Absolute Clinical Radiation Oncology Review

Daniel M. Trifiletti
Nicholas G. Zaorsky
Editors

Springer

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Contents

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Abbreviations

2D	Two-dimensional
3D	Three-dimensional
3D-CRT	Three-dimensional conformal radiation therapy
5-FU	5-Fluorouracil
ABMT	Autologous bone marrow transplant
APBI	Accelerated partial breast irradiation
abnl	Abnormal
ACTH	Adrenocorticotropic hormone
ADH	Antidiuretic hormone
adj	Adjuvant
Adr	Adriamycin
AFP	Alpha-fetoprotein
AIDS	Acquired immune deficiency syndrome
AJCC	American Joint Committee on Cancer
aka	Also known as
alk phos	Alkaline phosphatase
Alt	Alternated with
am	Morning (ante meridian)
ANC	Absolute neutrophil count (lab)
ant	Anterior
anterolat	Anterolateral
AP	Anterior-posterior
APC	Adenomatous polyposis coli (gene mutation)
appx	Approximately
APR	Abdominoperineal resection
ARUBA	A Randomized Trial of Unruptured Brain Arteriovenous Malformations
ASCUS	Atypical squamous cells of undetermined significance
ASTRO	American Society for Radiation Oncology
AUC	Area under the curve
avg	Average
BAT	B-mode acquisition and targeting
b/c	Because
b/t	Between
bFFP	Biochemical freedom from progression
b-HCG	Beta-human chorionic gonadotropin
bid	Twice daily

bilat	Bilateral
BM	Bone marrow
BMI	Body mass index
BMP	Basic metabolic panel
BMT	Bone marrow transplant
BTSG	Brain Tumor Study Group
BWS	Beckwith-Wiedemann Syndrome
Bx	Biopsy/biopsies
C	Cervical (spine level)
c/w	Compared with
CA19-9	Cancer antigen 19-9
CA 125	Cancer antigen 125
CALGB	Cancer and Leukemia Group B
C/A/P	Chest/abdomen/pelvis
CBC	Complete blood count (lab)
CCCG	Colorectal Cancer Collaborative Group
cCR	Clinical complete response
CD	Cone-down
CD4	Cluster of differentiation 4 (for immune cells)
CEA	Carcinoembryonic antigen
CESS	Cooperative Ewing Sarcoma Study
CHART	Continuous Hyperfractionated Accelerated Radiotherapy Trial
chemo	Chemotherapy
CHF	Congestive heart failure
CIN	Cervical intraepithelial neoplasia
CIS	Carcinoma in situ
cm	Centimeter/centimeters
CMP	Complete metabolic panel (lab)
c-myc	Proto-oncogene, part of the Myc gene family
cN0	Clinically node-negative
CN	Cranial nerve
CNS	Central nervous system
Co-60	Cobalt-60
COG	Children's Oncology Group
contralat	Contralateral
CPT	Common procedural terminology
Cr	Creatinine
CR	Complete response
CRT	Chemoradiation
CSF	Cerebrospinal fluid
CSI	Craniospinal irradiation
CSM	Cancer-specific mortality
CSS	Cause-specific survival
CT	Computed tomography
cT	Clinical T-stage
CTV	Clinical target volume
Cx	Cervical (spine level)
CXR	Chest x-ray

D/C	Discontinue/discontinued
D&C	Dilation and curettage
DCC	Deleted in colorectal cancer (gene)
DDx	Differential diagnosis
DFS	Disease free survival
DI	Diabetes insipidus
DLBCL	Diffuse large-B cell lymphoma
DLCO	Lung diffusion capacity testing
DM	Distant metastasis
DMFS	Distant metastasis free survival
DOI	Depth of invasion
DRE	Digital rectal examination
DSS	Disease-specific survival
d/t	Due to
DVH	Dose volume histogram
DVT	Deep venous thrombosis
Dx	Diagnosis/diagnoses
Dz	Disease/diseases
EB	External beam
EBRT	External beam radiation therapy
EBUS	Endobronchial ultrasound
EBV	Epstein-Barr virus
ECE	Extracapsular extension
ECOG	Eastern Cooperative Oncology Group
EFRT	Extended field radiotherapy
EFS	Event free survival
e.g.	For example
EGFR	Epidermal growth factor receptor
EM	Electron microscopy
ENI	Elective nodal irradiation
EORTC	European Organisation for Research and Treatment of Cancer
Epo	Erythropoietin
ESR	Erythrocyte sedimentation rate (lab)
et al.	And others
EUA	Exam under anesthesia
EUS	Endoscopic ultrasound
EWS	Ewing sarcoma
exam	Examination
f/b	Followed by
FAP	Familial adenomatous polyposis
FDA	Food and Drug Administration
FDG	Fluorine-18 2-fluoro-2-deoxy-D-glucose
FEV	Forced expiratory volume
FFS	Failure-free survival
FFTF	Freedom from treatment failure
FIGO	International Federation of Gynecology and Obstetrics
FH	Favorable histology
FHIT	Fragile histidine triad

FISH	Fluorescence in situ hybridization
FKHR	Forkhead (Drosophila) homolog 1 (rhabdomyosarcoma) (gene)
FLAIR	Fluid attenuation inversion recovery
F:M	Female to male ratio
FN	Rate false-negative rate
FNA	Fine needle aspiration
FOLFOX	5-FU/leukovorin/oxaliplatin
FPR	False-positive rate
FSH	Follicle-stimulating hormone
FSR	Fractionated stereotactic radiotherapy
fx	Fraction/fractions
GBM	Glioblastoma multiforme
GH	Growth hormone
GI	Gastrointestinal
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GnRH	Gonadotropin-releasing hormone
GTR	Gross total resection
GTV	Gross target volume
GU	Genitourinary
Gy	Gray
gyn	Gynecologic
H&N	Head and neck
H&P	History and physical
HA	Headache
HAART	Highly active antiretroviral therapy
HCG	Human chorionic gonadotropin (lab test)
HDC+SCT	High-dose chemotherapy with stem cell transplant
HDR	High dose rate
Hgb	Hemoglobin
HGG	High-grade glioma
HGSIL	High-grade squamous intraepithelial lesion
HIV	Human immunodeficiency virus
HNPCC	Hereditary nonpolyposis colon cancer
HPV	Human papilloma virus
hr/hrs	Hour/hours
HR	Hazard ratio
HRT	Hormone replacement therapy
HSV	Herpes simplex virus
HTN	Hypertension
HVA	Homovanillic acid
Hx	History/histories
Hyperfx	Hyperfractionation
IBCSG	International Breast Cancer Study Group
IC	Internal carotid
ICP	Intracranial pressure
IDL	Isodose line
i.e.	That is

IFN	Interferon
IgA	Immunoglobulin A
IGF	Insulin-like growth factor
IgG	Immunoglobulin G
IGRT	Image-guided radiation therapy
IJROBP	International Journal of Radiation Oncology, Biology, and Physics
IMA	Inferior mesenteric artery
IMRT	Intensity-modulated radiation therapy
inf	Inferior
INR	International normalized ratio
intraop	Intraoperative
IORT	Intraoperative radiation therapy
ipsi	Ipsilateral
IQ	Intelligence quotient
ITV	Internal target volume
IVC	Inferior vena cava
JAMA	Journal of the American Medical Association
JCO	Journal of Clinical Oncology
JCOG	Japan Clinical Oncology Group
JCRT	Joint Center for Radiation Therapy
JHH	Johns Hopkins Hospital
JNCI	Journal of the National Cancer Institute
JPA	Juvenile pilocytic astrocytoma
KPS	Karnofsky Performance Status
L	Lumbar (spine level)
LA	Lymphadenopathy
lab	Laboratory/laboratory test
LAD	Lymphadenopathy
LAMP	Locally Advanced Multimodality Protocol
LAO	Left anterior oblique
lat	Lateral
LC	Local control
LDH	Lactate dehydrogenase
LDR	Low dose rate
LE	Lower extremity
LEEP	Loop electrosurgical excision procedure
LF	Local failure
LFT	Liver function test
LGSIL	Low-grade squamous intraepithelial lesion
LH	Luteinizing hormone
LINAC	Linear accelerator
LLL	Left lower lobe
LML	Left middle lobe
LN	Lymph node
LND	Lymph node dissection
LOH	Loss of heterozygosity
LP	Lumbar puncture

LPO	Left posterior oblique
LR	Local recurrence
LRC	Locoregional control
LRF	Locoregional failure
LRFS	Local recurrence free survival
LRR	Locoregional recurrence
LUL	Left upper lobe
LVI	Lymphovascular invasion
LVSI	Lymphovascular stromal invasion
MALT	Mucosa-associated lymphoid tissue
max	Maximal/maximum
MB	Medulloblastoma
MDACC	MD Anderson Cancer Center
med	Medication
MEN	Multiple endocrine neoplasia
mets	Metastasis/metastases
M:F	Male to female ratio
MFS	Metastasis free survival
MGMT	O6-methylguanine DNA-methyltransferase
MI	Myocardial infarction
MIBG	Metaiodobenzylguanidine
min	Minimal/minimum
MLD	Mean lung dose
MN	Mediastinal node
mo/mos	Month/months
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MS	Median survival
MSKCC	Memorial Sloan Kettering Cancer Center
MTD	Maximum tolerated/tolerable dose
Mtx	Methotrexate
MVA	Multivariate analysis
NB	Neuroblastoma
N/C	Nuclear to cytoplasm ratio
NCCN	National Comprehensive Cancer Network
NCCTG	North Central Cancer Treatment Group
NCI	National Cancer Institute
NCIC	National Cancer Institute of Canada
NED	No evidence of disease
NEJM	New England Journal of Medicine
neoadj	Neoadjuvant
NF	Neurofibromatosis
NGGCT	Nongerminomatous germ cell tumor
NHL	Non-Hodgkin lymphoma
NPCR	National Program of Cancer Registries
NPV	Negative predictive value
NPX	Nasopharynx
NR	No response

NSABP	National Surgical Adjuvant Breast and Bowel Project
NSAID	Nonsteroidal anti-inflammatory drug
NSE	Neuron-specific enolase
NSS	Not statistically significant
NTR	Near-total resection
n/v	Nausea/vomiting
NWTS	National Wilms Tumor Study
NZ	New Zealand
OPX	Oropharynx
OR	Odds ratio
ORN	Osteoradionecrosis
ORR	Overall response rate
OS	Overall survival
PA	Posterior-anterior
PAP	Papanicolaou smear
PCI	Prophylactic cranial irradiation
PCNSL	Primary CNS lymphoma
PCP	Pneumocystic pneumonia
PCR	Polymerase chain reaction
pCR	Pathologic complete response
PDGFR	Platelet-derived growth factor receptor
PEG	(Tube) Percutaneous endoscopic gastrostomy tube
periop	Perioperative
PET	Positron emission tomography
PF	Posterior fossa
PFS	Progression free survival
PFT	Pulmonary function test
Plt	Platelets
pm	Afternoon (post meridian)
PM	Para-meningeal (for rhabdomyosarcoma)
PMH	Princess Margaret Hospital
pN0	Pathologically node negative
PNET	Primitive neuroectodermal tumor
PNI	Perineural invasion
PNS	Paranasal sinuses
PORT	Postoperative radiation therapy
post	Posterior
posterolat	Posterolateral
postop	Postoperative
PPV	Positive predictive value
PR	Partial response
PrA	Para-aortic (for lymph nodes)
PrT	Paratesticular (for rhabdomyosarcoma)
preop	Preoperative
PS	Performance status
PSA	Prostate-specific antigen
pt/pts	Patient/patients
PTHrP	Parathyroid hormone–related peptide

PT	Prothrombin time
pT	Pathologic tumor stage
PTV	Planning target volume
PUVA	Psoralen and long-wave ultraviolet radiation
q	Every
qd	Daily
QOL	Quality of life
QUANTEC	Quantitative analysis of normal tissue effect in the clinic
R1	Microscopically positive margin
R2	Macroscopically positive margin
RAO	Right anterior oblique
RASSFIA	Ras association (RalGDS/AF-6) domain family member 1A
RB	Retinoblastoma
RBE	Relative biologic effectiveness
RCC	Renal cell carcinoma
RCT	Randomized controlled trial
rcv	Receive/received
RFS	Relapse free survival
RLL	Right lower lobe
RML	Right middle lobe
RMS	Rhabdomyosarcoma
r/o	Rule out
ROM	Range of motion
RPO	Right posterior oblique
RR	Relative risk
RT	Radiation or radiation therapy
RTOG	Radiation Therapy Oncology Group
RUL	Right upper lobe
RUQ	Right upper quadrant
Rx	Prescription/prescriptions
S	Sacral (spine level)
SBO	Small bowel obstruction
SC	Spinal cord
SCC	(or SCCa) Squamous cell carcinoma
SCV	Supraclavicular
Sg	Surgery
SEER	Surveillance Epidemiology and End Results (data)
SFOP	French Society of Pediatric Oncology
Sg	Surgery
SIADH	Syndrome of inappropriate secretion of antidiuretic hormone
SIL	Squamous intraepithelial lesion
SQ	Subcutaneous
s/p	Status post
SPECT	Single photon emission computed tomography
SRS	Stereotactic radiosurgery
SS	Statistically significant
SSD	Source to skin distance
ST	Soft tissue (as in sarcoma)

STD	Sexually transmitted disease
STR	Subtotal resection
STS	Soft-tissue sarcoma
sup	Superior
SVC	Superior vena cava
Sx	Symptom/symptoms
T	Thoracic (spine level)
TD	Tolerance dose
TFT	Thyroid function test
tid	Three times a day
TMZ	Temozolomide
TNM	Tumor/node/metastasis
trilat	Trilateral
TRUS	Transrectal ultrasound
TSH	Thyroid-stimulating hormone
Tx	Treatment/treatments
UA	Urinalysis
UCSF	University of California at San Francisco
UE	Upper extremity
UH	Unfavorable histology
UK	United Kingdom
unilat	Unilateral
US	Ultrasound
U.S.	United States
UV	Ultraviolet
VALCSG	Veterans Administration Lung Cancer Study Group
VCE	Vincristine, carboplatin, etoposide (chemo regimen)
VMA	Vanillylmandelic acid
vs.	Versus
w	With
WBC	White blood cell
WBRT	Whole brain radiation therapy
WHO	World Health Organization
wk/wks	Week/weeks
WLE	Wide local excision
yo	Year old/years old
yr/yrs	Year/years

Symbols

+	Meaning with or and (as in Surgery + RT)
→	Meaning followed by
↑	Meaning increasing, high(er), or elevated
↓	Meaning decreasing or low(er)

General Principles of Radiation Oncology

1

Nicholas G. Zaorsky, Daniel M. Trifiletti, and Daniel W. Golden

Abstract

This chapter discusses the general management and thought process used by radiation oncologists. Several broad and basic principles of radiation oncology are discussed.

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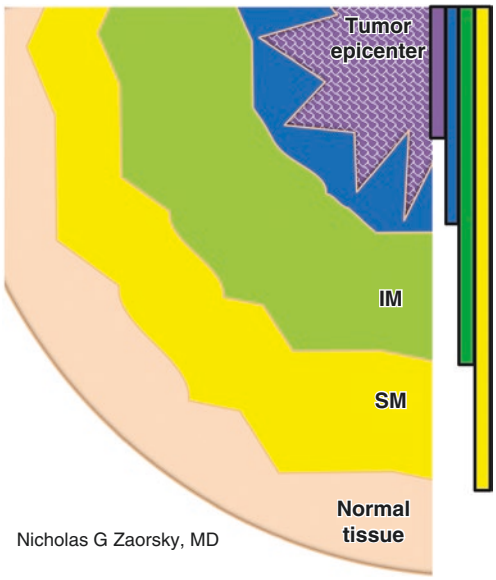

GTV: gross tumor volume

- All tumor that can be seen on a scan
- For reference, a 1 cm tumor has about 10^9 billion cells

CTV: clinical target volume

- The volume that has to be treated to achieve cure or palliation
- Should be defined before choosing a treatment modality
- Includes "crablike" extensions of the cancer, which contain:
  - microscopic cancer cells that cannot be seen on a scan
  - “Elective” lymph nodes that we think the cancer spread to
- CTV = GTV + a margin of where we think microscopic disease is located

IM: internal margin

- Variations in size, shape, and position of CTV relative to anatomic reference points (e.g. from breathing)

ITV: internal target volume

- Volume that encompasses movement of the CTV and the IM
- ITV = CTV + IM

SM: setup margin

- Uncertainties in patient positioning and alignment of therapeutic beams during treatment planning, and all treatment sessions

PTV: planning target volume

- Volume that encompasses movement of the CTV, the IM, and errors in setup / position of the patient and penumbra
- PTV = CTV + IM + SM

Disease	Scenario	General protocol	CTV	PTV	Dose	Chemo	Outcome
WHO IV (GBM) and WHO III (AA, AO, AOA) 1p19q non-codel; Unidel; AA Rim-enhancing (signifying central necrosis), irregular. Pathology: pseudo-palisading necrosis. High grade = Mitoses, Endothelial prolif, Atypia, Necrosis. IDH 1 WT = molecular GBM IDH1 = 2ndary GBM (LGG =>HGG)	Standard (Stupp): < ~65–70 yo, KPS > ~60–70	MRI in 48h of surg. Send tissue for MGMT, IDH1/2, TERT promoter, EGFR	CTV46 = Post-op T2 **FLAIR** + cavity **+ 2 cm** CTV60 = **post-op** cavity + residual **enhancement + 2 cm** (cropped to 5 mm at natural barriers)	+ 3 mm w daily CBCT	46 Gy to **FLAIR**, 60 Gy to **enhancement**	+TMZ 75 mg/m2 QD, then 1m break, then 150 mg x 5d q 28d x 6c. Consider TTF No Avastin upfront	GBM RPA III: 22 m RPA IV: 15 m RPA V: 10 m
	>65–70 yo and good KPS	Decadron + PPI Keppra 500 mg BID if sz	CTV = T1post enhancement + **2 cm**	+ 3 mm w daily CBCT	**40 Gy / 10 @** 4 + TMZ → TMZ (Perry) **40.05 Gy / 15** @2.7 Gy (Roa 1; also WHO III KPS≤60), 75% of dose **25 Gy / 5 @ 5** Gy (Roa 2: 40/15=25/5) **34 Gy / 10** @ 3.4 Gy (Nordic: 34/10 better than 60/30)	No TMZ in Canada/Roa, yes TMZ in Nordic/Perry	Perry: MST 9.3 vs 7.6 m
	KPS ≤ 60				**TMZ alone** (Nordic) for poor KPS		
	Recurrence		GTV	+ 3 mm w daily CBCT	35 Gy / 10	Bev alone	
WHO III (AA, AO, AOA);	1p19q co-del (all are IDH1mut); others per WHO IV standard	MRI in 48h of surg. Send tissue for 1p/19q and IDH1 for oligo (all 1p19q codel are also IDH1 mut)	CTV45 = Post-op T2 FLAIR + cavity + 2 cm (cropped to 5 mm at natural barriers) CTV59.4 = If enhancing: post-op cavity + residual enhancement **+ 2 cm** (cropped to 5 mm at natural barriers). If non-enhancing: T2-FLAIR **+5mm**	+ 3 mm w daily CBCT	**45 Gy** to FLAIR, and **59.4 Gy** to conedown / 1.8 Gy	Adjuvant PCV q6w x 6c	94–02 GIII AO, AOA: RT vs RT, adj PCV 1p/19q co-del (all IDH1 mut): 7yr vs. 14.9yr 1p/19q intact, IDH1 mut: 3.3 vs. 5.5 Intact/WT: 1.3 vs. 1.0
LGG (diffuse astro: oligo, astro, mixed oligoastro; pilomyxoid; pleomorphic xanthoastro) G1 subtypes: JPA, pleomorphic xanthoastro, SEGC astrocytoma, subependymoma, gangliogliomas	**New hi risk**: > 40 yo or STR **Old hi risk** (also): size 6+ cm, astrocytoma, neuro deficit preop, cross midline, 1p19q non-co-del, IDH1/2 non-mut	**options:** RT + adjuvant PCV RT + concurrent TMZ (prefer for MGMTm) Decadron + PPI Keppra 500 mg BID if sz	CTV = T2 FLAIR + tumor bed + **1 cm**	+ 3 mm w daily CBCT	**50.4–54 Gy**	**High Risk options:** RT + adjuvant procarbazine POD8–21, CCNU d1, vincristine (PCV) RT + concurrent TMZ **Low risk option:** TMZ alone if 1p19q co deleted	Low risk: OS5 = 90%; PFS5 = 50% High risk: OS5 = 70%; PFS5 = 50%
	Low risk: <40 yo AND GTR	**Options:** Obs vs RT alone if sx or difficult to salvage vs. TMZ alone if 1p19q codel					
Ependymoma, brain	G1 = subependymomas and **myxopapillary** G2 = classic ependymomas G3 = **anaplastic** ependymomas	MRI in 48h of surg. RT in 8w.	CTV = initial tumor vol, tumor bed + 1 cm	+ 3 mm w daily CBCT	G2: **54 Gy** G3: **59.4 Gy**. If MRI spine/LP+, CSI to 36 Gy. Boost spine GTVs to **45 Gy**	Chemo no proven benefit	EFS5 GTR: 80% EFS5 STR: 40%
Ependymoma, spine		R0 = observe (only G1/2) R+ = limited field RT Spine mets = CSI + boost		+ 3 mm w daily CBCT	Limited field = **50.4 Gy.** If MRI spine/LP+, CSI to 36 Gy. Boost spine GTVs to **45 Gy**		
Ependymoblastoma	treat like STPNET/high risk medullo				CSI 36 Gy. Boost to **55.8 Gy**		
Meningioma		G1 Simpson1–3 (R0): obs G1 Simpson4–5 (R+): obs vs RT hi risk vol Recur: surg vs RT G2-3 (<10%): EBRT	Do not cover dural tail!!! **G1:** CTV54 = GTV + bed + **1 cm** **G2/3:** CTV54 = GTV + bed + **2 cm** CTV60 = GTV + bed + **1 cm**	+ 3 mm w daily CBCT	RTOG 0539: **PTV54** to tumor/bed +1–2 cm **PTV60** to G2/3 tumor bed + 1 cm Consider SRS 13 Gy (up to 17 Gy if G3), but not 1st choise. Optic n sheath: 45 Gy		G1: 90% LC in def EBRT, R0, R1+EBRT G2: MST 12y. LC 60% if R0, 70% LC surg + EBRT G3: MST 3y. OS5 50%.
Pituitary adenoma: Macro: ≥ 1 cm, micro < 1 cm PRL (30%), GH (25%), ACTH (15%). PRL: amenorrhea, galactorrhea. Cushing (ACTH): obesity, HTN, DM, hirsutism, skin, osteoporosis. Acromegaly (GH): bones, HA, cardiac dz	**RT if:** Inoperable; TSH secreting (always post-op); R+ with persistent hypersecretion or residual near critical structures; Recur after surg	Endo panel: TSH, FSH, LH, GH/IGF-1, cortisol, ACTH, PRL. Dex text.	CTV= GTV + bed + **2 mm**	+ 3 mm w daily CBCT	Functioning: **54 Gy**. Or SRS 20 Gy Non-functioning **50.4 Gy.** Or SRS 18 Gy	GH or TSH: Somatostatin ACTH: Ketoconazole	If no hormone normalization after surg, RT, meds,: Cushing's => adrenalectomy TSH => thyroidectomy
AVM	SRS best if < 3 cm, deep, defined focus			+ 1 mm	SRS 16–20 Gy	None	SRS reduces bleed risk 50% in latency period, 88% after obliteration. 2y obliteration = 90%
Acoustic neuroma	No mass effect. If mass effect, needs surg	Audiometry to check serviceable hearing	SRS: if < 3 cm. GTV = PTV. FSRT: if > 3 cm. PTV = GTV + 3 mm.	SRS = none FSRT = +3 mm w daily CBCRT	SRS = 12.5 Gy FSRT = 50.4 Gy in 1.8 Gy or 25 Gy / 5	No	
PCNSL		Vz exam. Slip lamp exam (20% ocular involvement). CBC, CMP, HIV, EBV, testicular exam, MRI spine. Bx first. No steroids bc 40% response.	If no ocular involvement, iso at bony canthi and ½ beam block. Cover post 1/3 orbit if slit lamp neg. Cover brain and cribriform, down to C2/3.		Chemo. If CR, WBRT to 23.4 Gy. If PR, WBRT to 30, boost GTV to 45 Gy If orbit involved, and if CR, 23.4 Gy to orbit; if PR 36 Gy. If no chemo: WBRT 36 Gy, boost GTV to 45 Gy. Avoid RT if > 60yo	R-MPV x 7c + IT MTX first (per RTOG 93–10)	80% CR to chemo OS5: 80% for pts who received WBRT PCNSL = Ocular involvement in 20% Ocular lymphoma = 80% risk of PCNSL later
Primary ocular DLBCL			36 Gy / 1.8 Gy fx. Half beam block post at post optic canal (tx CN II). If only 1 eye, tx ipsi globe, CN II.				
Trigeminal neuralgia		MRI thin slices	Single 4-mm isocenter; target is 3–6 mm anterior from junction of the trigeminal nerve and pons		**SRS 80 Gy to 100 % IDL.**		Median time to pain relief: 1–2m 60% pain free, 20% have decrease, 15% no change. <10% facial numbness
Brian mets		MRI w contrast. Always do workup for primary: breast, lung, RCC most common	Intact = GTV Post-op = cavity + 2 mm	+ 1 mm	RTOG 90–05. SRS to 80% IDL on linac. 0–2cm: 24 Gy, but use **22 Gy,** >2–3 cm: **18 Gy,** >3–4 cm: **15 Gy**		

Disease	Association	Workup	Treatment
HL CD15/30+, I-II F	MC = EBV LD = HIV, old	CBC, CMP, LDH, HIV, pregnancy test, EBV, albumin, ESR, albumin, echo, excisional bx, CSF if HIV+/testicular	**ABVD x 2**, restage w/ PET , Deauville 1–3, **ISRT 20 Gy,** Deauville 4, **ISRT 30 Gy** UK RAPID: ABVD x3, interim PET. D1–2: observe or ABVDx1; D3–4 ABVDx1, then ISRT 30 Gy.
HL CD15/30+, I-II UF		+ BM bx	**ABVD x 4**, restage w/ PET, Deauville 1–3 = **ISRT 30 Gy** Deauville 4 , **ABVD x 2**, restage w/ PET Deauville 1–3, **ISRT 30 Gy** Persistent Deauville 4 or 5 needs bx, if (+) it is refractory
HL III-IV (MASH ALL): Male, Age ≥45, Stage IV, Hgb <10.5, Alb <4, Leukocytosis >15k, lymphocytopenia <0.6k/mL (or <8%)]		+ BM bx	**ABVD x 2**, restage w/ PET Deauville 1–3 = **ABVD x4**, then observe Deauville 4 = **ABVD x 4**, restage w/ PET Deauville 1–3 ISRT to bulky sites to **36 Gy**
NLPHL CD20/45+, I-II			**ISRT 30 Gy (larger margin than HL)**, then PET. CR = observe. PR = R-CHOP or ABVD.
NHL relapse/refractory			RT after salvage chemo in pero-txp prior. Pre transplant 24–30 Gy / 20 fx BID 6 hours apart. Post txp 30 Gy in 17–20 Gy. If non-txp candidate, then 30 Gy for CR.
NHL, high grade: • Burkitt, lymphoblastic	t(8:14): Burkitt's lymphoma	+ beta2 micro, + LDH, + HBV, + EGD, + CSF, + BM bx	da-R-EPOCH or R-CHOP x 6c, then PET-CT, then **30 Gy ISRT** for PR
NHL, G2, Stage I–II: • follicular (G3B), mantle cell, DLBCL, T/NK cell, peripheral T cell, anaplastic large cell IPI: APLES: Age > 60, Performance >2, LDH > ULN, 2+ E sites, Stage III/IV	t(11:14): BCL-1, mantle cell lymphoma "Double hit": bcl-2, c-myc "Triple hit": above + bcl-6	Above, but no CSF + c-scope for mantle	I-II (non-X, i.e. < 7.5 cm): For IPI 0-1, **RCHOP x 3c**. Then PET. Then ISRT **30–36 Gy.** Boost FDG-avid residual dz to 40–46 Gy. For IPI 2–4 or X, **RCHOP x 6c.** Then PET. Then **+/–ISRT 30–36 Gy.** If unable to tolerate chemo, then 36–45 Gy ISRT,boost to 40–46 Gy. If high IPI, clinical trial for high dose chemo with autologous stem cell rescue. ISRT 36 Gy only to initial bulk dz.
NHL, intermediate grade, III–IV			III-IV: If high IPI, clinical trial for high dose chemo with autologous stem cell rescue. **R-CHOP x 4**, restage w/ PET. If CR, **R-CHOP x 2**, observe. Consider ISRT only to initial bulk (**36 Gy**), per German group. If PR, R-CHOP x 2, restage w/ PET. If PET negative: ISRT only to initial bulk (**36 Gy**) If PET positive: refractory, go to transplant.
• DLBCL, gastric			R-CHOP x 3, ISRT **30 Gy**
• DLBCL, testicular			Orchiectomy, R-CHOP x 6 w/ IT-MTX, scrotal RT to **30 Gy.** Electrons 9–12 MeV. No bolus.
• DLBCL, bone			R-CHOP x3c, ISRT **30 Gy if CR, 40 if PR**
• DLBCL, breast			R-CHOP x 6c + RT **36 Gy** to whole breast
Primary mediastinal B cell lymphoma (PMBCL)	35yo woman		DA-EPOCH-R x 6c. **NO RT** unless persistent focal dz, then 30 Gy.
Mediastinal gray zone lymphoma (GZL)	35yo man		DA-EPOCH-R or R-EPOCH x 6c. Always consolidate **30 Gy** + 10 Gy boost for PR.
NHL, low grade / indolent: • FL G1–2, MZL, MALT, SLL/CLL, MF FLIPI for FL ("*NoooooLASH*"): Sites: ≥5, LDH > ULN, Age ≥60, Stage III/IV, Hgb < 12. FLIPI-2: B2 micro, BM, Hgb < 12, LN > 6 cm, age ≥ 60	t(14:18), BCL 2, follicular lymphoma del13, t(14,19), tri12, SLL, CLL		Stage I–II, G1, no X: ISRT, **24–30 Gy** / 2 Gy fx Stage I–II, X, or unfav molecular: Chemo w R-bendamustine, then ISRT, **24–30 Gy** / 2 Gy fx Stage I–II G1, non-X and non-contiguous: chemo alone Stage III–IV: no cure. Palliate PRN. **2 Gy x 2**
• MALT, gastric	t(11:18) usually abx refractory	EGD, urea breath test, bacteria test	Bismuth, lansoprazole, tetracycline, metronidazole. Wait 1 year. **30 Gy / 20 (@1.5)** ISRT if refractory. Tx planning: NPO, 4D, 100 cc PO contrast.
• MALT, orbital	Chlamydia psittaci	bacteria test	Doxycycline. RT if refractory, **24 Gy / 12 fx.** Treat whole orbit.
• MALT, salivary	Sjogren		Abx. Surg. If R0, observe. Else, RT **24 Gy / 12 fx.**
• MALT, small bowel	Campylobacter jejuni	bacteria test	Abx. Surg. If R0, observe. Else, RT **24 Gy / 12 fx.**
• MALT, testis			RT **24 Gy / 12 fx** to contralattestis.
• MALT, thyroid	Hashimoto		Surg. If R0, observe. RT **24 Gy / 12 fx.**
• MALT, spleen	HCV		Surg. If R0, observe. RT **24 Gy / 12 fx.**
• MALT, breast			RT **24 Gy / 12 fx.** WBI.
• MALT, lung			Surg. If R0, observe. RT 24 Gy / 12 fx. Advanced stage: chemo + ISRT
• MALT, skin (Primary cutaneous MZL)	Borrelia burgdorferi		Surg. If R0, observe. RT 24 Gy / 12 fx. CTV = GTV + 1 cm. Palliate 2 Gy x 2.
Plasmacytoma			
• SEP	Lesion visible, plasmacytoma by bx (<5% plasma cells), no CRAB	CRP, LDH, ALP, albumin, B2 micro, Ca, SPEP/UPEP, serum free light chain. Bx. No Tc99 BS.	PTV1 to 50.4 Gy, ENI to 40 Gy.
• SBP			Bone with 2–3cm margin. Spine: whole VB Standard tx is RT, 40–50 Gy
MM	BM bx > 10% plasma cells, M-spike on SPEP or UPEP, CRAB		Bortezomib and dexamethasone x 2 c. Palliative **30 Gy / 10 fx**
MF			T1: PUVA, steroids, topical chemo, local electrons **24 Gy / 2 Gy** T2–4: TSEBT **24 Gy / 12 fx**, 4 days per week, 3 positions QOD.
Nasal NK/T cell NHL	EBV		Concurrent Chemo-RT (54 Gy) to involved dz w/ concurrent cisplatinum, 3c DeVIC
Chloroma / myeloid sarcoma			**24 Gy / 12 fx**

Site	Work-Up	Scenario	Treatment	CTV	PTV	Dose	Chemo	Follow-Up	Outcomes
Esophageal	- H/P: GERD, alcohol, smoking, dysphagia, weight loss - EGD + Bx -CT C/A/P +C -EUS if M0 -PET/CT -Smoking Cessation -PEG/PEJ -Bronch if above carina (25cm)	T2–4 or N+	Neoadjuvant CRT (followed by restaging PET/CT +/– EGD w/ Bx in 4 weeks) → surgery Or Definitive CRT	ITV + 4cm sup/inf and 1cm radial ENI: SCLV if proximal 1/3; celiac if distal 1/3; paraesophageal for everyone	CTV + 0.5cm	50.4Gy [can also do 45Gy + 5.4Gy CD if preop – CD volume = GTV + 1cm per RTOG 1010]	Neoadjuvant: Carbo AUC 2/ Taxol 50mg/m2 weekly Definitive: cisplatin 75mg/m2 + 5FU 1000mg/m2 on weeks 1, 5, 8, 11	H/P Q 3–6mos for yrs 1–2, then Q6–12mos for yrs 3–5, then annually CT C/A/P Q4–6mos yr 1, then decr freq EGD Q 3–6mos for yrs 1–2, then Q6mos yr 3	5-Yr OS: Stage I: > 90% Stage II: 40% Stage III: 10% Stage IV: < 5% pCR=30% R0=90%
Gastric	-H/P: satiety, hematemesis, detailed nodal exam (cervical axillary, periumbilical, SCLV), ascites, HSM -EGD + Bx -CT C/A/P +C -PET/CT if >T2,N+,M0 -EUS if M0 -Nutritional c/s +/– PEJ -Laparoscopy if >T1b or N+	High risk T2 [G3, LVSI, PNI, no D2 dissection] T3–4 or N+	Surgery → Adjuvant CRT	Gastric Bed Anastomosis LNs: SMA, perigastric, celiac for all; add paraesophageal + splenic If proximal/GEJ; add pancreaticoduodenal and splenic if middle; add pancreaticoduodenal + duodenal stump if distal	CTV = 0.5cm	45Gy in 25 fractions 5.4Gy boost if +SM 9Gy boost if GRD	1c of capecitabine (1000mg/m2 BID)D1–14 followed by 825mg/m2 BID capecitabine concurrent with RT followed by 2c of capecitabine (1000mg/m2 BID)D1–14	H/P Q 3–6mos for yrs 1–2, then Q6–12mos for yrs 3–5, then annually Monitor for B12 and iron deficiency Labs, imaging and EGD as clinically indicated	5-yr OS: Stage I: 65% Stage II: 40% Stage III: 15% Stage IV: 5%
Pancreas	-H/P: painless jaundice, abdo exam, weight loss -Pancreatic protocol CT -EUS + FNA Bx -ERCP w/ stent if obstructed -CT chest	Any	If resectable: resect → chemo (4c Gem/abraxane or FOLFOX) → CRT If unresectable: 4c chemo → CRT	Resected: CTV: [(proximal 1.5cm of CA, prox 3cm of SMA, PV, PJ, preop tumor volume) + 1cm] + [Aorta + (3cm to the R + 1cm to the L + 2cm anteriorly + 0.2cm posteriorly)] Definitive: ITV (gross disease and involved LNs) + 1cm	CTV + 0.5cm	50.4Gy in 28Fx	Capecitabine 825mg/m2 BID on radiation days	H/P Q3–6mos for 2 yrs, then Q6–12mos w/ CA 19–9 and CT (cat 2B) Pancreatic enzyme replacement	Resectable: MS 2 yrs , 3-yr OS=30%, LC 70–80% Unresectable: MS 10mos, 2-yr OS 10–20%
Rectal	-H/P: anemia, prior RT, IBD, DRE, pelvic exam in women, FHx -CEA -colonoscopy, proctoscopy -EUS or MRI -CT C/A/P +C	[TAE alone if: <8cm from verge, <30% circum, <3cm, G1, margin >3mm, no LVSI] T3–4 or N+	Neoadjuvant CRT → Surgery → adjuvant CT If cT1/2 taken for surgery and found to be T3/4 or N+ or +SM, give postop CRT → CT	Mesorectum up to rectosigmoid or 2cm superior to gross dz (whichever is more proximal) and 2cm distal to gross dz Presacral and internal iliac LNs If T4 : ext iliac If anal canal involved:+/– inguinals	CTV + 0.7cm Fields: PA: L5/S1 → 3cm below tumor + 2cm on pelvic brim laterally Lats: behind PS (in front if T4) → behind sacrum	45Gy to whole pelvis f/b 5.4Gy boost to GTV + 2cm	Concurrent Capecitabine 825mg/m2 BID on radiation days f/b 4 months of CAPOX or FOLFOX [total of 6 months of chemo]	H/P Q3mos for 2yrs w/ CEA if elevated at dx, then Q6 mos for yrs 3–5 Colonoscopy in 1 yr then Q5yrs CT C/A/P annually for 5yrs	50% LRF reduction w/ RT LRR < 10% at 10yrs with naCRT; 30% DMs 5-yr OS: Stage I: 90% T3 or N+: 75% T4N+: 50% M1, resectable liver: 30–40%
Anal	-H/P: sphincter tone, HIV, IBD, prior RT, pelvic exam with pap and HPV testing in women -Labs: HIV -Anoscopy + Biopsy -CT C/A/P +C -PET/CT	Any	Definitive CRT	CTV_A: [GTV + anal canal] + 2–2.5cm CTV_B: Involved LN(s) + 1cm CTV_C: Elective LNs (internal iliac, external iliac, inguinal) + 1cm	CTV + 1cm	T2N0: 50.4 Gy in 28Fx to CTV_A and 42Gy in 28Fx to CTV_C T3/4N0: 54Gy in 30Fx to CTV_A and 45GY in 30Fx to CTV_C N+: 54Gy in 30Fx to CTV_A., 54Gy in 30Fx to CTV_B if LN > 3cm OR 50.4Gy in 30Fx to CTV_B if LN < 3cm; 45Gy in 30Fx to CTV_C	Concurrent MMC 10mg/m2 and 5-FU 1000mg/m2 on D1 and D29	H/P in 8–12 weeks. If CR, DRE and inguinal nodal exam Q3–6mos for 5 yrs; Anoscopy Q6–12mos for 3 yrs, CT C/A/P annually for 3 yrs If persistent disease at 8–12 weeks, re-evaluate at 4 weeks. If persistent disease, restage. If progressive dz at 8–12 weeks, re-stage.	5-yr OS: Stage I: 85% Stage II: 75% Stage III: 50% Stage IV: 5%

Disease	Workup	Scenario	Contraindications	Treatment	CTV	PTV	Dose	Systemic tx
Prostate	PSA, MRI, Biopsy	VLR, LR		AS			PSA q 6m, DRE/bx no more than q 12m After 12-month bx, alternate mpMRI w/ bx. Indications to tx: ↑ in # cores, % involvement, ≥ G4; PSA DT < 3 years	No
		LR (T1-T2a, GS6, PSA <10)		EBRT	Prostate + prox SVs	+ 5 mm	78 Gy	No
	+ BS if T2 and PSA >10	IR (T2b-c, GS7, PSA 10–20)		EBRT	Prostate + prox SVs Distal SVs	+ 5 mm	PTV1 = 80 Gy PTV2 = 46 Gy	Consider ADT 6m in unfav IR
	+ BS + T, LFTs, CBC, CMP, Dexa, Ca, Vit D	HR (GS 8+, T3+, PSA >20)		EBRT + ADT	Prostate + prox SVs Distal SVs + pelvic LNs	+ 5 mm	PTV1 = 80 Gy PTV2 = 46 Gy	ADT x 2–3y Lupron (7.5 mg = 1 month; 22.5 mg = 3 months) = GnRH agonist (Degarelix = GnRH antagonist). Menopausal sx. Bicalutamide (50 mg/day) = anti-androgen. Check LFTs monthly. Diarrhea.
			> 60 cc, < 20 cc (if too large give ADT to shrink by 1/3) TURP defect Large median lobe	LDR-BT	Prostate	0 mm	I125, 145 Gy mono 110/50.4 Gy boost Pd103, 110 Gy mono, 100/50.4 Gy boost	
			Pubic arch interference IPSS > 15 (> 20 absolute) Anesthesia/sedation risk IBD/prior RT	HDR-BT	Prostate	0 mm	13.5 x 2, one week apart 15 Gy + 50.4 Gy	
	MRI BS if PSA > 10	Post RP Adjuvant: T3, R+ Salvage: Persistent or rising PSA post-RP			1 cm below UVA, lat to obturator internus, post to rectum, ant entire bladder below pubic symphysis, and 1 m of it superior to it. Pelvic LNs if pLN+	+ 5 mm	68 Gy. 74 Gy if GTV	aRT, N0 = RT alone (shared decision making about ADT) aRT, N+ = RT + 2y of ADT (Messing was life) sRT, N0 = RT + 6 months ADT if pre-RT PSA <0.7 ng/mL; else, 2y sRT, N+ = RT + 2y of ADT
Bladder	GU/rectal/GYN exam Cystoscopy w/ mapping + TURBT + random biopsies [Trigone/neck → urethral] CT C/A/P w/ CT urethrogram to evaluate UUT for synchronous lesions and evaluate LN ALP or sx → BS	Ta-LG		Obs				
		CIS		BCG x 6				
		cT1/Ta-HG		reTURBT, then BCG x6 → residual: BCG x 6 or cystectomy				
		cT2-T4aN0	Tumor>5cm, Hydronephrosis, multifocal, poor bladder fx, carcinoma in situ (CIS), incomplete TURBT, non-TCC histology, M+ disease, near ureteral orifices	RT	Bladder, prostate, prox urethra	+ 5–7 mm	60 Gy, 66 Gy / 30 fx	Cisplatin (40 mg/m2 weekly)
Testicular	LDH, HCG, AFP; do bilat testicular exam, supraclav and inguinal LN exam; CBC, CMP; CT CAP; fertility; sperm bank	IS: Any pT N0 M0 S1-3 IA/B: T1-T4 but N0 M0 S0		obs				
				Carbo1c AUC7				Carbo1c AUC7
				20 Gy PA	T11/12-L5/S1 CTV= (IVC+1.2cm) + (Aorta + 1.9cm)	PTV= CTV + 0.5 cm. A 0.7cm uniform margin around PTV to block edge accounts for penumbra.		
		IIA: T1–4 N1 (all ≤ 2cm (no more than 5 total pN+) S0-2		20 Gy DL + 10 Gy CD	From T11/T12, contour aorta and IVC down to the ipsilateral iliac arteries and veins stopping at the top of the acetabulum	PTV = CTV + 0.7cm to block edge Block edge CD = LN + 2 cm		
		IIB: T1–4 N2 (all 2 -≤ 5cm, or more than 5 pN+, or ECE) S0-2		20 Gy DL + 16 Gy CD				
		III						BEP 3c

General Principles [1–22]

Cancer Death Worldwide

1. Lung 1.59 M
2. Liver 745 K
3. Stomach 723 K
4. Colorectal 694 K
5. Breast 521 K
6. Esophagus 400 K

Cancer Visibility and Tumoricidal Dose

Number of cells	CT scan visibility	Example case	Dose necessary to kill cells (EQD2)
10^8	Not visible	R1 resection status post-chemo with CR	~50 Gy
10^9	1 cm^3	R2 resection Most visible cancers, including LNs	~66–70 Gy
10^{10}	10 cm^3	Bulky disease	

Dose necessary to kill 1 log = ~10–20 Gy

Resection Nomenclature

Resection type	Definition	CNS and peds protocol terms	CNS and peds protocol description
R0	Negative margins	GTR1	Not visible on operative microscope or postoperative imaging
R1	Grossly negative but pathologic positive margin	GTR2	Visible on operative microscope Not visible on postop imaging
R2	Grossly positive margin (surgeon can see with their eye)	NTR	Residual evident on postop imaging, nodularity <5 mm. Linear "streak" enhancement
		STR	Surgically removing tumor tissue Residual evident on postoperative imaging, nodularity >5 mm

Radiobiology

The "4 Rs" of Radiobiology

- Redistribution
- Repopulation
- Repair
- Reoxygenation
- Lethal damage = DNA double-strand breaks
- 1 Gy of radiation = ~20–40 DSBs
- Majority of radiation-induced cell death = mitotic catastrophe

Cell Cycle and Radiosensitivity

- Cell cycle: G1 → S → G2 → M
- Cells in late G2/mitosis = most radiosensitive
- Cells in late S/early G2 = most radioresistant

Blood Vessel Radiosensitivity

- Capillaries > arteries > veins.
- Arteries can tolerate 50–70 Gy CFRT.
- Veins are highly radioresistant.

Physics

- 1 Gray (Gy) = 1 Joule/Kg energy deposited in tissue
- The difference between γ-rays and X-rays is the source. γ-ray = natural decay of radioisotope, e.g., Cobalt-60, X-ray = manmade, e.g., linear accelerator
- Photon nuclear interactions:
  - (1) Coherent scattering (≈E)
  - (2) Photoelectric effect (≈Z^3/E^3) used for diagnostic imaging
  - (3) Compton effect (≈electron density) **dominates in radiotherapy**
  - (4) Pair production (≈E)

Clinical Care Path

- Consultation → Simulation → Treatment planning → Quality assurance → Treatment → Follow-up

LN Metastasis Nomenclature

- Sister Mary Joseph nodule: periumbilical met through falciform ligament
- Virchow's node: L supraclavicular mass where thoracic duct inserts into left venous angle and thoracic duct drains from cisterna chyli
- Krukenberg tumor: ovarian metastasis from breast, gastric, and others
- Irish LN: L axillary mass
- Blumer's shelf: tumor spread to retrouterine or rectovesical space (pouch of Douglas)

Preoperative vs Postoperative RT

Advantages of preop	Advantages of postop
Improved blood supply/ tumor oxygenation	Smaller target volume after resection/debulking
Target delineation more clear	Plan based on pathologic information
Radiated tissue is resected	
No tumor repopulation during healing	

Young Patients

- Fertility counseling
- Pregnancy testing
- Consider options to minimize normal tissue exposure (reduced RT protocol, protons)

Life Expectancy (US Social Security Data)

	M	F
65 y/o	18 y	20 y
70 y/o	14 y	17 y
75 y/o	11 y	13 y
80 y/o	8 y	10 y
85 y/o	6 y	7 y

TEACHH Model: Life Expectancy of M+ Patients

- Type of cancer. +1 if not breast or prostate
- ECOG. +1 if 2. + 2 if 3–4.
- Age. +1 if > 60
- Chemo (prior courses). +1 if >2
- Hospitalizations. +1 if yes
- Hepatic mets. +1 if yes

Groups

- A (0–1): 20 m
- B (2–4): MST 5 m
- C (5, 6): MST 2 m

Palliative Care

- Temel, NEJM, 2010: 151 NSCLC M+ patients randomized to SOC +/− early palliative care. Palliative care is meeting with palliative care team member within 3-week enrollment, and then monthly. Improved QOL, lower depression, less aggressive end-of-life care (54% vs 33%), more resuscitation preferences documented in medical record, and longer OS (11.6 m vs 8.9 m MST).
- ENABLE II: n = 322. Randomize to nursing-led multicomponent psycho-educational intervention vs usual care. Improved QOL, symptom intensity, and mood. No difference in resource usage.
- ENABLE III, Alabama (Bakitas, 2015): advanced cancer patients and oncologist determined prognosis 6–14 months. Randomize to early (at enrollment) vs delayed (after 3 m) palliative care. Palliative care is telehealth RN coaching session, monthly FU. One year OS was improved in early intervention group. KM

1-year OS 63% vs 48%, a 15% absolute benefit. No change in QOL between groups.

– Kumar, JCO 2017: interview 2300 families of deceased patients with advanced lung or colorectal cancer. Patients enrolled in hospice had more pain, the right amount of pain med, help with dyspnea, EOL wishes followed, excellent quality with EOL care, and highest QOL.

KPS vs ECOG

KPS	ECOG	Description
90	1	Restricted in strenuous activity
70	2	Unable to work. Out of bed >50% of waking hours
50	3	Limited self-care. Out of bed <50% of waking hours
30	4	No self-care