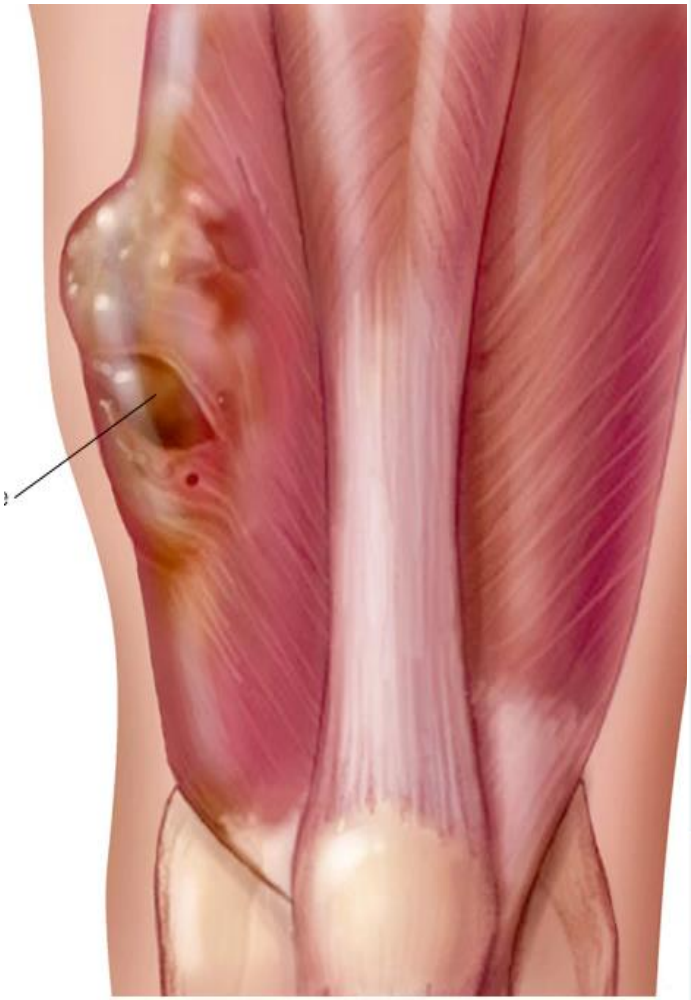
Organ sparing Brachytherapy in soft tissue sarcomas -- Evidence & Planning

Dr. Ritika Harjani Hinduja
P. D. Hinduja Hospital, Mumbai

MD, DNB,
FRCR (Clinical Oncology),
Clinical Fellow, Extracranial SBRT, Ottawa, Canada



- **Varied locations**
- **Distinct HP types**

T Primary tumor					
TX	Primary tumor cannot be assessed				
T0	No evidence of primary tumor				
T1	Tumor 5 cm or less in greatest dimension				
T1a	Superficial tumor				
T1b	Deep tumor				
T2	Tumor greater than 5 cm in greatest dimension				
T2a	Superficial tumor				
T2b	Deep tumor				
N Regional lymph nodes					
NX	Regional lymph nodes cannot be assessed				
N0	No regional lymph nodes metastases				
N1	Regional lymph node metastasis				
M Distant metastasis					
M0	No distant metastasis				
M1	Distant metastasis				
Stage I	A	G1, GX	T1a-1b	N0	M0
	B	G1, GX	T2a-2b	N0	M0
Stage II	A	G2, G3	T1a-1b	N0	M0
	B	G2	T2a-2b	N0	M0
Stage III		G3	T2a-2b	N0	M0
		Any G	Any T	N1	M0
Stage IV		Any G	Any T	Any N	M1

Surgery- primary definitive treatment

LRR- 5-20%

LRR- 30-60%

The Treatment of Soft-tissue Sarcomas of the Extremities

Prospective Randomized Evaluations of (1) Limb-sparing Surgery Plus Radiation Therapy Compared with Amputation and (2) the Role of Adjuvant Chemotherapy

STEVEN A. ROSENBERG, M.D., PH.D.,* JOEL TEPPER, M.D.,† ELI GLATSTEIN, M.D.,† JOSE COSTA, M.D.,‡
ALAN BAKER, M.D.,* MURRAY BRENNAN, M.D.,* ERNEST V. DEMOSS, M.D.,* CLAUDIA SEIPP, R.N.,*
WILLIAM F. SINDELAR, M.D., PH.D.,* PAUL SUGARBAKER, M.D.,* ROBERT WESLEY, PH.D.§

Between May 1975 and April 1981, 43 adult patients with high-grade soft tissue sarcomas of the extremities were prospectively randomized to receive either amputation at or above the joint proximal to the tumor, including all involved muscle groups, or to receive a limb-sparing resection plus adjuvant radiation therapy. The limb-sparing resection group received wide local excision followed by 5000 rads to the entire anatomic area at risk for local spread and 6000 to 7000 rads to the tumor bed.

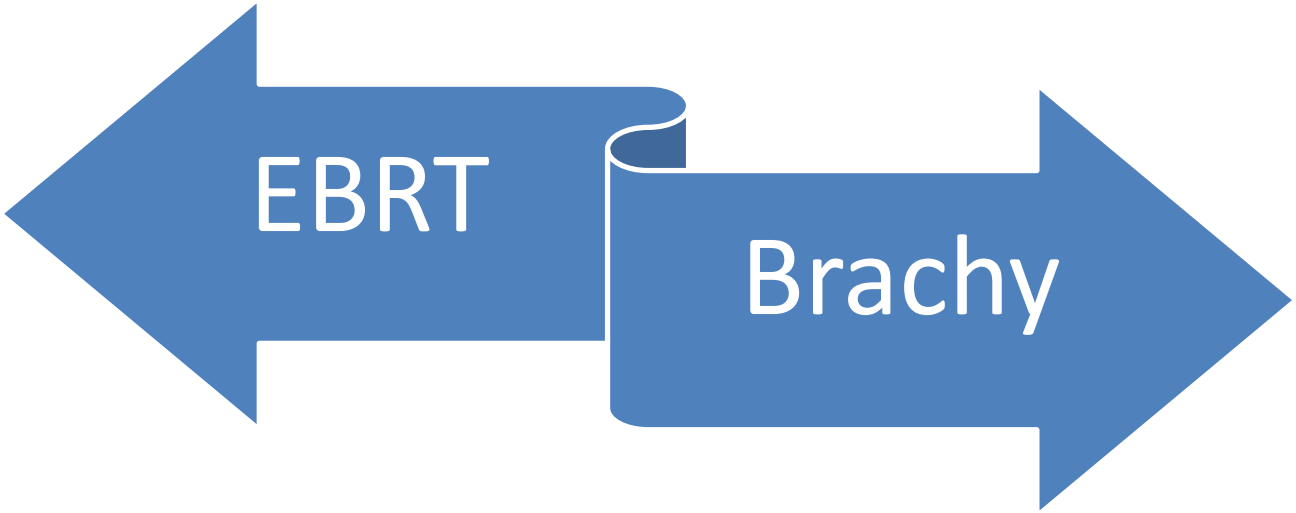
From the National Cancer Institute, Bethesda, Maryland

SOFT-TISSUE SARCOMAS are malignant tumors that arise in the extraskeletal connective tissues of the body. Though a large number of different pathologic

-Equivalent Disease specific survival
-Annals of Surgery; Sept, 1982.

Barring T1A, low grade, negative margins (>1cm),

All require radiation therapy



Brachytherapy

Advantages

- As applicators in tumour bed- high dose to target and rapid dose fall off- reduced dose to normal tissues
- This could translate to lower risk of lymphedema/subcut fibrosis/ bone fracture
- Short duration of treatment
- Early treatment in post op period has shown to improve LC (avoiding tumour repopulation, efficacy in less hypovascular/ fibrosed tumour)

Disadvantages

- Limited as compared to EBRT in its volume coverage
- Depends on skill of the radiation oncologist

Evidence

● *Clinical Original Contribution*

LONG-TERM RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL OF ADJUVANT BRACHYTHERAPY IN THE MANAGEMENT OF COMPLETELY RESECTED SOFT TISSUE SARCOMAS OF THE EXTREMITY AND SUPERFICIAL TRUNK

LOUIS B. HARRISON, M.D.,* FRANK FRANZESE, M.D.,* JEFFREY J. GAYNOR, PH.D.† AND MURRAY F. BRENNAN, M.D.‡

Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021

IJROBP, 1993

Long-Term Results of a Prospective Randomized Trial of Adjuvant Brachytherapy in Soft Tissue Sarcoma

By Peter W.T. Pisters, Louis B. Harrison, Denis H.Y. Leung, James M. Woodruff, Ephraim S. Casper, and Murray F. Brennan

JCO, 1996

- Local control was significantly better with BT in high grade tumours
- No difference in local control of low grade tumours
- No difference in Distant metastases free period
- No difference in disease specific period

Interstitial Brachytherapy in Soft Tissue Sarcomas

The Tata Memorial Hospital Experience

Ashok J. Chaudhary[1], Siddharth Laskar[1], Rajesh Badhwar[2]

- Strahlentherapie Und Onkologie, 1998

- Retrospective
- Most common were spindle cell sarcomas f/b liposarcomas

- For brachytherapy alone- Local control was 75%, improved to 82% after salvage (med f/u -30 mos)
- For brachytherapy+EBRT, LC was 71% which after including salvaged patients- rose to 86%.

- Treatment related complications <1%

Annals of Surgical Oncology **14**(2):560–567
DOI: 10.1245/s10434-006-9137-2

Perioperative Interstitial Brachytherapy for Soft Tissue Sarcomas: Prognostic Factors and Long-Term Results of 155 Patients

Siddhartha Laskar, MD,[1] Gaurav Bahl, MD,[1] Ajay Puri, MS,[2] Manish G. Agarwal, MS,[2] MaryAnn Muckaden, MD,[1] Nikhilesh Patil, MD,[1] Nirmala Jambhekar, MD,[3] Sudeep Gupta, DM,[4] Deepak D. Deshpande, PhD,[5] Shyam K. Shrivastava, MD,[1] and Ketayun A. Dinshaw, FRCR[1]

155 adults with STS treated with Sx, BT with/without EBRT

Cumulative Radiotherapy dose > 60Gy had a significant positive impact on

- **Local Control**
- **Disease Free Survival**
- **Overall Survival**

Indications for Brachytherapy as monotherapy

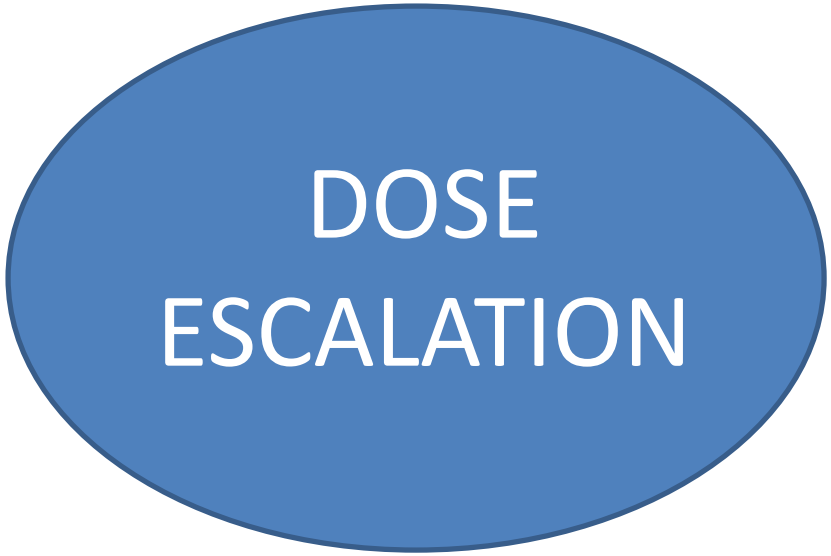
- Medium sized tumours (<10cms)
- High grade
- Negative surgical margins
- Preferable primary lesion

- Re-irradiation
- Paediatric STS

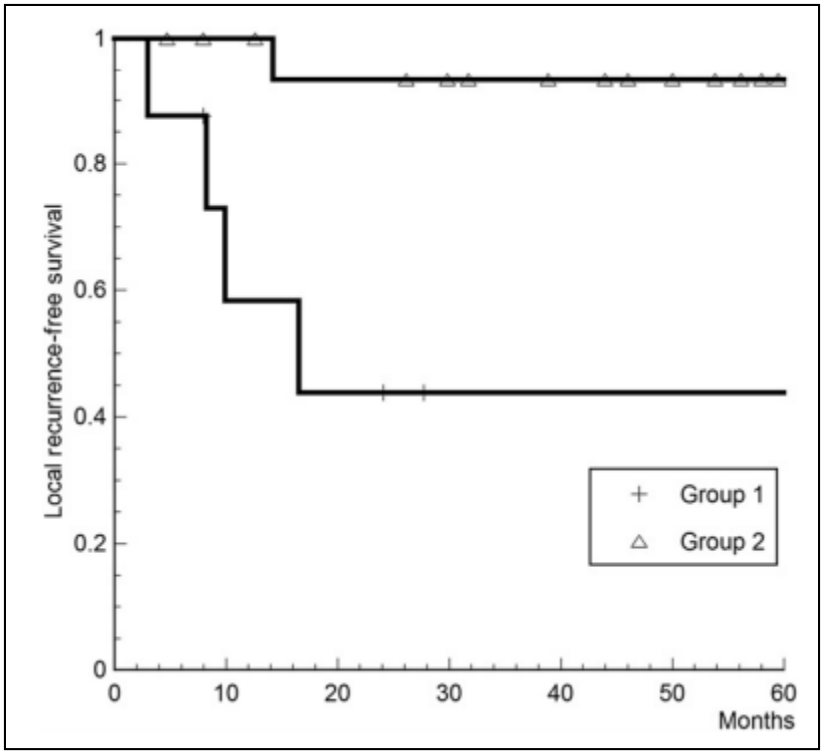
Brachytherapy +EBRT

EBRT will add to benefit along with Brachytherapy in

- BT cannot adequately cover
  - unfavourable geometry/ OAR restriction
  - skin ulcer
- High risk of recurrences
  - >10cms
  - positive margins
  - recurrent disease
  - deep location



HDR brachytherapy alone in post-op soft tissue sarcomas with close or positive margins. Jun Itami et al, (Japan) Brachytherapy, 2009



The local recurrence free survival was 43.8% if the patient had positive margin or a recurrent lesion vs 93.3% if it was a primary lesion with adequate margin

In Group 1 lesions, addition of a wide field EBRT seems to be necessary to improve the local control rate

Also, evidence for EBRT boost in positive margins by Alekhteyar et al IJROBP 1996

Author (year) [reference number] Institute	Inclusion criteria (*n*)	EBRT dose (Gy) Median (range)	BT dose (Gy) Median (range)	Local control (%)	Survival	Complication rate (%)
Shiu *et al.* (1991) [7], Memorial Sloan-Kettering Cancer Centre, USA	Locally advanced/candidate for amputation (33)	–	LDR 44 (25-54)	At 3 yr, 88% At 5 yr, 70%	–	39% (overall)
Harrison *et al.* (1993) [8], Memorial Sloan-Kettering Cancer Centre, USA	After gross tumor resection BT (intra-operative insertion) vs. no BT, randomized control trial (166)	–	LDR 42-45	At 5 yrs, 82% vs. 67%	5 yr DFS 81% vs. 80% (NS)	14% vs. 10% (NS) (wound complication)
Chaudhary *et al.* (1998) [9], Tata Memorial Hospital, India	Non-metastatic STS in adults (177)	45 (12-70)	HDR alone 30 (29-50)	At 30 months, 70%, After salvage, 86%	–	< 1%
Rosenblatt *et al.* (2003) [10], Haifa, Israel	Non-metastatic STS (32)	39.2 (16.2-45)	LDR 33 (18-49), HDR 16	At 3 yrs, 87.5%	At 5 yrs DFS 56%, OS 70%	Wound complication 16%, Late local toxicities 19%
Laskar *et al.* (2007) [11], Tata Memorial Hospital, India	Non-metastatic STS, children, (median age 13 yrs) (50)	45 (30.6-45)	HDR alone 36 (30-40) EBRT + HDR BT 21 (15-36)	At 51 months, 82%	At 51 months, DFS 68%, OS 71%	Wound complication 4%, Late toxicities 20%
Laskar *et al.* (2014) [12], Tata Memorial Hospital, India	Non-metastatic STS, children, (Median age 15 yrs) (76)	–	–	At 70 months, 85%	At 70 months, DFS 74%, OS 77%	Wound complication 8%, Late local toxicities 31%
Cortesy *et al.* (2017) [13], Italy	Primary or recurrent STS (107)	46 (mean)	LDR and PDR 20 (mean?)	At 5 yrs, 80.5%	At 5 yrs, DFS 58.6% OS 87.4%	
Current study	Primary STS (27)	50 (30-50)	HDR alone 60.7 (33.4-67.4) EBRT + HDR BT 66.6 (42-78)	At 5 yrs, 85.7%	DFS 39.7 ±3.9 months OS 42.4 ±3.4 months	≥ grade 2 skin toxicity in 14.8% patients

Specific situation	Preferred treatment	Treatment considerations
Extremity/trunk		
Low grade: Superficial, <5 cm, and wide margin (≥1 cm)	Surgery alone	Limb-sparing surgery
High grade: <10 cm and negative margin	BT alone	30–50 Gy
Low grade: deep, >5 cm, or negative margins (<1 cm)	BT + EBRT	BT + EBRT >60 Gy
High grade: >10 cm, negative margin		
All grades: close/positive margin	BT + EBRT	BT + EBRT ≥65 Gy
Recurrent (not previously radiated)	BT + EBRT	BT + EBRT ≥65 Gy
Re-irradiation	BT alone	30–50 Gy

ABS, Naghavi et al, Brachytherapy,2017

When not to do Brachytherapy?

- Location very close to skin/ skin compromised
- Bone (periosteum removed) and exposed

- Irregular tumour bed with doubtful catheter stability/ possibility of kink

- Acral and phalangeal sites

Procedure and Planning

Pre- procedure work-up

General pat. assessment- - tolerance of treatment (PS, comorbidities, prev RT)
- Limb function
- risk of wound complications (DM, baseline edema)

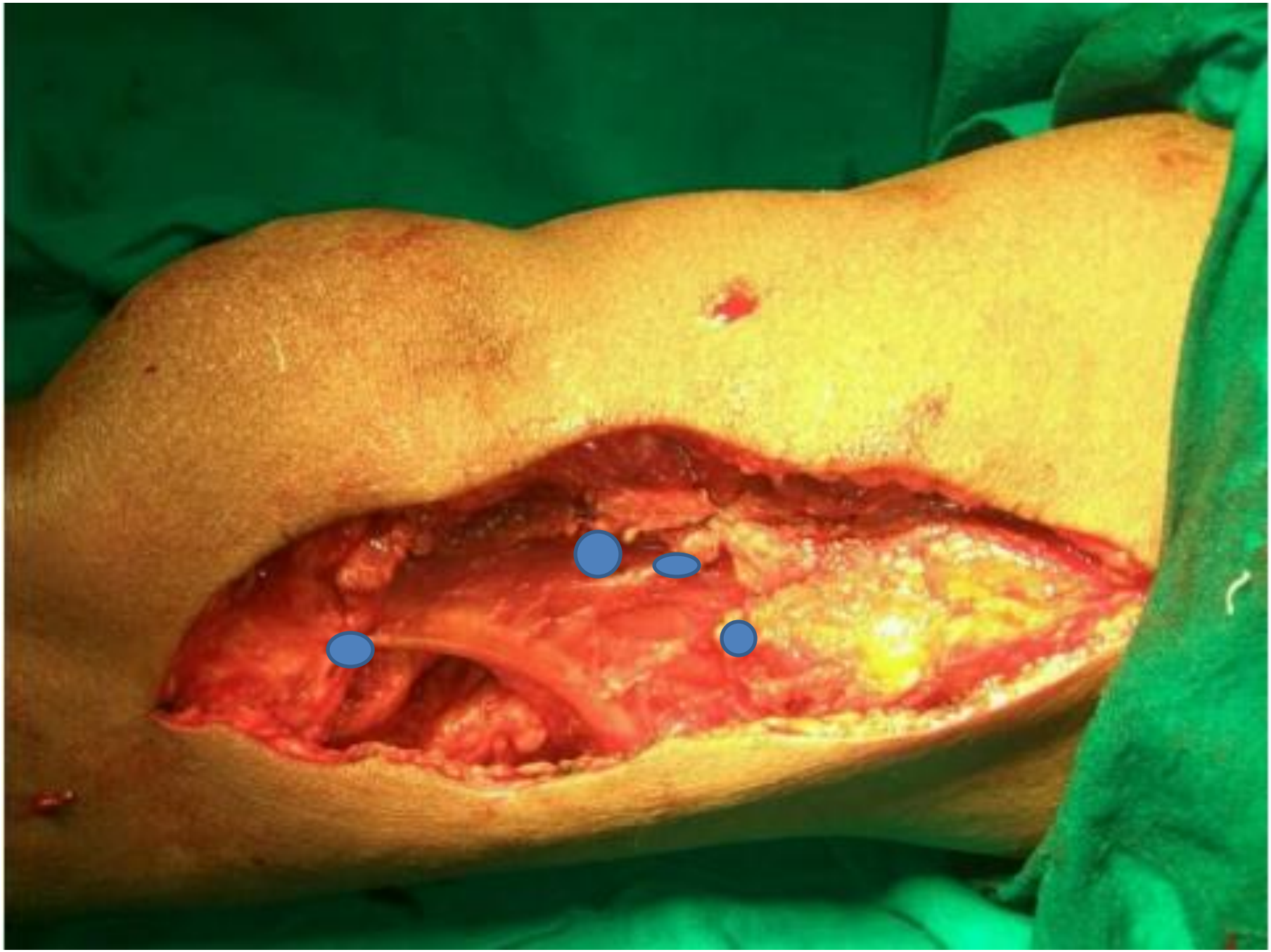
Evaluation of primary-
Imaging- disease extent, resectability, relation to bone/neurovascular bundle
- Commonly MRI.
Biopsy- carefully planned, by same surgeon

Nodal evaluation- in
S-ynovial sarcoma
C-lear cell sarcoma
A-ngiosarcoma
R-habdomyosarcoma
E-pitheloid sarcoma

Evaluation for Distant metastases-
- Chest CT for all.
- Histopathology based abdominopelvic/CNS imaging

Most commonly, catheters inserted intra-operatively during surgical resection

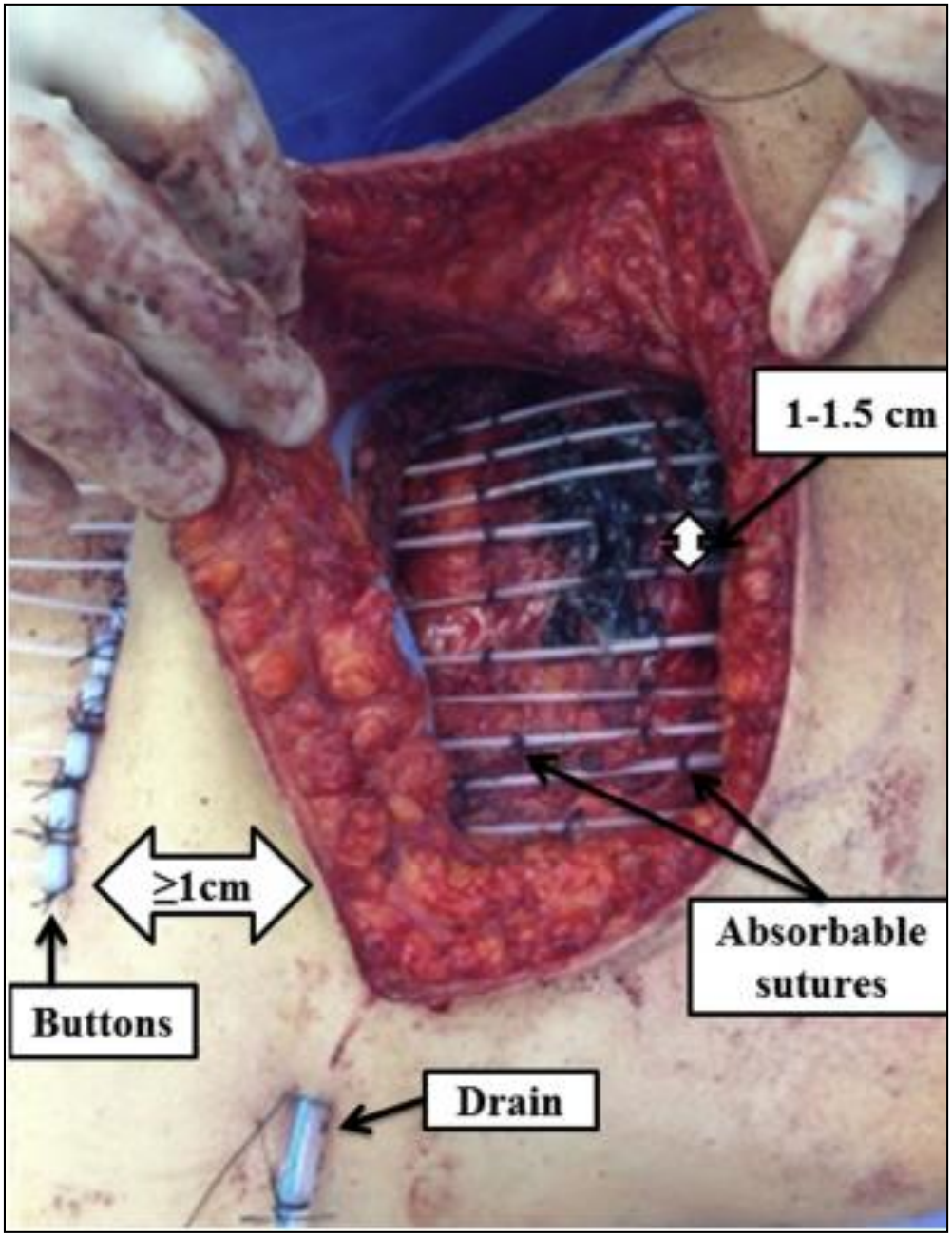
Surgeon places clips to demarcate tumour bed and any areas at high risk or to demarcate critical structure, eg. - NVB



Hollow flexible plastic catheters are placed with the aid of steel needles over the tumour bed

- Can be along or perpendicular to incision line

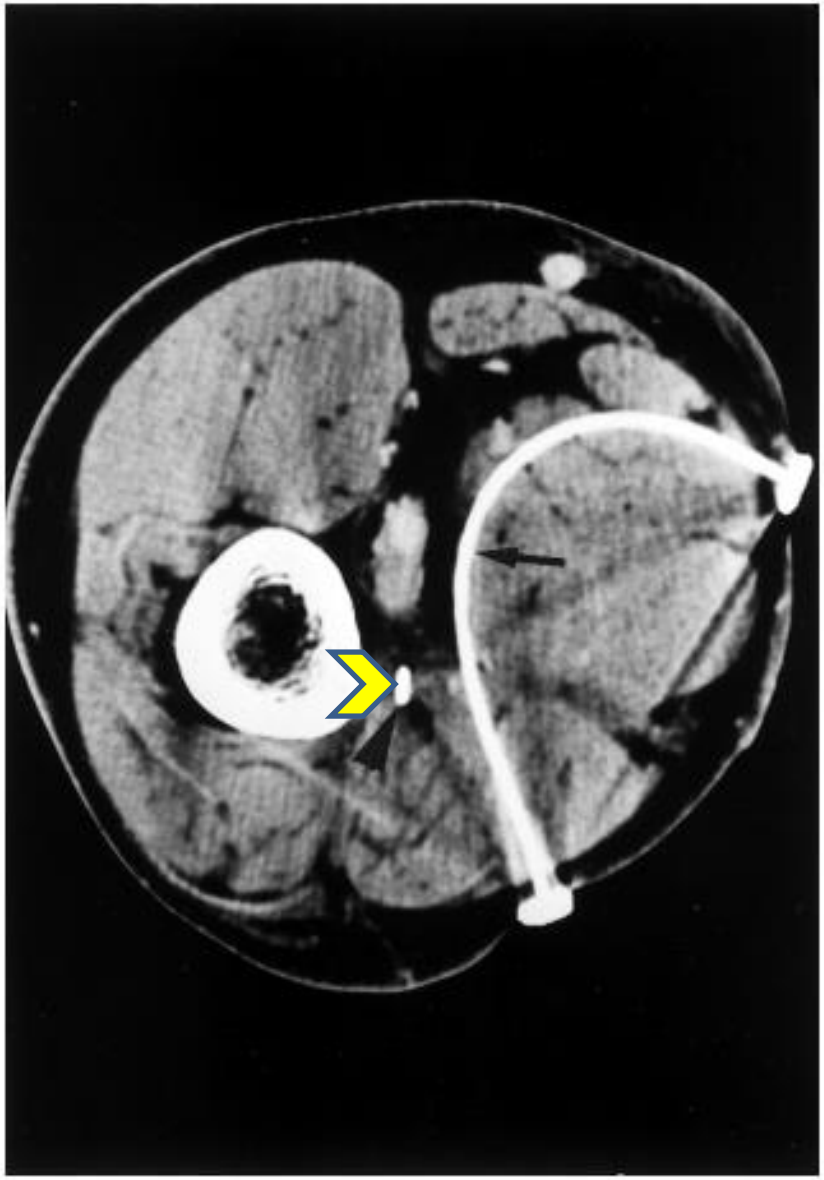
- Parallel placement
- 1-1.5cms separation
- Avoid penetrating blood vessels
- Pass through the tumour bed (Sutures to stabilize catheters to tumour bed)



Avoid direct contact to bones and nerves

May consider muscle/gelfoam/bone wax (maintaining 0.5cms distance)– Mison Chun et al, JJCO 2001

Commonly, single plane is sufficient



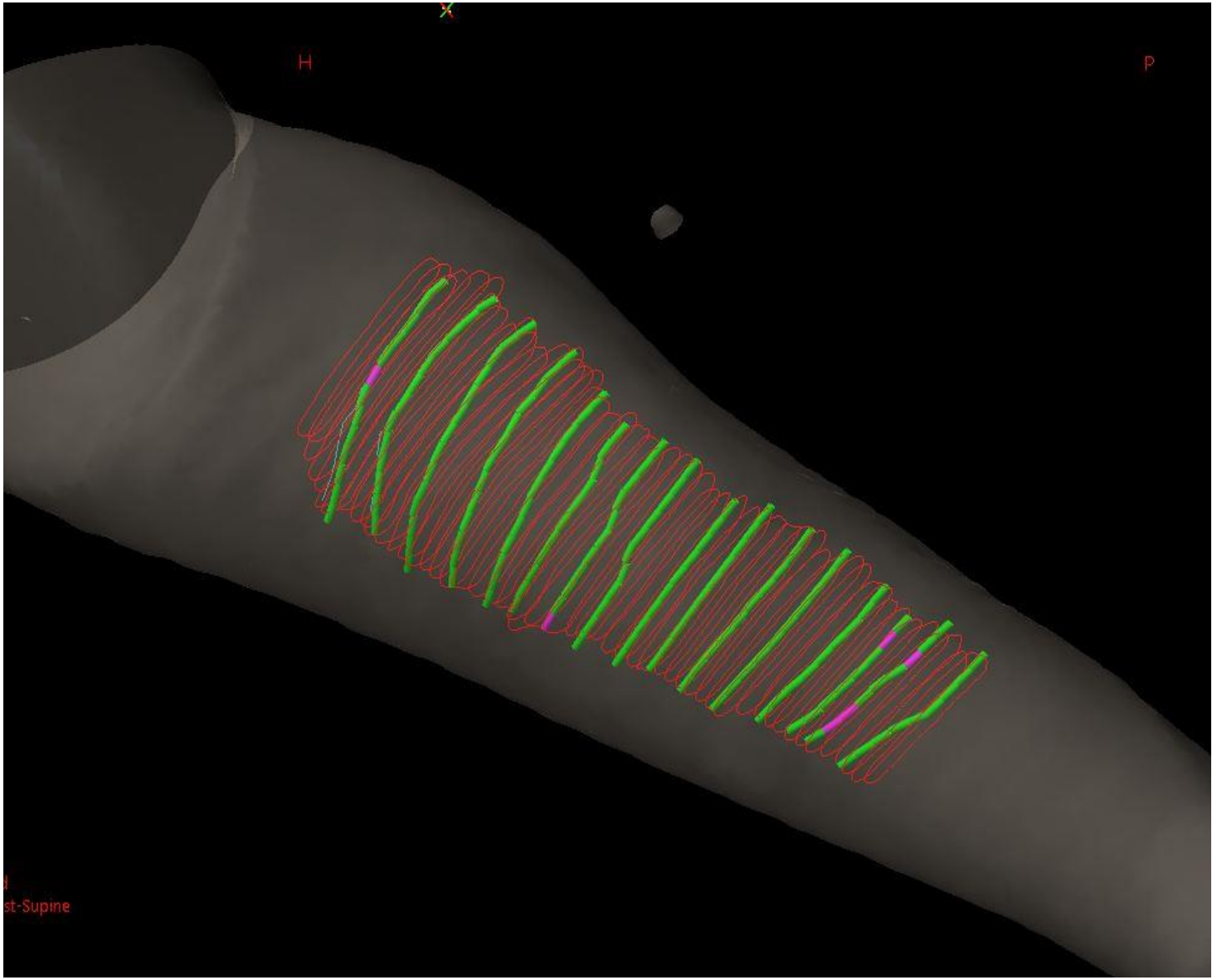
- Entry and exit points of the catheters should be kept 2 cm away from incision line
- Buttons/balls to be placed in both ends of the catheters.
- Adequate gap of 5 mm between end buttons and skin to encompass post-operative tissue edema.

After a gap of 4-6 days,

Planning CT scan is done – 2.5 - 3 mm thickness

Adjust position accordingly that applicator digitization is not difficult.

Measurement and cutting of applicators to remove the dummy, numbering. Followed by digitization

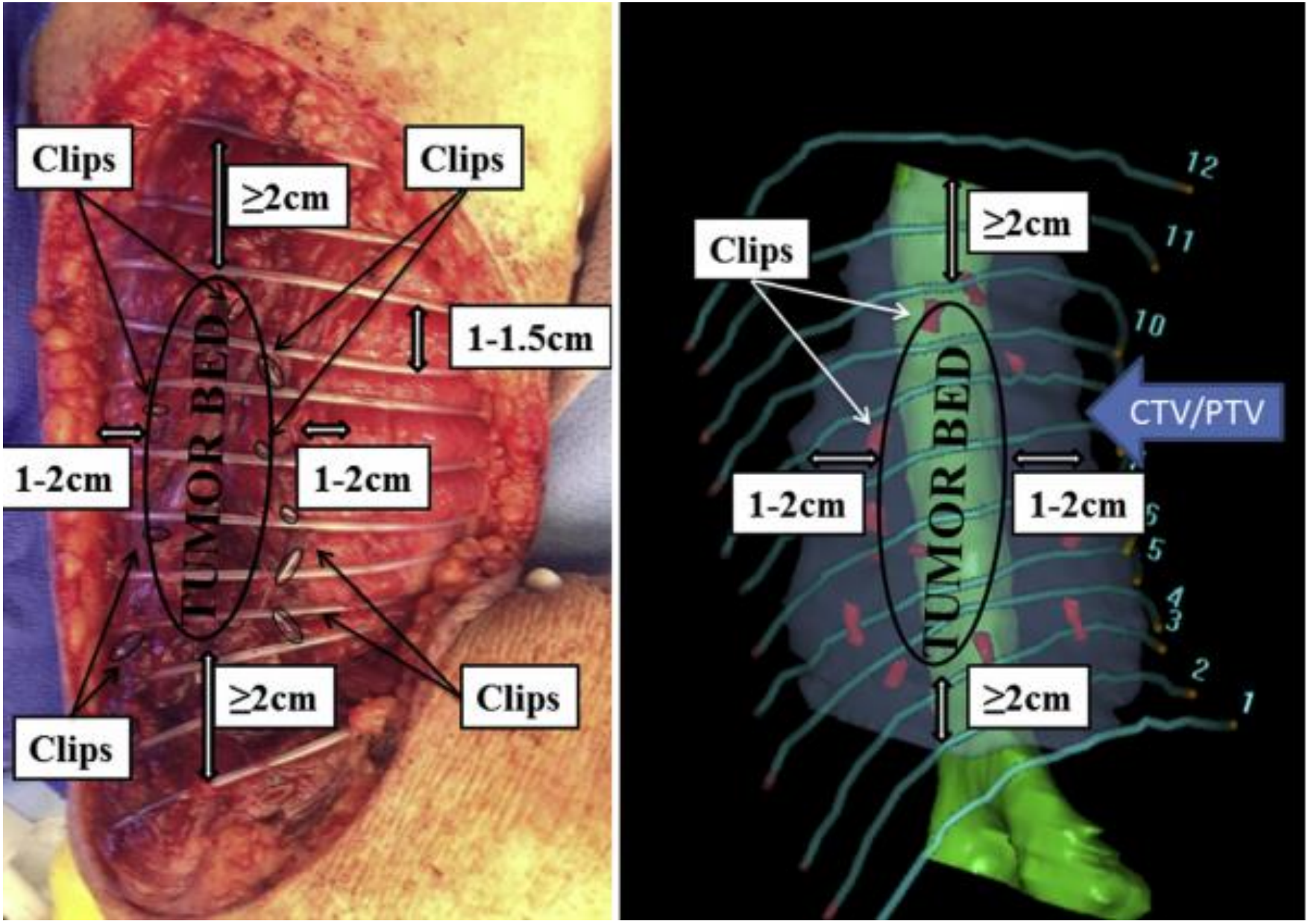

H
P
st-Supine

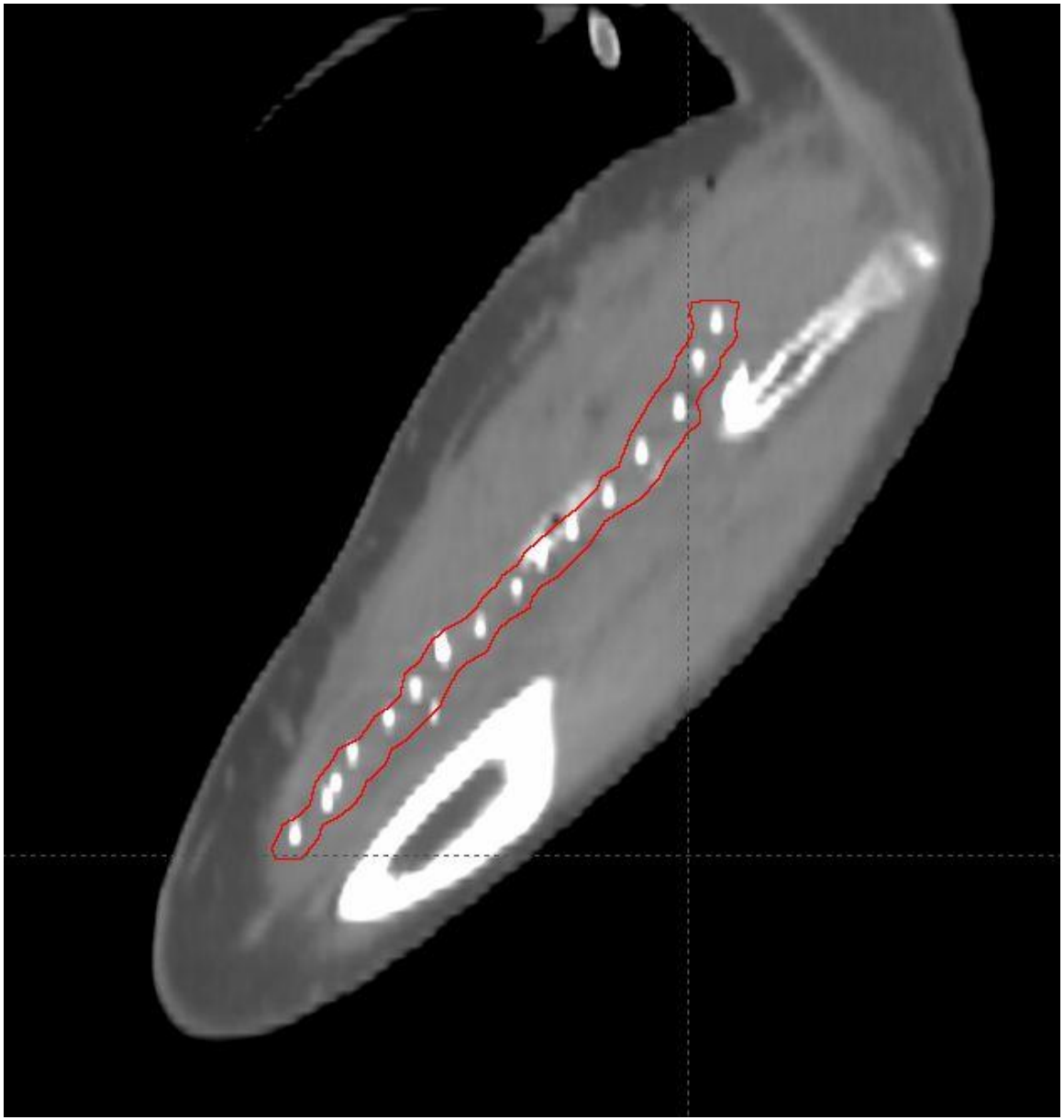
BT- CTV consists of the surgical bed with a margin,

- ≥ 2 cm craniocaudally
- 1-2 cm laterally
- scar and drain sites not included
- Clips defining tumour bed help

No PTV expansion in BT

Contour appropriate OARs (bone, skin, NVB, where applicable)


Clips
≥2cm
Clips
1-1.5cm
TUMOR BED
1-2cm
1-2cm
Clips
≥2cm
Clips
Clips
≥2cm
CTV/PTV
TUMOR BED
1-2cm
1-2cm
≥2cm
12
11
10
5
5
4
3
2
1



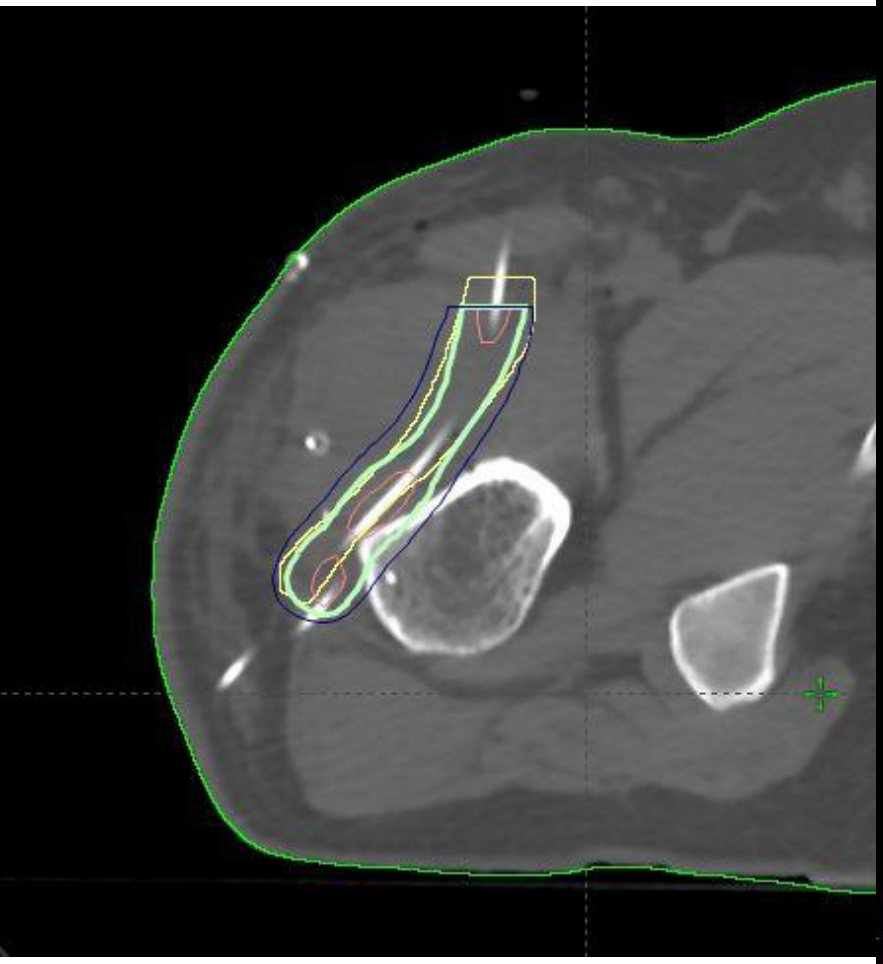
EBRT delineation will be more generous with greater longitudinal margin, including scar and drain sites

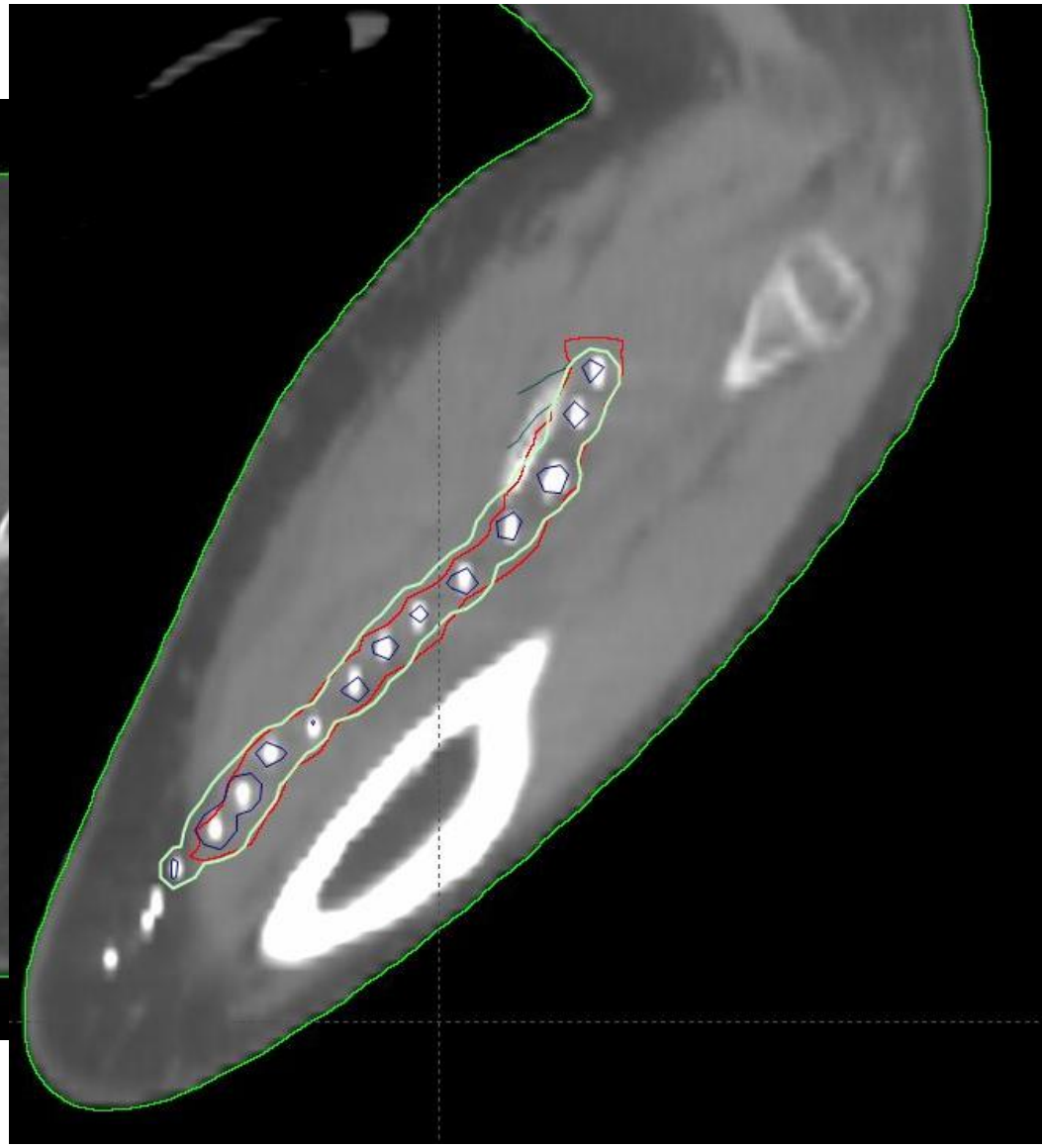
Longitudinal margin to tumour bed while placing applicators in BT can be accordingly modified.

BT type	Modality	EBRT (Gy)	BT (Gy)
LDR/PDR	BT		45–50
	BT + EBRT	45–50	15–25
HDR	BT		30–50
	BT + EBRT	45–50	12–20
IORT	IORT + EBRT	45–50	10–20

- Dose- 3-4Gy/fractions
- Boost- 6 fractions, Brachy alone- 10-12 fractions

Recommendations: 36Gy/10Fr definitive and 18-21Gy/ 6-7fr as boost



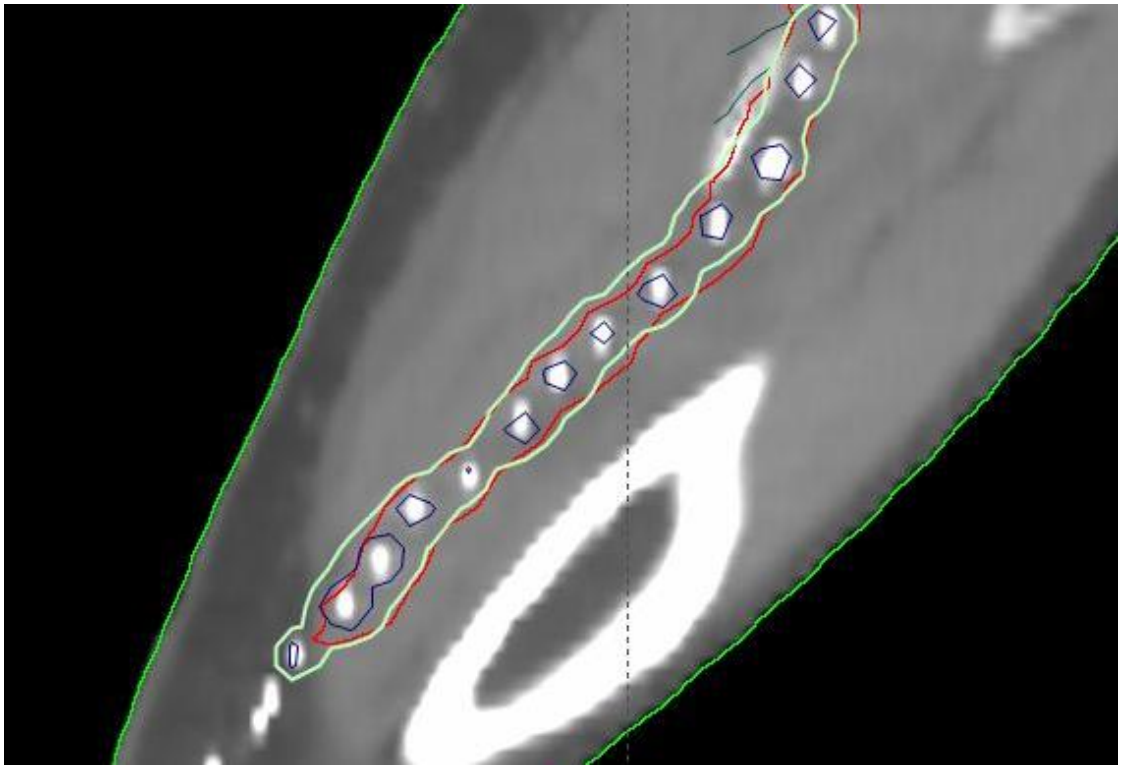


Volume	Constraints	Common	Ideal
CTV	V_{100}	≥90%	≥95%
	V_{150}	≤50%	≤40%
	D_{90}	≥90%[a]	≥100%[a]
	DHI	≥0.6	≥0.8

30%

DHI = [V100 - V150]/V100; 0.8 means 80% of volume receiving 100-150% of the prescribed dose and <20% of the volume receiving >150%

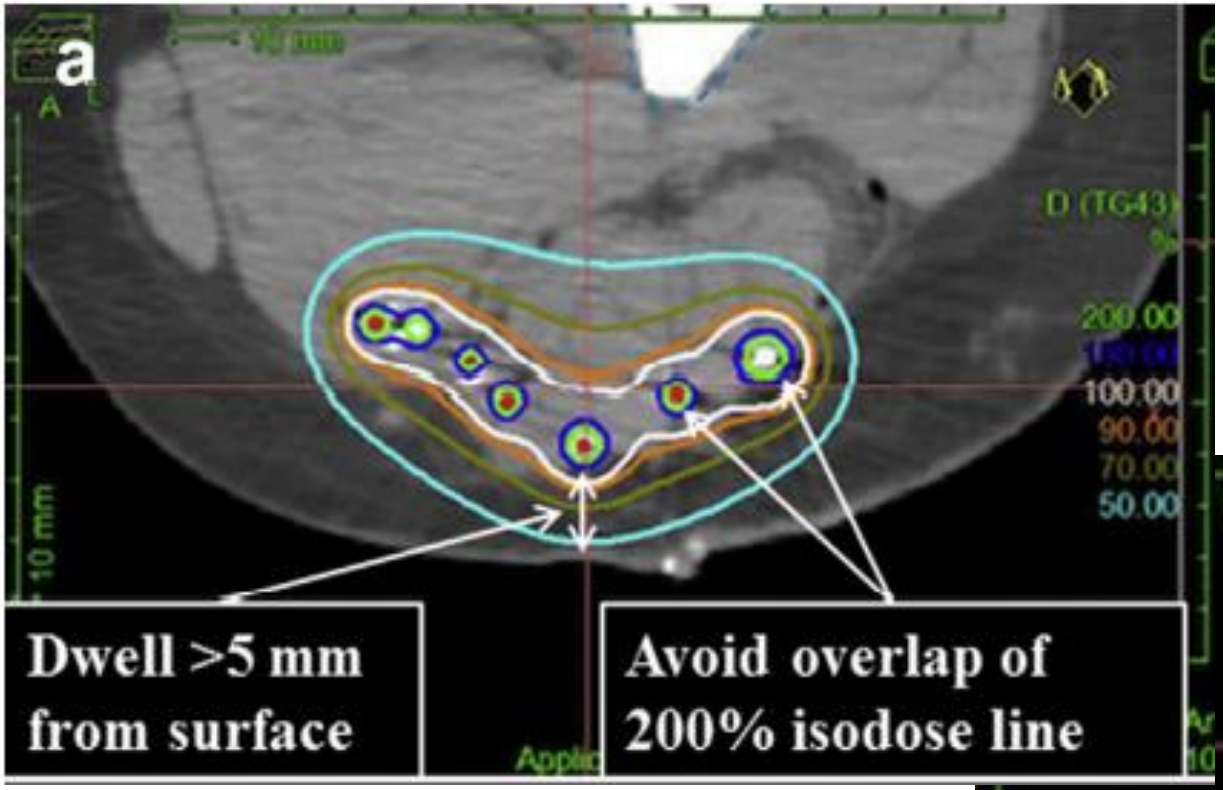
Alternately, visualizing isodoses of 150% and 200% for overlap

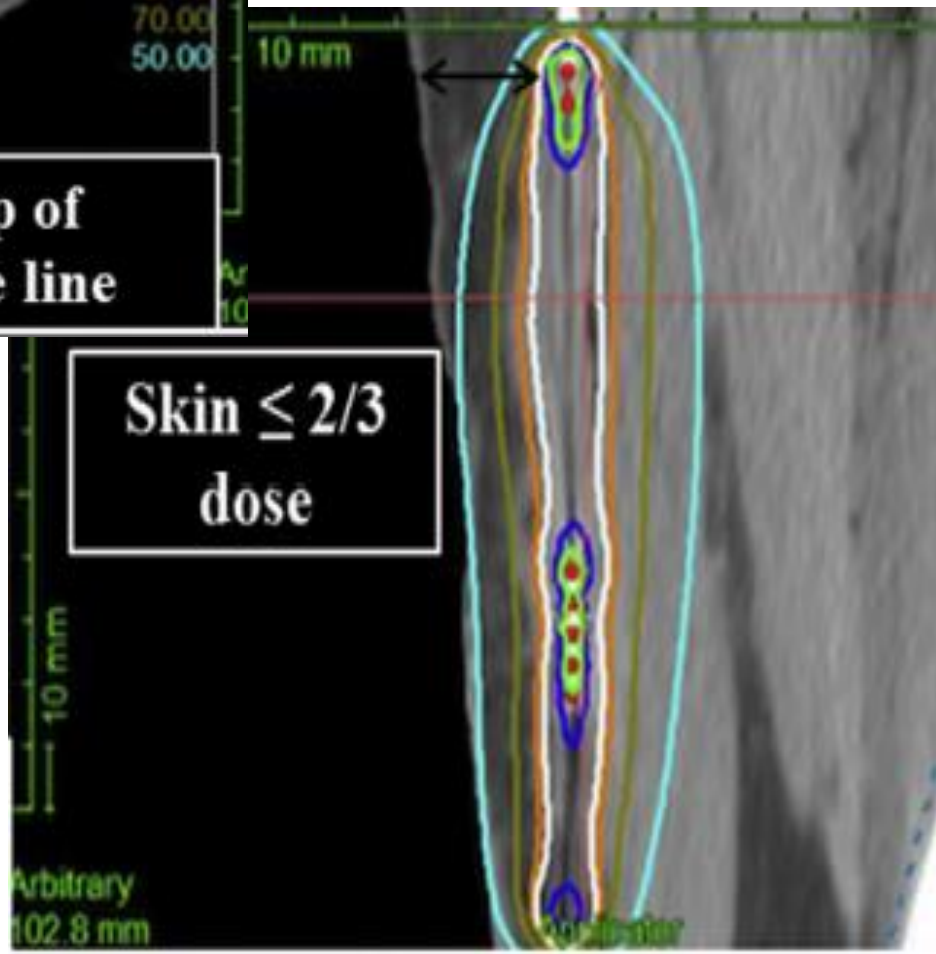


OAR should receive < 100% of prescription dose, unless required i/v/o tumor involvement.

To minimize skin toxicity,

- the dose to the skin should be less than 2/3rd the prescribed dose
- Source loading should be ≥0.5 cm from skin


a
D (TG43)
200.00
100.00
90.00
70.00
50.00
10 mm
Dwell >5 mm from surface
Avoid overlap of 200% isodose line


10 mm
Skin ≤ 2/3 dose
10 mm
Arbitrary
102.8 mm

Site care

- Avoid major movements to prevent kinks
- Do not wet
- Antiseptic ointment
- Removal procedure

Side effects

Acute

Wound related complications- dehiscence/ gaping/edema
(Skin- tautness during procedure and wound closure)

Wound complications can be reduced by treating 5 days post surgery and catheter insertion Alektiar et al, IJROBP 2000

Local pain and erythema at site for few days, generally self-resolving

Chronic

- Hypo pigmentation
- Telengiectasia
- Skin atrophy
- Subcutaneous fibrosis
- Stiffness at site, joint stiffness
- Neuropathy (cumulative LDR dose >90Gy; gel foam)*
- Bone fracture (<5% risk, related to periosteal stripping)

*Zelefsky et al IJROBP 1990

Complications depend on-----

- Total treatment dose
- BT dose, BT dose per fraction
- No of catheters, Tumour volume-150
- Addition of EBRT (fibrosis, chronic edema, joint)

Emory et al 2012; Laskar et al 2007

- Lower limb as compared to upper limb
- Joint proximity
- Acral/distal lesions
- Reirradiation


THANK
YOU
ROMANS 1:8

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