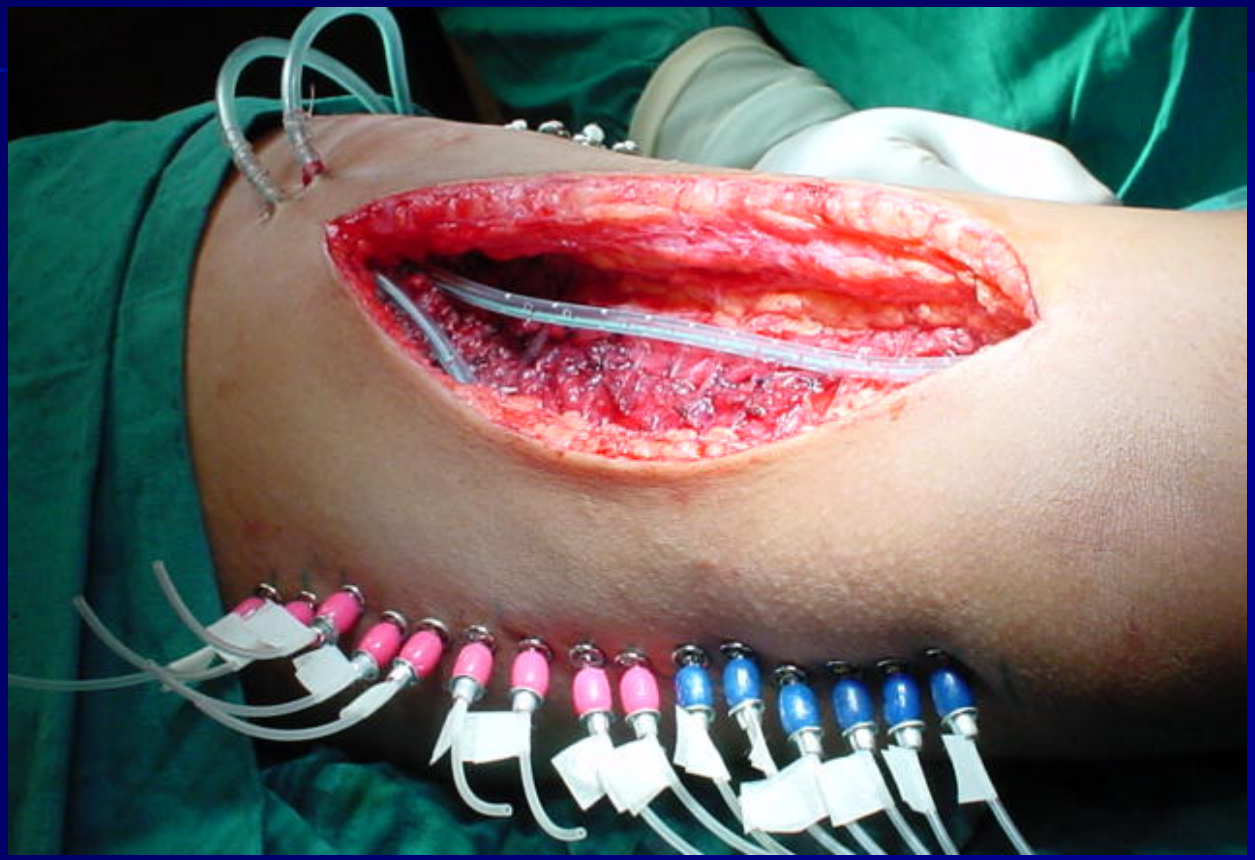
INTERSTITIAL BRACHYTHERAPY FOR SOFT TISSUE SARCOMAS



Siddhartha Laskar
Professor
Department of Radiation Oncology
Tata Memorial Hospital, Mumbai, INDIA
(laskars2000@yahoo.com tmc.gov.in)

SOFT TISSUE SARCOMAS

NON-ROUND CELL STS

Tumors of fibrous tissue:
- Fibromatoses (desmoid tumors)
- Adult and infantile fibrosarcoma
- Dermatofibrosarcoma

Fibrohistiocytic tumors:
- Malignant fibrous histiocytoma

Tumors of adipose tissue:
- Liposarcoma

Tumors of smooth muscle:
- Leiomyosarcoma

Tumors of blood and lymph vessels:
- Angiosarcoma
- Hemangiopericytoma

Tumors of peripheral nervous system:
- Malignant schwannoma (MPNST)

Tumors of bone and cartilage:
- Extraskeletal osteosarcoma
- Extraskeletal myxoid chondrosarcoma
- Extraskeletal mesenchymal chondrosarcoma

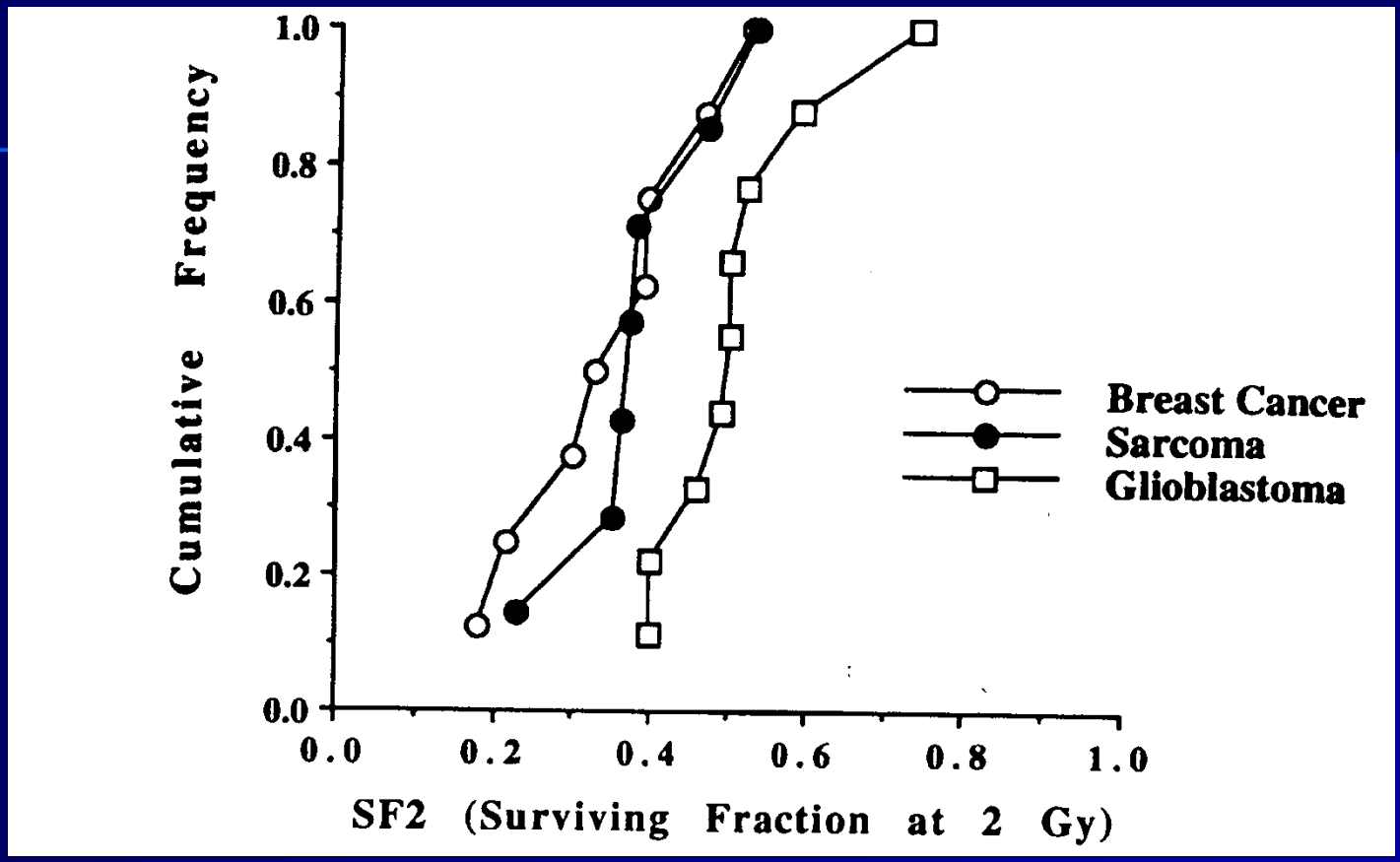
Tumors of more than one tissue type:
- Malignant mesenchymoma
- Malignant Triton tumor

Tumors of unknown histogenesis:
- Alveolar soft part sarcoma
- Epithelioid sarcoma
- Clear cell sarcoma (nonrenal)
- Synovial sarcoma
- Desmoplastic small round cell tumor

ROUND CELL STS

Rhabdomyosarcoma
Extraskeletal Ewing's Sarcoma

RADIOSENSITIVITY OF SARCOMA CELLS



Cumulative frequency of surviving fraction of clonogens at 2Gy

Ruka W et al, JCO 1996

LOCAL RECURRENCE RATES AFTER SURGERY

Author	Amputation/ Rad. Resection (%)	Wide Excision (%)	Marginal Resection (%)
Cantin et al	18	30	42
Gerner et al	8	60	93
Abbas	8	36	65
Liebel et al	13	28	70
Enneking et al	4	25	50

"The value of adjuvant radiotherapy is in 'extending the margin' of limb salvage surgery that otherwise has a high risk of recurrence"

William F. Enneking, Surgical Oncologist

"The management of this condition (STS) should be radical surgery & no help, as a curative measure, should be expected from radiotherapy either as pre-op or post-op procedure"

Ralston Patterson, Radiation Oncologist

IS LIMB CONSERAVATION FEASIBLE ?
Amputation vs. Limb Conservation

High Grade Extremity STS (n=43)

Amputation (n=16)

LSS + Radiotherapy (n=27)
RT:50Gy (WF) + 10-15Gy (Boost)

Both groups received: Doxo + Cyclo + High Dose MTX Chemo

Median Follow-up: 56 mths.

Local control: Amputation - 0%
LSS + RT - 14%
p=0.06
Overall Survival: No Difference

Rosenberg et al. Ann Surg 1982
Level II Evidence

NIH Consensus development conference on Limb Conservation:
Combined Conservative Surgery + Radiotherapy as standard of care
(Cancer Treatment Symp. 1985)

IS BRACHYTHERAPY EFFECTIVE ?

MSKCC Trial *(Pisters PWT et al, JCO 1996)*

Extremity / Superficial Trunk STS (n=164)

LSS Alone (n=86)

LSS + Interstitial Brachytherapy (n=78)

Brachytherapy: 42-45Gy in 4-6 days

Median FU: 76mths

Local Control

LSS Alone: 69%

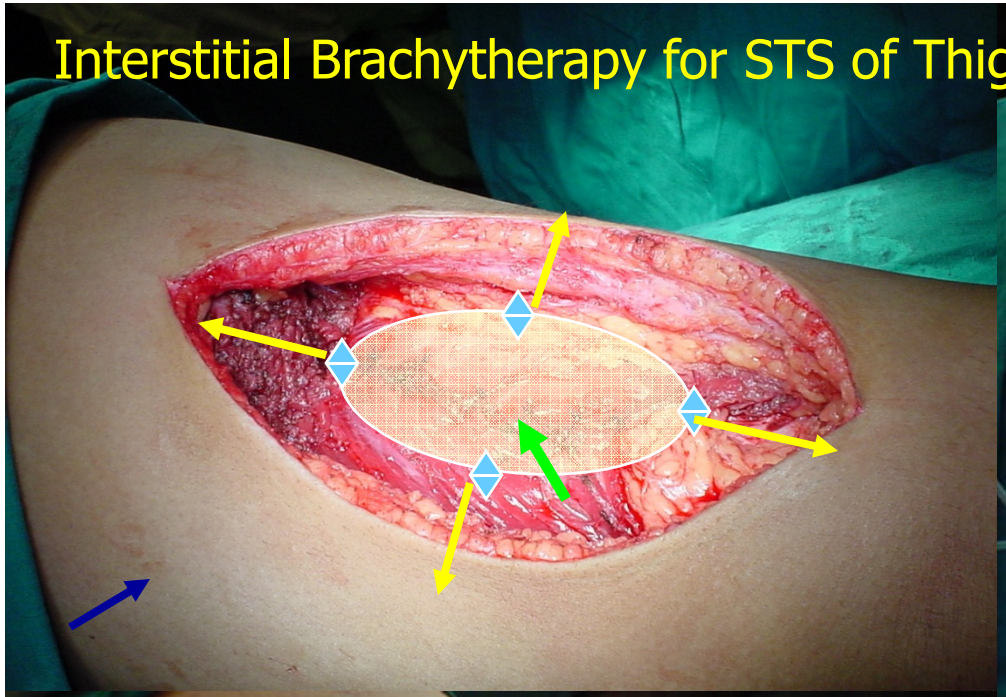
LSS + Interstitial Brachytherapy: 82%

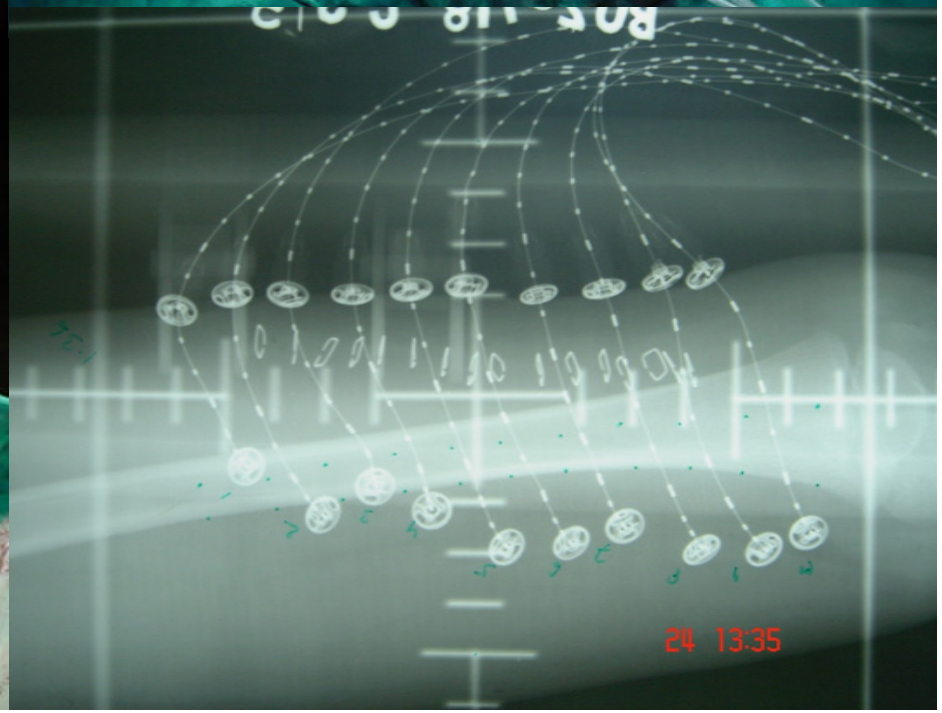
p=0.04

+ve impact in 119 pts. with high grade sts only
no improvement in 45 pts. with low grade sts

Level I Evidence

Interstitial Brachytherapy for STS of Thigh





GUIDELINES

TARGET VOLUME

Radical brachytherapy : Gross tumour volume + 4cm margin

Brachytherapy as boost: Gross tumour volume + 2cm margin

SIMULATION done on 4-5th day after surgery

DOSIMETRY

LDR Manual afterloading technique: Paris system

HDR remote afterloading:
Stepping Source Dosimetric System
Dose point (0.5cm from implant plane)
+ Geometric Optimization
Prescription at 85% of basal dose

DOSE

Radical (LDR): 45-50Gy @ 45-50cGy/hr, (HDR): 36Gy/9# @ 4Gy/# x 2 #/ day

Boost (LDR): 15-20Gy @ 45-50cGy/hr, (HDR): 15Gy/5# @3Gy/# x 2#/ day

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 49, No. 4, pp. 1033–1043, 2001

0360-3016/01/$–see front matter

PII S0360-3016(00)01534-0

CLINICAL INVESTIGATION **Sarcoma**

THE AMERICAN BRACHYTHERAPY SOCIETY RECOMMENDATIONS FOR BRACHYTHERAPY OF SOFT TISSUE SARCOMAS

SUBIR NAG, M.D.,* DANIEL SHASHA, M.D.,† NORA JANJAN, M.D.,‡ IVY PETERSEN, M.D.,§ AND MARCO ZAIDER, PH.D.‖ for the American Brachytherapy Society

*Ohio State University, Columbus, OH; †Beth Israel Medical Center, New York, NY; ‡U.T.M.D. Anderson Cancer Center, Houston, TX; §Mayo Clinic, Rochester, MN; ‖Memorial Sloan Kettering Cancer Center, New York, NY

Purpose: This report presents the American Brachytherapy Society (ABS) guidelines for the use of brachytherapy for patients with soft tissue sarcoma.

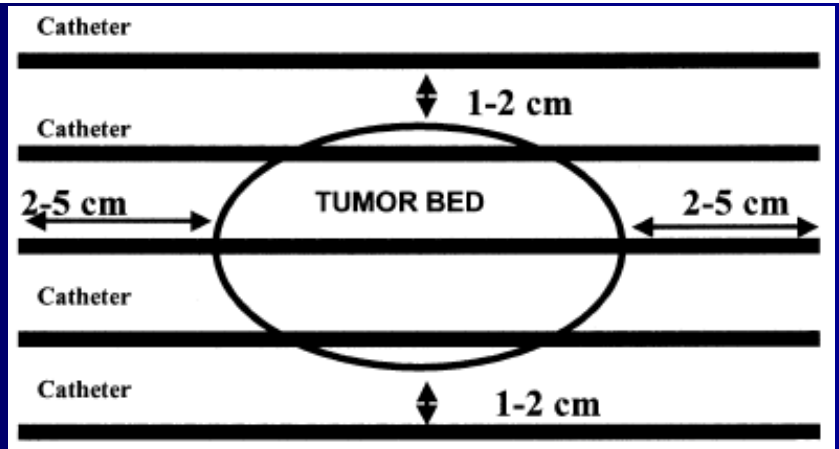


Fig. 1. Catheters are placed 1–2 cm beyond the lateral edge of the clinical target volume (CTV) and 2–5 cm beyond the CTV in the longitudinal direction.

RESULTS WITH LDR BRACHY ALONE

Table 2. LDR iridium 192 brachytherapy used alone as adjuvant therapy for intermediate-high grade primary and recurrent soft tissue sarcoma of the extremity or superficial trunk

Author	Year	*n*	FU (mos)	LC (%)	Cxs (%)
Nonrandomized series					
Shiu *et al.* (61)	1984	33	36	82	39
Habrand *et al.* (23)	1991	50	82	65	35
Cionini *et al.* (11)	1992	12	51	75	6
Chuba *et al.* (10)	1996	22	50	82	48
Gerbaulet *et al.* (22)	1996	50	NS	82	38
Chaudhary *et al.* (9)	1998	33	40	71	1
Rosenblatt *et al.* (58)	1999	9	27	67	15
Randomized series					
Harrison *et al.*, Pisters *et al.* (24, 55)	1996	56 (+BRT)	76	89	14 (>5d)*
		63 (−BRT)	76	66	48 (<5d)*

Abbreviations: LDR = low dose rate; BRT = brachytherapy; *n* = number of patients; FU = follow up (months); LC = local control, Cxs = complications.

* Major factor influencing complication was the time of loading of catheter.

Local Control: 65 – 90%

Adverse Effects: 1 – 50%

RESULTS WITH HDR BRACHY ALONE

Table 4. HDR iridium-192 brachytherapy used as adjuvant therapy for intermediate-high grade primary STS of the extremity or superficial trunk

Author	Year	*n*	FU (mos)	LC (%)	Cxs (%)
Nonrandomized					
Donath *et al.* (16)	1993	19	12	70	16
Alekhteyar *et al.* (2)	1994	13	16	77	NS
Chuba *et al.* (10)	1996	32	50	82	48
Yoshida *et al.* (63)	1996	13	24	72	8
Crownover *et al.* (12)	1997	10	12	100	0
Koizumi *et al.* (37)	1999	16	30	50	6

Abbreviations: HDR = high dose rate; STS = soft tissue sarcoma; *N* = number of patients; FU = follow up (months); LC = local control; Cxs = complications; NS = not stated.

Local Control: 50 – 100%

Adverse Effects: 0 – 50%

RESULTS WITH LDR BRACHY + EBRT

Table 3. LDR brachytherapy used in combination with EBRT as adjuvant therapy for intermediate-high grade primary and recurrent STS of the extremity or superficial trunk

Author	Year	*n*	FU (mos)	LC (%)	Cxs (%)
Nonrandomized series					
Schray *et al.* (59)	1990	63	20	96	10 (early)
Gemer *et al.* (20)	1991	25	36	80	36
Cionini *et al.* (11)	1992	33	51	91	6
O'Connor *et al.* (50)	1993	68	40	91	22
Chaudhary *et al.* (9)	1998	118	40	71	1
Delannes *et al.* (13)	2000	58	54	89	61
Rosenblatt *et al.* (58)	1999	16	27	94	15 (severe)

Abbreviations: LDR = low dose rate; STS = soft tissue sarcoma; EBRT = external beam; *n* = number of patients; FU = follow up (months); LC = local control; Cxs = complications.

Local Control: 70 – 90%

Adverse Effects: 1 – 60%

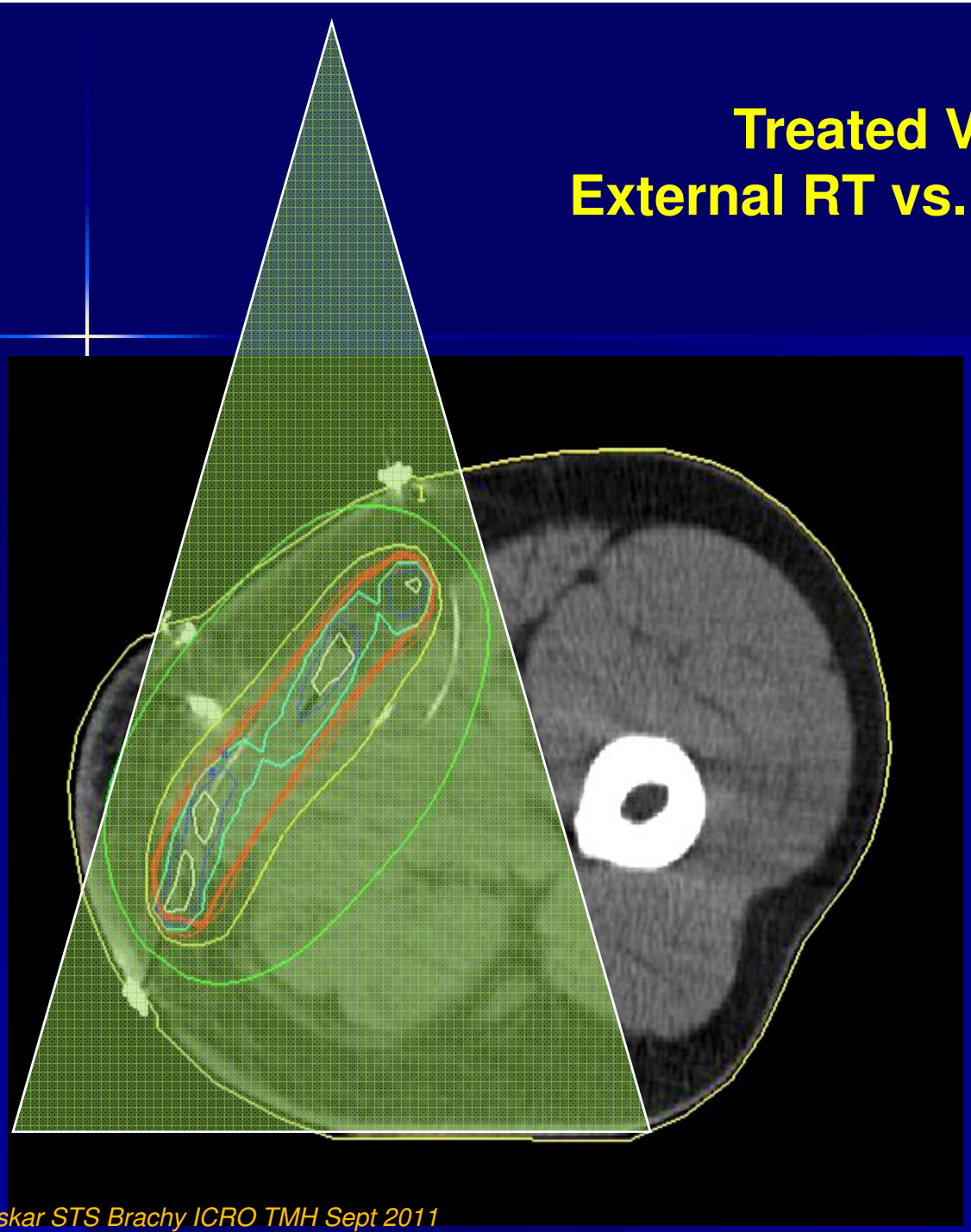
BRACHY vs. EBRT

Table 6. Advantages of monotherapy using LDR-brachytherapy compared to EBRT for adjuvant STS irradiation

	Brachytherapy	EBRT
Planning target volume (PTV)	Tumor + 1.5–2 cm	Tumor + 5 cm
Muscle compartment irradiated	No	Yes
Entire scar irradiated	No	Yes
Drain site irradiated	No	Yes
Overall treatment time	10–14 days	7–8 weeks after discharge
Cost of radiation treatment	Less	More
Intermediate-high grade STS local control	Equivalent	Equivalent
Low grade STS local control	Inferior	Superior
Survival	Equivalent	Equivalent
Radiation hazard to caregivers	Present	Absent
Functional outcome	Equal or better	Equal or worse

Abbreviations: STS = soft tissue sarcoma; EBRT = external beam radiation therapy; LDR = low dose rate.

Treated Volumes: External RT vs. Brachytherapy



Local Control

Adverse Effects

INTERSTITIAL BRACHYTHERAPY AT TMH

1981 - Introduced Ir 192 Interstitial Brachytherapy

1981 - Low Dose Rate, Iridium 192 Manual Afterloading System

1987 - Low Dose Rate, Iridium 192 Remote Afterloading System

1994 - High Dose Rate, Iridium 192 Remote Afterloading System

PLATO, Brachytherapy Treatment Planning System

Interstitial Brachytherapy in Soft Tissue Sarcomas

The Tata Memorial Hospital Experience

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

Background: Soft tissue sarcomas are relatively rare tumors with an aggressive natural history associated with a high propensity for local recurrence following conservative surgery. It accounts for 1.8% of all cancers seen at the Tata Memorial Hospital, Mumbai. Organ preserving surgery and tumor bed brachytherapy have revolutionized the management of soft tissue sarcomas.

Patients and Methods: One hundred and seventy-seven patients with histologically proven non-metastatic cases of soft tissue sarcomas in the age group of 16 to 79 years (median 41 years) were treated at the Tata Memorial Hospital between January 1983 and December 1992. One hundred and fifty-one patients who had completed a minimum of 24 months of treatment were studied. There were 100 males (66%) and 51 females (33%). The majority had recurrent lesions (70.3%). Extremities were involved in 75% of patients. Spindle cell sarcoma was the major histologic variant (30%). The patients underwent function preserving surgery and temporary afterloading Ir-192 tumor bed brachytherapy with or without external radiotherapy.

Results: In patients receiving brachytherapy only, 25 out of 33 (75%) were locally controlled after a median follow-up of 30 months. After successful salvage of local failures the overall local control improved to 82%. Similarly in the patients who received both interstitial brachytherapy and external irradiation, the local control rate after a median follow-up of 40 months was 71% which improved to 86% after successful salvage. The overall treatment related complication rate was less than 1%. The only marginally significant prognostic factor for local control was tumor grade ($p = 0.06$).

Conclusions: The sequential combination of limited surgery and tumor bed brachytherapy with or without external radiotherapy has been established as an effective alternative to more ablative procedures like amputation. Histologic grade has proven to be a significant factor determining local control.

Key Words: Soft tissue sarcomas · Brachytherapy · Organ preservation

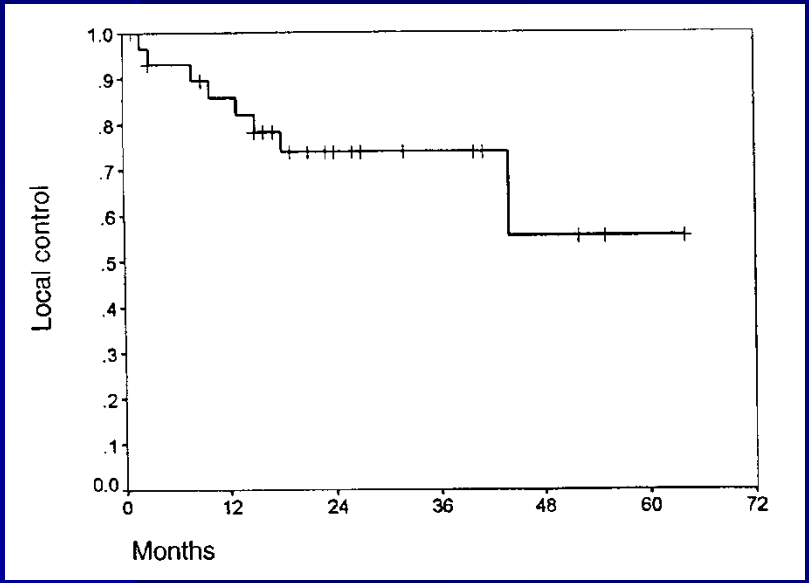
Strahlenther Onkol 1998

TATA MEMORIAL HOSPITAL EXPERIENCE

1983-1992 (n=151)
Age:17–79 Yrs (Median: 41Yrs)

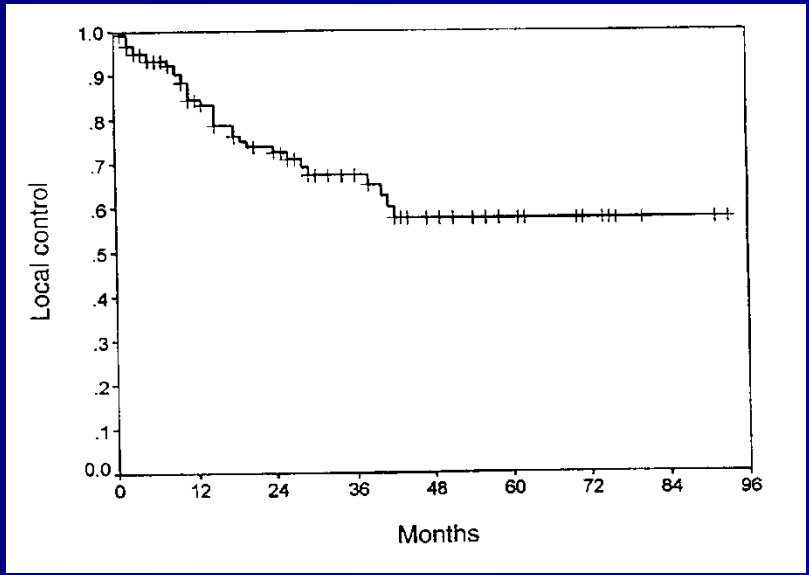
LSS + Brachy alone (n=33)
Brachy Dose: 29-50Gy (median:30Gy)

Median FU: 30 months
Local Control: 76%



LSS + Brachy. + Ext. RT (n=118)
Ext. RT Dose: 40-60Gy
Brachy. Dose: 15-20Gy

Median FU: 40 months
Local Control: 71%



Strahlenther Onkol 1998

What did we learn ?

Prognostic Factors for Local Control (Brachytherapy Alone):

Tumor Grade:

Gr I – 86%, Gr II – 67%, Gr III – 67%

Tumor Length:

< 5cm: 65%, 5 – 10cm: 90%, > 10cm: 80%

Site:

Extremity: 76%, Others: 75%

Disease Status:

Primary: 67%, Recurrent: 81%

Surgical Margins:

+ve: 50% failed locally, -ve: 19% failed locally

What did we learn ?

Prognostic Factors for Local Control (Brachytherapy + External RT):

Tumor Grade:

Gr I – 91%, Gr II – 79%, Gr III – 71%

Tumor Length:

< 5cm: 94%, 5 – 10cm: 80%, > 10cm: 80%

Site:

Extremity: 72%, Others: 65%

Disease Status:

Primary: 73%, Recurrent: 71%

Surgical Margins:

+ve: 77% failed locally, -ve: 21% failed locally

INFERENCES

BRT Alone or BRT + Ext. RT: Similar Outcome

BRT affective also for low grade tumors

Tumor size not a contraindication for BRT if coverage achievable

Extremities had better outcome

Surgical margins very crucial for local control

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]

Background: The goal of this study was to evaluate the efficacy of temporary interstitial brachytherapy (BRT) for patients undergoing combined modality management of soft tissue sarcomas (STS).

Methods: From January 1990 to December 2003, 155 adults 18–88 years of age (median = 42 years) with STS who had received BRT as part of locoregional treatment were included in this review. Sixty-four percent were males. Sixty-nine percent had primary lesions. Sixty percent had lesions involving the lower extremities. Spindle cell sarcoma (28%) and synovial sarcoma (16%) were the most common histologic types and 51% had grade III lesions. Treatment included wide local excision of primary tumor with BRT with or without external beam radiotherapy (EBRT).

Results: After a median followup of 45 months, the local control (LC), disease-free survival (DFS), and overall survival (OS) for the entire cohort was 71%, 57%, and 73%, respectively. DFS was superior for superficial tumors compared with that for deep tumors (96% vs. 54%, $P = .02$). Patients with a tumor less than 5 cm had superior OS (88% vs. 63%, $P = .05$). Cumulative radiotherapy dose greater than 60 Gy had a significant positive impact on LC ($P = .003$), DFS ($P = .003$), and OS ($P = .048$). Subcutaneous fibrosis (21%) was the major complication.

Conclusions: Temporary perioperative iridium-192 interstitial BRT with or without EBRT after function-preserving surgery results in satisfactory outcome in patients with STS. Both low dose rate and high dose rate BRT are equivalent in terms of disease control and complications when used alone or in combination with EBRT. BRT results in fewer complications compared with the combination of BRT and EBRT.

Key Words: Soft tissue sarcoma—Radiotherapy—Interstitial brachytherapy..

Laskar et al, Ann Surg Oncology 2007

Results

Prognostic factors		n	Local control %	Local control Significance	Disease-free survival %	Disease-free survival Significance	Overall survival %	Overall survival Significance
Overall		155	71		57		73	
Age	≤40 yr	69	81	$P = .32$	65	$P = .33$	58	$P = .27$
	>40 yr	85	59		48		81	
Gender	Male	99	80	$P = .63$	60	$P = .17$	72	$P = .11$
	Female	56	61		56		78	
Size	≤5 cm	67	87	$P = .79$	78	$P = .22$	88	$P = .05$
	> 5cm	86	62		46		63	
Depth	Superficial	37	96	$P = .20$	90	$P = .05$	93	$P = .18$
	Deep	118	54		42		67	
Site	Upper limb	30	84	$P = .91$	69	$P = .46$	70	$P = .33$
	Lower limb	93	60		47		67	
	Trunk	32	72		62		92	
Tumor	Primary	106	90	$P = .19$	71	$P = .61$	61	$P = .46$
	Recurrent	48	52		44		85	
Grade	Gr I	38	83	$P = .89$	78	$P = .31$	81	$P = .72$
	Gr II	38	72		59		84	
	Gr III	79	67		49		67	
Surgical margin	+ ve	8	45	$P = .29$	66	$P = .70$	46	P = .07
	Close	6	100		100		100	
	− ve	141	51		63		72	
Symptom duration	≤3 mo	52	83	$P = .51$	67	$P = .72$	73	$P = .43$
	>3 mo	102	69		56		73	
RT type	BRT	54	63	$P = .13$	50	$P = .38$	52	$P = .76$
	EBRT + BRT	100	74		59		79	
EBRT + BRT Group:								
Dose rate	LDR	57	73	$P = .72$	58	$P = .73$	78	$P = .84$
	HDR	43	97		84		89	
Cumulative dose	≤60 Gy	7	0	$P = .0003$	0	$P = .003$	36	$P = .048$
	>60 Gy	93	97		79		84	
Radical BRT Alone Group:								
Dose rate	LDR	40	65	$P = .44$	52	$P = .58$	56	$P = .0016$
	HDR	14	50		44		40	

Patterns of Failure

	Local recurrence	Distant metastasis	Local and distant failure
Tumor size			
≤5 cm (n = 67)	3 (4%)	6 (9%)	1 (1%)
> 5cm (n = 85)	4 (5%)	14 (16%)	2 (2%)
Depth			
Superficial (n = 37)	1 (3%)	2 (5%)	0 (0%)
Deep (n = 117)	6 (5%)	18 (15%)	3 (3%)
Site			
Upper limb (n = 30)	2 (7%)	3 (10%)	1 (3%)
Lower limb (n = 92)	3 (3%)	14 (15%)	2 (2%)
Trunk (n = 32)	2 (2%)	3 (9%)	0 (0%)
Tumor type			
Primary (n = 107)	3 (3%)	15 (14%)	2 (2%)
Recurrent (n = 48)	4 (8%)	5 (10%)	1 (2%)
Grade			
I (n = 38)	1 (3%)	2 (5%)	1 (3%)
II (n = 38)	2 (5%)	5 (5%)	0 (0%)
III (n = 78)	4 (5%)	13 (17%)	2 (3%)
BRT alone			
LDR (n = 41)	3 (7%)	5 (12%)	1 (2%)
HDR (n = 14)	1 (7%)	0	1 (7%)
BRT + EBRT			
LDR (n = 57)	3 (5%)	9 (16%)	1 (2%)
HDR (n = 43)	1 (2%)	5 (12%)	0

Toxicities

Complications	Pts. (%)	BRT (%)	BRT + EBRT (%)
Subcutaneous fibrosis	33 (21%)	3/55 (5%)	30/100 (30%)
Distal limb oedema	15 (10%)	–	15/100 (15%)
Wound dehiscence	10 (6%)	3/55 (5%)	7/100 (7%)
Impaired joint movement	8 (5%)	–	8/100 (8%)

Literature Review

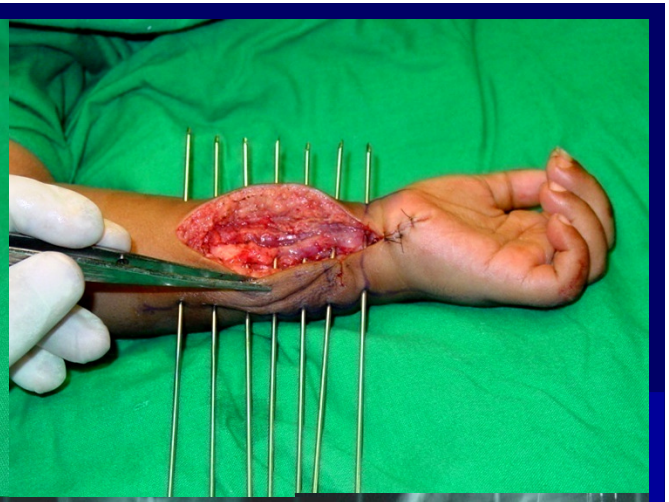
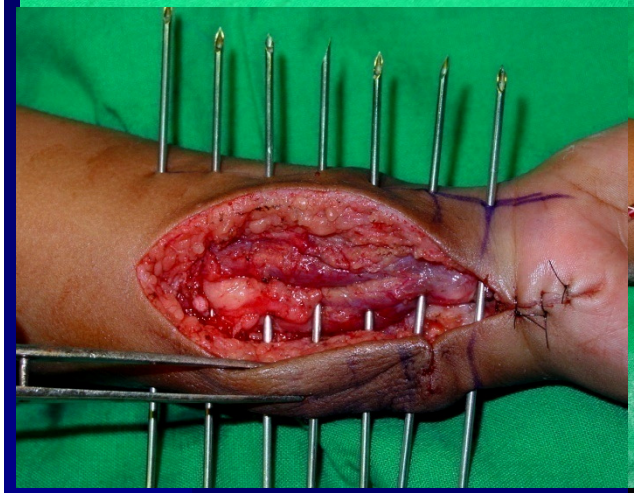
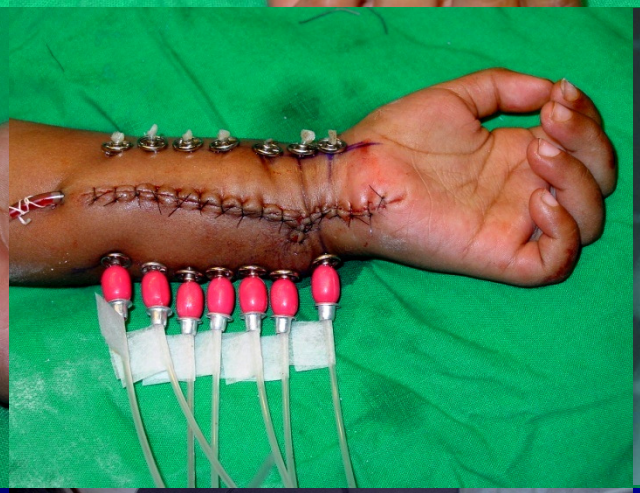
CENTER	PTS	BRACHY	LC(%)
MSKCC (Pister et al.)	164	LDR/HDR	89
Tata Memorial Hosp. (1983-92)	151	LDR	71
Fox Chase	130	LDR/HDR	82
MSKCC (Harrison et al.)	126	LDR	82
Inst. Claudius Regaud	112	LDR/HDR	89
MSKCC (Alekhteyar et al.)	105	LDR	86
Institute Gustave Roussy	50	LDR	62
Tata Memorial Hospital (1990-2003)	155	LDR/HDR	71

Table 4. HDR iridium-192 brachytherapy used as adjuvant therapy for intermediate-high grade primary STS of the extremity or superficial trunk

Author	Year	*n*	FU (mos)	LC (%)	Cxs (%)
Nonrandomized					
Donath *et al.* (16)	1993	19	12	70	16
Alekhteyar *et al.* (2)	1994	13	16	77	NS
Chuba *et al.* (10)	1996	32	50	82	48
Yoshida *et al.* (63)	1996	13	24	72	8
Crownover *et al.* (12)	1997	10	12	100	0
Koizumi *et al.* (37)	1999	16	30	50	6

Abbreviations: HDR = high dose rate; STS = soft tissue sarcoma; *N* = number of patients; FU = follow up (months); LC = local control; Cxs = complications; NS = not stated.



SIMULATOR 19.8.0

SIMULATOR 19.8.02



2008
S Laskar STS Brachy 04
S Laskar STS Brachy ICRO TMH Sept 2011

TLD Measurements of Dose To Normal Tissues

Measurement done using Lithium Fluoride TLD chips

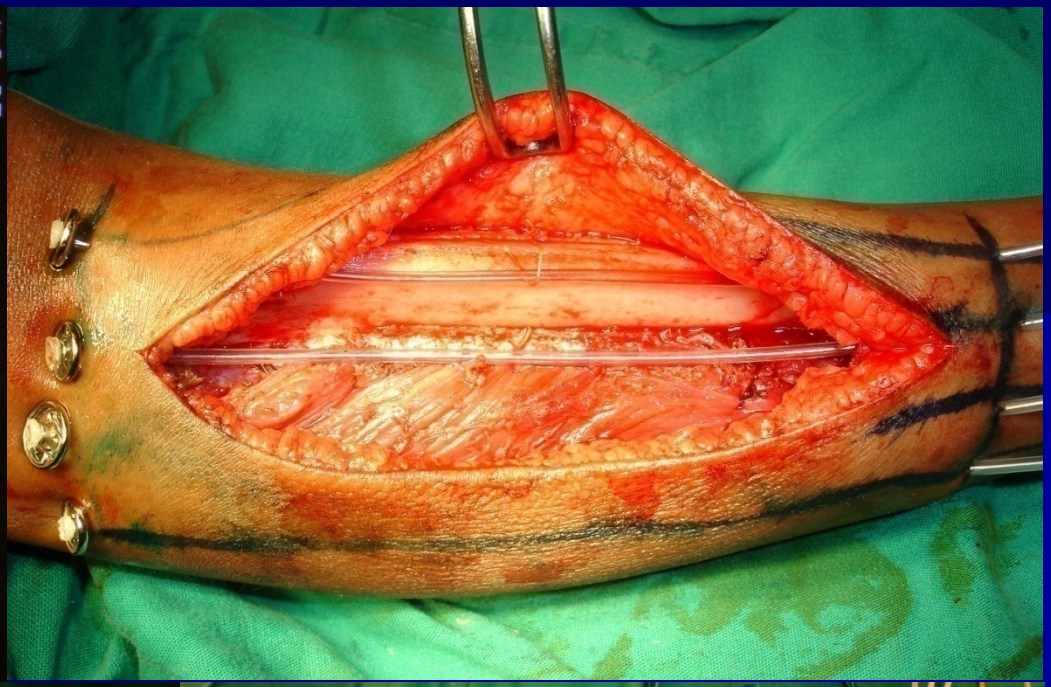
Site of disease: Right ankle

Dose per fraction : 400cGy HDR (Iridium 192)
Total Planned Dose : 400cGY x 9# = 36Gy

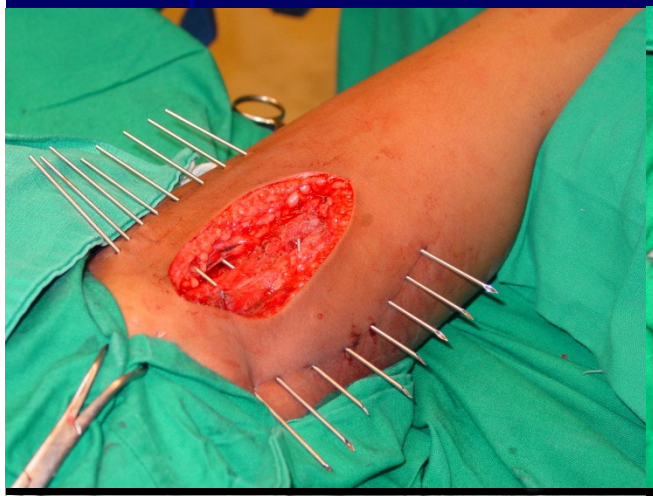
Dose to right side of scrotum: 2.35cGy / fraction
Dose to left side of scrotum : 1.57cGy / fraction
Dose to thyroid gland : almost nil / fraction

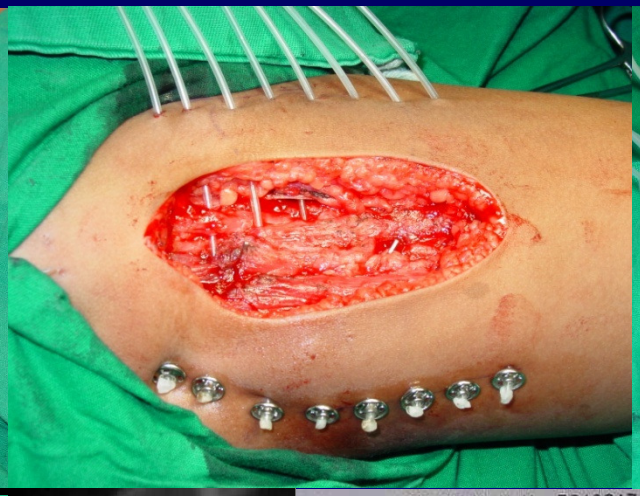
Total Dose (max) received by gonads: 2.35 x 9 = 21.15cGy
Average skin dose: 20%

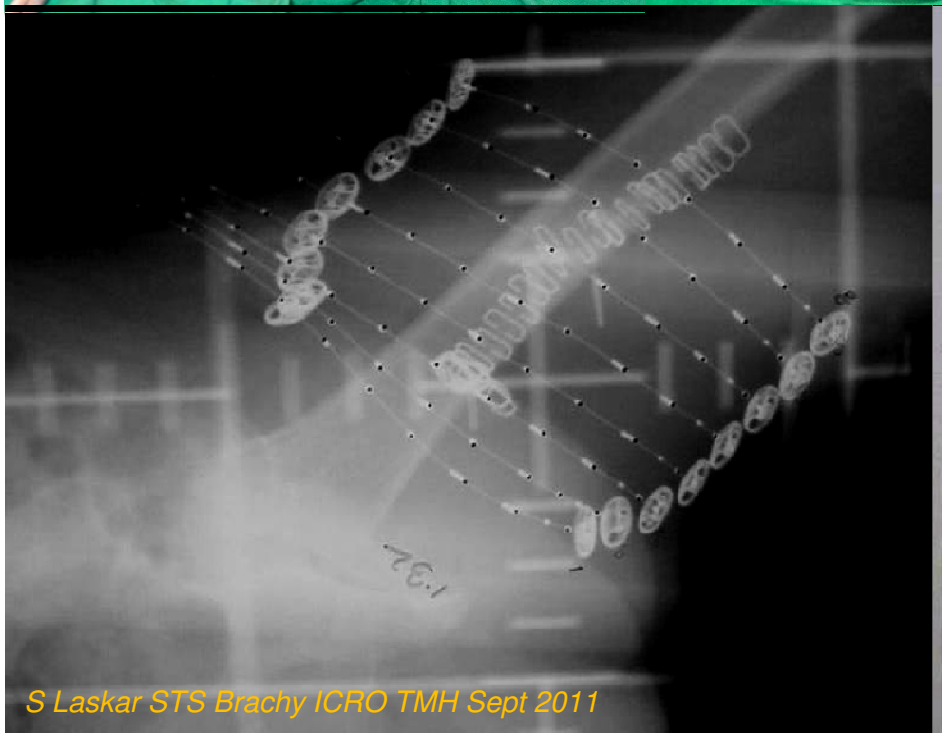

Signa 1.5T SYSMCEMSOW
Ex: 3923
Se: 104
Im: 7
DAx 539.2
MRI CENTRE MAHAWATI HOSPITAL
RAD HARSHITA BABY
F 3 63950
09 Jan 2009
02:34:13 PM
HRP
SJA

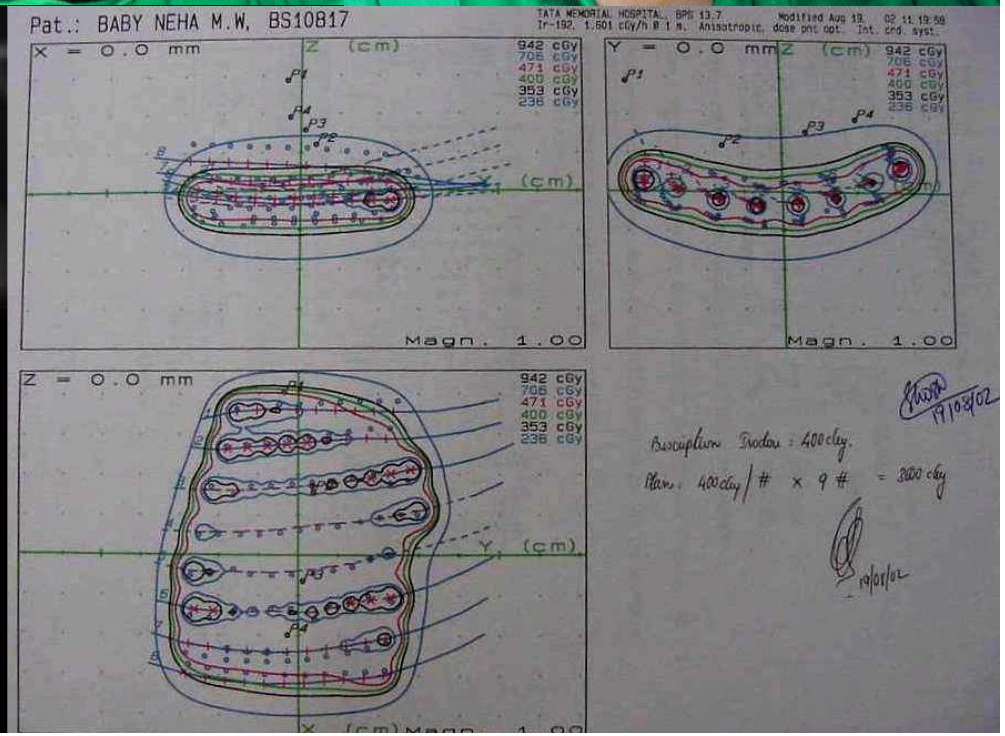


STS LEFT GROIN AND FEMORAL REGION

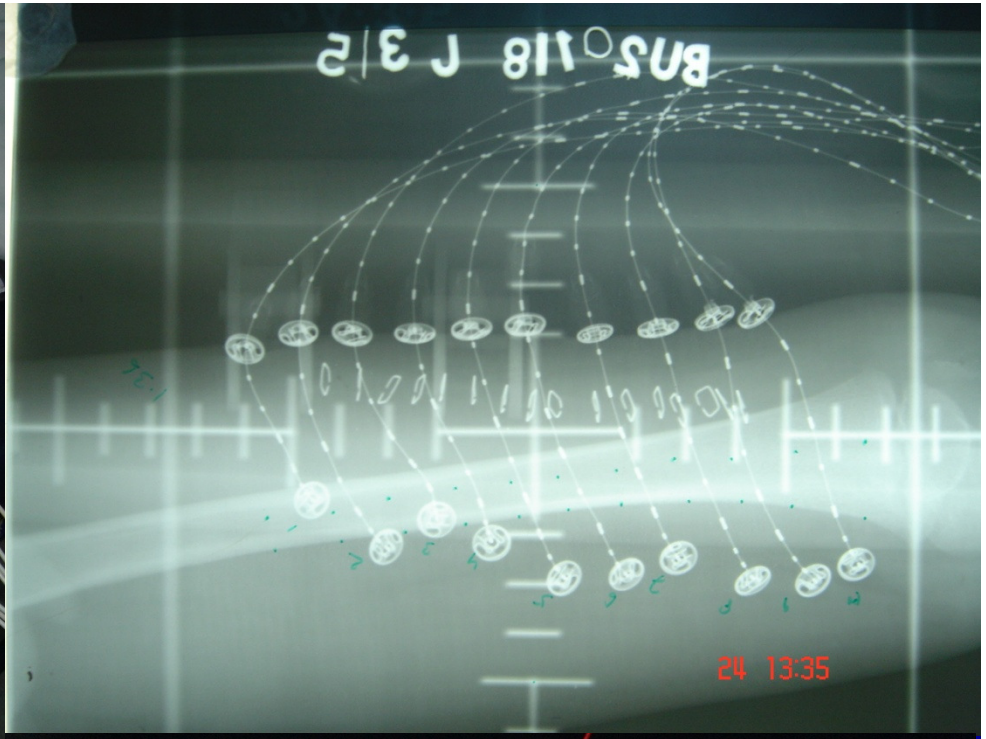


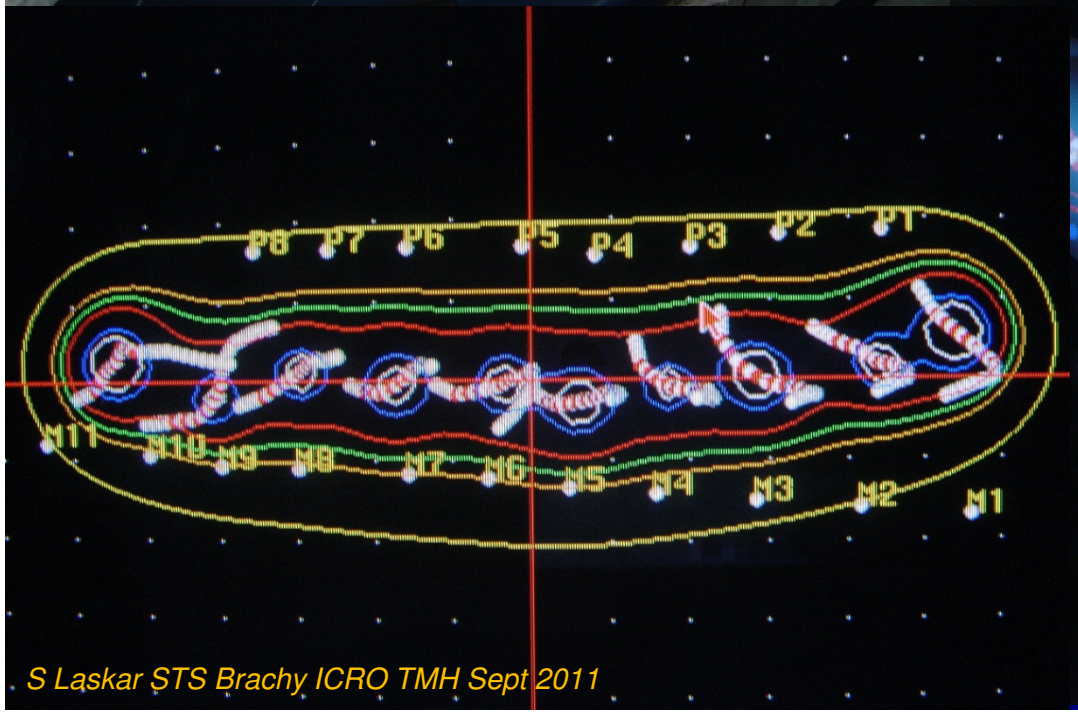


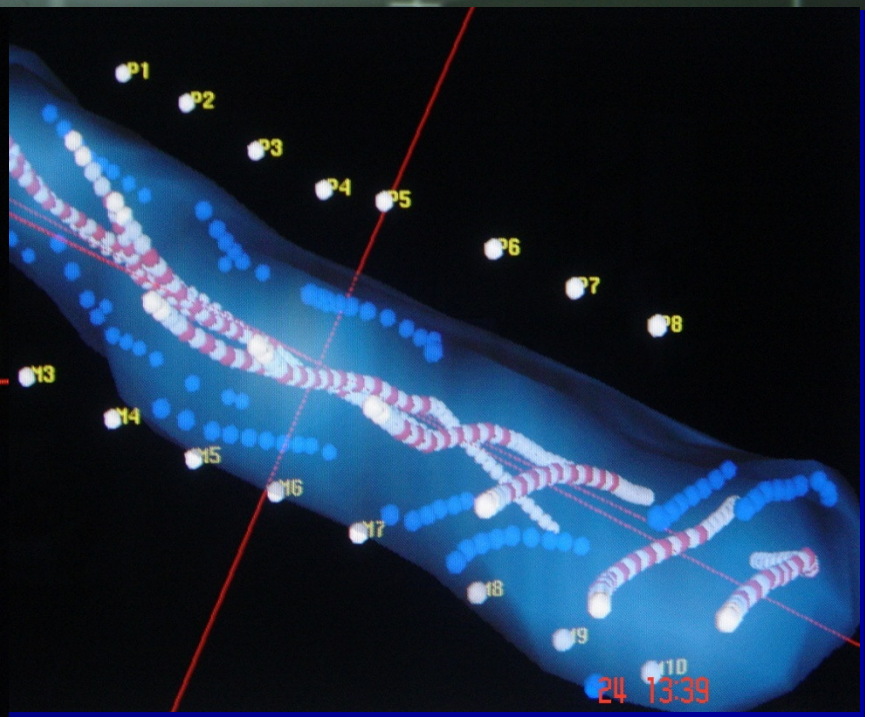





24 16:02

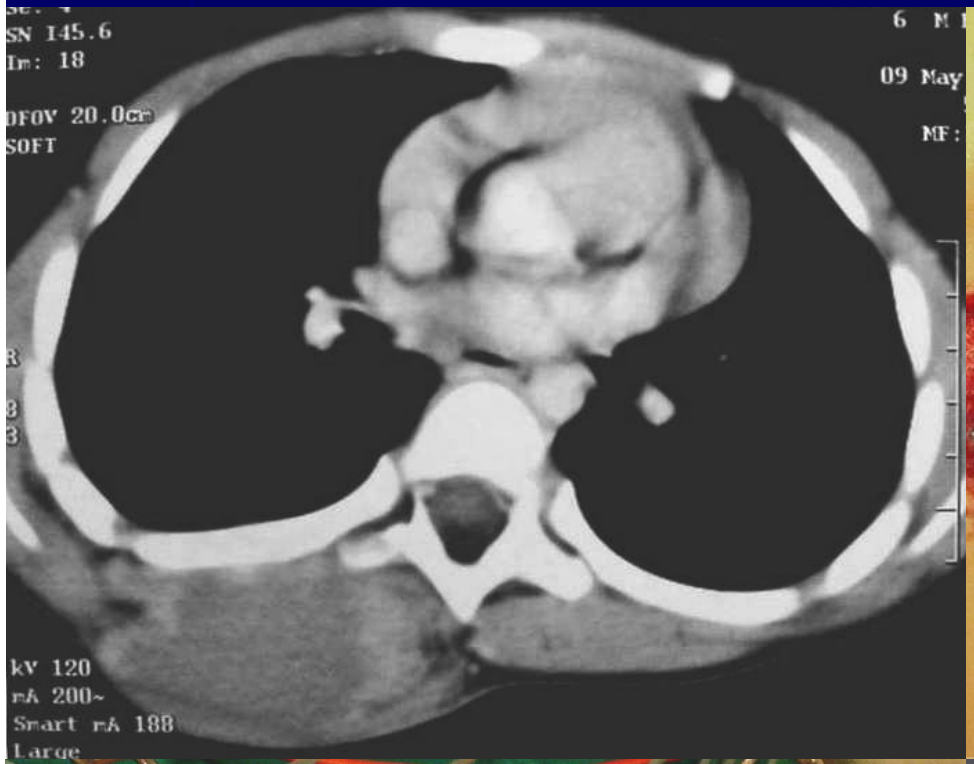

24 13:35

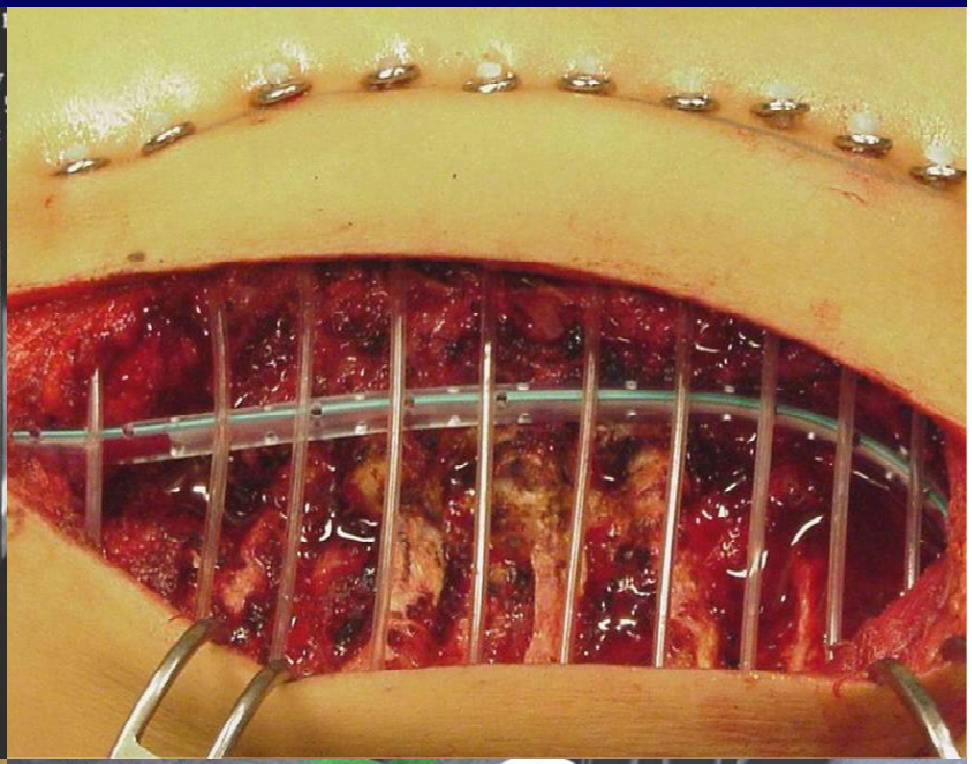

P8 P7 P6 P5 P4 P3 P2 P1
M11 M10 M9 M8 M7 M6 M5 M4 M3 M2 M1
S Laskar STS Brachy ICRO TMH Sept 2011

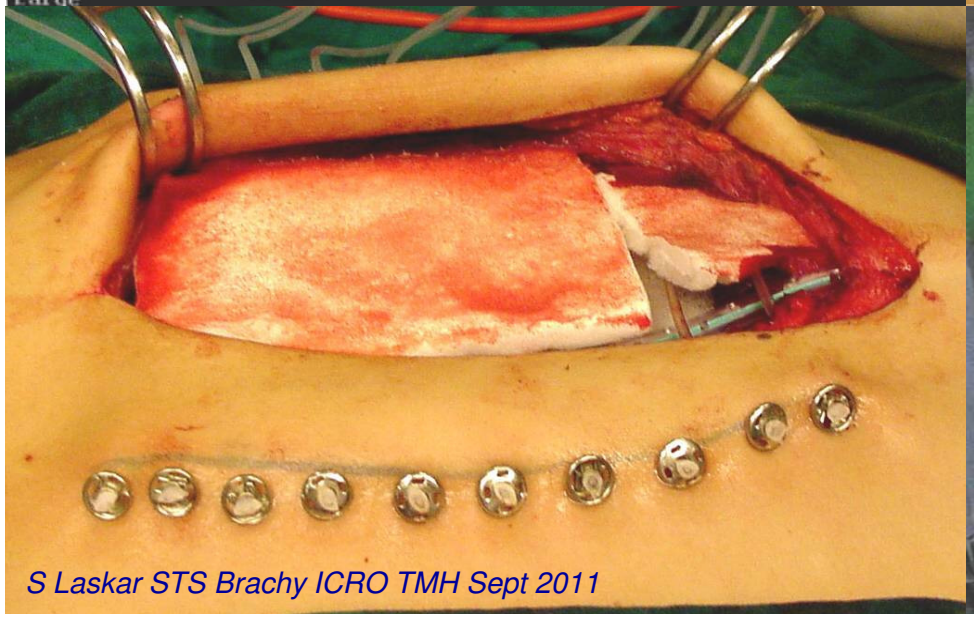

P1
P2
P3
P4
P5
P6
P7
P8
M3
M4
M5
M6
M7
M8
M9
M10
24 13:39

RECC STS Lt MALAR REGION

CHEST WALL & PARASPINAL







Pediatr Blood Cancer

Interstitial Brachytherapy for Childhood Soft Tissue Sarcoma

Siddhartha Laskar, MD,[1]* Gaurav Bahl, MD,[1] Mary Ann Muckaden, MD,[1] Ajay Puri, MS,[2] Manish G. Agarwal, MS,[2] Nikhilesh Patil, MD,[1] Shyam K. Shrivastava, MD,[1] and Ketayun A. Dinshaw, FRCR[1]

Background. To evaluate the efficacy of interstitial brachytherapy (BRT) in children undergoing combined modality treatment for soft tissue sarcomas (STS). ***Procedure.*** From September 1984 to December 2003, 50 children (median age 13 years, range 1 to 18) with STS who received BRT as part of loco-regional treatment were included. There were 30 males and 20 females, the majority (68%) had primary lesions, synovial sarcoma (32%) was the most common histological type, and 26% had high-grade lesions. Treatment included wide local excision and BRT with or without external beam radiotherapy (EBRT). Thirty children (60%) received BRT alone. ***Results.*** After a median follow-up of 51 months, the local control (LC), disease-free survival, and overall survival were 82%, 68%, and 71%, respectively. LC was superior in patients with tumor size ≤ 5 cm versus >5 cm (96% vs. 67%, $P=0.04$), symptom duration <2 months versus >2 months (100% vs. 73%, $P=0.05$), and Grade I versus Grade II versus Grade III tumors (100% vs. 93% vs. 57%, $P=0.03$). Children receiving a combination of BRT and EBRT had comparable LC to those receiving BRT alone (78% vs. 84%, $P=0.89$). There was no significant difference in LC for patients receiving LDR versus HDR BRT (77% vs. 92%, $P=0.32$, for BRT alone; and 67% vs. 100%, $P=0.17$, for BRT+EBRT). ***Conclusion.*** Interstitial BRT with or without EBRT appears to result in satisfactory outcome in children with STS. Radical BRT alone, when used judiciously in select groups of children, results in excellent local control and functional outcome with reduced treatment-related morbidity. Pediatr Blood Cancer

Key words: interstitial brachytherapy; pediatric; radiotherapy; soft tissue sarcoma

Laskar et al, Pediatric Blood & Cancer 2007

Results

Prognostic factor	5-year local control (LC)	5-year disease free survival (DFS)	5-year overall survival (OS)
Sex			
Male	80%	62%	60%
Female	83% ($P=0.99$)	76% ($P=0.66$)	92% ($P=0.28$)
Age			
≤10 years	81%	81%	100%
>10 years	82% ($P=0.65$)	63% ($P=0.67$)	63% ($P=0.15$)
Symptom duration			
<2 months	100%	100%	100%
>2 months	73% ($P=0.05$)	51% ($P=0.01$)	55% ($P=0.04$)
Tumor depth			
Superficial	92%	92%	100%
Deep	78% ($P=0.41$)	56% ($P=0.11$)	65% ($P=0.08$)
Size of tumor			
≤5 cm	96%	89%	93%
>5 cm	67% ($P=0.04$)	44% ($P=0.01$)	52% ($P=0.06$)
Primary site			
Extremities	82%	66%	69%
Axial/trunk	86% ($P=0.99$)	86% ($P=0.65$)	100% ($P=0.38$)
Type of lesion			
Primary	89%	71%	71%
Recurrent	67% ($P=0.09$)	56% ($P=0.22$)	68% ($P=0.57$)
Tumour grade			
Gr I	100%	100%	100%
Gr II	93%	75%	81%
Gr III	57% ($P=0.03$)	29% ($P=0.03$)	36% ($P=0.12$)
Surgical margins			
Negative	82%	68%	68%
Positive/close	80% ($P=0.74$)	67% ($P=0.88$)	100% ($P=0.45$)
Treatment			
BRT alone	84%	84%	95%
BRT + EBRT	78% ($P=0.89$)	45% ($P=0.11$)	55% ($P=0.10$)
Radiotherapy type (BRT + EBRT)			
LDR	67%	28%	31%
HDR	100% ($P=0.17$)	100% ($P=0.05$)	100% ($P=0.17$)
Radiotherapy type (BRT alone)			
LDR	77%	77%	90%
HDR	92% ($P=0.32$)	92% ($P=0.33$)	100% ($P=0.34$)

Multivariate Analysis of Prognostic Factors

	Local control			Disease free survival		
Variable	*P*-value	HR	95.0% CI	*P*-value	HR	95.0% CI
Size of tumor >5 cm	0.024	5.88	1.26–27.44	0.042	3.69	1.06–13.03
Grade III (high grade) tumor	0.004	14.39	2.84–39.53	0.001	11.78	2.87–48.36
Recurrent tumor	0.657	1.76	0.14–21.45	0.517	1.92	0.27–13.67
Symptom duration >2 months	0.235	4.64	0.82–26.23	0.121	5.22	0.35–7.69
Brachytherapy alone	0.448	0.53	0.10–2.76	0.358	0.57	0.15–1.98

Literature Review

CENTRE	PTS.	BRACHY	LCR(%)	TOX
Institute Gustave Roussy	127	LDR	81	22
Tata Memorial Hospital*	50	LDR/HDR	82	-
St. Jude Childrens Research Hospital	46	LDR	86	26
University of California	8	LDR	63	38
JCRT	7	LDR	100	14
Austrian Data	12	# HDR	75	0
Ohio State University	12	# HDR	91	17
Ohio State University	13	IO-HDR	95	23
MSKCC	10	IO-HDR	80	20

Subir Nag et al.IJROBP,Vol.51,No.3,p 729-735,2001
Laskar et al. Pediatric Blood and Cancer 2007

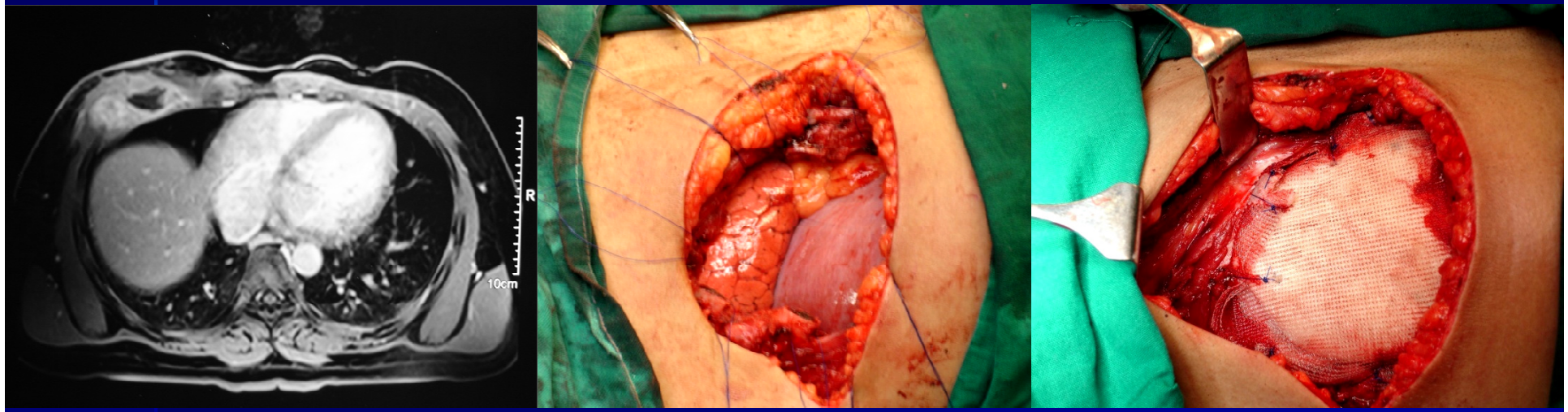
BRACHYTHERAPY WITH PLASTIC RECONSTRUCTION

Interstitial Brachytherapy

With

Plastic Reconstruction

CHEST WALL TUMOR BED IRRADIATION WITH BRACHYTHERAPY



Brachytherapy Tubes and Free Tissue Transfer After Soft Tissue Sarcoma Resection.

- N = 36
- W/E + Free flap → Brachytherapy after 5 days
- Avg F-up = 54 months
- Major complications 3 cases
  - Revision of anastomosis before radiation therapy
  - Delayed Deep wound infection (2 months) and required a second flap
- Minor complications
  - Hematoma,
  - Partial skin graft loss
  - Superficial infections

Aflatoon Et Al Clin Orthop Rel Res 2003

Reconstruction After Soft Tissue Sarcoma Resection In The Setting Of Brachytherapy: A 10-year Experience.

- N = 17, Recurr. STS
- Sx→ 5-7 days post-op →brachytherapy 1600-4500 Gy → Flap reconstruction
- 100% flap retention.
- Two patients developed postradiation partial-thickness skin necrosis with delayed secondary wound healing
- One patient developed venous thrombosis requiring re-surgery for flap salvage

Ann Plast Surg 2004

TOLERANCE OF TISSUE TRANSFERS TO ADJUVANT RADIATION THERAPY IN PRIMARY SOFT TISSUE SARCOMA OF THE EXTREMITY

MARNEE M. SPIERER, M.D.,* KALED M. ALEKTIAR, M.D.,* MICHAEL J. ZELEFSKY, M.D.,* MURRAY F. BRENNAN, M.D.,† AND PETER G. CORDIERO, M.D.†

- **N =43 adult patients Primary high-grade soft tissue extremity sarcomas**
- **Limb-sparing surgery and reconstruction → adjuvant RT**
- **N = 16 recd. Brachytherapy (Alone 45 Gy or EBRT 45 Gy + Boost 20 Gy)**
- **5-year overall wound reoperation rate was 6% (95% CI: 0–14%).**
- **Wound complications: BRT vs. EBRT (actuarial 17% vs. 0%, *p* 0.06);**

MSKCC IJROBP 2004

COMPLICATIONS

BRACHYTHERAPY FOR SHOULDER

Wound Complications In the Multimodality Treatment of Extremity and Superficial Truncal Sarcomas.

- N = 105 extremity and superficial truncal sarcomas
- Wide local excision with or without adjuvant perioperative brachytherapy (BRT) and/or chemotherapy.

	BRT	Non- BRT	
Major wound complications:	9 / 41 (22%)	2 / 64 (3%)	p = .002
Major + Minor complications:	18 / 41(44%)	9 / 64 (14%)	p = .0006
Median duration to complete resolution:	189 days	49 days	p = .0005

- A subset of 54 cases were studied in a randomized manner and yielded similar results
- Mean time to loading of radioactive sources: 4.1 days

Arbeit et al, JCO 1987

BMC Cancer

Nerve tolerance to high-dose-rate brachytherapy in patients with soft tissue sarcoma: a retrospective study

Tadahiko Kubo*[1], Takashi Sugita[2], Shoji Shimose[1], Toshihiro Matsuo[1], Ken Hirao[2], Hiroaki Kimura[3], Masahiro Kenjo[4] and Mitsuo Ochi[1]

- N= 7 STS involving the neurovascular bundle
- Limb-preserving surgery, followed by fractionated radical HDR brachytherapy (50 Gy @ 5 Gy/#)
- HG = 6 (one c/m +) LG = 1
- Median f-up 4 years
- 5-year actuarial OAS = 83.3%
- No HDR brachytherapy-induced peripheral neuropathy.
- 3 of 5 survivors → Normal motor nerve conduction velocity of the preservedperipheral nerve

Int. J. Radiation Oncology Biol. Phys., Vol. 47, No. 5, pp. 1273–1279, 2000

0360-3016/00/$–see front matter

PII S0360-3016(00)00587-3

CLINICAL INVESTIGATION **Sarcoma**

MORBIDITY OF ADJUVANT BRACHYTHERAPY IN SOFT TISSUE SARCOMA OF THE EXTREMITY AND SUPERFICIAL TRUNK

KALED M. ALEKTIAR, M.D.,* MICHAEL J. ZELEFSKY, M.D.,* AND MURRAY F. BRENNAN, M.D.†

Departments of *Radiation Oncology and †Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose: We have previously shown that adjuvant brachytherapy (BRT) improves local control in soft tissue sarcoma (STS) of the extremity and superficial trunk. A detailed assessment of the morbidity of this approach has not been examined. The purpose of this study was to evaluate the toxicity associated with adjuvant BRT in terms of wound complications, bone fracture, and peripheral nerve damage.

Table 2. Clinical and pathologic risk factor analysis for wound reoperation

Factor	No. of patients	No. of patients with wound reoperation (%)	*p* Value
Age			
≥60 yr	60	4 (7)	0.66
<60 yr	104	4 (4)	
Sex			
Male	94	4 (4)	0.95
Female	70	4 (6)	
Underlying diseases			
Yes	61	5 (8)	0.25
No	103	3 (3)	
Grade			
High	119	7 (6)	0.57
Low	45	1 (2)	
Size (cm)			
Proximal extremity	120	7 (8)	0.7
Distal extremity	21	1 (5)	
Size (cm)			
≥5	83	6 (7)	0.29
<5	81	2 (2)	
Depth			
Superficial	49	2 (4)	0.93
Deep	115	6 (5)	
Presentation			
Primary	147	6 (4)	0.42
Recurrent	17	2 (12)	
Skin width			
≤4 cm	90	1 (1)	0.02
>4 cm	70	7 (10)	
Skin area			
≤100 cm^2	128	4 (3)	0.08
>100 cm^2	32	4 (13)	
Resected specimen size			
≤1000 cm^3	107	3 (3)	0.18
>1000 cm^3	56	5 (9)	

Table 3. Treatment risk factor analysis for wound reoperation

Factor	No. of patients	No. of patients with wound reoperation (%)	*p* Value
Prior excision			
Yes	81	2 (2)	0.29
No	83	6 (7)	
BRT randomized			
Yes	78	8 (10)	0.006
No	86	0 (0)	
BRT dose rate (Gy/hr)			
≤42	35	4 (11)	0.88
>42	39	3 (8)	
Dose to skin (Gy)			
≤30	52	5 (10)	0.78
>30	18	2 (11)	
Interval between BRT and surgery			
<5 days	22	3 (14)	0.71
≥5 days	52	4 (8)	
Antibiotics use			
Yes	133	7 (5)	0.81
No	31	1 (3)	
Postoperative chemotherapy			
Yes	64	2 (3)	0.54
No	96	6 (6)	

LATE TOXICITIES

Complications	Pts. (%)	BRT (%)	BRT + EBRT (%)
Subcutaneous fibrosis	33 (21%)	3/55 (5%)	30/100 (30%)
Distal limb oedema	15 (10%)	–	15/100 (15%)
Wound dehiscence	10 (6%)	3/55 (5%)	7/100 (7%)
Impaired joint movement	8 (5%)	–	8/100 (8%)

Laskar et al, Annals of Surgical Oncology 2006

BRACHYTHERAPY FOR RE-IRRADIATION

Soft tissue sarcoma of the extremity. Limb salvage after failure of combined conservative therapy[1]

- N = 25 Post Sx+ RT recurrence
- 10 cases treated with W/E + Re-Irradiation

  BRT = 6 BRT + EBRT = 1 EBRT = 3
- Median retreatment dose 49.5 Gy
- Median cumulative soft tissue dose 100 Gy
- At 24 mths Median F up,

  Local Control W/E alone 36%

  W/E + BRT 100%
- However, Major Complications 60%
- Also Superior Functional Scores over Sx alone

Radioth Oncol 1996 Princess Margaret hospital

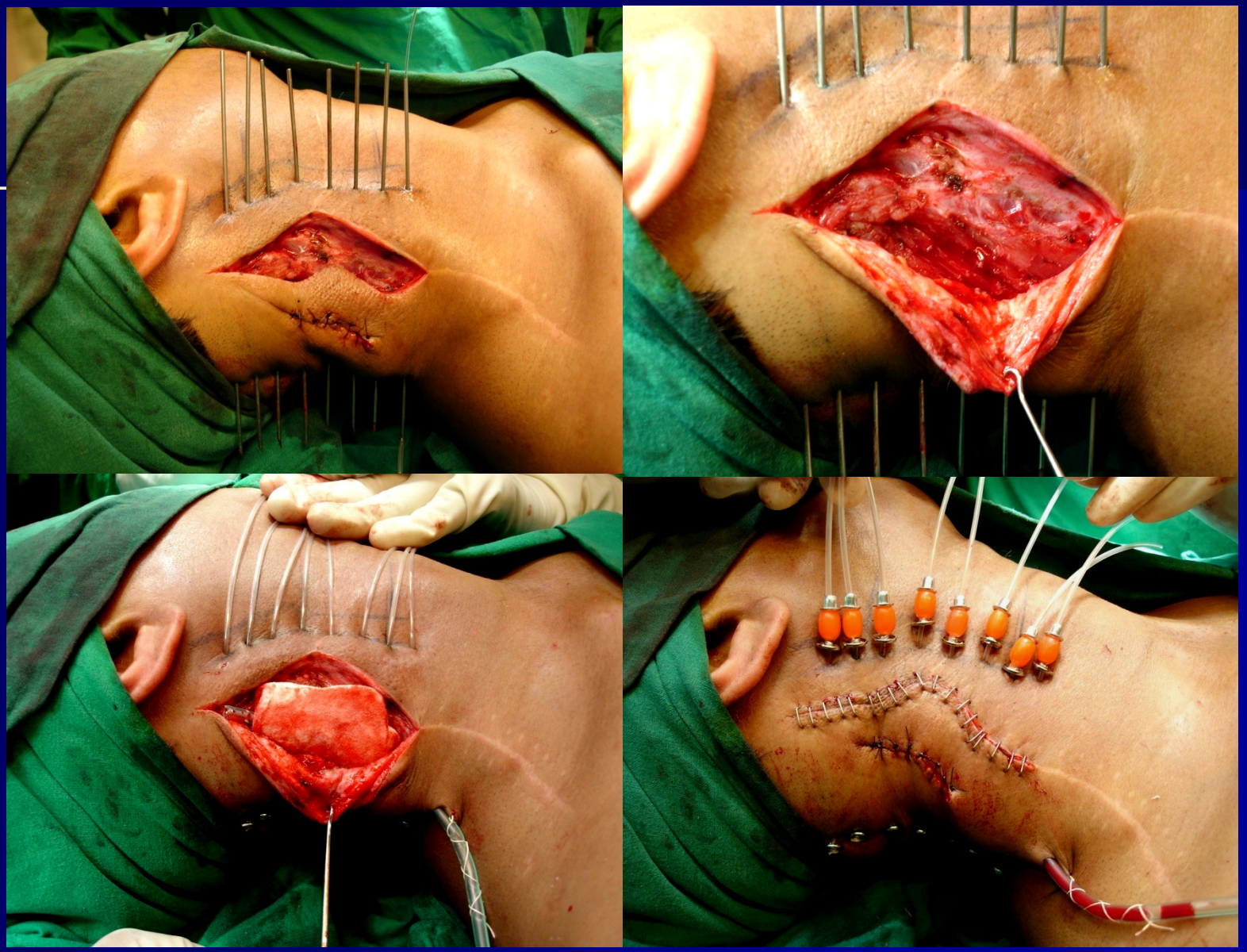
Re-Resection with Brachytherapy For Locally Recurrent Soft Tissue Sarcoma Arising in a Previously Radiated Field.

- N = 26 Recurrent STS Median F-up16 months
- 50% with flaps.
- All In-field Recurrences
- Post-op Interstitial Brachytherapy given only after 5-7 days.
- Mean dose 47.2 Gy +/- 1.6 Gy
- **Complications**: 5 / 26 cases. → 3 Wound breakdown
  → 1 Osteonecrosis
  → 1 Neuralgia

➢ 5-yr local RFS & OAS both 52%

Pearlstone et al 1999 Cancer J Sci Am MDACC

POST OP RE-IRRADIATION WITH BRACHYTHERAPY



CONCLUSIONS

Questions Answered:

Interstitial Brachytherapy useful tool in management of STS

Similar results of Brachy alone vs. Brachy. + Ext. RT

Can be used along with flaps used for plastic reconstruction

Useful tool for salvage of recurrence at primary site

Complications are not significant

Questions Unanswered:

Target volume: needs further definition

Ideal number of planes

HDR vs. LDR Brachytherapy

BRACHYTHERAPY

Results:

- Optimal disease control
- Reduced toxicity

Advantages over Ext. Radiotherapy:

- Shorter overall treatment time (4-6 days vs. 5-6 wks)
- Post-op RT can be started sooner
- Smaller irradiated volume --- functional advantage

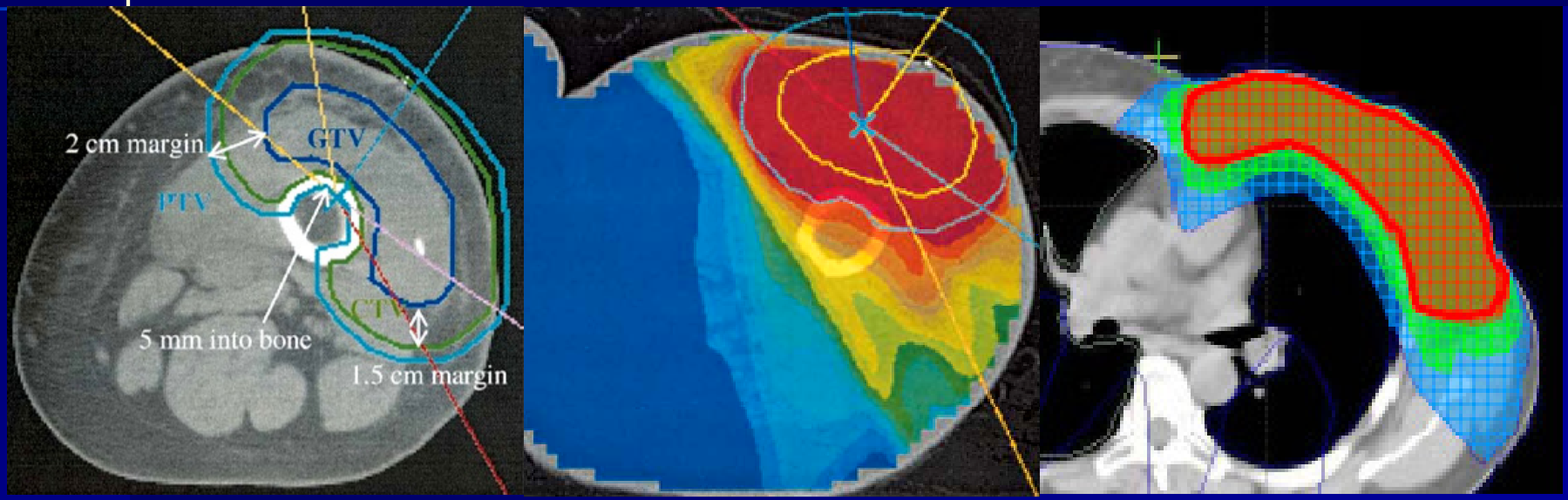
Disadvantages:

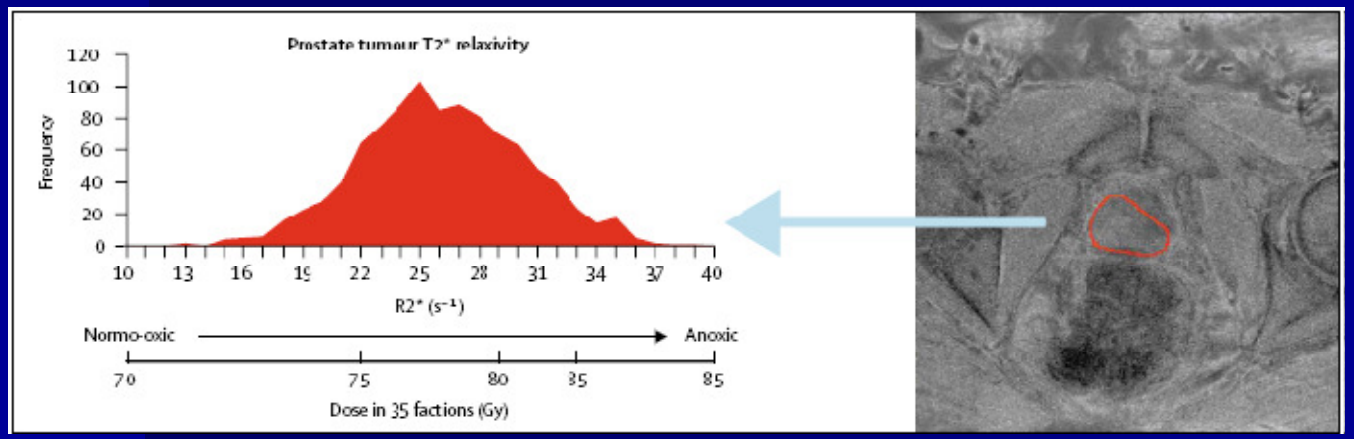
- Restricted target coverage
- Difficult for lesions close to neurovascular bundle
- ? Efficacy in Low Grade Tumours

Issues:

- Brachy. vs. Extetrnal RT – No Randomized Comparision
- ? Need for Multi-Planar Implant (Volume)

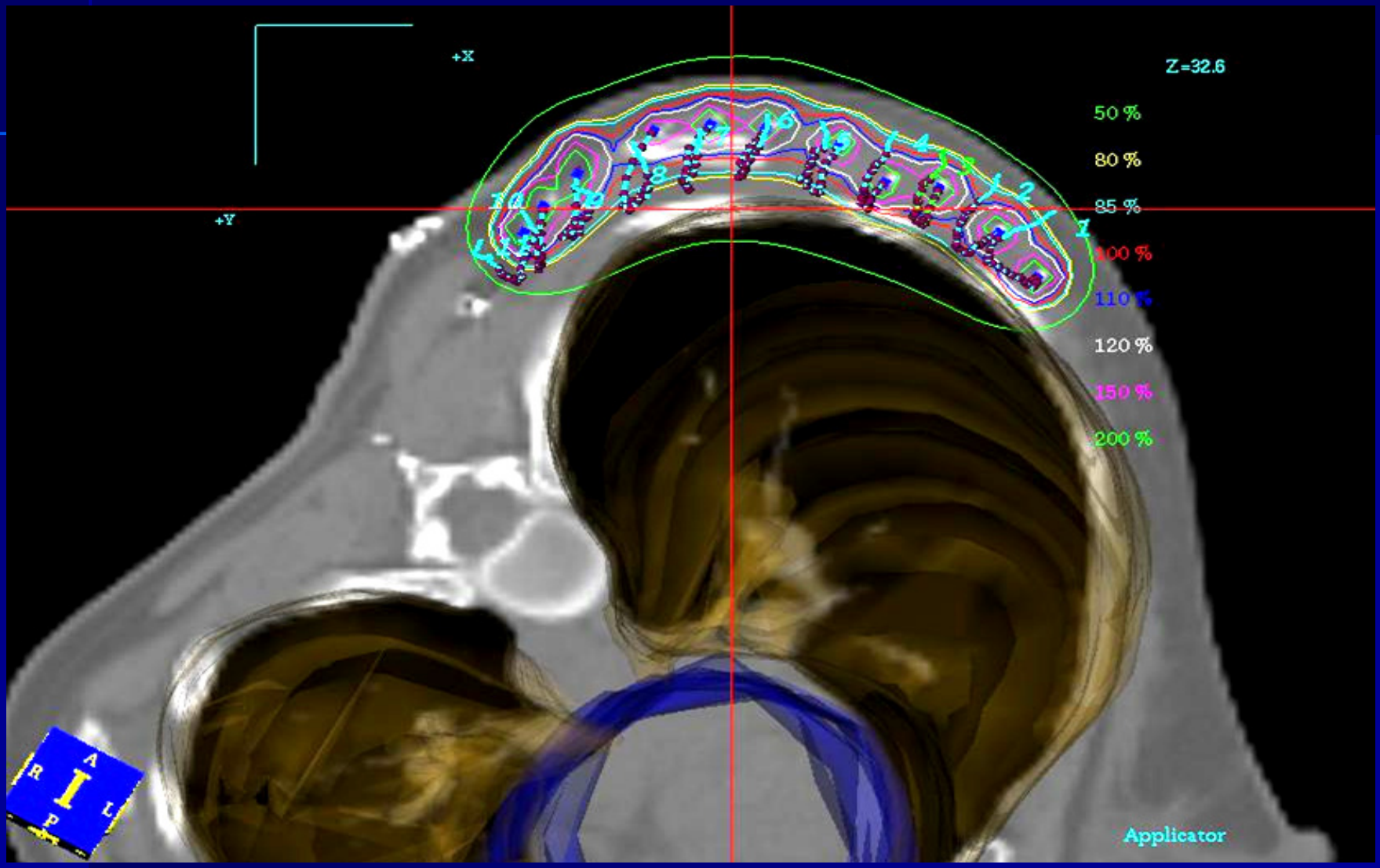
INTERSTITIAL BRACHYTHERAPY IN THE ERA
of
IMRT / IGRT / DOSE PAINTING WITH NUMBERS

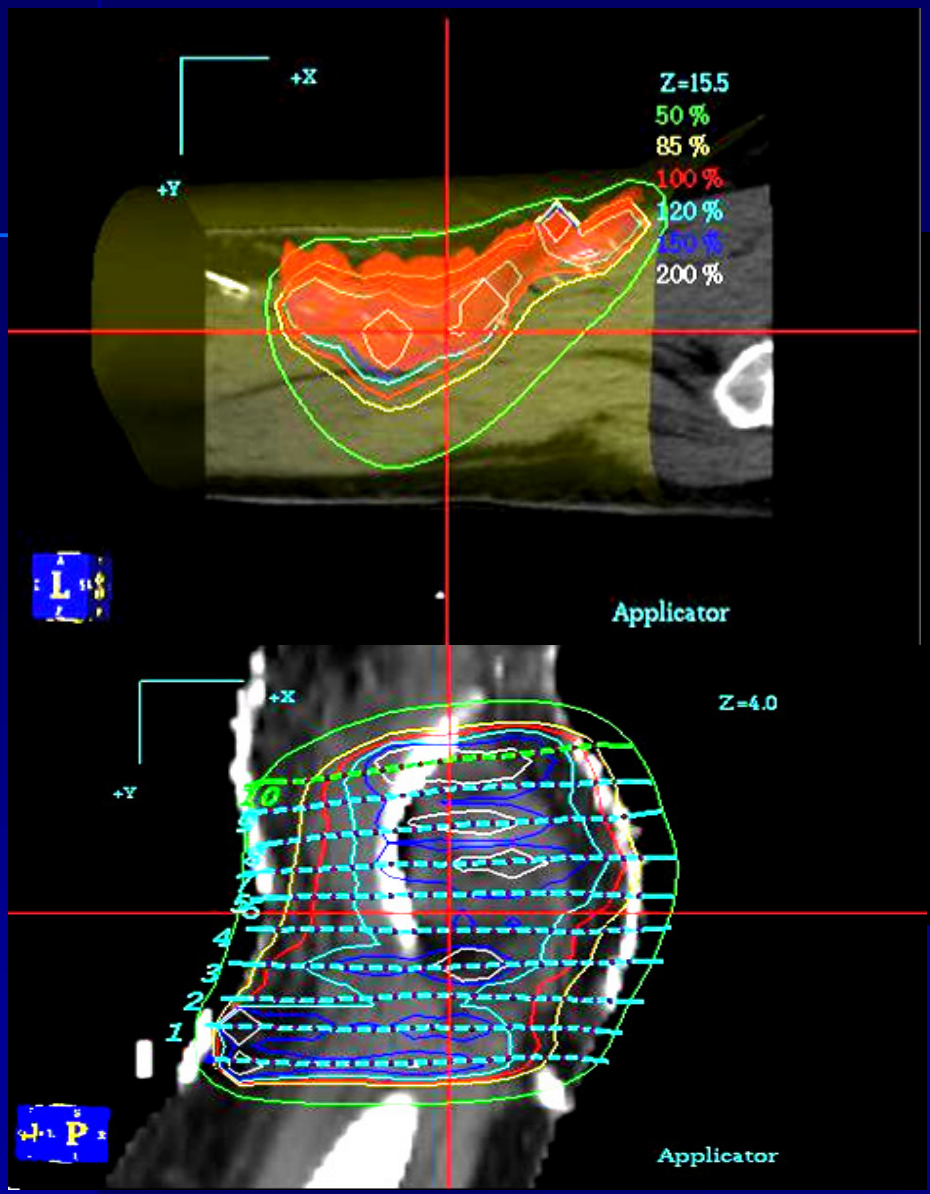




Hong et al., IJROBP 2004
Lancet Oncology 2006

IMAGE GUIDED BRACHYTHERAPY




+X
+Y
Z=15.5
50 %
85 %
100 %
120 %
150 %
200 %
Applicator
+X
+Y
Z=4.0
Applicator


4th TMH Annual Radiotherapy Practicum: Brachytherapy- Techniques & Clinical Applications
29 September - 1st October 2006
Tata Memorial Hospital, Parel, Mumbai

Thank You