Is There a Role for Radiation In the Management of Lymphoma?

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Presenter Disclosure

- **Faculty:** Naseer Ahmed

- **Relationships with commercial interests:**
  - **Grants/Research Support:** PharmaCorp ABC
  - **Speakers Bureau/Honoraria:** XYZ Biopharmaceuticals Ltd.
  - **Consulting Fees:** MedX Group Inc.
  - **Other:** Employee of XXY Hospital Group
- Not applicable

Mitigating Potential Bias

- [Explain how potential sources of bias identified in slide 1 have been mitigated].

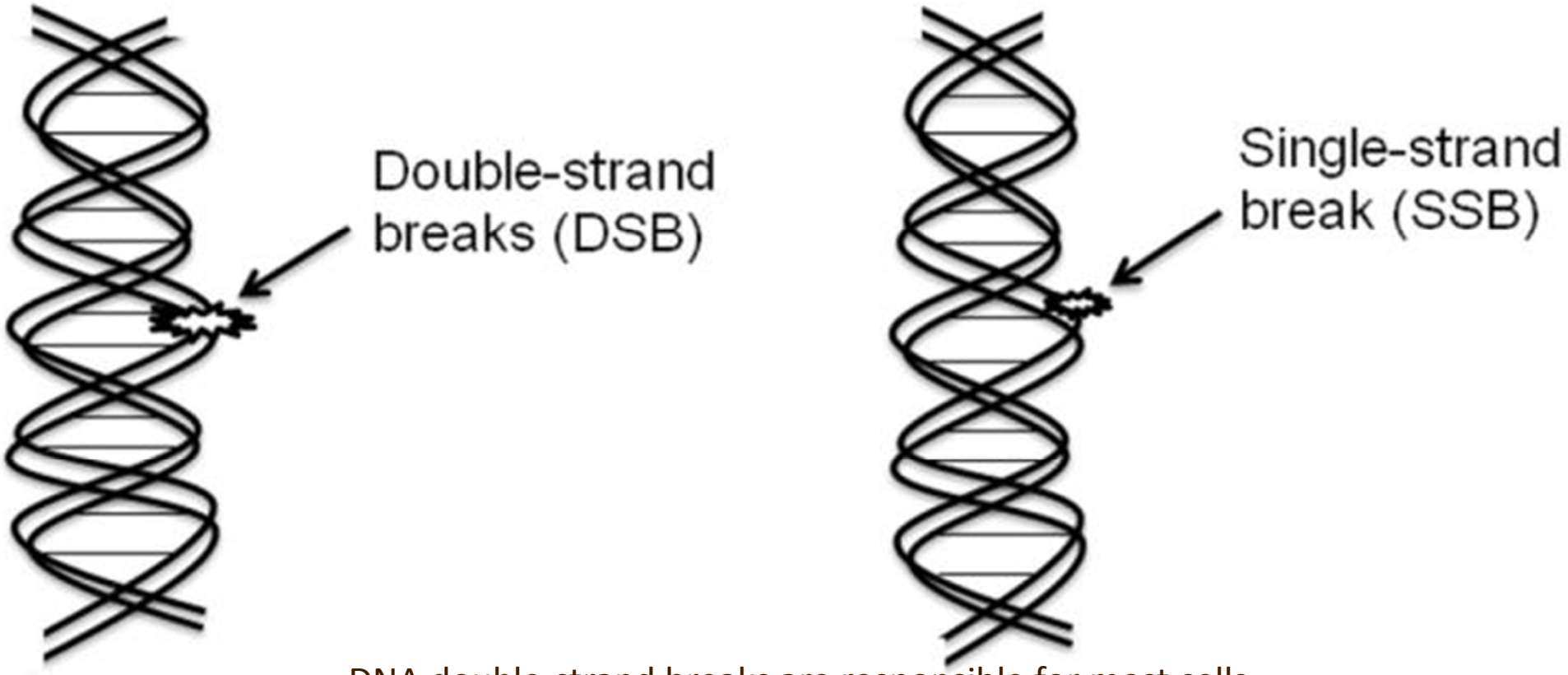
- Not applicable

Role of radiotherapy in lymphomas

1. A conceptual overview of radiation
2. Indications of radiation in lymphomas
3. How effective is the radiation ?
4. Potential toxicity of the treatment

Linear Accelerator –the most common source of radiation

The biological target of radiation



DNA double-strand breaks are responsible for most cells killing,

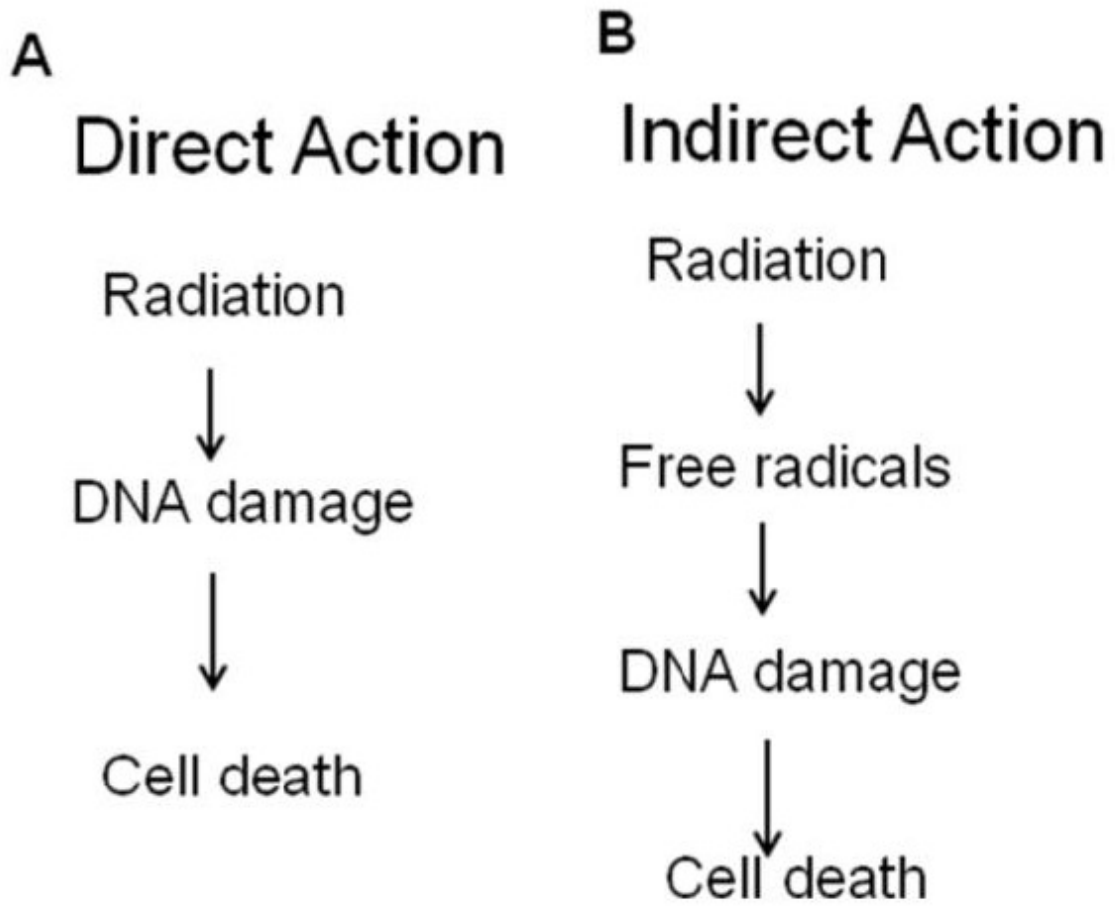
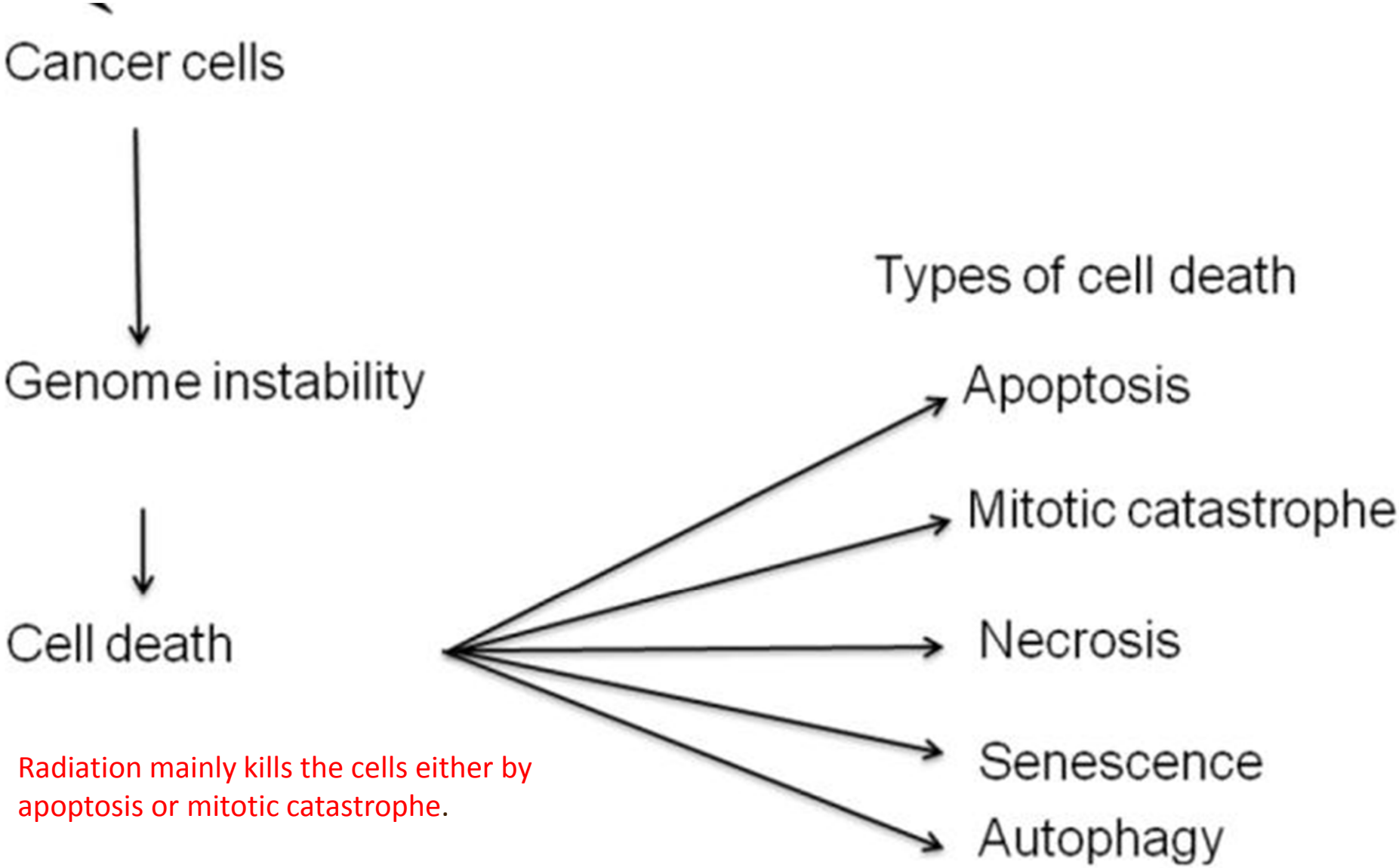
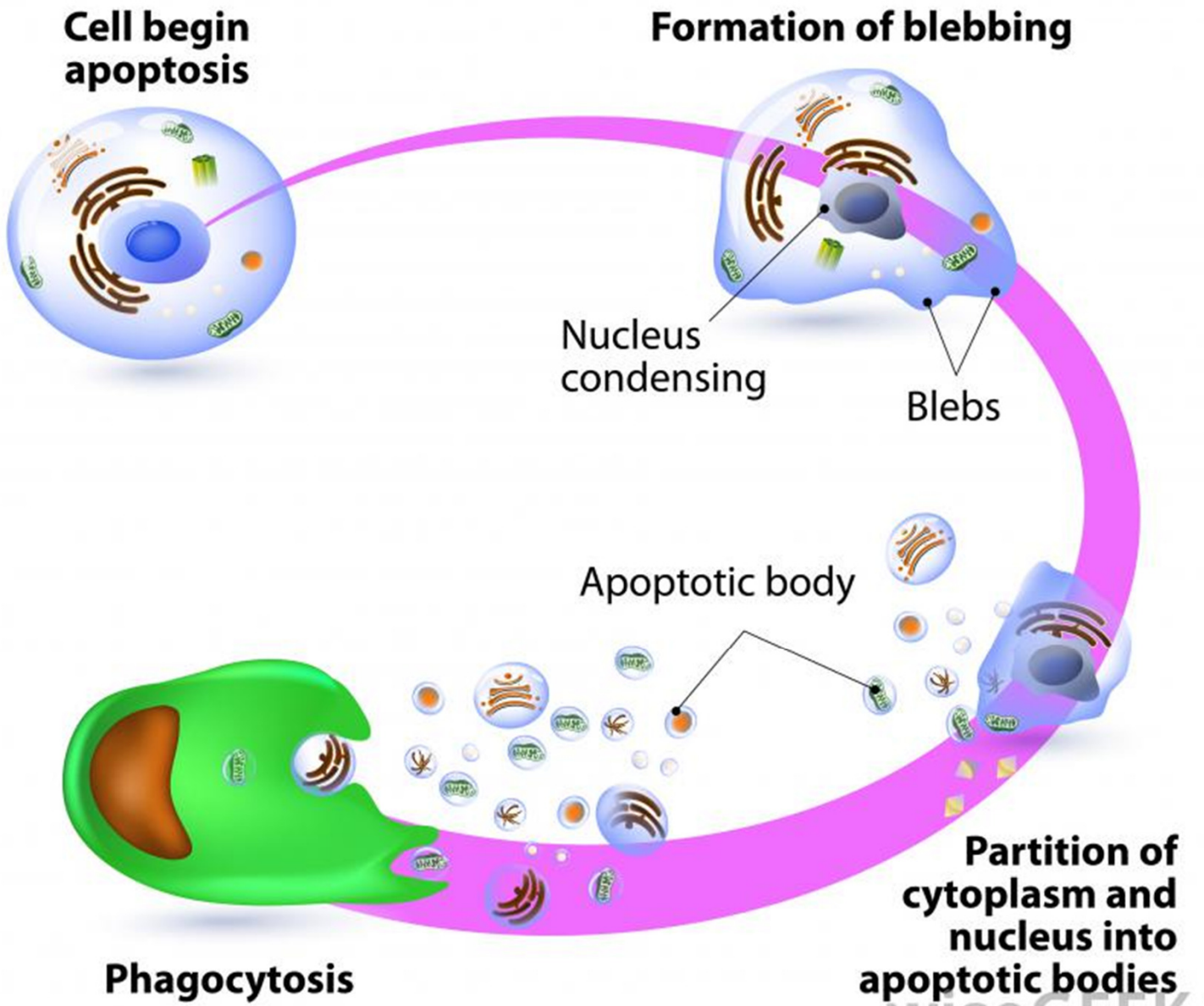


Figure 2. Radiation act directly or indirectly on the cellular DNA.



Radiation mainly kills the cells either by apoptosis or mitotic catastrophe.

APOPTOSIS



How patients are prepared for radiation?

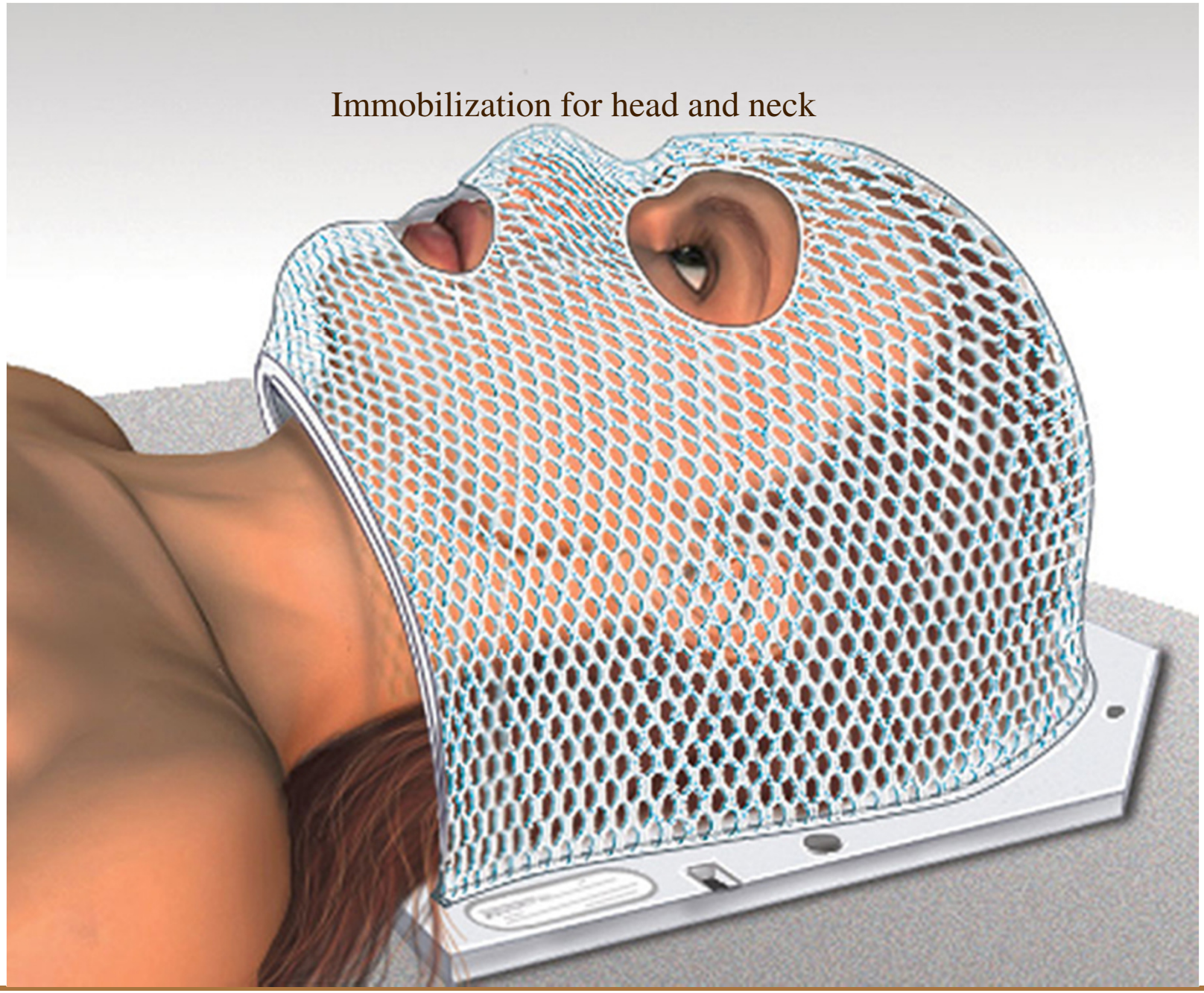
What is involved in radiation delivery?

RO

Medical Physicist

Radiotherapist

Immobilization for head and neck



Immobilizati
on for chest

CT SIMULATOR

RT planning and delivery

- Volume delineation
- 3D CRT (Conformal Radiotherapy)
- IMRT(Intensity Modulated Radiotherapy)

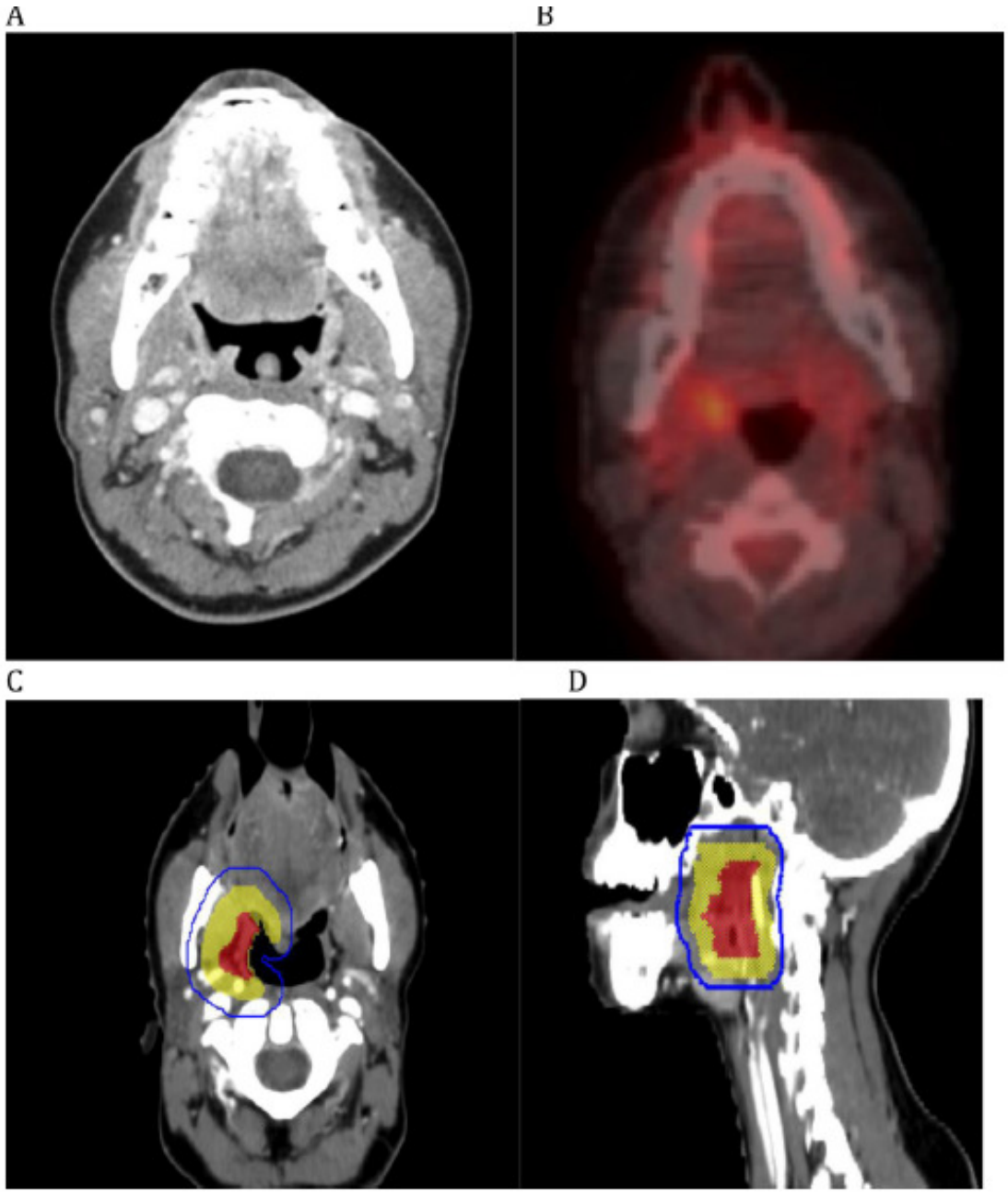
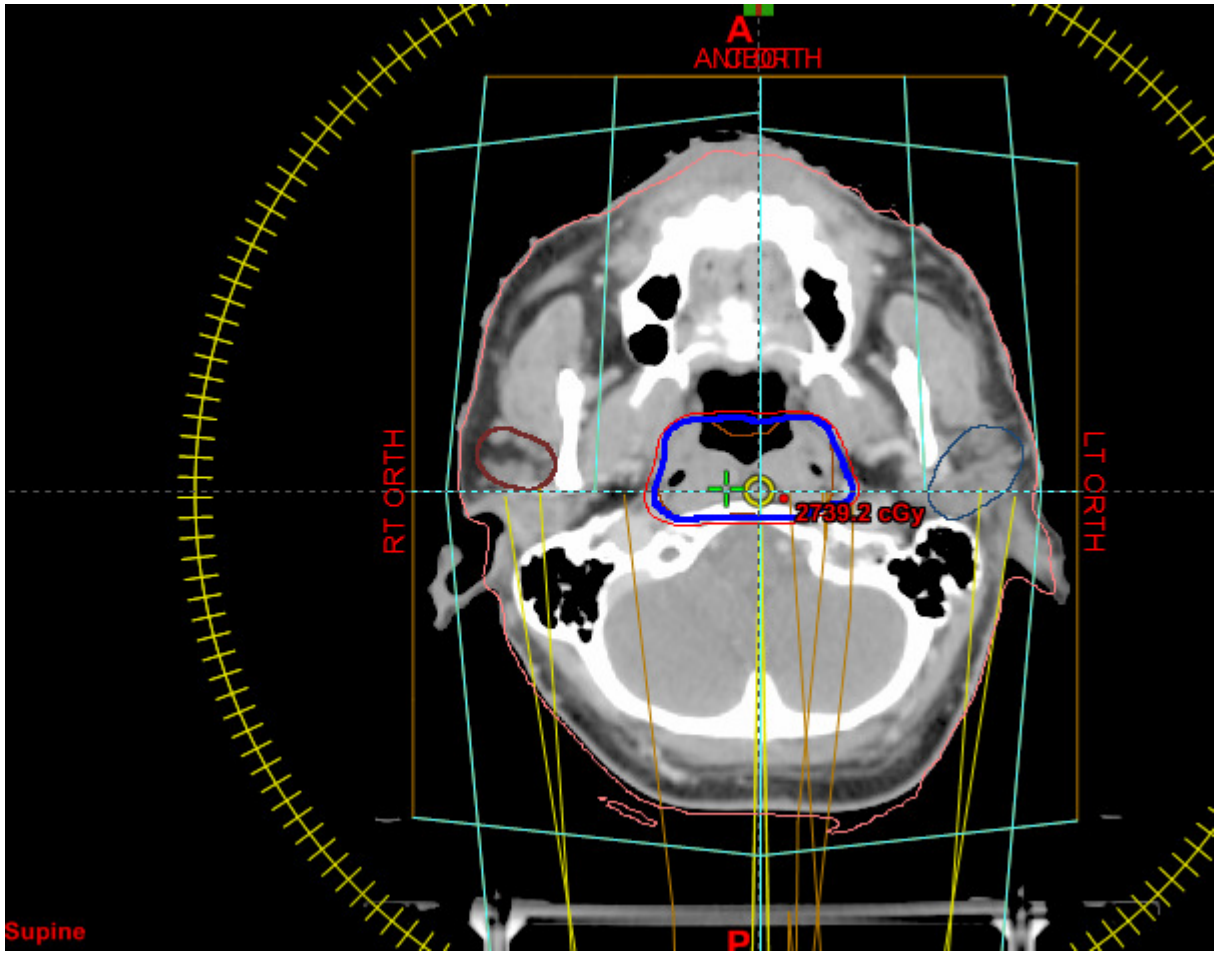
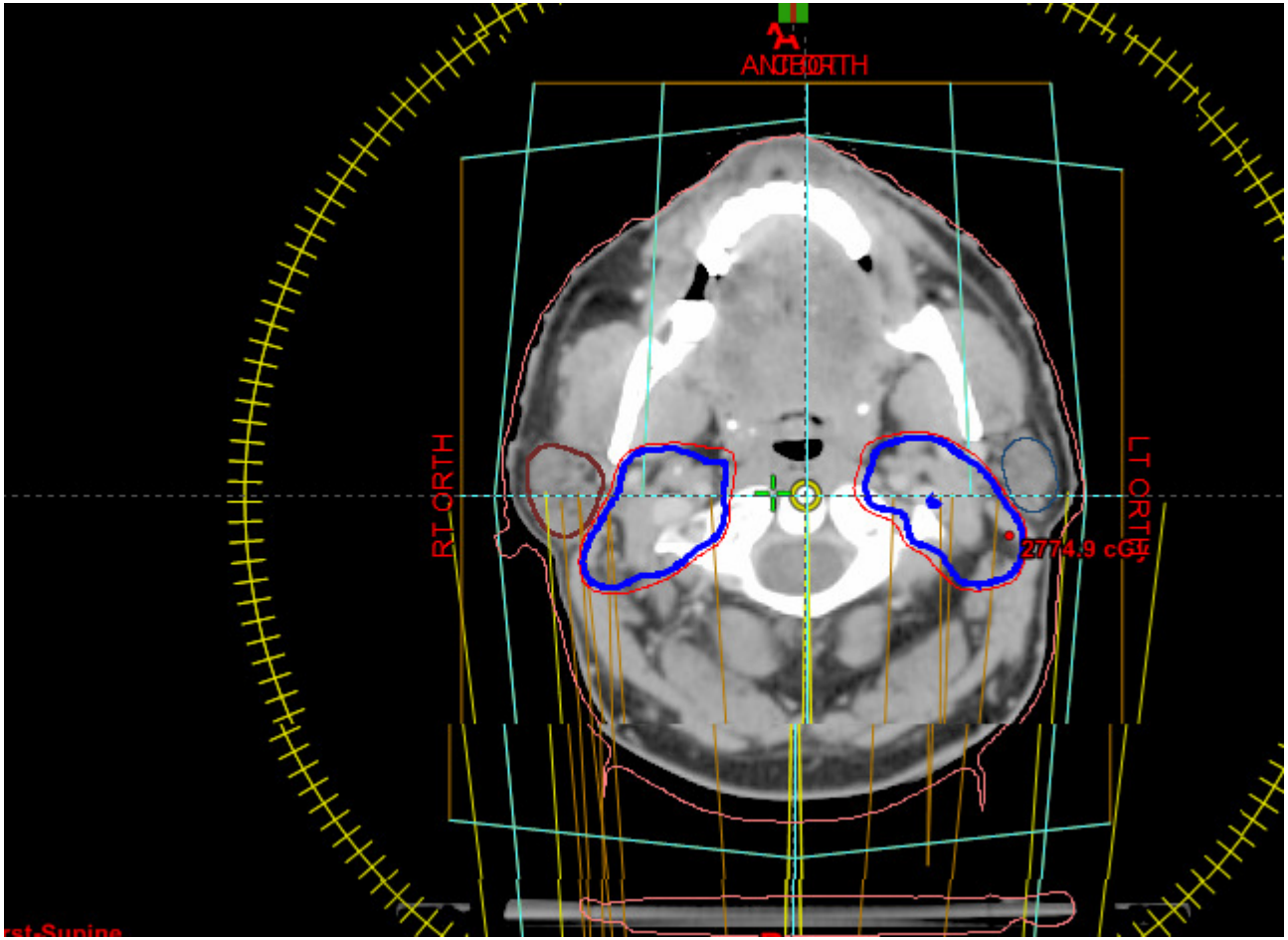


Fig. 4. (A, B) Lymphoma of the tonsil in a 42-year-old man after right tonsillectomy showing diffuse large B-cell lymphoma of right tonsil alone. (C, D) Received short chemotherapy followed by involved site radiation therapy to tonsil of 30 Gy with intensity modulated radiation therapy; gross tumor volume, red; clinical target volume, yellow; planning target volume, blue.

Nodular Lymphocyte predominant HL-IMRT planning




RT ORTH
LT ORTH
2774.9 cGy

Radiation is indicated in------

- Early Stage HL – Combined Modality
- Advanced HL- Residual disease
- Early Stage NHL – As a primary treatment
- Combined Modality
- Advanced NHL- Residual disease
- TBI
- TSI- Mycosis Fungoides
- Low dose palliative RT

ES HL Prognostic factors

Unfavourable Risk Factors in Early-stage HL: Risk stratification

Risk factor	EORTC	GHSG	NCIC/ECOG	NCCN 2010
Med Mass	>0.35 at T/6	>1/3	<1/3 or 10 cm	> 1/3 or >10 cm
Histology			MC or LD	
Age	≥50 years old		≥40 years old	-
EN disease	-	Any		>1
ESR and B Sx	≥50 or ≥30 and B Sx	≥50 or ≥30 and B Sx	≥50	≥50 or any B Sx
Number of nodal sites	>3	>2	>3	>3

EORTC – European Organization for Research and Treatment of Cancer; ESR – erythrocyte sedimentation rate;

ES HL

- CT+RT or CT alone are recommended treatment options for patients with early-stage non-bulky Hodgkin lymphoma.
- RT delivered (3 weeks post chemo) after 2 cycles of ABVD in FHL and after 4 cycles in UFHL
- 20 Gy/ 10F-2weeks for patients with FHL and between 30 to 36 Gy/15-18F in 3-3.5 weeks for UFHL
- NLPHL : RT alone may be sufficient – 30Gy/3 weeks

Advanced Stage HL

- ABVD x 6 /BEACOPP x 6
- Prior bulk > 10cm with PET positive residual mass
- RT: 30Gy/15 F/3 weeks

Localized Indolent NHL Lymphomas

- CLL/SLL
- Follicular lymphoma
- Marginal zone lymphoma:

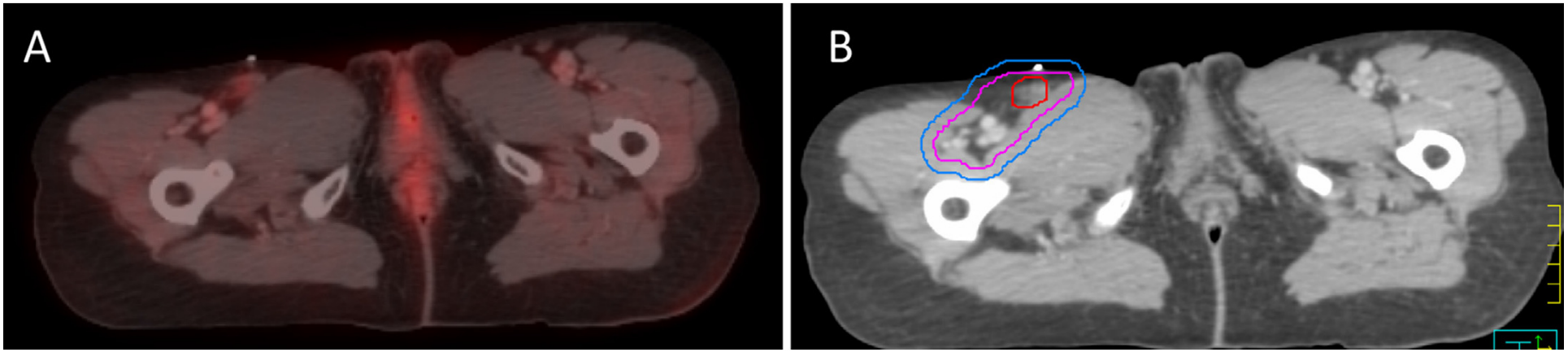
  Gastric

  Conjunctiva, Parotid, Thyroid

  24-30 GY in 2 G P/F 2.5 to 3 weeks - ISRT

Early Stage NHL – As a primary treatment

- Follicular Lymphomas stage 1&2 (Grade 1,2 and 3A
- Involved Site Radiation
- 24-30 Gy in 2.5- 3 weeks



A 63-year-old woman with stage 1A follicular lymphoma of the right inguinal region presented with right groin mass. Excisional biopsy. At simulation the patient was placed in frog-leg position, and the scar was wired.

Outcome of patients with stage1/11 FL treated with RT

- LC: 97%
- 15 years OS: 57%
- 15 years PFS: 46%

*Barzenje DA, Småstuen MC, Liestøl K, Fosså A, Delabie J, Kolstad A, Holte H. Radiotherapy compared to other strategies in the treatment of stage I/II follicular lymphoma: a study of **404 patients** with a median follow-up of 15 Years. PloS one. 2015 Jul 6;10(7):e0131158.*

Palliation

- Low dose radiation primarily for indolent low grade) lymphomas
- SLL
- FL MZL
- MCL
- 2 Gy x 2 which may be repeated as needed
- Rapid and durable response
- MINIMAL OR NO TOXICITY

4 Gy versus 24 Gy radiotherapy for patients with indolent lymphoma (FORT): a randomized phase 3 non-inferiority trial

- UK. Lancet Oncology

	24 Gy	4 Gy
All patients*		
Complete regression	176 (68%)	137 (49%)
Partial regression (>30%)	60 (23%)	90 (32%)
Stable disease (including <30% regression)	22 (8%)	44 (16%)
Progression	2 (<1%)	10 (4%)
Total	260	281
Follicular lymphoma		
Complete regression	152 (67%)	116 (48%)
Partial regression (>30%)	53 (23%)	78 (32%)
Stable disease (including <30% regression)	19 (8%)	40 (16%)
Progression	2 (<1%)	9 (4%)
Total	226	243
Marginal zone lymphoma		
Complete regression	24 (71%)	21 (55%)
Partial regression (>30%)	7 (21%)	12 (32%)
Stable disease	3 (1 %)	4 (11%)
Progression	0	1 (3%)
Total	34	38

Data are number of sites (%). *Patients who withdrew before treatment or with missing treatment data have been excluded, as have the three patients who switched from 4 Gy to 24 Gy after the trial was closed. There were also 43 (20 in the 24 Gy group and 23 in the 4 Gy group) with no measurable disease at baseline and 17 (13 in the 24 Gy group and four in the 4 Gy group) with missing response data.

Table 2: Response (randomised sites) at week 12

Aggressive Early Stage Lymphomas(DLBCL or PTCL)

- Consolidation after chemotherapy CR: 30-36 Gy
- Complimentary after PR: 40-50 Gy
- RT as primary treatment for refractory or non-candidates for chemotherapy: 40-55 Gy
- In combination with stem cell transplantation: 20-36 Gy, depending on sites of disease and prior RT exposure

- NK-T cell lymphoma
  - RT as primary treatment 50-65 Gy
  - RT in combined modality therapy 45-60 Gy

Mycosis Fungoides

- Mycosis fungoides (MF) is the most common subtype of cutaneous T-cell lymphoma
- Total Skin Electron Beam
- 12-36 Gy
- 3 fractions a week

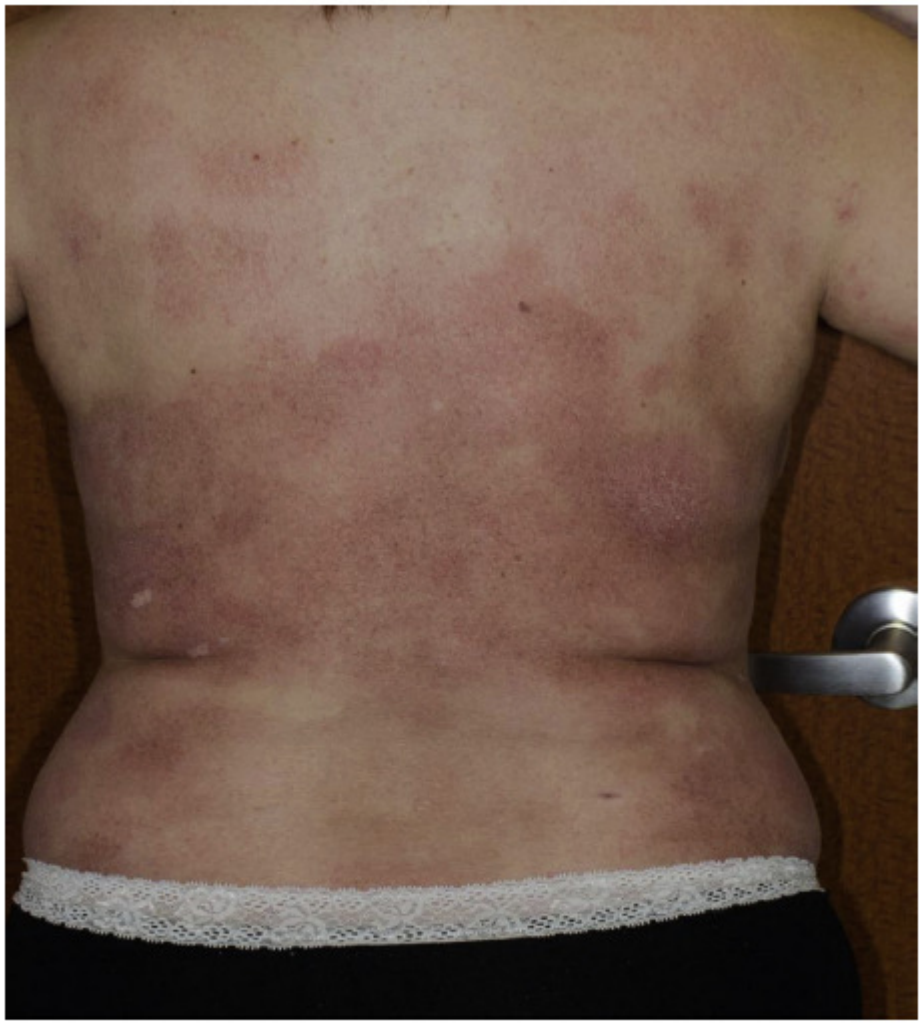
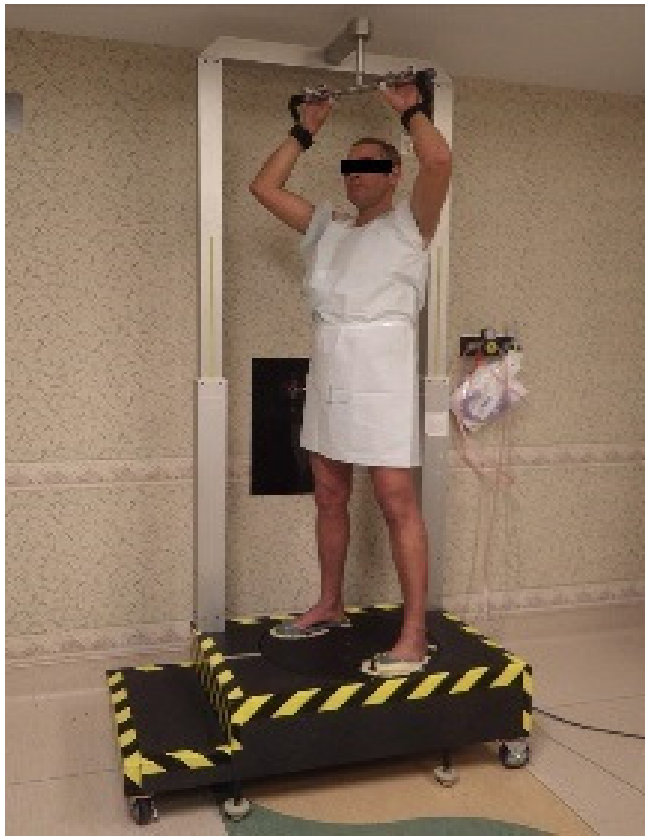
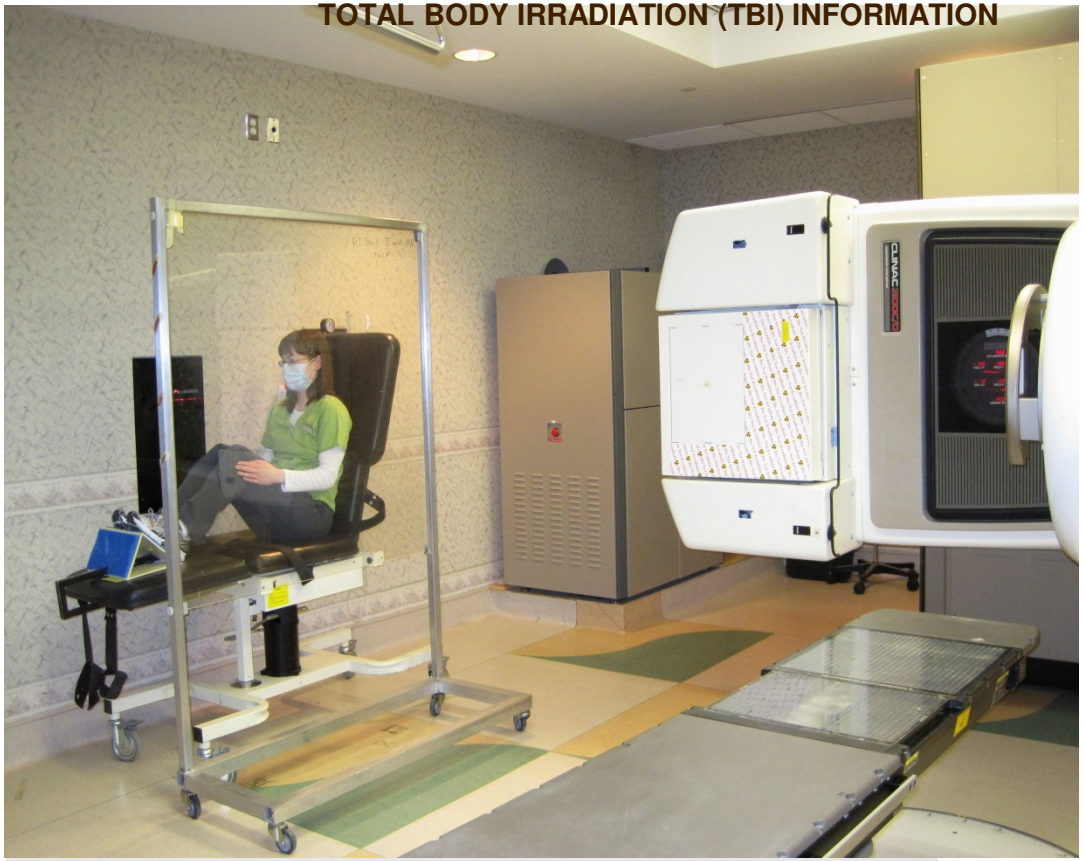


Fig. 6. Mycosis fungoides with widespread patches.

Fig. 7. Mycosis fungoides with numerous plaques.



Total Body Irradiation



Acute and sub acute toxicity

- Skin Reaction
- Peak 7-10 days after therapy.
- Skin Desquamation and chronic skin changes rare
- Alopecia:
- Regrowth3-4 months after treatment
- Complete recovery expected

Acute and sub acute toxicity

- Depends on the anatomical site of treatment
- Dysphagia: Complete resolution with in one month. Antacid+ Xylocaine Viscous 2%
- Temporary taste alteration
- Xerostomia: Full Recovery expected
- L'Hrmitts Sign: Electric shock like sensation in the extremities by neck flexion
- 3 months after RT- Disappears after 6 months

Acute and sub acute toxicity

- Radiation Induced Pneumonitis:
- Dry cough , dyspnea 1-3 months post RT
- < 5%
- Self limiting
  - Steroids
- Oral prednisone,40 to 60 mg daily for 1 to 2 weeks followed by taper (reducing ~10 mg every 1–2 weeks).

Managing Mucositis

- **Magic Mouth wash**
- 0.56 ml dexamethasone 4mg/ml
- 120ml diphenhydramine elixir 2.5mg/ml suspension
- 30 ml of Nystatin 100,000 units/ml in suspension
- 30 ml of tetracycline 125mg/ml suspension
- 200 ml of sterile water
- Swish 10 mL for 3 minutes and swallow every 6 hours while awake

Late Effects

- Hypothyroidism
- Can occur as late as 26 years after RT
- Second malignancies
  - Breast cancer
  - Lung cancer
- GI
- Risk of developing NHL

Late Effects

- Cardiovascular disease
- CAD
- Valvular disease
- Cardiomyopathy

Take Home Messages

- Radiation has a definite and curative role in limited stage low grade lymphomas

- Radiation has an important contribution combined with other treatments for lymphoma