IHH Healthcare

Advanced Surgeries for Complex Neuroblastoma

KEY PROCEDURE HIGHLIGHTS

1. **Survival rate improves with multimodality therapy**: Combination of surgery, aggressive chemotherapy, stem cell transplant and immunotherapy [5]

2. **Optimal management strategy and surgical outcome** is supported by accurate disease staging and risk classification

3. **Higher 5-year overall survival and event-free survival rates** in patients treated exclusively at Mount Elizabeth Hospital [5]

WHAT IS NEUROBLASTOMA

Neuroblastoma is the most common soft-tissue malignancy of early childhood. The primary tumour originates from anywhere along the sympathetic nervous system, but most frequently arises from the adrenal medulla or paraspinal ganglia. Neuroblastoma typically encases vital vessels, rendering surgery both challenging and threatening.

In low- to-intermediate risk neuroblastoma, the prognosis after treatment is excellent and some tumours may regress spontaneously. High-risk neuroblastoma, on the contrary, has guarded prognosis.

Accurate disease staging and risk classification therefore provide **critical insights** to developing an **optimal management strategy** for neuroblastoma.

NEUROBLASTOMA STAGING AND RISK CLASSIFICATION

The International Neuroblastoma Risk Group Staging System (INRGSS) is a 4-stage system based on clinical criteria and preoperative tumour imaging.

INRG Staging System

Staging		Recommended Treatment
L1	Localised disease without IDRFs ^	Upfront Surgery
L2	Localised disease with one or more IDRFs	Chemotherapy, followed by surgery
M	Distant metastatic disease (except MS)	Chemotherapy, followed by surgery, followed by other modalities
MS	Distant metastatic disease confined to skin and/or liver and/or bone marrow	Keep under observation or for treatment

^ Image-defined risk factors

The INRG stage, together with other prognostic factors, forms the INRG Classification Consensus to stratify the 4 risk groups that determine the optimal management strategy. The focus is to minimize or avoid treatment in low-risk patients while intensifying treatment in high-risk patients to improve survival.

INRG Classification Consensus

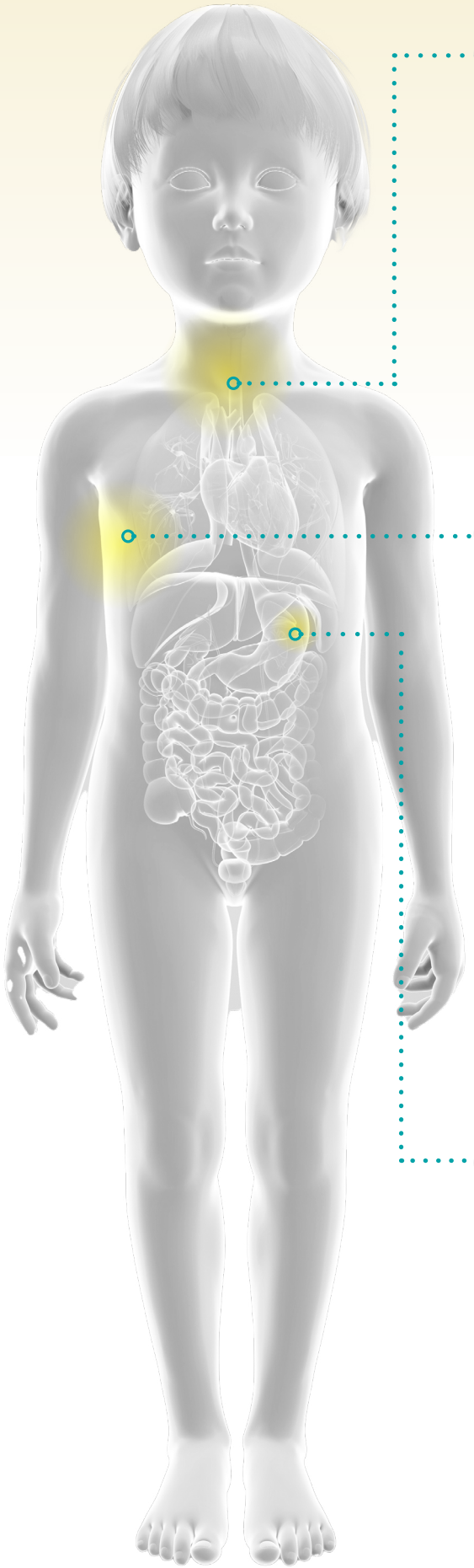
Prognostic Factors		Risk Group	5-year Event-free Survival
INRG stage	MYCN amplification	Very Low	>95%
Age	11q aberration	Low	75-85%
Histopathological grading	Ploidy	Intermediate	50-75%
		High	<50%

CLINICAL PRESENTATIONS OF HIGH-RISK COMPLEX NEUROBLASTOMA

Complex neuroblastoma consists of high-risk group tumour with the following presentations, deeming the tumour a surgical challenge to resect:

- **Encasement of vital vessels**
- **Multi-compartmental tumour**
- **Contiguous organ infiltration**
- **Significant spinal extension**
- **Airway compression**

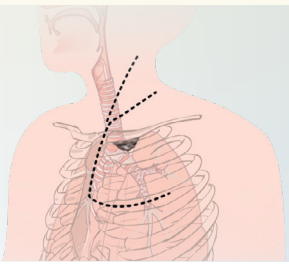
ADVANCED SURGERIES FOR COMPLEX NEUROBLASTOMA



Complex Neuroblastoma: Cervicothoracic and Apical thoracic Neuroblastoma

Key Challenges: Surgical management is challenging due to the tumour's unique location and limited access within the shallow thoracic cavity and fluid chest wall of children. There are also risks associated with vascular encasement of the subclavian, vertebral and/or carotid arteries.

Advanced Surgical Approach: Trapdoor thoracotomy offers good access, exposure, and control of the vascular structures. It promotes radical tumour resection with low incidence of complications such as damaging the mobility of the clavicle or scapula. This surgical method also provides a good opportunity for early blood vessel control, and early identification and preservation of stretched nerves to prevent or reduce trauma. [4]

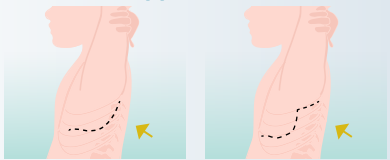


Complex Neuroblastoma: Thoracoabdominal Neuroblastoma

Key Challenges: These tumours involve two major body compartments – the abdomen and thorax. They are usually extensive and manifest as solitary or multifocal tumours. Each disease pattern has its own unique anatomical characteristics with surgical and prognostic implications. Solitary tumour features IDRFs of dual compartment infiltration, diaphragmatic infiltration, and T9–T12 costovertebral involvement. In contrast, multifocal tumours lacked a common pattern of IDRFs.

Advanced Surgical Approach: Thoracoabdominal surgery requires multiple incisions, multi-staged operations, and surgeons with different expertise. In solitary tumour, surgical approaches include thoracoabdominal approach, laparotomy-cum-transdiaphragmatic approach, and laparotomy-cum-thoracotomy. In multifocal tumour, surgical approaches include laparotomy accessed via transdiaphragmatic approach, trapdoor anterior thoracotomy or posterolateral thoracotomy. [3]

Single incision thoracoabdominal approaches



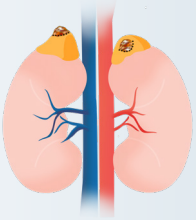
(A) Oblique thoracoabdominal incision (broken line)

(B) Thoracoabdominal incision with 'S' modification

Complex Neuroblastoma: Bilateral Adrenal Neuroblastoma (BAN)

Key Challenges: Compared with unilateral disease, patients with BAN are usually younger and are more likely to have distant metastasis. Traditional approach of bilateral radical tumour adrenalectomies would result a lifetime dependency on adrenal replacement therapy and the risk of life-threatening Addisonian crisis.

Advanced Surgical Approach: Adrenal-sparing surgery for BAN is a less aggressive surgical approach with the aim of preserving adrenal function. The approach includes various combinations of bilateral adrenal observation, unilateral tumour adrenalectomy (TA) with contralateral adrenal observation, unilateral TA with contralateral adrenal-sparing tumorectomy (AST), and bilateral AST. [2]



ADVANCED MULTIMODALITY THERAPY

High-risk complex neuroblastoma often presents a suboptimal outcome. However, survival rates have been shown to improve with a multimodality therapy of surgical treatments with:

Pre-operative Chemotherapy
renders high TVR, high tumour necrosis and reduced IDRFs #. Hence, it creates favorable conditions to significantly improve resection, especially for MYCNA neuroblastoma which is often unresectable at initial diagnosis.[1]

High-dose Chemotherapy with Autologous Stem Cell Transplant:
The use of high-dose chemotherapy with autologous bone marrow or peripheral blood stem cell rescue **further improved prognosis with survival rates around 50%.**[5]

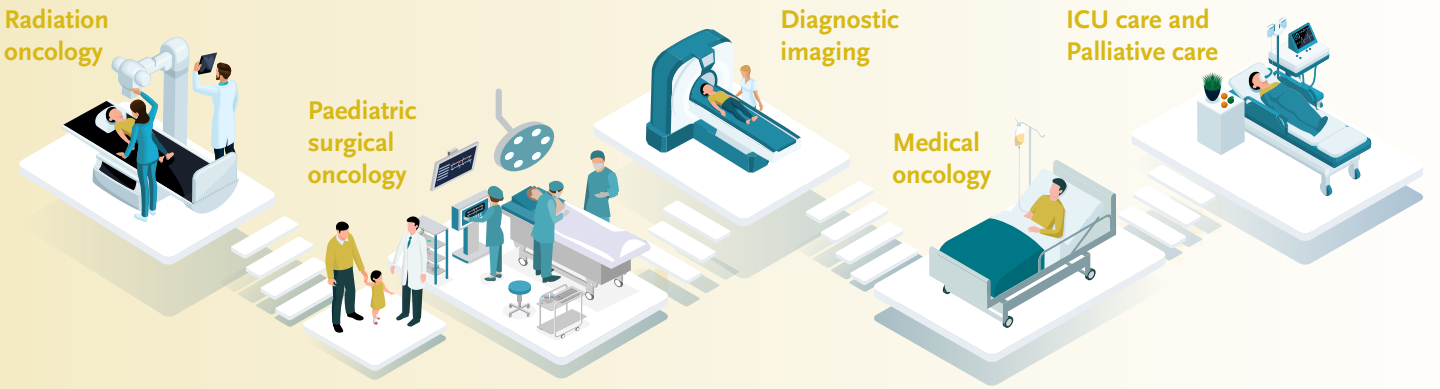
Immunotherapy with anti-GD2 monoclonal antibody
Immunotherapy is associated with a significantly improved outcome * as compared with standard therapy at 2 years.[7]

On completion of pre-operative chemotherapy, 85.5% patients had tumour volume reduction (TVR) of >50%, 75.8% tumours had necrosis of >50%, 42.9% responded with reduced IDRFs

* At 2 years, event-free survival (66±5% vs. 46±5%) and overall survival (86±4% vs. 75±5%).

MULTIDISCIPLINARY FRAMEWORK AT PARKWAY HOSPITAL

At Mount Elizabeth Hospital, our multidisciplinary team focuses on delivering comprehensive cancer care from early detection to treatment regimen, pre and post-operative therapies intensity, and supportive care services.



On the surgical front, we are a high-volume centre with established protocols and strong oncology expertise.[5]

Expertise with more than **15 YEARS** of managing high-risk neuroblastoma

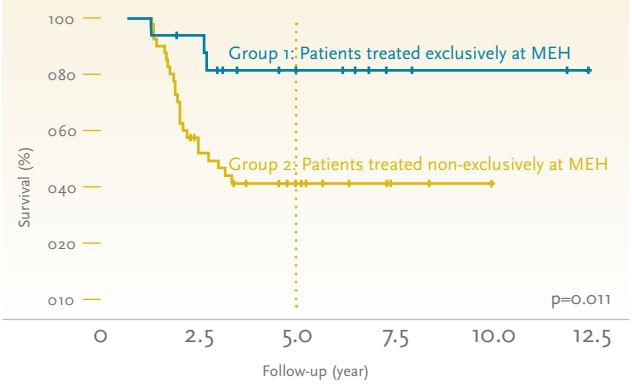
Our surgeons achieve **>90%** of tumour resection in all cases & **GROSS TOTAL RESECTION** in majority of the cases[5]

Impact of strong multimodality therapy expertise in Mount Elizabeth Hospital

High-risk neuroblastoma patients treated exclusively at Mount Elizabeth Hospital present with a higher 5-year overall survival rate and event-free survival than patients who had received treatment prior to admission to Mount Elizabeth Hospital.[5]

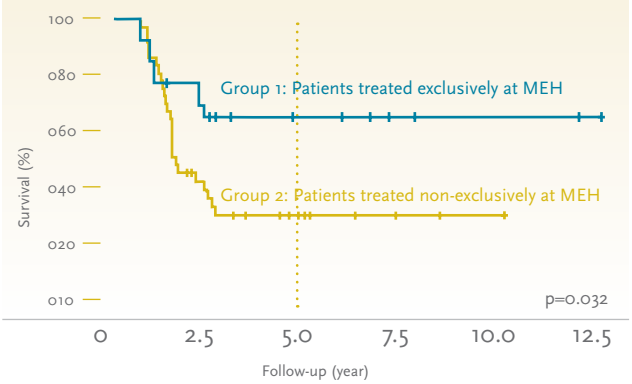
Clinical Outcomes for High-Risk neuroblastoma patients treated at Mount Elizabeth Hospital (MEH)[5]:

Higher 5-year overall survival rate at 81.6%



Group 1 (n = 17, 81.6%, 95% CI, 63.2 - 100%)
Group 2 (n = 40, 41.1%, 95% CI, 25.4 - 56.8%)

Higher 5-year event-free survival at 69.7%



Group 1 (n = 17, 69.7%, 95% CI, 47.4 - 9.20%)
Group 2 (n = 40, 36.1%, 95% CI, 20.9 - 51.3%)

WHEN TO REFER TO MOUNT ELIZABETH HOSPITAL

- Uncertainty in diagnosis
- Inability to complete staging process
- Inability to achieve adequate tumour resection for non-high-risk groups
- Inability to achieve >90% tumour resection and provide high-risk therapy for high-risk groups
- Tumour recurrence

REFERENCES

1. Chui, C. (2020). Effects of preoperative chemotherapy on neuroblastoma with MYCN AMPLIFICATION: A surgeon's perspective. World Journal of Pediatric Surgery, 3(2). https://doi.org/10.1136/wjps-2020-000129
2. Chui, C. H., & Chang, K. T. (2020). The feasibility of adrenal-sparing surgery in bilateral adrenal neuroblastoma. Journal of Pediatric Surgery, 55(12), 2836–2839. https://doi.org/10.1016/j.jpedsurg.2020.06.038
3. Chui, C. H., & Lee, A. (2019). Management of thoracoabdominal neuroblastoma: A 13-Year experience. World Journal of Pediatric Surgery, 2(2). https://doi.org/10.1136/wjps-2019-000055
4. Chui, C. H., & Thirugnanam, A. (2020). Trapdoor anterior thoracotomy for cervicothoracic and apical thoracic neuroblastoma in children. Pediatric Surgery International, 36(8), 891–895. https://doi.org/10.1007/s00383-020-04692-2
5. Lee, A. C.-W., Chui, C. H., Kwok, R., Kim, S. L., Chee, M. F., & Wong, W. H. (2021). Treatment and outcomes of high-risk neuroblastoma in Southeast Asia: a single institution experience and review of the literature. Singapore Med J. https://doi.org/10.11622/smedj.2021164
6. Rojas Y, Jaramillo S, Lyons K, et al. The optimal timing of surgical resection in high-risk neuroblastoma. Journal of Pediatric Surgery. 2016;51(10):1665-1669. https://doi.org/10.1016/j.jpedsurg.2016.05.021
7. Yu AL, Gilman AL, Ozkaynak MF, et al. Anti-GD2 antibody with GM-CSF, interleukin-2, and isotretinoin for neuroblastoma. New England Journal of Medicine. 2010;363(14):1324-1334. doi:10.1056/nejmoa0911123

IHH Healthcare

IHH Healthcare has a global network of 83 hospitals and ancillary services in 10 countries.

As a patient at Gleneagles Hospital Singapore, Mount Elizabeth Hospital, Mount Elizabeth Novena Hospital and Parkway East Hospital, you enjoy easy access to a full spectrum of integrated healthcare services under the IHH Healthcare ecosystem.

For more information, contact us at: