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The Role of Radiotherapy towards Pediatric Cancer

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Abstract

Cancer is the leading cause of death in children worldwide. Pediatric cancer is challenging to detect early because it generally appears with signs and symptoms that are not typical. The increase in cancer cases in pediatric must be followed by an increase in cancer management in all fields of scientific disciplines. Radiation oncology, as one of the areas of science, has an essential role in definitive, adjuvant, palliative, and prophylactic cancer in pediatric. Apart from these uses, radiation management is a significant contributor to the complications of pediatric cancer survivors. Complications that arise can be in the form of growth retardation, tissue changes, secondary cancer, neurocognitive changes, infertility, or other hormonal dysfunction and pre-term labor. An increase in radiation techniques followed the development of treatment machines able to reduce radiation-related morbidity and mortality rates. In pediatric radiotherapy, the entire process from the pre-procedure anesthesia to radiotherapy requires special attention. Psychological issues are also worth observing. This study will briefly discuss these matters and the management of some of the most common pediatric cancers in Dr. Cipto Mangunkusumo Hospital.

Keywords: pediatric cancer, radiotherapy, brainstem glioma, nasopharyngeal carcinoma, retinoblastoma, medulloblastoma, soft tissue sarcoma

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Background

Cancer is the leading cause of death in pediatric. It could happen in every cycle of human life, from the beginning of life until the geriatric phase.¹ In 2018, Globocan estimated about 272.600 new cases, and 101.000 death in children age 0-19 years old are caused by cancer. The most common malignancy in pediatric is leukemia, central nervous system tumor, and lymphoma.² Higher incident prediction is reported by Baseline Model (BM) that is formed based on America's Surveillance, Epidemiology and End Results (SEER) in 2015. The BM estimated about 360.114 cancer cases in pediatric worldwide, 54% in Asia, and 28% in Africa region.³ In Indonesia, pediatric accounted for 3%-5% from all cancer.^{4,5}

World scientific development, especially in cancer, could increase the survival rate in pediatric. In Europe, Gatta et al. reported that 1,3,5 survival years rate in all types of pediatric cancer is 90,6%, 81%, and 77,9 %.

The most significant is Acute Lymphoid Leukemia (ALL) with a 90% five-year survival rate.⁶ However, children with cancer in Low-middle Income Countries (LMICs) have not got that same benefit and chances of that developed science yet. The probability of death incidents of children who live in LMIC is fourfold higher than kids in High-Income Countries (HIC). The main factor of death rate in pediatric cancer who lives in LMIC is drug availability, drug insufficiency, lack of Centers of Excellence for pediatric cancer, waiting list problem because of an inadequate hospital bed, human resources availability, especially pediatric oncologists, delayed diagnostic and relapse.^{6,7} Cancer's impact on child is very complex; cancer will significantly affect children's growth and development, less school attendance, and disability and eventually will affect the country itself because the country will lose the momentum for human development.

Radiotherapy is an integral part of pediatric cancer treatment.⁸ Synergizing Radiation Oncology with other multidisciplinary significantly decreases the potential morbidity and mortality. The goal of radiation therapy is to obtain optimum therapeutic ratio and lowering acute and late toxicity risk. This review will give a perspective, a strategy, and some significant contribution in radiation oncology towards the most common cancer in our institution and the effect of radiotherapy in pediatric cancer. This strategy and guideline might benefit for radiotherapy centers in performing radiotherapy for each institution.

Materials and Methods

This retrospective analysis was taken from cancer registration in hospital and Instalasi Pelayanan Terpadu Onkologi Radiasi (IPTOR) RSUPN Dr. Cipto Mangunkusumo year 2008-2014. The data was analyzed based on age and the most common cancer type treated by radiotherapy for curative or palliative intense. Four types of most common cancer would be reviewed towards radiotherapy treatment guideline based on literature review and International Atomic Energy (IAEA) Training course on Pediatric radiation Oncology RAS 6086, that was held in Jakarta on September, 2nd-6th, 2019

Results

Demography characteristic

From January 2008 until December 2014, there are 2.986 children diagnosed with cancer, and 751 children are treated with radiotherapy (RT). The most pediatric cancer that treated with RT is central nervous system malignancy (n=333;44%), eye and adnexa malignancy (n=131,17%), nasopharyngeal carcinoma (n=78;10%) and bone and soft tissue malignancy (n=71,9%).

Table 1. Total pediatric patient in IPTOR at Dr. Cipto Mangunkusumo Hospital from 2008 until 2014

No	ICD 10	Diagnosis	n (%)
1	C71	Malignant neoplasm of brain	333 (44)
2	C69	Malignant neoplasm of eye and adnexa	131 (17)
3	C11	Malignant neoplasm of nasopharynx	78 (10)
4	C40	Malignant neoplasm of bone and articular cartilage of limbs	38 (5)
5	C49	Malignant neoplasm of other connective and soft tissue	33 (4)
6	C42	Malignant neoplasm hematopoietic and reticuloendothelial system	31 (4)
7	C76	Malignant neoplasm of other and ill-defined sites	14 (2)
8	C31	Malignant neoplasm of accessory sinuses	11 (1)
9	C34	Malignant neoplasm of bronchus and lung	11 (1)
10		Other Neoplasm	71 (9)

Treatment Recommendation

Medulloblastoma

Medulloblastoma (MB) is the most common brain cancer in pediatric cancer with a peak at 6-8 years old.⁹ Clinical manifestations of MB are an increase in intracranial pressure, cerebellum disorder, and cranial nerve disorder.¹⁰ The treatment for MB is a combination of surgery, radiation, and chemotherapy. The risk level of MB is divided into an average risk (age ≥ 3 years old, M0, local, gross total /near-total resection, remaining tumor $<1,5 \text{ cm}^2$) and high risk (age < 3 years old, $>M0$, disseminated, subtotal resection/biopsy, remaining tumor $>1,5 \text{ cm}^2$, anaplastic type/ large cell).¹⁰⁻¹² The five -year survival rate for the average-risk group is 80% and 60-65% for the high-risk group.¹¹ The goal of the operative procedure is optimum resection followed by radiation at the craniospinal axis and booster for the remaining tumor.

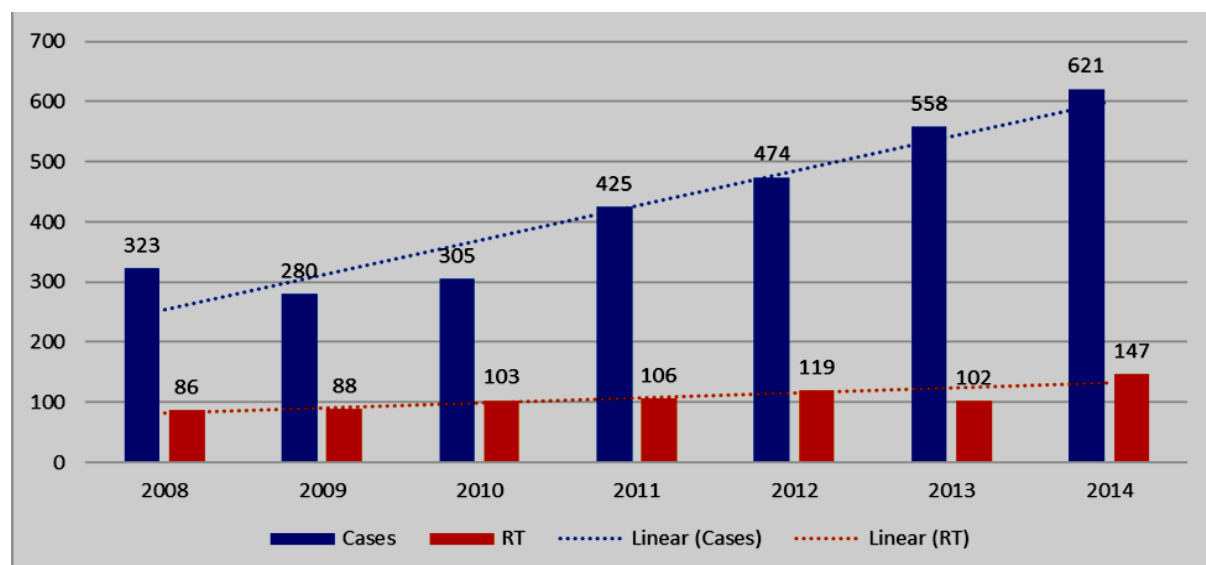


Figure 1. Total new cases of pediatric cancer treated by RT at Dr. Cipto Mangunkusumo Hospital from 2008 until 2014

Radiation is given via craniospinal irradiation (CSI) with dosage 23,4 Gy if followed by chemotherapy and 35-36 Gy if not followed by chemotherapy. Booster dosage is given to fossa posterior and the remaining tumor with maximal dose at 54-55 Gy.¹⁰

The outcome of CSI lower dose in the average-risk patient group is even if given without chemotherapy, the Event Free Survival (EFS) will be the same as if the chemotherapy is given along with radiation and post-radiation.⁸ There are no different EFS between post-radiation chemotherapy and chemotherapy pre radiation.⁸ The outcome of postponed post-operative radiation will not be as good as immediate post-operative radiation followed by chemotherapy.¹³

The radiation target of CSI is the whole CSF area. The booster is given to the whole fossa posterior and the tumor bed. Clinical Target Volume (CTV) (Table 2) include the cribriform plate, optical canal of sphenoid, superior orbital fissure, foramen rotundum, foramen ovale, internal auditory meatus, jugular foramen, and hypoglossal canal. The PTV limit is according to each department policy, usually for CTVcranial is 3-5 mm and CTVspinal is 5-8 mm. Delineated Organ at Risk (OAR) is an eyeball, lens, parotid gland and submandibular, larynx, esophagus, thyroid and women's breast, lung, liver, heart, gaster, colon, pancreas, kidney and gonad. The radiation technique is 3DCRT, IMRT, VMAT, Tomotherapy and proton therapy.¹⁴

Pontine Glioma (DIPG) is still poor, with a survival rate of <10 % even with aggressive medication. However, focal and exophytic brain stem tumor's prognosis is quite good, with a reported survival rate between 50-100%.¹⁵⁻¹⁸

Brain stem glioma, including low-grade Focal Brain Stem Glioma/FBSG (WHO type I-II) and high-grade DIPG. Brain stem tumors developed in a crucial and eloquent area. Usually, FBSG developed symptoms within three months, and DIPG diagnosed within 3-6 months after the first symptoms appear.^{16,17}

Children with brain stem glioma usually have a prior neurologic disorder such as eyeball movement, diplopia, unsymmetrical smile, equilibrium disorder, and hemiparesis. The triad of clinical symptoms is cranial neuropathy, ataxia, and long tract sign. At least two-thirds of those symptoms are assessed to diagnose brain stem glioma clinically.^{15,19} Biopsy no needs to be performed if the patient shows classic symptoms and typical imaging. This thing is related to post-biopsy complication risk; also, the aggressive operative procedure would not be done.^{15,18} MRI is the golden standard in BSG characterization and excellent modality for assessing therapy responsiveness and prognosis.

Surgery is a preferable choice, if possible. Radiation is an alternative for non-operable patients or patients with progressive disease after the procedure performed. In the delineation process, MRI Imaging should combine

Table 2. Guideline of delineated CSI according to SIOPE and COG trials

SIOPE (PNET4/5, SIOP CNS GCT II)	COG (ACNS0332, ACNS 0331, ACNS 0122)
<p><i>Cranial CTV:</i> 'includes brain with entire frontal lobe and cribriform plate. The geometric edge of the shielding should extend at least 0.5 cm inferiorly below the cribriform plate and at least 1 cm elsewhere below the base of the skull'</p> <p><i>Spinal CTV:</i> 'extend laterally to cover the intervertebral foramina. Inferior border of Spinal CTV must be determined by imaging the lower limit of the thecal sac on a spinal MRI; inferior treatment field border should be set 1 cm below this'</p>	<p><i>Cranial CTV:</i> 'whole-brain field shall extend anteriorly to include the entire frontal lobe and cribriform plate region. Inferiorly, the CTV shall be at least 0.5 cm below the base of the skull at the foramen magnum'</p> <p><i>Spinal CTV:</i> 'The spinal target volume will be the entire thecal sac. The field to cover this volume should extend laterally on both sides to cover the recesses of the entire vertebral bodies, with at least a 1 cm margin on either side. The inferior border of the treatment volume will be placed after review of the spinal MRI. The border will be 2 cm below the termination of the subdural space'</p> <p><i>Proton therapy</i></p> <p>'For proton therapy, the spinal target volume will include the vertebral bodies for skeletally immature patients to minimise the risk of unequal vertebral growth. The spinal target volume in skeletally mature patients will include the spinal subarachnoid space with a margin of 3-5 mm into the vertebral body to allow for interfraction set up variation'</p>

Source: reference no. 14

Brainstem Glioma

Around 12,4 % of all central nervous system tumors in children from 0-14years old are developed in the brainstem. The average age of children with brain stem glioma is 6-7 years old, with an equal ratio between girls and boys. The prognosis of Diffuse Intrinsic

with the CT scan imaging. Gross Tumor Volume (GTV) best defined in T2-weighted or Flair MRI. The border of CTV is 1-1,5cm, which anatomically bordered by bone and sometimes tentorium. Planning Target volume is 0,3-0,5 cm. Using a sophisticated technique like IMRT is needed to reduce preparation

time that might delay the treatment process. Usually, the dosage of RT is 30-31 fractions for six weeks.^{16,20,21} An alternative fractionation schedule has been studied towards patients with DIPG. Hyperfraction RT 1-1,26 Gy is given twice a day with a total dosage until 78 Gy in order to increase the control tumor. In much continuous research in North America in the 1980-1990s, dosage 76-78 Gy does not show any benefit; instead, more prominent morbidity are appearing, such as prolonged steroid use and the vascular event is found within the study. RT with an accelerated fraction (common fraction 1,8 Gy which given twice a day) with total dosage 48,6-50,4 Gy. A study in England shows that medication method with fractionation is not superior, although it can be tolerated and considered favorable because the patient and their family can spend less time on medication procedure. Hypofraction RT also has been studied. Compared to conventional RT in one prospective study, hypofraction RT with total dose 39-45 Gy (3 Gy once a day) is also safe and effective.¹⁸

A systematic review was written by Matthew Gallitto et al. in 2019 about the role of radiotherapy in DIPG management is, there is no significant difference between conventional radiation with hyperfraction and one-year survival rate (30,9% vs. 27%) or median time progressivity (6 vs. 5 months). Higher hyperfraction (total dose 75,6 Gy given twice a day in 60 fractions) did not increase the outcome of DIPG. Otherwise, hypofraction radiation is not statistically inferior if compared with conventional radiation.¹⁷ Large scale exploration, multi-institutional, is needed to identify an optimal technique, total dose, and fractionation for definitive radiation in DIPG.

Retinoblastoma

Retinoblastoma (RB) is the most common eye malignancy in pediatric, presenting 2,5-4% form total pediatric cancer and 11% cancer in the first year of life.²² RB incidence in worldwide constantly sit in 1 per 15.000-20.000 live births rate, around 9000 new cases every year.²³ In a developed country, RB is diagnosed in an early stage (intraocular). Nevertheless, in low-middle income countries (LMIC), 60-90 % of children come to the doctor with an extraocular tumor. The critical treatment for RB depends on the capability of detecting and perform therapy in early-stage/intraocular tumors. The staging is correlated with delayed diagnosis, growth, and development from the retina that only happens after the tumor reaches a bigger intraocular dimension.²² The extension of RB is started with spreading to choroid and sclera and optic

nerve. The loco-regional spread occurs with direct extension to the orbital and preauricular lymph nodes. The extra orbital disease manifested as intracranial spreading and hematogenic metastasis to the bone, bone marrow and liver.^{22,24}

The main goal of RB management is to increase the survival rate, eyesight preservation, and minimize toxicity and side effect.^{22,24,25} The treatment is different for each patient depends on unilaterality, eyesight potential (Reese-Ellsworth classification), stage's disease (International Retinoblastoma Staging System dan International Intraocular Retinoblastoma Classification).²⁶⁻²⁸

Radiotherapy is an effective modality for RB treatment. Indication RT to RB is grade A/grade B RB with progressive local tumor after focal therapy (15%); RB multifocal and patients with near macula tumor or optic nerve with goal eyesight preservation (20%); large tumor and extension to vitreous which not responds to systemic chemotherapy (40%); extraocular RB (post-operative RT); and palliative RT.²⁵ RT dose is depending on International Intraocular Retinoblastoma Classification; total dosage 45 Gy with 1,8 Gy/fraction for RB classification 1, classification 2, and post-operative with the microscopic residual lesion. The other option for RB classification 3,4,5 and gross residual RT post-operative is total dosage 50,4 Gy with 1,8 Gy /fraction. The target volume for RT is the whole retina through ora serata and extends to a minimal 1 cm from the optic nerve with 3D technique or IMRT. While doing RT planning, very important to minimize spreading dosage towards the contralateral eye, optic chiasma, pituitary gland, and spinal cord.²⁵

Nasopharyngeal carcinoma

About 5 % of primary malignant neoplasm developed in the head and neck area, whereas nasopharyngeal carcinoma (NPC) represents around 2% in the children's age group. The incident increases gradually along as they get old. In adults, Nasopharyngeal carcinoma is a common type of cancer in head and neck with the variant incident rate worldwide.²⁹ NPC in children is different from adults towards correlating with EBV, non-differentiated histology type and advance loco-regional incident rate.^{30,31}

SEER study aims to compare NPC in pediatric and adult found that children and adolescents showing a better result than adults, although there is advanced disease. This patient group has higher long term complication risk, including increasing secondary cancer risk.³²⁻³⁴

The early new diagnosis gold standard of NPC is with nasopharyngeal endoscopy biopsy. Radiologic imaging might help in staging and disease spreading. Compared with the CT scan, MRI is an excellent modality. T1 MRI will show asymmetric mass, which is hypointensity, and figure T2 shows mild hyperintensity. Mass invasion to the skull base is easier to detect by MRI because of the clivus bone marrow signal change (decreasing in T1 and increasing in T2). Besides those imaging modalities, PET CT is also used for local and early assess distant metastasis.³⁵

Treatment for pediatric nasopharyngeal carcinoma is complying with adult's nasopharyngeal carcinoma guideline with early chemotherapy tendency to neoadjuvant form. In the last couple of years, the congruent superiority of chemoradiation / concurrent chemoradiotherapy (CCR) towards adult NPC was proven. This development of CCR usage to adults with NPC is studied. One of them is the ARAR 0331 protocol developed by Children's Oncology Group to assess chemotherapy induction feasibility and benefit, followed by CCR. From this study, the induction of chemotherapy and CCR is giving an excellent outcome near 90% in 5 years, and reducing radiation dose is considered to patient who is responsive toward induction chemotherapy. Operative procedures in NPC usually could not be performed because of the complex anatomical area. Therefore radiation is an option. Radical neck dissection is considered when the primary tumor has been controlled, or there is persistent neck node after chemoradiation or neck local relapse after radiation.^{29,35,36}

Radiotherapy in pediatric NPC is given with a total dose of 50-70Gy in 33-35 Gy fraction to the primary tumor and neck lymph node.^{33,37} These are the term of the delineated guideline in pediatric NPC, which comply with the adult delineated guideline.³⁷

Primary CTV dan high dose node (CTVp1 and CTVn1)

CTVp1: distance from GTVp

GTVp + 5 mm (\pm whole nasopharyngeal), could reduce to minimum 1 mm (if close to the critical organ)

CTVn1: distance from GTVn

GTVn + 5 mm (consider 10 mm if there is extracapsular extension)

Primary CTV - moderate dose (CTVp2)

Margin from GTV

GTVp + 10 mm + whole nasopharyngeal, could reduce to minimum 2 mm (if close to the critical organ)

Nasal cavity – posterior part

At least 5 mm from choana

Maxillary sinus – posterior part

At least 5 mm from the posterior wall

Posterior ethmoid sinus

Vomer included

Skull Base

Foramen ovale included rotundum, lacerum, and petrous tip

Cavernous sinus

If T3-4 (only involved side)

Pterygoid fossa and parapharyngeal space

Whole

Sphenoid sinus

Inferior $\frac{1}{2}$ if T1-2; whole if T3-4

Clivus

$\frac{1}{3}$ if there is no invasion; whole if there is an invasion

CTV nodal – moderate dose (CTVn2)

CTVn1 + 5 mm

Lymphatic node–bilateral retropharyngeal, level II, III, and Va

Level VIIb + at least one level ipsilateral under the involved level

Level Ib

Include if involved: the submandibular gland, the flowing structure to level Ib as first echelon (oral cavity, $\frac{1}{2}$ anterior nasal cavity), level II with extracapsular extension.

CTV nodal – low dose (CTVn3)

Level IV and Vb through clavicular regio

Ignore if N0 or N1 based on retropharyngeal lymphatics node involvement.

Soft tissue sarcoma

Soft tissue sarcoma (STS) is a group of malignant neoplasm that comprises embryonic mesenchymal tissue during the differentiated process to become muscle, fascia, and fat.³⁸ This malignancy is around 6-8 % of total pediatric cancer, and 50-60 % is Rhabdomyosarcoma (RMS). Furthermore, the rest of it is known as non-RMS STS (NRSTS), a classification that comprises all kind of soft tissue tumor that is rare including Ewing sarcoma, fibrosarcoma, synovial sarcoma ad malignant peripheral nerve sheath tumor (MPNSTSs).³⁹ Two-thirds of RMS are diagnosed before age six years old, and the incident rate is decreased as they got old. Otherwise, adolescents have a higher risk of developing NRSTS than a younger child. RMS can develop in any body area, including head and neck (35%), genitourinary (24%) and extremity (19%)

RMS needs a multidiscipline approach between surgery, chemotherapy, and RT. RT itself is the pillar for increasing local control. Treatment of RMS depends on the risk stratification based on Intergroup Rhabdomyosarcoma Study (IRS) Clinical Grouping, TNM staging, and histopathology.⁴¹ IRSG Study establishes the standard guideline for RMS dose in pediatric; 50,4 Gy and 41,4 Gy with 1,8 Gy per fraction for gross tumor and microscopic disease, respectively.⁴² RMS with low group risk stratification based on D9602 and ARST0331 study criteria could be given a reduced total dose to 36-45 Gy.⁴³ The five-year survival rate and local control in RMS are good. The survival rate is 90-95% for low-risk stratification, 68-78% in a mild risk group, and 25% in a high risk group.⁴²

Determine the target delineation of RMS is essential. Basic Gross Tumor Volume (GTV) delineation is diagnostic imaging before the treatment. CTV is determined by giving margin +2cm from GTV, adding post-operative area, and the involved lymph nodes. PTV is determined with giving margin 5 mm towards CTV.⁴⁴ IMRT is preferable for Head and neck RMS, with a reduction to 1 cm CTV margin giving 95% 3-year control loco-regional result with minimum toxicity.⁴⁵

COG study ARST0332 determines treatment recommendation for RT and chemoradiation in NRST. Indication determined by local vs. metastasis, operability status, post-operative margin status, grades, and tumor size (**Figure 2**). In a delayed plan operative, neoadjuvant chemoradiation with 45 Gy is preferable. Tumor with positive post-operative margin and gross tumor, so, the preferable RT is a total dose for each is 55,8 Gy and 64,8 Gy, respectively.⁸

Toxicity and secondary malignancy

Pediatric cancer survivors are facing the next effect of prior cancer therapy.^{46,47} Various type of tumor, location and body shape are correlated with various tumor radiosensitivity and combination with other treatment. Radiation therapy that is given in growthful and immature tissue will cause a significant anatomic and functional problem.⁴⁸

The radiation late effect is different for each dose, organ disposition, and age spectrum.^{48,49} The arising effect can be seen as growth resistance, tissue change, secondary cancer, neurocognitive change, infertility, or other hormonal dysfunction, and premature labour. 20 Gy radiation dose towards breast could stop its growth, while 10 Gy towards breast will cause hypoplasia.⁴⁶ Low dose (2-3 Gy) to testicle will cause permanent

azoospermia.^{46,48} Ovarium function disorder occurs if the radiation dose is 12-15 Gy⁴⁸ with 2-12 years healing period.⁴⁶ If the heart obtains a dose of 2,5-3 Gy, it will cause an increase in coronary heart risk, stroke and heart disease with dose 1-4 Gy in vascular, cataract with 2,3-3 Gy, diplopia and dry eye with dose 5-12 Gy,⁴⁸ Lung cancer risk are increasing with dose >9 Gy in post-radiation Hodgkin's patient. The advanced effect will aggravate other cancer therapy modalities.

A carcinogenic effect from radiation, chemotherapy, and a combination of both can cause secondary malignancy. The risk is getting higher 3-6 fold in pediatric cancer survival.⁴⁷ Secondary malignant latent growth happens 7-20 years after the primary tumor was diagnosed.^{47,48} The most common type is secondary AML, which related to chemotherapy, and could happen at least three months after radiation with a 10-year peak risk. The second most common is a secondary solid tumor, which depends on radiation dose, with median 9,5 years.⁴⁸

Nevertheless, this radiation is very much needed because it could treat tumors effectively. Radiations also related to long term survival rates. Pediatric cancer survival is a unique population with a unique problem and need. With the increase of the outcome, there is still some problem that is not solved yet, so research and adequate intervention is still needed to lowering or prevent it.

Special consideration

Children are not adult miniature. There are many physiologic, anatomic, and psychological diverse, which make treatment approach toward children is different. Mostly pediatric cancer is sensitive to radiation, but on the other side, the toxicity effect and advance is being distinctive considered in RT benefit to pediatric cancer.⁵⁰

Limited sources are the main challenge in radiotherapy for children in LMIC countries, particularly Indonesia. Pediatric cancers need a specific approach, which could reduce adverse effects for the body and children psychosocial. This approach has to prioritize the maximal clinical outcome and excellence of patient safety and quality assurance.⁵¹ Prophylaxis and trauma psychological management through family and staff support is essential during the journey.

The benefit of radiotherapy with the best technique is the top priority in pediatric cancer management. The goal is to maximize therapy dose towards tumor and minimize the effect on healthy tissue.⁵² So that, conformal RT with IMRT, IGRT, and SRS/SRT is a

top recommendation in RT treatment. This recommendation also needs adequate human source through continuous training (multidiscipline team, medical staff, anesthesia, nurse, medical physician radiation technologist) and adequate immobilized equipment.⁵¹ According to the recommendation, an integrated referral to a qualified facility is a must for therapeutic goals in pediatric cancer management.

Immobilization itself is a challenging moment for giving RT treatment to children. Children under five years old have a difficult time in immobilization during simulation and therapy; in these circumstances, mostly children having anxiety and afraid because of being

minimalize risk and save planned anesthesia procedures. Kids friendly RT procedure room and save anesthesia with scared distraction equipment during the therapy is needed. Providing particular anesthesia recovery room and resuscitation with adequate emergency equipment for pediatric cancer.⁵¹

Special attention to the psychological issue is needed in pediatric cancer comprehensive management. Pediatric cancer generates a serious problem in the children themselves and their families. Children could not choose their medications, and parent is the key to decide the therapy. Healing chance, the growth, development, and their next quality of life significantly

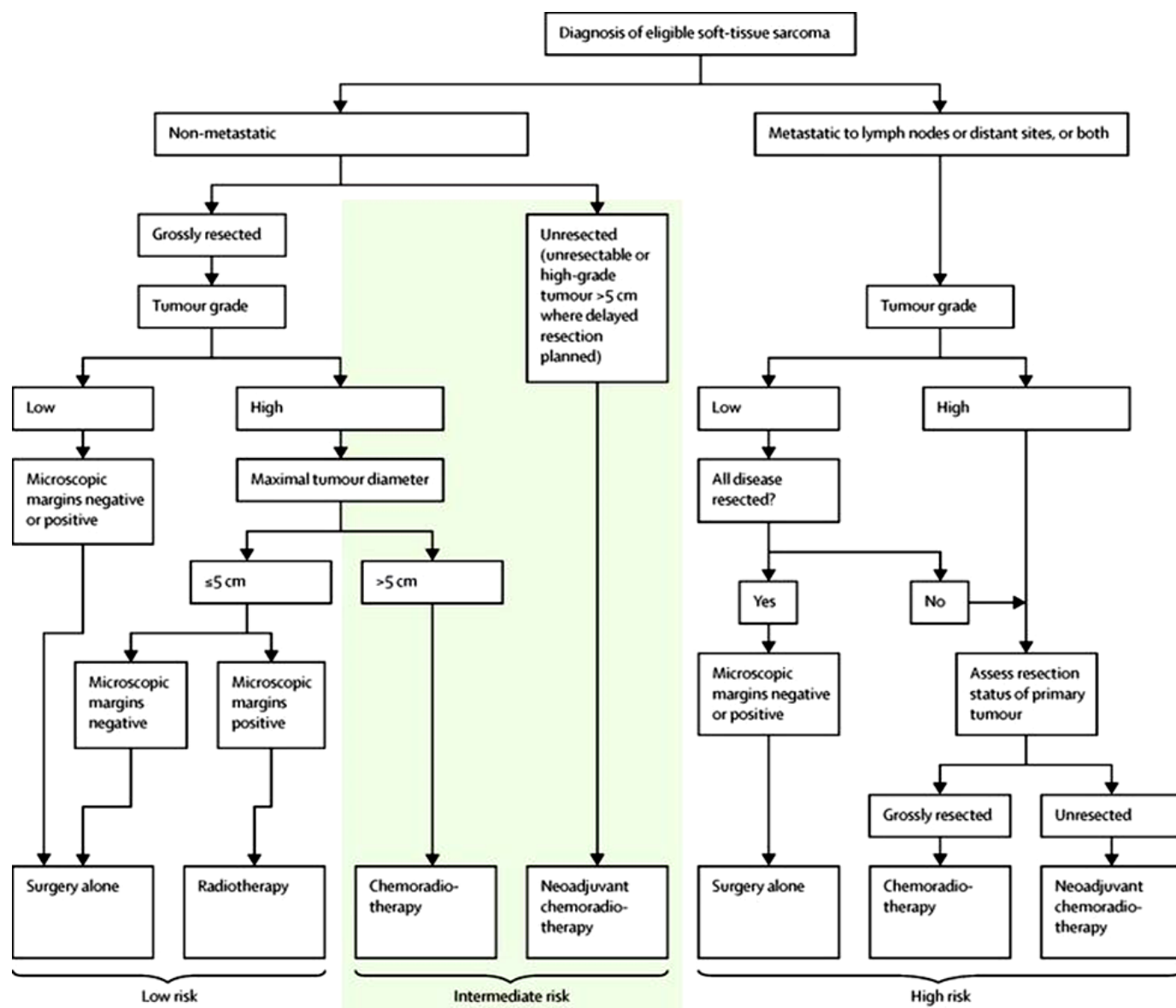


Figure 2. Group Risk and Treatment Guideline of NRSTS based on Children Oncology Group ARST 0332

Source: reference no. 8

apart from their parents and uncomfortable medical procedure. Anesthesia procedure is needed to maintain their position and immobilization during the process. Integrated and save anesthesia procedure is the key to minimalize children's trauma and risk. Anesthesia pre-procedure assessment must as accurate as possible to

depend on the parent's choice. The interpersonal approach and empathy from dedicated medical staff during the medication process have to make sure that the parents got accurate information and fully understand the effect to the child so that information will help the parents to decide the right decision.

Conclusions

Multidisciplinary care is a must in managing pediatric cancer. Cancer therapy needs a particular diagnostic and therapeutic and also the ability to manage potential complications. RT has a significant positive effect on the development of pediatric cancer treatment; the newest effective technique increases survival rate and cancer control, decrease late side effect and has an excellent palliative modality.

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