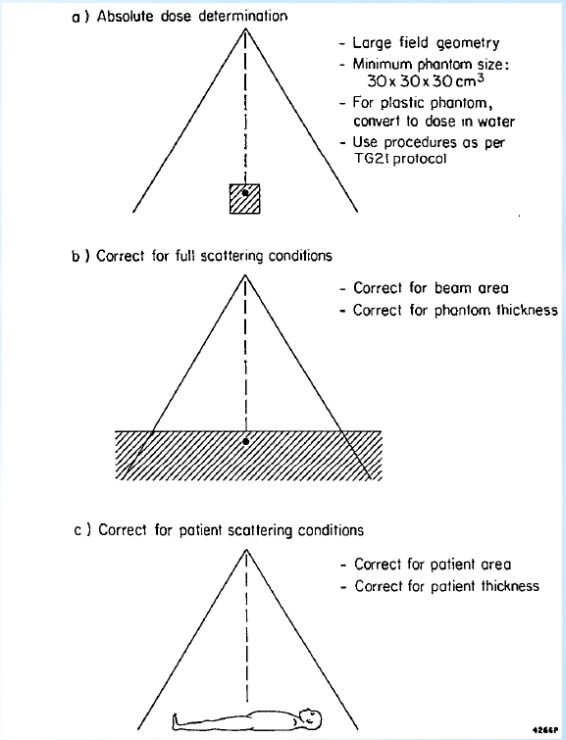
Step 3: For patient treatments, corrections should be made for patient dimensions both in terms of the area of the patient intersecting the radiation beam as well as patient thickness.

Basic Dosimetry

New measurements at TBI SAD

(IAEA protocol for non reference conditions)

- Beam calibration
- Depth dose curves;
- Beam profiles;
- Scatter factor
- Wall and floor scatter factor
- Beam spoiler attenuation



Basic Dosimetry

Measurements of PDD /TMR at large SAD, Profiles at TBI set-up

Table 2 Measured tissue maximum ratios (6 MV).

No.	Depth 'd' cm	TMR 1.0m SAD (40 × 40 cm)		TMR 3.5m SAD (140 × 140 cm)	TMR 4.0mSAD 160 × 160 cm	
		RH	BJR 25 Ref [13]		Open	1.5 cm BS
1	1.5	1.000	1.000	1.000	1.000	1.000
2	3.0	0.983	0.983	0.975	0.976	0.973
3	5.0	0.948	0.949	0.934	0.937	0.932
4	10.0	0.844	0.848	0.819	0.828	0.819
5	15.0	0.740	0.741	0.703	0.714	0.704
6	20.0	0.633	0.638	0.595	0.610	0.601
7	25.0	0.525	0.528	0.496	0.518	0.510

Ravichandran R, et al., ***Beam configuration and physical parameters of clinical high energy photon beam for total body irradiation (TBI)***, Physica Medica (2010)

- *Water phantoms dedicated to horizontal beams*
- *As an alternative large sized plastic phantom or placing near diffusor bodies*
- *Films? Diode Array? Others?*

Basic Dosimetry

Measurements of scatter factors at TBI Set-up

The scatter is not dependent on field size (normally 40x40 cm^2) but the patient's sizes (district):

$$S_{cp} = S_c(40) \times S_p(pz)$$

S_p depends only by the energy of the beam for which should be approximately the same as in SAD, otherwise measures with phantoms of various sizes

Ravichandran R, et al., ***Beam configuration and physical parameters of clinical high energy photon beam for total body irradiation (TBI)***, Physica Medica (2010)

In vivo Dosimetry

Target volume of high dose TBI

➢**Whole body,** including the skin, as the *target cells* are widely disseminated, all manifest or occult clones of malignant cells, including those circulating and the whole cellular immune system.

➢***Organs with a high risk of recurrence*** ("homing phenomenon") and ***primary extended*** ("bulky") ***tumour regions*** like meninges, testes, or abdominal lymph nodes may require additional concurrent local radiotherapy.

In vivo dosimetry

In vivo dosimetry is of particular relevance in case of Total Body Irradiation before bone marrow transplantation for different reasons:

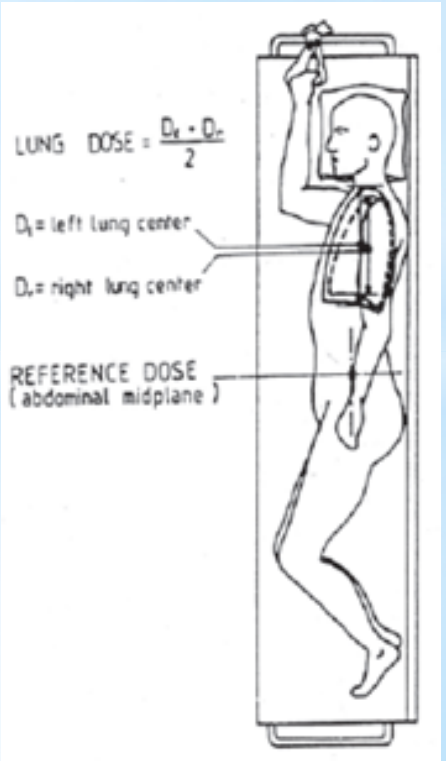
- ***difficulties in calculation of the dose at different points in the patient***
- ***increased risk of patient movements due to the long duration of the treatment***
- ***in single fraction regimen, need to correct the dose before the end of the session.***

The ***in vivo measurements*** are to be considered not only as an independent check, but rather as an integral part of the overall dosimetric approach for this particular treatment technique.

In vivo dosimetry

Tasks for in vivo dosimetry

- Evaluation of the dose at the dose specification point, usually taken at mid-pelvis or mid-abdomen
- to estimate the homogeneity of the midline dose distribution at different loci in cranio-caudal direction
- to monitor the dose at the level of organs at risk (lungs, liver, etc).



In vivo dosimetry

Target dose, simplified approach :

- symmetrical , with respect to the midline point, expansion or compression of the real patient to a thicker or thinner "water patient"
- tissue inhomogeneities should be symmetrical and equally distributed with respect to the midline

❖**In LL direction good approximation**

❖**In Antero- Posterior direction not realistic approximation**

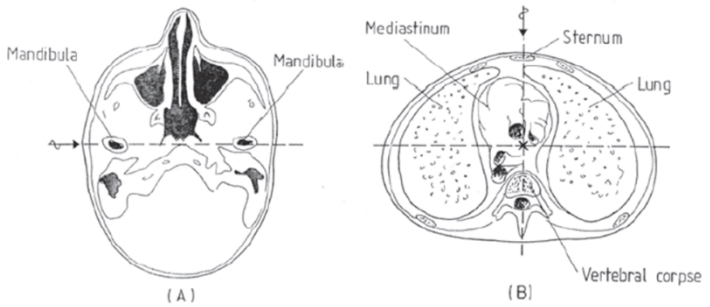


Figure II.5: Examples of symmetrical (A) and asymmetrical (B) disposition of the tissues, with respect to the midline depth. For the head-and-neck fields (A) the method of target dose determination is applicable, while it is not for the thorax fields (B).

In most clinical cases, the arithmetic mean of entrance and exit dose may be a quite reasonable approximation for Dose at midline.

In vivo Dosimetry

Dosimeters set-up

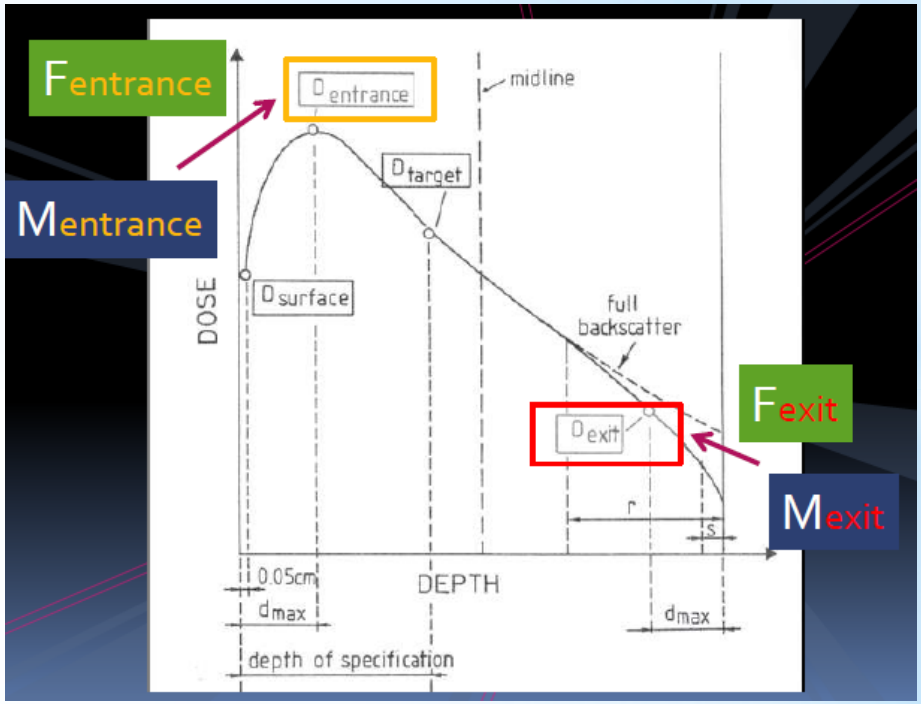
The dosimeters must be placed on the skin of the patient in pairs (one "*in entrance*" and the other "*in exit*") in the point of reference (abdomen) and in several body districts, like head, neck, mediastinum, lungs (possibly on both lungs if they are not "dosimetrically symmetrical", like the irradiation AP-PA in lateral decubitus), navel, knees and ankle.

Subsequently, for every district, the pair of measured values must be used in order to calculate the "***dose at half thickness***"

In vivo Dosimetry

An algorithm for calculation of the **"dose at half thickness"** in TBI uses:

- the **entrance dose**, corrected by the distance from "centre field";
- the **"equivalent depth in water"**, determined on the base of its dosimetric correlation with the **"exit dose / entrance dose" ratio**;
- the correlation between the **"equivalent depth in water"** and the **data of attenuation**



The detectors must be previously calibrated in TBI conditions, for comparison with the ionization chamber.

In vivo Dosimetry

Main Detectors for *in-vivo Dosimetry*

- TLD
- MOSFET
- DIODI

And now in Trieste

- Gafchromic film

In vivo Dosimetry

Semiconductor detectors

Advantage:

- elevated sensitivity to radiation,
- small dimensions
- immediate reading of the value of absorbed dose

Disadvantage:

- influenced by the accumulated dose, the dose rate, the temperature and the beam-detector angle
- indispensable to carry out the calibration of the semiconductor in the geometric-physical conditions of TBI.

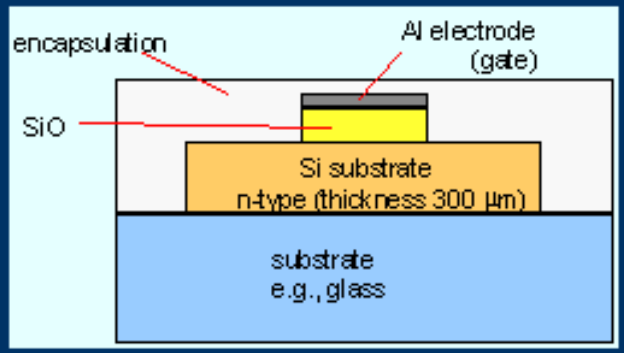
AAPM REPORT NO. 8 DIODE IN VIVO DOSIMETRY FOR PATIENTS RECEIVING EXTERNAL BEAM RADIATION THERAPY
Report of Task Group 62 of the Radiation Therapy Committee February 2005

Calibration of semiconductor detectors for dose assessment in total body irradiation
N. Jornet, M. Ribas, T. EudaldoRadiotherapy and Oncology 38 (1996) 247-251

In vivo Dosimetry

MOSFET dosimeter is

a Metal-Oxide Semiconductor Field Effect Transistor.



Principle:

- Ionizing radiation generates charge carriers in the Si oxide.
- The charge carries moves towards the silicon substrate where they are trapped.
- This leads to a charge buildup causing a change in threshold voltage between the gate and the silicon substrate.
- MOSFET dosimeters are based on the measurement of the threshold voltage, which is a linear function of absorbed dose.
- The integrated dose may be measured during or after irradiation

In vivo Dosimetry

MOSFET dosimeter

Advantages

☺MOSFETs are small

☺Although they have a response dependent on radiation quality, they do not require an energy correction for mega-voltage beams.

☺During their specified lifespan they retain adequate linearity.

☺MOSFETs exhibit only small axial anisotropy (±2% for 360º).

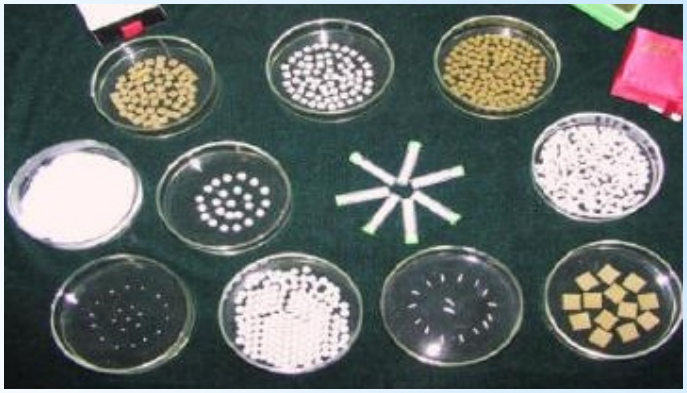
Disadvantages

☹MOSFETs are sensitive to changes in the bias voltage during irradiation (it must be stable).

☹Similarly to diodes, they exhibit a temperature dependence.

In vivo Dosimetry

TLD Detectors



Advantage:

- small dosimeters
- good sensitivity to radiation
- small dependency on dose rate and energy
- do not need to be connected to electrometers through cables and are therefore easily applied to the patient's skin.

Disadvantage

- They cannot be used for dosimetry in real time, due to the complexity of the reading procedure.

QA in TBI procedure

TBI demands specific additional protocols of quality control , not required for standard treatments:

❖*Base controls*

Related to the dosimetric and geometric parameters of the specific treatment unit in TBI condition, to the performances of the employed treatment planning systems (verification of the algorithms for distances superior to conventional ones and fields larger than the dimensions of the patient) and to the dosimetric systems for the determination of the absolute and relative dose.

❖*Pre-irradiation controls*

Related to the dosimetric systems, and to the verification of the accessories (absorber and diffusers, couch /seat, etc.) for the positioning during irradiation, to be specifically carried out for each patient.

QA in TBI procedure

Table 4. TBI specific base controls in addition to those prescribed for conventional radiotherapy

Object	Parameter to control	Modality of control
Basic dosimetriy	Dose in standard phantom at reference depth	Audit or external confrontation in TBIconditions; calibration according to international protocols
LINAC or telecobalt	OAR profiles	Dosimetric measures in standard phantom in TBI condition
LINAC or telecobalt	PDD or TPR	Dosimetric measures in standard phantom in TBI condition
Treatment planning system (TPS)	Dose in anthropomorhic phantom with lung type inhomogeneity: absolute values and dose distribution.	Dosimetric measures in TBI condition
In vivo dosimetry system	Entrance and exit dose and algorithm of calculation at half thickness	Dosimetric measures in TBI condition
"Standard phantom" is that recommended by the dosimetric protocol of reference		
LINAC or telecobalt	Dose	Control of constancy
Personalize beam modifiers (protection, shields, compensators, bolus)	Attenuation of the shields Consistency of compensators and bolus	Dosimetric measures
Positioning devices	Geometric parameters (distance from the source, height from the pavement etc.)	Metric control
In vivo dosimetry	Sensitivity	Calibration in terms of absorbed dose or control relative to the response

Experience of Trieste

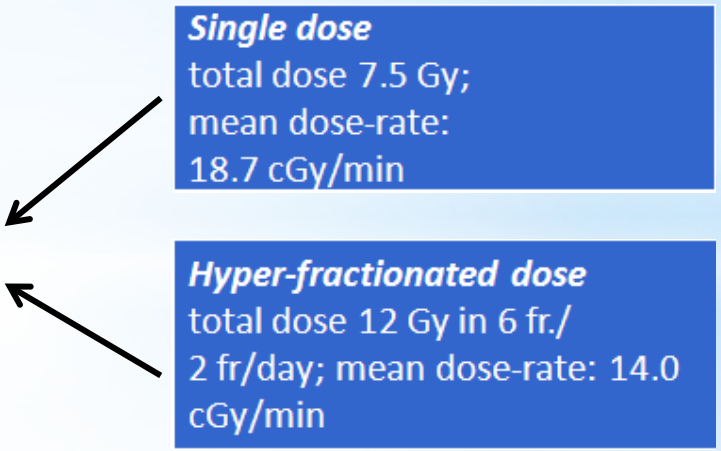
Total body irradiation (TBI) in pediatric patients:

Since 1984 pediatric patients have been treated with TBI as a conditioning regimen for autologous and allogeneic BMT, at the Radiotherapy Center of Trieste

Patients	***36***
Median Age	12 (6-19)
Female *Male*	10 26
Disease	
ALL *I or II CR* *> II CR* *PR* *relapse/refractory*	33 22 2 3 6
AML *I CR*	1
AML/ALL *I or II CR*	2

Experience of Trieste

Conditioning regimen	***N***
THIO, EDX *EDX* *FLU, EDX, THIO* *FLU, EDX, THIO, DAUNO* *Others*	14 *5* *3* *3* 11
TBI	
Single dose	14
Hyper-fractionated dose	22
Type of donor	
MRD	13
MUD	7
Haploidentical	14
Autologous	2



Experience of Trieste

Linear Accelerator, 6MV X-rays
Maximum Radiation Field
Source Axis Distance ~ 4 m
Collimator rotated
Parallel opposed lateral fields

Patients were treated in the seated-supine position. The lateral position of the arms provided partial lung shielding

Experience of Trieste

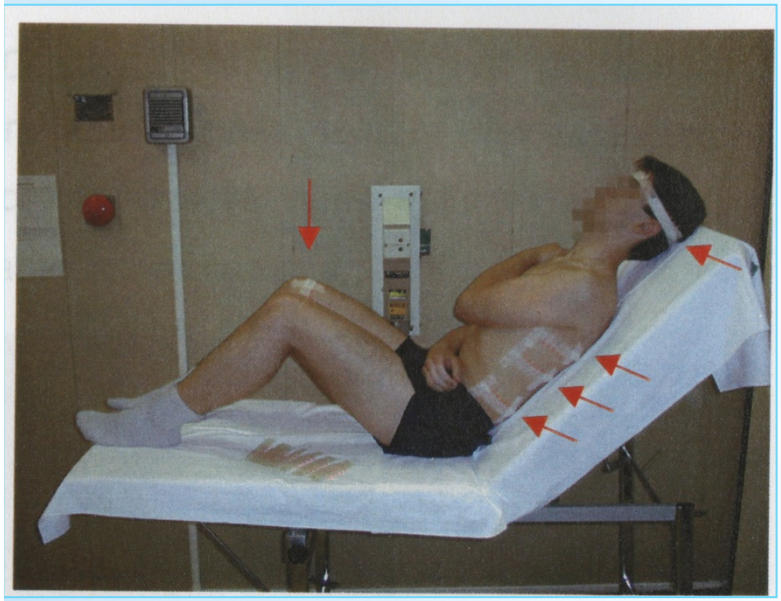
Before treatment: many dosimeters measure entrance and exit dose and allow to evaluate the mean patient axis dose:

- ***until 2005*** *sets of calibrated LiF TLDs (cylindrical micro-rods of length 6 mm and with diameters of 1 mm) were applied to 9 body sites*

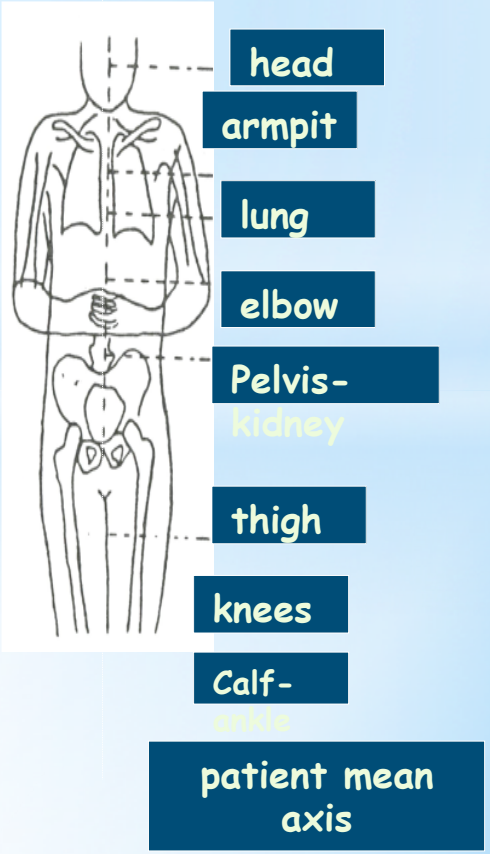
- ***since 2006*** *sets of EBT gafchromics are used at 9 body sites before treatment (STBI) or at the first fraction (HFTBI)*

During treatment: *one ionization chamber is set in right armpit, and one in the axis of legs check the actual irradiation and the reproducibility of the treatment*

Dosimeters distribution and measured dose values

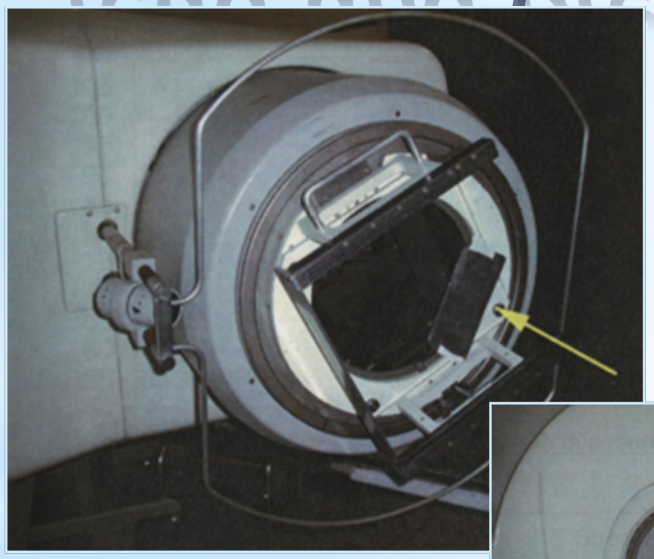


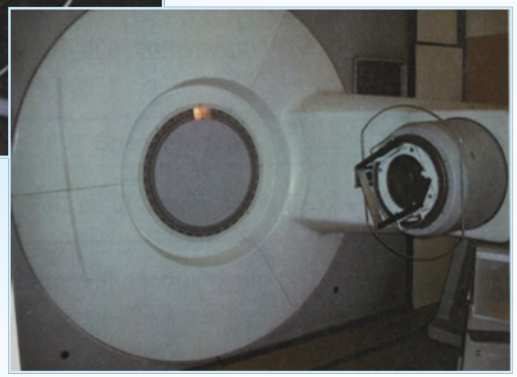
	Medium Dose (Gy)	Min. Dose %	Max Dose %
Head	1.98	-6	5
Armpit	2.00	-6	10
Lung	1.98	-8	6
Elbow	2.01	-5	6
Abdomen	2.07	-6	13
Thigh	2.04	-9	9
Knee	2.04	-5	11
Calf	2.05	-4	10
Ankle	2.14	-1	13

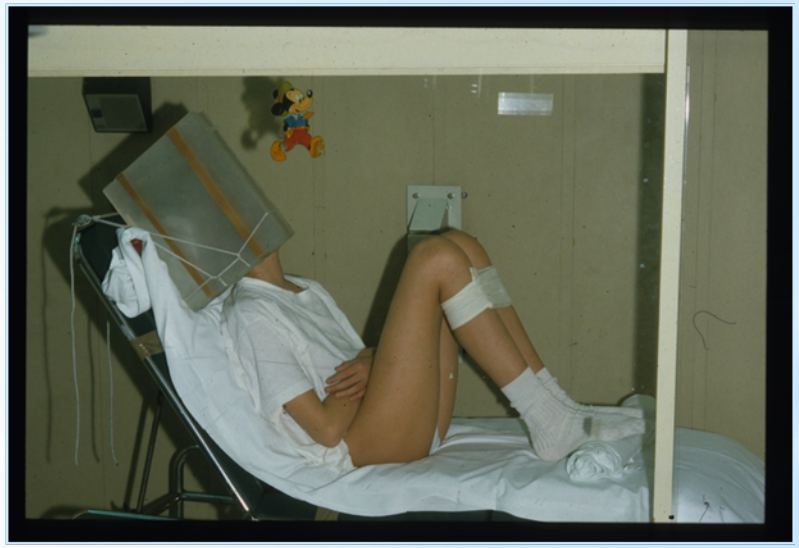


Monitor units are calculated by the mean value of three body dose points: armpit, lung and elbow

In vivo dosimetry: lead and plexiglass shielding







1-2 mm lead shielding

for the leg dose homogenity

4-9 cm plexiglass slabs

to compensate thin head

Trieste experience: Adverse events

Outcomes	N
GvHD	22 (61%)
VOD	1 (2.78%)
Interstitial pneumonia *Adenovirus* *Actinomyces* *CMV* ***Idiopathic interstitial pneumonia***	4 (11.1%) 2 1 1 **0**
Neurological toxicity	6 (16.67%)
Renal failure	2 (5.56%)
Cataract	0
Hypothyroidism	0
Secondary tumours	0

Acute GvHD: 15 (41.6%)

Chronic GvHD: 7 (19.4%)

Lung complications were diagnosed by clinical, radiological and micro-biological examinations: IP was considered idiopathic when no infectious agent was detected

Dosimeters distribution and measured dose values

gaf code	pre irradiation reading	post irradiation reading	log (LG no irr/LGirr)	Calculated Dose	district	medium dose / 1200UM	Δ %	medium dose / 1330UM	shielding	Δ % per 1330 UM	
1	44.356	31308	0,151297	172,54	TESTA DX	178,0	-1,1	197,3			
2	44.194	30648	0,158961	183,47	TESTA SN						
3	44.101	30289	0,163164	189,58	COLLO DX	192,7	7,1	213,6	200,8	2,4	
4	44.391	30191	0,167417	195,85	COLLO SN						
5	44.103	30799	0,155932	179,12	ASCELLE DX	178,1	-1,1	197,4			
6	43.938	30785	0,154501	177,08	ASCELLE SN						
7	43982	30975	0,152264	173,90	POLMONE DX	175,3	-2,6	194,3			
8	43286	30350	0,154189	176,63	POLMONE SIN						
9	43.955	30494	0,158794	183,23	ADDOME DX	187,1	4,0	207,4			
10	43.852	30050	0,164145	191,02	ADDOME SN						
11	43.738	29699	0,168117	196,89	COSCIA DX	198,7	10,4	220,3		12,4	0 mm pb
12	44.004	29711	0,170575	200,56	COSCIA SN						
13	44.216	29848	0,170664	200,70	GINOCCHIO DX	201,5	11,9	223,3		13,9	0 mm pb
14	43.962	29605	0,171712	202,27	GINOCCHIO SN						
15	43.973	28821	0,183477	220,31	CAVIGLIA DX	221,9	23,3	246,0	217,2	10,8	1 mm pb
16	44.169	28814	0,185514	223,51	CAVIGLIA SN						
gaf measured medium dose at reference point:				176,7	cGy per 1200UM per parte						
armpit Dose (i.c.):				180,0	cGy per 1200UM per parte						
Legs Dose (i.c.):				197,1	cGy per 1200UM per parte						
gaf measured medium dose at reference point:				195,8	cGy per 1330UM per parte						
UM / 200 cGy:				2660							
Doserate (160UM/min):			11,8	cGy/min							

CASTELLO DI MIRAMARE. Veduta del porticciolo, riserva marina del WWF. © APT Trieste - ph.: Alessandro Savella.