41st ICRO teaching Course

Nuances of Brachytherapy in Pediatric Malignancies

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Radiation and children

- A child is NOT a small adult
- Structure and function preservation
- Varies sites
- Varied tolerance
- Effect NOT dose dependent
- Second cancers!!
- Lack of robust evidence
- Suboptimal understanding

Radiation in pediatric malignancies

- Multi-modality treatment program that includes surgery, chemotherapy, and radiation. Better outcomes!!

- Significant long-term toxicity (especially retardation of growth of bones and organs) including radiation induced second cancers.

- The use of brachytherapy is an attractive alternative because brachytherapy irradiates small volumes and can thus potentially minimize complications.

Brachytherapy an attractive option!!

- Rapid dose fall off → Sparing of surrounding normal tissues
- Higher local dose delivered in short period of time/ less in patient days; cost effective (biologically very effective dose) → better outcome and better compliance in children
- Cosmetic superiority → older children
- Functional preservation of organs → long term survivors
- Second cancers !!

Is high dose per fraction a problem in children

- Dose per fraction and late toxicity
- Single dose per day (and not twice a day)
- Lesser volume

- Selection of cases!!

- Techniques very similar to adults

Dose required and volume irradiation should be less

Brachytherapy in children

- Soft tissue sarcoma extremities (Dr D N Sharma)
- Plaque brachytherapy for Retinoblastoma (Dr A Kumar)
- Pelvic (Bladder/ Prostate RMS)
- Vaginal intracavitary and Moulage technique (Botryoid RMS)
- Orbital (Orbital RMS)
- Auditory canal (auricular RMS)
- Re irradiation
- HDR better than LDR

Limitations

- Inaccessible sites
- Limitations in geometry of tumor bed
- Close proximity to bone or NV structures
- Invasive procedure requires GA (peri-operative Vs post-operative)
- Additional surgical intervention
- Labor intensive
- Higher dose inhomogeneity
- Precision and expertise required
- Potential of a miss

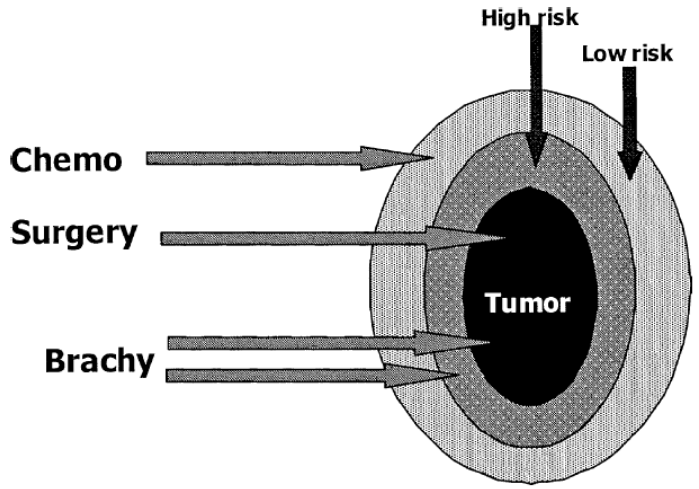
Few institutes use
brachytherapy for children!!

Intra operative HDR brachytherapy

- See and do!!
- Preferably, the radiation oncologist should be present during Sx
- Single plane implant/ multiple plane
- General anesthesia/ mild sedation
- Limb or body immobilization/ plaster casts
- Gonadal shielding for boys whenever necessary and feasible
- IORT (electron beam)

Margins in pediatric malignancies

- What constitutes adequate margin is controversial a depends on histology, grade, and location.
- Limited margins; evolving In cases of extremity
- Chemosensitive and radiosensitive tumors
- Adjuvant brachytherapy to volumes at high risk of relapse
- Brachytherapy as “definitive” RT (vaginal/ orbital)



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Principles of EBRT and Brachytherapy remain the same!!

Table 2
Comparisons among various intraoperative and perioperative techniques

Parameter	IOHDR	IOERT	LDR	F-HDR	Permanent I-125
Treatment time	Minutes	Minutes	2–7 days	6–8 days	Months
Personnel radiation hazard	Nil	Nil	High	Nil	Low
Typical doses used	10–15 Gy	10–15 Gy	45 Gy	36 Gy	140–160 Gy
Sites	Any	Limited	Any	Any	Deep
Dosimetry*					
Surface dose	200%	80%	N/A	N/A	N/A
2 cm depth dose	30%	90%	N/A	N/A	N/A
Radiobiology					
Reoxygenation	None	None	Yes	Yes	Yes
Redistribution	None	None	Yes	Yes	Yes
Repair of SLD	None	None	Yes	Yes	Yes
Rx of micro disease	With EBRT	With EBRT	Alone or w/EBRT	Alone or w/EBRT	Alone or w/EBRT
Rx of gross disease	Limited	Limited	Alone or w/EBRT	Alone or w/EBRT	Alone or w/EBRT
Rx in previous RT field	Limited	Limited	Yes	Possible	Yes

IOHDR = intraoperative high-dose-rate brachytherapy; IOERT = intraoperative electron beam radiation; LDR = low-dose-rate brachytherapy; F-HDR = fractionated high-dose-rate brachytherapy. EBRT = external beam radiation. N/A = not applicable; SLD = sublethal damage; Rx = treatment.

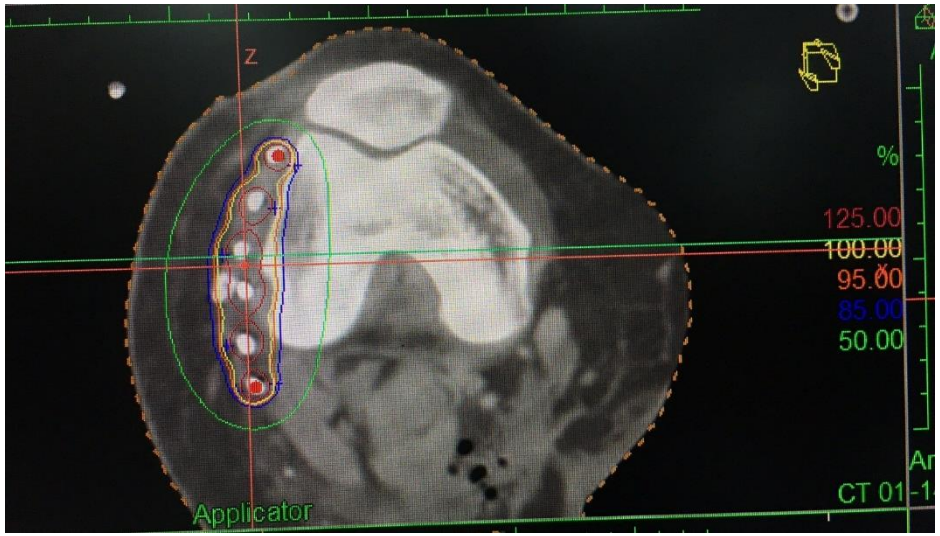
* Dosimetry profile for a 6 MeV electron beam prescribed to 90% isodose at 0.5 cm depth. The dose prescription for brachytherapy techniques is 100% at 0.5 cm.

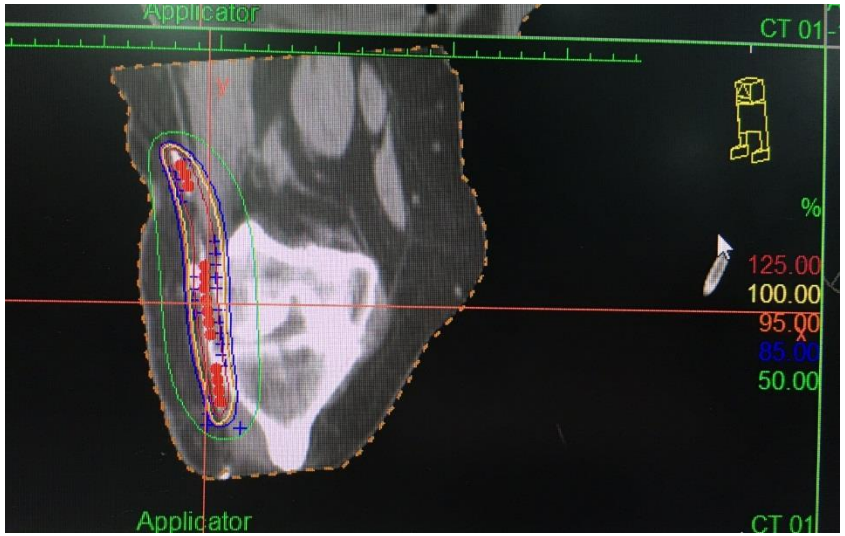
Extremity sarcoma in children

- Wide local excision + adjuvant RT
- Sparing of normal tissue specially the joints and NVB
- Proximity to bone and NVB is a challenge
- Selection is the key!!
- Expertise and experience!!

- Long term sequelae
  - Skeletal deformity
  - Second cancers

Close to joint?



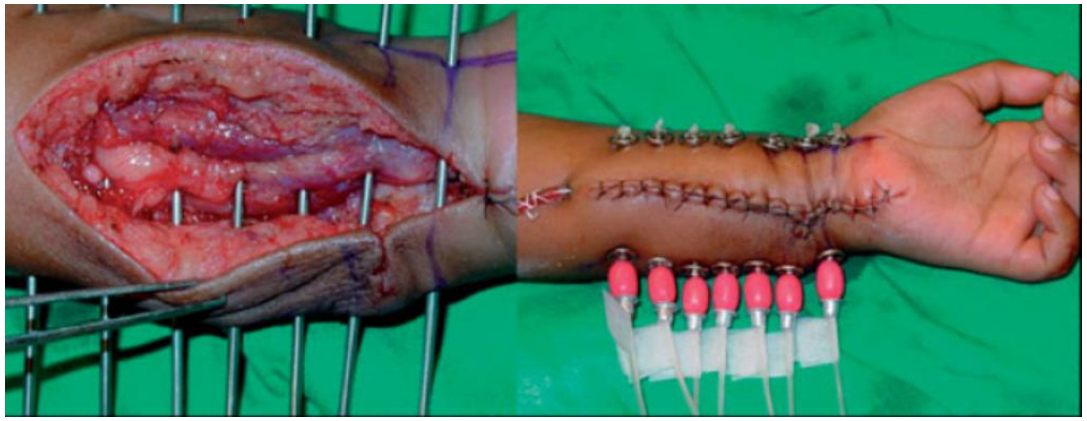


Bone/ joints can be spared
Lesser volume of normal tissues irradiated
Integral dose much less

IDEAL for children

Close to the bone and neurovascular bundle?

- Not an absolute contraindication
- Bone and thick nerves are relatively resistant in adults
- Gelfoam can be used as a spacer
- Muscle strips can be pulled from surrounding without altering the anatomy of the tumor bed
- Selection is the key!!



Can it be considered with flaps/ plastic reconstruction/ skin graft?

Take care of the vascular pedicle
Careful evaluation of brachy plan wrt doses at skin and suture line
BT to start NOT before 72 hours

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RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer

Interstitial brachytherapy for pediatric soft tissue sarcoma: Evolving practice over three decades and long-term outcomes

Siddhartha Laskar[1] | Avinash Pilar[1] | Nehal Khanna[1] | Ajay Puri[2] |

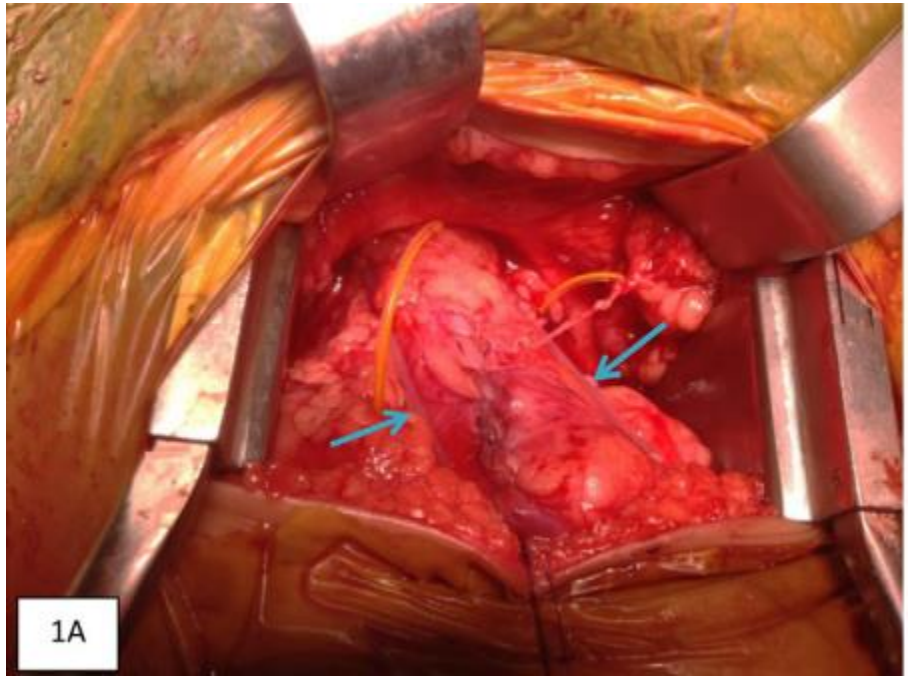
- 1984 – 2014, 105 children WLE + Brachytherapy
- Median follow-up of 65 months
  - 10 year Local control – 83%
  - 10 yr disease-free survival (DFS) – 66%
  - 10 yr overall survival (OS) – 73%
- Sequelae
  - Wound complications were seen in 6%.
  - Subcutaneous fibrosis (25%), Limb edema (6%)
  - Skeletal abnormalities (3%), and
  - Neuropathy (1%) were the late complications.
  - One child (0.9%) developed a second malignancy after 7 years
- Late toxicity is minimal and results in good functional outcome in most patients.

Bladder and prostate RMS

- Historically, the standard treatment was based on total cystectomy or cysto-prostatectomy → severe urinary and sexual sequelae
- Multimodal conservative approach
- Long term survival!!
- Pelvic EBRT → risk of late GI/ GU toxicities remains a major issue in children

- Conservative surgery + brachytherapy 

- Four single leader plastic tubes are implanted through transperineal route under perioperative guidance, encompassing the prostate/bladder neck.
- Two loops encompassed the prostate/urethra and/or the bladder neck and systematically sutured to the bladder wall



C. Chargari et al. Radiotherapy and Oncology 2017

How is it done?

- Principle - avoiding partial bladder neck resection and resection of the whole bladder wall, to minimize long-term urinary morbidity

- For tumors located in the anterior part of the bladder wall and extending above the trigona level, a partial cystectomy was performed with free upper margins, respecting the bladder neck.
- When the trigona was involved, only a resection of the tumor and the mucosa was performed, without resection of the muscular layers.
- Bilateral ureteral reimplantation was performed to avoid a stenosis of the ureteral orifices.
- For tumors involving the prostate, partial prostatectomy was performed with urethra preservation.

R+ resection acceptable

- The surgery is never intended to be microscopically complete at the level of the prostate and/or bladder neck, to avoid the genitourinary sequelae of a radical surgery.

- A macroscopically tumor residuum is accepted, on the basis of the rationale that brachytherapy could sterilize residual tumor cells.

Outcomes

- Brachytherapy Institute Gustave Roussy, France
- Largest prospective database
- Close collaboration between surgeons and brachytherapists
- Separate intervention for removal

Table 3 Oncologic outcome

Parameter	Value
No. of patients	100
Median follow-up (range)	64 mo (6 mo-24.5 y)
Relapses	
Total no. of patients with relapse	12
Local	6
Nonlocal	1
Local and nonlocal	5
Kaplan-Meier estimated survival times	
5-y overall survival (%) (95% CI)	91 (87-95)
5-year disease-free survival (%) (95% CI)	84 (80-88)

C Chargari et al. IJROBP 2017

Multiple publications by Cyrus Chargari, Christine Haie-Meder and Helene Martelli

Functional outcomes

- 78% had a normal diurnal urinary continence
- 11 had diurnal dribbling (3 with night-time incontinence).
- Urodynamic studies showed a small bladder capacity with hyperactive or not compliant bladder in 6 patients
- Two patients required intermittent catheterization.
- Significant rectal and vaginal complications were as follows
  - Painful rectal ulceration – 2 pts
  - Rectal stenosis requiring dilatations – 1 pt
  - Vaginal stenosis - 2 pts
  - No bowel complication was reported.
  - Erectile dysfunction – 1 pt
  - No second cancer
  - To date, no patient had offspring.

Quality of life and functional outcome of male patients with bladder-prostate RMS treated with conservative surgery and brachytherapy during childhood

- 18 male pts; Median age at Sx - 24 mths; Median followup -10 years
- Normal QOL – 13/18
- Normal urinary continence 9/13
- Rare occasions of diurnal dribbling 4/13.
- All pubertal patients considered themselves as having normal erections. Three sexually active patients reported having satisfying sex and orgasms. Two patients had normal ejaculations.

- Conclusion - The majority of long-term male survivors (76%) within this cohort considered themselves as having a normal QOL

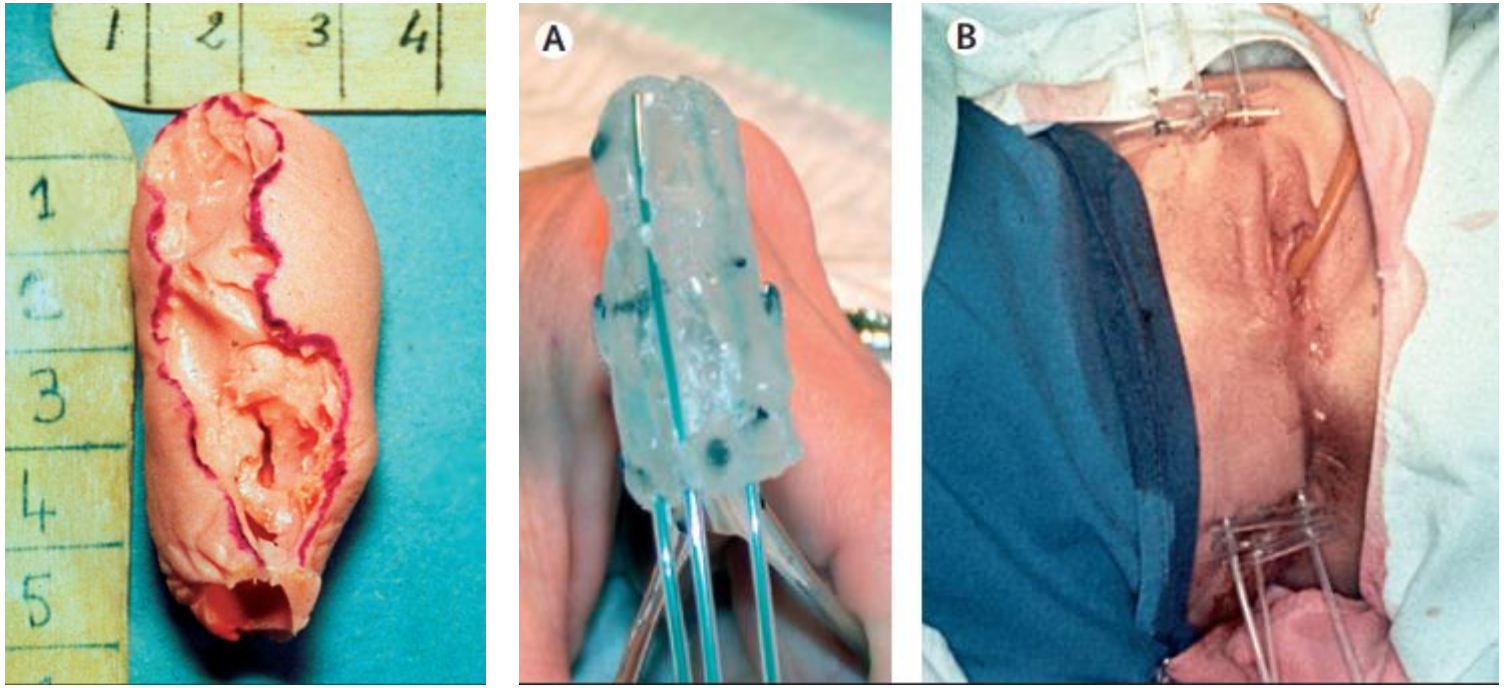
Helene Martelli et al. Brachytherapy 2016

Genital tract RMS in girls

- Recognized as one of the most curable forms of RMS
- Multimodal Rx
- RT can be an alternative to Sx
- Concerns with EBRT
  - Fertility
  - Future pregnancy potential
  - Sexual QOL

- Brachytherapy can be an alternative to EBRT
- Vaginal brachytherapy
  - Moulage technique
  - Customised implants

How is it done?



- A vaginal impression that accurately shows the topography and extension of the tumour as well as the anatomy of the vagina.
- A vaginal mould/ moulded applicator

Nicolas Magné et al. Institute Gustave Roussy, Lancet 2007

Dose prescription in vaginal brachytherapy

- Doses for vaginal cylinders are usually prescribed at 5 mm depth in adults
- Treatment of vaginal RMS in young girls requires consideration of a smaller vagina and relatively closer proximity of the rectum and bladder.
- Doses prescription at
  - 2 mm depth for girls younger than 1 year
  - 3 mm for girls between 1 and 3 years
  - 4 mm for girls between 3 and 6 years
  - 5 mm for girls older than 6 years.
- This results in a vaginal mucosal dose of approximately 60 Gy for most cases.

S Nag 2013 IJROBP

Outcomes

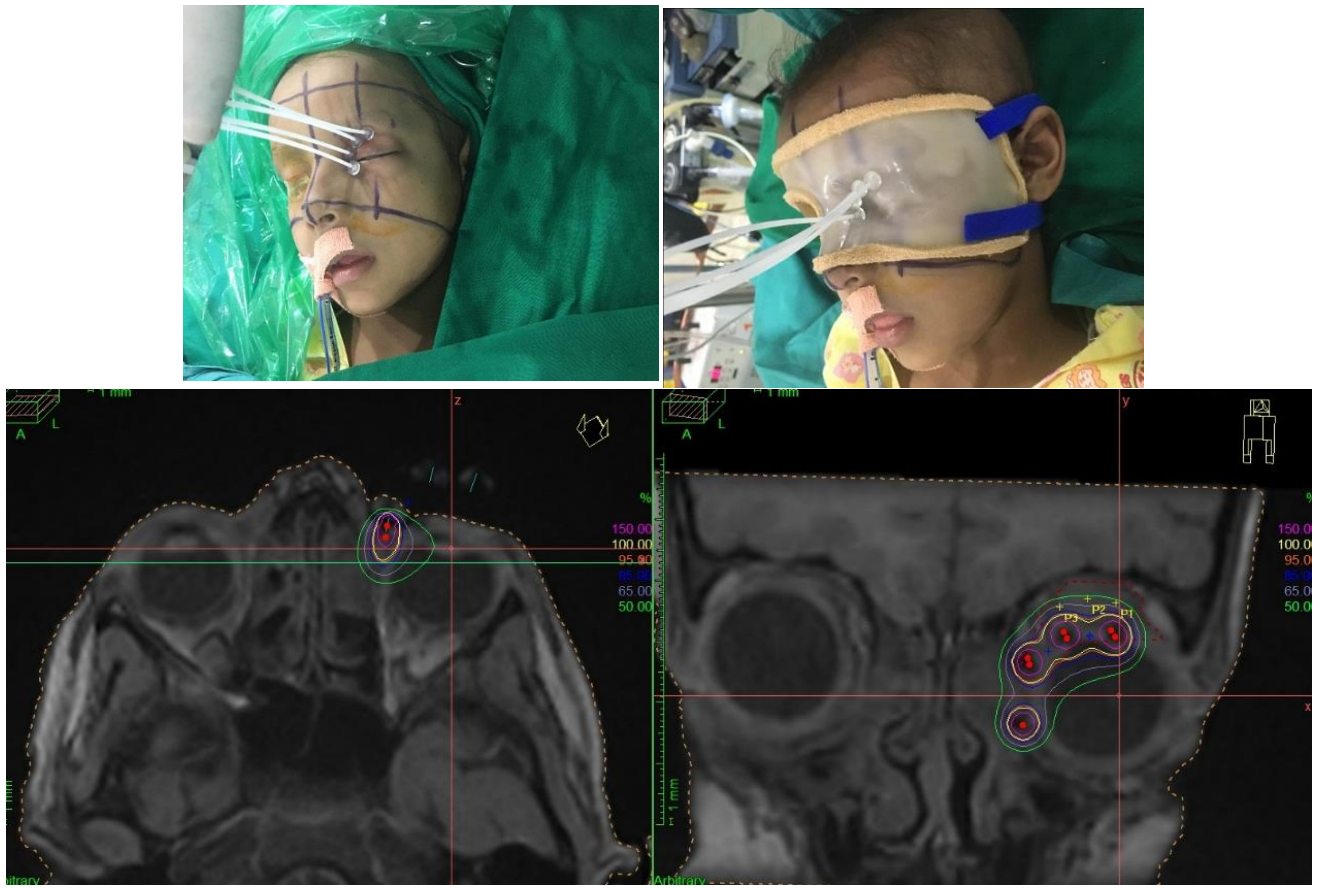
- More than 90% survival
- In a study assessing the effect of dose on myocontractility, which is thought to give a good indication for pregnancy success, a dose of more than 30 Gy to the uterus was seen to greatly impair myocontractility.
- Thus, brachytherapy should be discussed when a dose higher than 30 Gy to the uterine myometrium is to be delivered, especially if conservative surgery such as cervical amputation or trachelectomy is an alternative.
    - Haie-Meder C et al. Consequences of brachytherapy (BT) on uterine myocontractility. Radiother Oncol 2004; 71: S54.
- Brachytherapy restricted to the vagina or vulva has fewer consequences on fertility.

Nicolas Magné et al. Institute Gustave Roussy, Lancet 2007

Orbital Brachytherapy

- Orbital RMS
- Young pts
- Favorable site and histology (excellent 5 year survival)
- Radiation is the “local Rx” (definitive RT)
- EBRT 50.4Gy/28#s over 6 weeks conformal RT

- Sequelae
  - Cataract
  - Musculo skeletal abnormality, cranio-facial asymmetry/ deformity
  - neuroendocrine
  - Second cancers

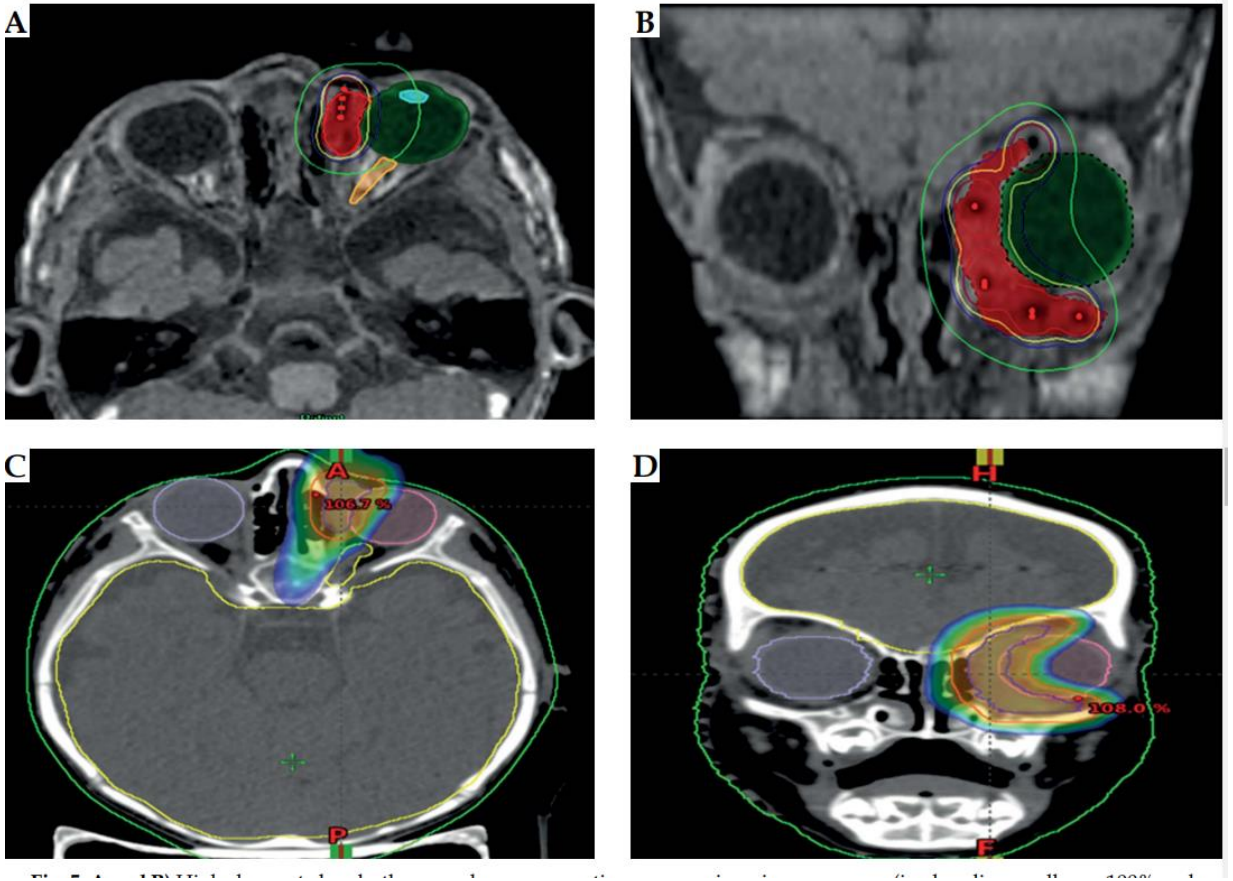


4 yr old girl, RMS orbit,
Underwent definitive Brachytherapy

Interstitial brachytherapy for orbital soft tissue sarcoma: an innovative technique

Siddhartha Laskar, MD[1], Avinash Pilar, MD[1], Nehal Khanna, MD[1], Yogesh Ghadi, MSc[2]

[1]Department of Radiation Oncology, [2]Department of Medical Physics, Tata Memorial Hospital, Mumbai, India



Various innovative techniques of interstitial brachytherapy for orbital tumors have also been reported previously with excellent local control and cosmetic/ functional outcomes

Step 1:

Pre-planning

1. Ideal catheter positions
2. Depth of insertion for each catheter
3. Catheter insertion co-ordinates with reference to bony landmarks (Figure 2)

Step 2:

Retainer fabrication

1. Extrapolation of needle entry points on skin
2. Fabrication of customised retainer
3. Transfer entry points onto the retainer and drill holes (Figure 3)

Step 3:

Implantation technique

1. Washers used to guide depth of insertion
2. Needles inserted carefully avoiding injury
3. Retainer guided over catheters secured using wahers and glue
4. Retainer secured using Velcro straps (Figure 4)

Step 4:

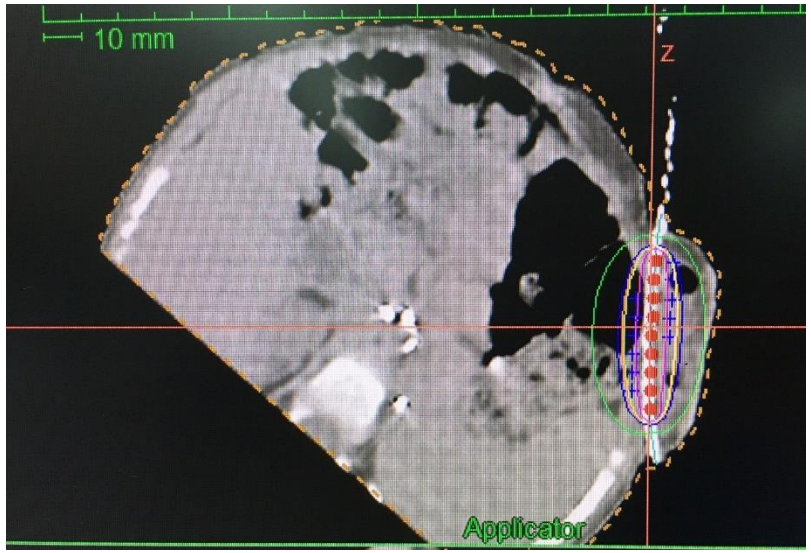
Treatment planning and delivery

1. MRI based BT planning and optimisation (Figure 5)
2. Plan evaluation using DVH (Table 1)
3. Treatment delivery under sedation

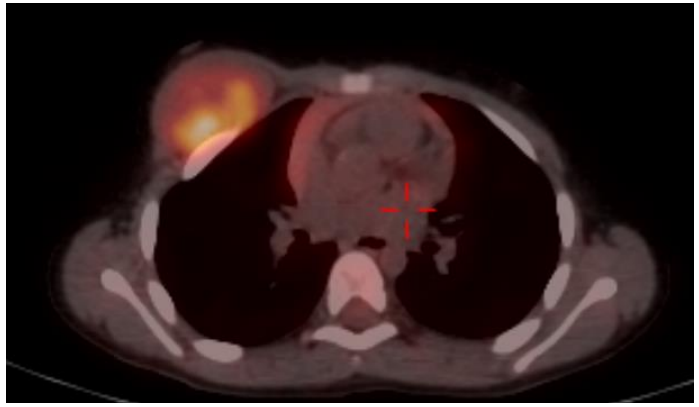
Fig. 7. Flowchart of the procedure

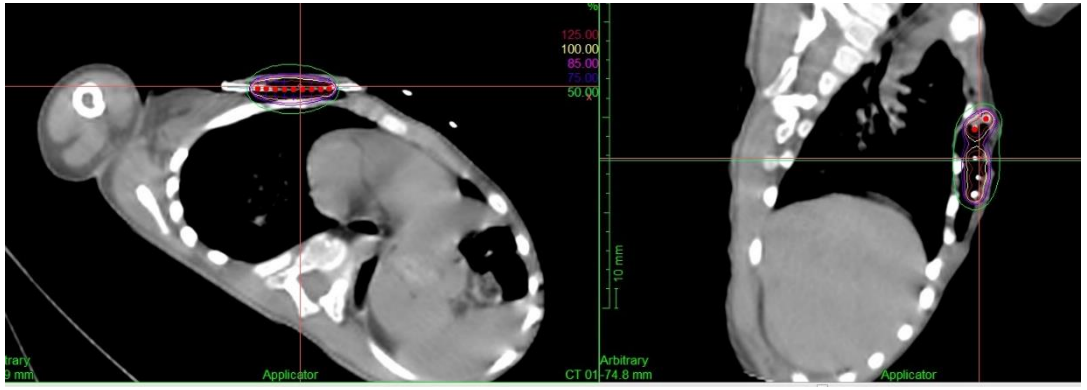
Abdominal wall brachytherapy ?

- 2 yr old boy
- Treated case of Renal PNET
- Relapsed as a 3cm nodule on the abdominal wall
- Underwent WLE + Brachytherapy
- Tolerated RT well



Chest wall brachytherapy



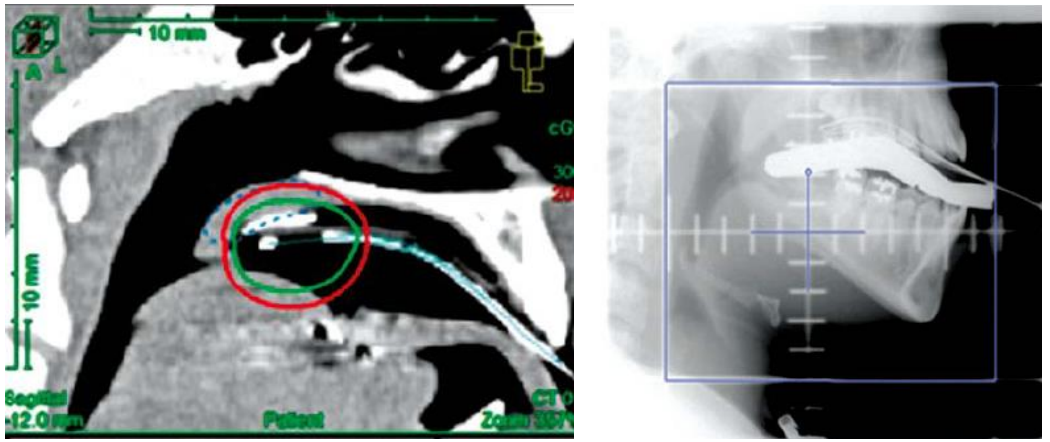


Doses to heart and lung?

Head and Neck malignancies in children

Dose to salivary organs, mandible and oral cavity

Used for easily accessible sites specially for cases which require reirradiation – buccal mucosa, lip, etc



Customised soft palate implant 2014
E Eklewundu et al. J of Contemporary Brachytherapy

Re-irradiation with brachytherapy

- Improvement in LC has been shown with adjuvant RT
- Side effects lesser as compared to EBRT

MDACC 26 patients Re RT with Brachytherapy
Plastic reconstruction in 13 cases
Optimum LC with acceptable morbidity

Pearlstone DB. Cancer J Sci Am 1999;5(1):26-33.

Conclusion

- Ideal for small accessible lesions
- Advantage over EBRT in children
- Data available on safety and efficacy
- Brachytherapy programs for training of students encouraging use of brachytherapy in children

- Heartfelt thanks to the **ICRO AROI** team (Dr S Pradhan, Dr V Srinivasan, Dr D N Sharma, Dr V A Reddy, Dr R Vashistha, Dr M Gupta), **Sri Sankara CHRC** team (Dr G V Giri, Dr Karthick Rishi), **Sun Oncology** and faculties of this course.