National University Cancer Institute, Singapore (NCIS)

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The NCIS brings together the expertise of the departments of Haematology, Radiation, Paediatric, Gynaecologic, Surgical, Nursing and Pharmacy Oncology to provide multi-disciplinary cancer care for patients through our specialised outpatient clinics spanning across Levels 8 to 10 at the NUH Medical Centre (NUH MC). It is the only facility in Singapore that treats both adult and paediatric oncology patients within the same premises. Other services include a Pharmacy, a Health Resource Centre (which helps patients learn and cope better with the disease) and the NCIS Concierge (which assists international patients).

**Our Outpatient Facilities**

The **Cancer Centre** is home to specialist outpatient clinics providing expert advice and care for cancer conditions. It has over 40 outpatient consult rooms including two VIP consult rooms for VIP patients, with a separate area for their entourage or security.

The **Chemotherapy Centre** provides infusion and oral therapy treating adult oncology patients in an outpatient setting and is currently equipped with capacity for up to 44 treatment chairs.

The **Viva-University Children's Cancer Centre** is a one-stop centre housing all paediatric cancer patients. With a team of dedicated and specialised paediatric oncology nurses, the centre is committed to meeting the standard of care required for managing patients undergoing chemotherapy and bone marrow transplant.

The **Stem Cell Therapy Centre** caters specifically to patients diagnosed with benign and malignant blood cancers and Haematopoetic Stem Cell Transplant needs.

The **Radiation Therapy Centre** is an outpatient centre providing radiation therapy treatment and specialist consultation for the management and care of both adult and paediatric cancers. It currently houses three Linear Accelerator machines and a brachytherapy machine, with additional capacity for future expansion.

The **Breast Care Centre** is a one-stop centre providing dedicated diagnosis and treatment for diseases of the breast with services such as breast imaging, breast surgery, as well as breast preservation and breast reconstruction.
Home Care @ NCIS – The Care Continuum

Ensuring patients’ smooth transition from hospital stay to normal life at home is a key focus the National University Cancer Institute, Singapore (NCIS) has heavily invested in. As such, informal home care was established in 2001 by Professor John Wong (Director of NCIS then) and Mdm Zarinah Hairom, Assistant Director of Nursing, to provide home care for cancer patients. At that time, it was only provided for special cases due to limited resources. In January 2014, the first official home care team at the NCIS was set up with the aid of government funding. The first patient was served on 22 January 2014. This programme was then named NCIS Transitional Care, also known as Caring Across Cancer Care [CA3C] P2, highlighting the continuity of cancer care from the point of diagnosis till end of life. Today, the team consists of three full-time dedicated haematology-oncology trained nurses working closely with multi-disciplinary team members.
The services offered under the CA3C P2 cater to the different needs of our patients during the various stages of their cancer journey.

**Services under the CA3C P2 programme**

- post-cancer therapy symptom management
- patient, family and caregiver education
- psychosocial and spiritual support
- medication reconciliation and administration
- referrals to community resources
- central venous catheter care
- wound and stoma care
- blood sampling
- home based treatment

Feasibility and safety of the CA3C P2 programme were analysed based on 82 patients with different cancers, specifically: lymphoma (31.7%), colon cancer (14.6%) and lung cancer (9.8%). There were a total of 341 home visits conducted over a period of eight months with no adverse events reported.

In December 2014, the government initiated a new model of care, the Frequent Admitter (FA) programme, to fund home visits for patients with at least three hospitalisations for the past one year, from the date of enrolment into the FA programme. The aim of the FA programme is to reduce unplanned readmissions to hospital. With this new initiative, we are able to reach out to more patients, allowing them to benefit from home care services while reducing their unplanned readmissions. To date, 79 patients have been recruited into the FA programme. A recent analysis found that 56.7% of patients in the FA programme experienced at least one admission in seven months compared to 78.4% in a control group. Patients in the FA programme were admitted for shorter durations (11 days versus 23 days), thus spending lesser on hospitalisation costs ($5,023 versus $11,186). All these were statistically significant.

A study was also conducted to assess patients and their caregivers’ responses to the home care programme. The study revealed that patients and their caregivers valued the home care service because of the following benefits:

- They are able to regain control of their daily routine
- They feel reassured and more confident in caring for themselves
- They are able to cope better with the physiological and emotional strains associated with cancer

In August 2014, the NCIS Home Care – a dedicated home care programme applicable to all cancer patients – was officially launched. This opened up the home care service to a wider range of patients who previously may not have qualified for the CA3C P2 and FA programmes. Similar to the CA3C P2 and FA programmes, this programme came with a fixed charge payable by patients. To date, the NCIS home care programme has made 165 home visits for cancer patients. Services provided include blood tests, intravenous hydration, central line care, antibiotic locks for central lines, post chemotherapy coping, medication delivery, wound care and removal of CADD pump post chemotherapy.

**Figure 1:** NCIS home care nurse administering Bortezomib therapy to a patient.

Moving forward, the NCIS Home Care Programme aims to provide disease-specific home care. One of the services includes administering Bortezomib in the comfort of myeloma patients’ homes. Bortezomib is a standard treatment for myeloma patients, which was conventionally done at our outpatient treatment centre. The programme has so far been positively received with over 20 patients being enrolled and more than 170 home visits have been made.
Supplementing the current home care services is a free counselling hotline, CancerLine, which is managed by our team of trained oncology nurses. CancerLine is the first point of contact for patients when they need help at home. It provides counselling and advice for the public as well as patients who experience side effects post-treatment. Our home care team also works closely with our haematologists and oncologists, medical social workers, nurse navigators, nurse counsellors and allied health professionals to provide our patients with an individualised and holistic care plan.

As the home care programme in the NCIS continues to evolve and expand, we aim to provide more bespoke treatment programmes to our patients while staying affordable. We believe that care goes beyond our patients’ homes – the birthplace of love, hope and dreams – and we are glad to be a part of their lives.

* This article was first published in SPARK by NCIS, January 2016 issue.
Early Phase Clinical Trials –

The NCIS Developmental Therapeutics Unit
HOW ARE CANCER DRUGS DEVELOPED FOR PATIENTS?
Drug development generally involves four phases: Phase I, II, III and IV. The traditional scope of phase I clinical trials are to evaluate safety and toxicity and to define optimal dosing in humans for future efficacy (phase II) trials of novel agents or combinations of agents after appropriate pre-clinical testing of safety, toxicology and pharmacology. Due to the fact that many of these novel compounds or combinations of compounds may be tested for the first time in humans (i.e. first-in-human studies) with unknown clinical efficacy and toxicity, these early phase trials usually enrol patients with advanced disease who have limited or exhausted standard treatment options. Nonetheless, all currently available standard-of-care treatments for cancer have also initially been developed through phase I clinical studies.

Once the optimal dose of the drug is established, the development of the drug moves into phase II where up to several hundred people with the disease/condition will be recruited to look at the effectiveness and further assess the side effects of the drug. After phase II, if the drug has shown sufficient efficacy, the development of the compound moves to phase III where the drug will be tested by comparing its efficacy against the current standard of care drug. Phase III studies can involve hundreds to thousands of patients and may take years to complete. If phase III studies successfully demonstrate an improvement in efficacy/outcome for the new drug when compared against an older drug, then the new drug will become the new standard of care and subsequently be considered and approved for use by the drug licensing authorities such as the Food and Drug Administration (FDA) in the United States and European Medicines Agency (EMA) in Europe. Once licensed, the drug development process moves into phase IV where further safety and efficacy evaluation will be carried out as patients start being treated with the new compound as a new standard of care.

WHY ARE EARLY PHASE TRIALS (PHASE I TRIALS) SO IMPORTANT?
A greater understanding of the biological networks and pathways implicated in the development of cancer has led to the identification of many potentially “druggable” therapeutic targets and a corresponding increase in the number of compounds suitable for clinical investigation. Disappointingly, despite the rapid expansion of available drug candidates for early phase testing, failures in translating the promise of these compounds to clinical reality remain prevalent[1, 2]. In 2004, data accumulated from a whole host of industry sponsored phase I trials between 1991-2000 showed that only less than 5% of cancer drugs tested in phase I end up obtaining marketing authorisation[3]. Most experts are of the opinion that the shortcomings in cancer drug development come down to several factors: 1) at the pre-clinical phase (i.e. laboratory development, pre-human testing phase) many compounds were not properly assessed with the appropriate pre-clinical disease models and hence were subsequently found to be ineffective even at the optimal dosage; 2) the drugs were too toxic and should never have been developed in the first place; 3) the drugs did not actually have any proof of mechanism i.e. there was no evidence that the drug actually hit its intended molecular target in cancer cells; and 4) drugs went on to be developed in later phase II and III studies despite the lack of demonstrable efficacy when the molecular target was “hit” in early phase (phase I) studies i.e. there was no early proof of concept.

Given the high costs associated with the conduct of later phase trials, especially randomised phase II or III trials, it is now increasingly common practice for many companies to discontinue development of their compounds if they cannot establish proof-of-mechanism by the end of phase I testing. Therefore, in addition to assessing toxicity and tolerability, many phase I trials have now assumed the role of “gate-keepers” in drug development, and are now an even more crucial first-step in the bench to bedside translational drug development process. Consequently, there is a growing consensus amongst cancer experts and the pharmaceutical industry that early phase or phase I clinical trials are now a fundamental component in the process of translating the preclinical data on the anti-cancer effects of a drug in the laboratory into real time clinical use for cancer patients. In the current era of precision medicine incorporating molecular-targeted therapy, “go-no-go” decisions are often made earlier on in the drug developmental process than during
the phase II to III interface\textsuperscript{30}. Notable successes in the development of novel anti-cancer therapeutic agents employing the approach of increased focus on phase I drug development include the drug ceritinib in lung cancer which was licensed based on the strength of the scientific and clinical data garnered from a well-designed and executed phase I study.

**A STATE-OF-THE-ART FACILITY FOR EARLY PHASE TRIALS: THE NCIS DEVELOPMENTAL THERAPEUTICS UNIT (DTU)**

Since its inception, the NCIS has developed a significant track record and reputation for running early phase studies in the region, due largely to the early efforts of Associate Professor Goh Boon Cher, Head and Senior Consultant of the Department of Haematology-Oncology, NCIS. His pioneering work in early phase drug development in Singapore was made possible by the development of an extensive administrative infrastructure provided by the Haematology-Oncology Research Group (HORG). The early phase drug development unit has since grown from strength to strength and has further benefited from the formal establishment of our Developmental Therapeutics Unit (DTU) in 2014, incorporating dedicated state-of-the-art inpatient and outpatient facilities for early phase clinical trials aided by funding from the Yong Siew Yoon (YSY) NCIS grant. Given the lack of Asian patients recruited to phase I trials which are generally carried out in western countries, the NCIS also recognised the need to establish a phase I unit that would specifically address the question of identifying optimal drug doses in Asian patients.

Setting up a formal DTU was a vital step in view of the need to maintain our current high standards for running early phase trials at the NCIS, and, given the anticipated increase in resources required to run multiple clinical studies of this nature, one that will also ensure our ability to accommodate further expansion of our early phase trial portfolio. These trials are highly intensive for both patients and the clinical team running the study given the requirements for frequent visits to the hospital for monitoring and testing before, during and after the study. These visits often include overnight stays in the hospital for repeated blood tests to assess drug metabolism (pharmacokinetic assessments) over a 24-hour period, and pre-/post- treatment tumour biopsies or blood tests to assess the biological effect of the drug on specific molecular targets in these tissues (pharmacodynamics studies). Additionally, it is also imperative that adequate facilities and appropriately trained staff are always available to evaluate and manage any issues encountered by early phase trial patients in a timely manner.

**THE NCIS DTU: A MULTI-DISCIPLINARY TEAM AT THE CUTTING EDGE OF CANCER CARE**

The NCIS DTU comprises a team of clinicians, nurses, allied health professionals and scientists, who work in a multi-disciplinary team to ensure the utmost standards of safety in conducting early phase trials. The DTU team currently runs a dedicated clinic every Monday and Thursday and meet weekly to discuss the clinical progress of each DTU patient on study and any

**Figure 1:** The NCIS Developmental Therapeutics Unit (DTU).
other trial related issues. Through the YSY grant, we have also been able
to develop a training fellowship programme in cancer drug development
in the DTU. Our current fellow is Dr Valerie Heong who was working as
a consultant medical oncologist in Melbourne, Australia before deciding
to take up the YSY fellowship in drug development at the NCIS last year.
Importantly, the establishment of the NCIS DTU has already helped attract
interest from drug companies seeking academic partners who have the
appropriate infrastructure in place to support early phase trials in Asia. This
has in turn benefited our patients by giving them access to cutting-edge
anti-cancer drugs. Currently available clinical trials of novel compounds in
the DTU are shown in the Table 1.

- P-TEFb inhibitor (Bayer)
- Trastuzumab + NK-cell therapy for HER2 amplified/
  overexpressed tumours
- Balanced PI3Ka/β inhibitor (Bayer)
- Exportin 1 (XPO1) inhibitor – selective inhibitor of nuclear export
  (Selinexor, Karyopharm)
- PDL-1 + MEK inhibitor (Roche)
- Pan- fibroblast growth factor receptor (FGFR) inhibitor (Bayer)
- AKT1 inhibitor (Astra Zeneca) in tumours with AKT1 mutations
- ASLAN001: HER1/2/4 inhibitor + carboplatin and paclitaxel
- PLK1 inhibitor (Tekmira)
- Wnt/Porc inhibitor (Experimental Therapeutics Centre/ D3
  A*STAR Singapore)

Table 1: DTU Phase I trials 2015.

Figure 2: Members of the Haematology-Oncology Research Group (HORG).
All our medical oncologists on the team are also leading experts in specific tumour types (see Table 2) and hence provide added clinical and scientific insight into the management of each patient referred to the DTU.

<table>
<thead>
<tr>
<th>Consultant</th>
<th>Tumour subspecialty</th>
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<tbody>
<tr>
<td>Goh Boon Cher</td>
<td>Head and Neck Cancers</td>
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<tr>
<td>Chng Wee Joo</td>
<td>Haematological Cancers</td>
</tr>
<tr>
<td>Lee Soo Chin</td>
<td>Breast Cancer and Cancer Genetics</td>
</tr>
<tr>
<td>Yong Wei Peng</td>
<td>Gastrointestinal Cancers</td>
</tr>
<tr>
<td>Chee Cheng Ean</td>
<td>Gastrointestinal Cancers</td>
</tr>
<tr>
<td>Andrea Wong</td>
<td>Breast and Central Nervous System Cancers</td>
</tr>
<tr>
<td>David Tan</td>
<td>Gynaecological Cancers</td>
</tr>
</tbody>
</table>

Table 2: List of DTU Consultant Medical Oncologists.

Given that many of the currently tested compounds target a specific molecular pathway aberration in cancer cells, patients in our DTU early phase trials are also offered molecular profiling of their tumours via our integrated molecular analysis of cancer (IMAC) programme to identify these “actionable” molecular aberrations in the tumour cells so that, based on their tumour molecular profile, patients can be matched to the most appropriate drug in early phase clinical trials. Our molecular profiling programme in DTU is currently led by Dr David Tan and is funded by a National Research Council of Singapore (NMRC) Transition Award and the NCIS centre grant. Through this programme, we have successfully matched patients with actionable mutations in their refractory cancer compounds with durable responses already noted.

FINDING AND DEVELOPING THE NEXT GENERATION OF ANTI-CANCER DRUGS

The next era of oncological therapy will inevitably evolve from a better understanding of the molecular aberrations in cancers allied with technologies that will facilitate a rapid and comprehensive characterisation of the unique biological features of each cancer patient’s tumour. The challenge for oncologists is to leverage on this wealth of scientific information to develop more effective therapeutic options for patients via well-designed and expertly executed early phase studies. The NCIS DTU is now fully equipped to embrace this challenge and lead the development of new drugs in the fight against cancer.

References:
Limb Salvage in Musculoskeletal Oncology

Musculoskeletal oncology (MSO) is a sub-specialty of surgical oncology that focuses on the diagnosis and multi-disciplinary approach to treatment of patients with benign and malignant tumours of bone and soft tissues.

The last few decades have seen rapid strides in the evolution of musculoskeletal oncology. What was once originally a specialty that involved a singular orthopaedic surgeon is now a specialty that requires a multi-disciplinary approach combining the expertise of orthopaedic surgeons, plastic and hand surgeons, paediatric and adult general surgeons, radiologists, radiation oncologists, paediatric and adult medical oncologists, and musculoskeletal pathologists.

<table>
<thead>
<tr>
<th>Red flags</th>
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<tbody>
<tr>
<td><strong>History</strong></td>
<td><strong>Physical Examination</strong></td>
</tr>
<tr>
<td>Rapidly growing lesion</td>
<td>General physical examination</td>
</tr>
<tr>
<td>Night pain</td>
<td>Size of the lesion – more than 5cm</td>
</tr>
<tr>
<td>Presence of constitutional symptoms</td>
<td>Depth of the lesion – lesions deeper to the subcutaneous layer</td>
</tr>
<tr>
<td>Personal or family history of cancer</td>
<td>Enlarged locoregional lymph nodes</td>
</tr>
<tr>
<td>Past history of chemo/radiotherapy</td>
<td>Signs of metastases</td>
</tr>
</tbody>
</table>

In the past, treatment aims in musculoskeletal oncology were centred on survival (overall and event free survival) as the main measurable outcome. The advent of better imaging modalities, more effective chemotherapy, improved radiotherapy techniques, a better understanding of the anatomy with continuous refinement in surgical techniques and advances in prosthesis design, biological techniques and materials have allowed for the focus of treatment to encompass limb preservation, joint preservation and growth plate preservation in paediatric patients where applicable[1]. As such, function and quality of life in these patients have become a significant goal of treatment in addition to overall and event free survival.

Limb salvage surgery, also known as limb-sparing surgery, is a highly complex operation done to remove a bone or soft tissue tumour and avoids amputation for patients with malignant tumours affecting the limbs. These are highly specialised procedures carried out in tertiary centres with sub-specialty experts in the field.

With the evolution of musculoskeletal oncology as a sub-specialty, amputation rates have undoubtedly gone down in most tertiary centres treating these conditions. We, as a surgical fraternity, are continuously pushing the boundaries of limb salvage surgery as we continue to evolve. Certain ‘absolute contraindications’ to limb salvage surgery are no longer relevant. For example, pathological fractures in patients with osteosarcoma were regarded...
as a contraindication to limb salvage surgery and amputation was frequently performed in these patients. Various studies have since shown that there are no differences in outcomes of limb salvage surgery and amputation, provided that the surgery is carried out in tertiary centres with sub-specialty experts performing the surgeries, and margin control attempts are aggressive [2, 3, 4].

The two case studies below illustrate limb salvage surgery in two different patients. Both patients are in the paediatric age group with osteosarcoma as the primary diagnosis. The reconstruction that has been performed in the first case is biological with the use of an allograft and the knee joint was preserved. In the second case, due to the extent of tumour, the knee joint could not be preserved and a specially designed tumour endoprosthesis was used.

**Case Study 1**
Mr AKK is an 11 year old boy who presents for increasing right thigh pain and swelling for two weeks. There was no history of recent trauma to his leg. No constitutional symptoms or similar lumps elsewhere were reported. X-rays (Figure 1) that were done revealed a poorly defined lytic lesion over the lateral aspect of the distal meta-diaphyseal region of the left femur. It had a large zone of transition and associated periosteal reaction.

The MRI scan (Figure 2) showed a 7.8 x 4.9 x 4.6 cm aggressive enhancing lesion in the meta-diaphyseal region of the right distal femur. The lesion extended up to his physeal plate but not into or beyond the epiphyseal plate. The lesion was within 2mm margins of the popliteal artery and vein, but there was no involvement of the neurovascular bundle.

A whole body bone scan (Figure 3) revealed no scintigraphic evidence of bony lesions elsewhere.

A computer topography (CT) scan of the thorax revealed no evidence of pulmonary metastases. This completed our preliminary investigations. An open biopsy confirmed that this was a high grade osteosarcoma. His case was discussed at the weekly multi-disciplinary tumour board where the consensus was for knee joint sparing surgery following neoadjuvant chemotherapy. Mr AKK subsequently underwent three months of neoadjuvant chemotherapy following which restaging imaging was done. The MRI (Figure 4) of his thigh revealed some evidence of tumour response to the neoadjuvant chemotherapy (2.9 x 0.9 vs 3.8 x 2 cm).
This correlated with the finding on the bone scan where the previously seen bony lesion in the distal right femur appeared less intense. Similar to the previous bone scan, no skip lesion was seen elsewhere.

![Figure 5: Restaging whole body bone scan.](image)

The CT thorax again showed no evidence of any pulmonary metastases. Highly precise preoperative planning and computer guided templating (Figure 6) was necessary to obtain an accurately matched structural bone allograft.

![Figure 6 (a – c): Rigorous templating carried out.](image)

A suitable match was found from a 25 year old donor from the USA. Multiple teleconferencing calls were necessary to ensure that the dimensions and the anatomical configuration of the allograft were appropriate for the patient. The allograft was flown over while maintaining a cold chain of transport prior to the surgery.

![Figure 7: Intra-operative photograph of the bone allograft after the thawing protocol and immersion in antibiotic soaked solution.](image)

The right distal femur resection and joint sparing allograft biological fixation went as planned. Excision (Figure 8) was performed 4 cm proximal to tumour margins (confirmed by intraoperative frozen section) and immediately distal to the physis (growth plate) under intraoperative imaging guidance.

![Figure 8: Excision of right distal femur sarcoma.](image)

Internal fixation (Figure 9) of templated allograft was then carefully carried out using a double plate technique.

![Figure 9: internal fixation of templated allograft.](image)
Post operatively, histopathological margins of the resected specimen were confirmed to be negative. Mr AKK recovered well and is completing adjuvant chemotherapy. He is now two months post-surgery. The distal interface of the host bone allograft has shown good healing. He is currently walking with crutch support and will be planned for full weight bearing ambulation in one month’s time.

Case Study 2
Mr ZBD is a 19 year old male who is a National Serviceman who presented for increasing right knee pain for one month accompanied by night pain. X-rays (Figure 10) that were done revealed a periosteal reaction at the lateral cortex of the diaphyseal region of the right distal femur.

MRI scans of the right thigh (Figure 11) and knee (Figure 12) showed a destructive lesion in the lateral aspect of the distal metaphysis of the right femur. No fracture or skip lesion was detected. There was no neurovascular involvement noted. However, in this case the tumour was extremely close to the knee joint.

The bone scan and CT thorax showed no evidence of distant metastases or skipped lesions. This completed our preliminary investigations. A frozen section open biopsy of the right distal femur confirmed high grade conventional osteosarcoma. After completing his neoadjuvant chemotherapy, his re-staging imaging was done. The MRI of his right thigh (Figure 13) revealed a smaller extraosseous soft tissue component and extent which suggested favourable treatment response to the neoadjuvant chemotherapy.

This was confirmed by the bone scan (Figure 14) on which the right distal femoral lesion was noted to be less intense than the previous scan.

After discussion at the tumour board, the decision was made to proceed with distal femur resection and joint replacement using a tumour endoprosthesis, as the tumour was adjacent to the joint and joint-sparing surgery would not be possible. The operation was done in early July and went as planned. Intra-operatively, the neurovascular bundle was found tethered to the femur but was not encased by tumour. Intra-operative frozen section confirmed that all resection margins were clear.
Post-operative imaging (Figures 16 & 17) showed a stable tumour endoprosthesis that was appropriately aligned and had no further complications.

Post-operatively, histopathological margins of the resected specimen were confirmed to be negative. There were no signs of infection or neurovascular compromise. Mr ZBD’s progress was monitored and he was discharged with no further complications. Mr ZBD is now nine months post-surgery. His x-rays done in clinic at nine months post surgery showed bone growing over the hydroxyapatite coating of the tumour endoprosthesis suggesting good integration. After going through physiotherapy, Mr ZBD is now ambulating independently and is back to riding a motorcycle.
FINAL THOUGHTS

These are highly complex surgeries and complications do occur, particularly in the context of ongoing chemotherapy and immunosuppression of these patients. However, the process of successfully treating multiple patients such as Mr AKK and Mr ZBD is an extremely rewarding one. The specialty of musculoskeletal oncology has seen vast amounts of rapid change in the last decade and we are fortunate to be able to bring this level of care to our patients. We hope to be able to help many more patients both locally and internationally.

*This article was also published in SPARK by NCIS, July 2016 issue.


A structured approach should be adopted when taking a family history of cancer. Include information of at least three generations on both the paternal and maternal side of the family; do not neglect the paternal family history when assessing for familial breast or ovarian cancers.

Young onset cancer (less than 40 years old for most solid tumours) or multiple primary cancers in a single individual should raise suspicion of a possible hereditary predisposition, even in the absence of family history.

Genetic testing can confirm the diagnosis of various hereditary cancer syndromes.

Advocate regular cancer screening to patients, especially for those who fall within the recommended age groups. Breast and Colorectal cancers are two of the top cancers in Singapore and both have established methods of screening.

Screening and preventive guidelines exist for many cancers and can result in early detection and reduction of cancer risk and mortality in high-risk individuals. It is important to close the loop with patients who have positive screening results. To make a patient referral, call 6773 7888 or email CancerApptLine@nuhs.edu.sg.
Stereotactic Ablative Radiotherapy (SABR) Programme –
Treating Our 100\textsuperscript{th} Patient And Beyond
BRIGHT NEW HOPE FOR CANCER PATIENTS

On 15th September 2015, the NCIS Radiation Therapy Centre treated its 100th SABR patient. From sending a team to undergo training at two renowned SABR centres in the United States in 2011 and treating our first SABR patient in the same year, to treating our 100th SABR patient, it has indeed been a long journey in attaining this significant milestone.

Stereotactic ablative radiotherapy (SABR), previously known as stereotactic body radiation therapy (SBRT), is a newly-developed cancer treatment technology. Utilising specialised and highly advanced equipment, software and procedures, a tumour’s location is precisely defined, and its size and shaped exactly mapped. During the treatment itself, the patient is precisely positioned, immobilised, and administered high-precision, high-dosage external radiation therapy. The technology allows intensely focused and highly precise treatment of the target area, with minimal effect on surrounding, healthy tissue.

SABR differs from conventional radiotherapy primarily in the precision of radiation delivery. Multiple, converging beam angles are used to safely deliver high-potency dosages. This reduces treatment time, minimises delay or disruption of systemic therapy, and results in greater convenience for the patient.

Currently at the NCIS, SABR is used in the treatment of tumours in the lungs and liver.

ADVANTAGES OF SABR

1. Treatment outcomes for eligible and properly selected patients are comparable to surgery, and certainly surpass conventional external beam radiation therapy techniques.

2. Treatment duration is reduced to just one to five sessions, each lasting about 30 minutes. Total treatment duration inclusive of preparation is about two weeks – up to 80% reduction compared to conventional fractionation.

3. Side effects may be relatively mild or absent, depending on tumour location. Patients experience less lethargy, esophagitis, and risk of pneumonitis.

4. The overall cost of SABR is slightly higher than conventional treatment. However, for Singaporeans, a significant proportion of the cost can be subsidised by Medisave and Medishield Life.

WHAT PATIENTS CAN EXPECT

1. Evaluation and patient selection
   The patient’s history will be reviewed, and his or her case will be evaluated for SABR suitability. The following factors will be considered during evaluation:

   Patient factors
   * Physical condition, including ECOG status, ability to lie still and to comply with instructions
   * Lung function (if treating the lung)
   * Liver function (if treating the liver)

   Disease factors
   * Size and location of tumour
   * Extent and control of systemic disease
   * Disease progression
   * Previous patient history of radiotherapy

Figure 1: Patient undergoing SABR treatment.
2. **Patient Consent**
   The full procedure, including possible risks, discomforts and alternative treatment options, will be explained to the patient. After the patient has fully understood the procedure, written consent to proceed will be obtained.

3. **Four-dimensional Computed Tomography (4D CT) simulation**
   A 4D Computed Tomography (CT) simulation will be carried out. Once completed, small, permanent marks will be made on the patient’s body. These will help in accurately positioning the patient at the time of treatment.

4. **Planning**
   The patient’s 4D CT images are imported to the planning software, and the tumour planning target volume (PTV) and normal-tissue organs are contoured. A treatment plan is produced, aimed at delivering the maximum prescribed radiation dose to the PTV, with rapid dose fall-off to the surrounding normal tissues.

5. **Quality Assurance**
   A series of procedures is now conducted to ensure the quality, accuracy and safety of procedural planning. This step is essential in the delivery of SABR as it ensures the quality of the approved plan and the safety of the delivery of the intended radiation dose. The medical physicist performs patient-specific quality assurance before each patient undergoes his or her first SABR session. As very high doses of radiation are delivered to the patient each SABR session, additional measures are employed to ensure patient safety.

6. **Treatment**
   The patient is taken to the treatment room, and positioned precisely as determined during the preparatory CT simulation step. The immobilisation device and body reference markings are used to ensure accurate positioning is achieved.

   Once the patient has been positioned, but before the actual treatment is administered, a 4D Cone Beam Computed Tomography (CBCT) scan is done, for final confirmation of the tumour’s position and dimensions.

   During the treatment itself, a SABR radiation oncologist will be at the treatment console, utilising all available on-board imaging technologies to deliver the treatment in close accordance with the original treatment plan. He or she will also take into account all potential patient-specific, tumour-specific, and organ-specific motion during treatment, in real time.

   The entire treatment takes about 30 minutes. The patient is awake throughout the procedure, and can expect to complete the treatment without pain. SABR patients can resume normal activity within a day.
7. **Follow-up**
Once treatment is complete, the patient will be scheduled for routine follow-up consultations. Follow-up scans and investigations will also be arranged, to evaluate results and response to treatment, as well as any possible side effects.

8. **Side Effects**
The side effects of SABR are minimal as the treatment is very precise and accurate.

Figure 3: Serial CT scans showing gradual resolution of the tumour after SABR.

**OUTCOMES**

Mr Tan, our 100th SABR patient, was a 75 year old chronic smoker who was recently diagnosed with early lung cancer. He had multiple medical comorbidities and limited lung function due to his chronic smoking and was not keen to undergo surgery. Before the availability of the SABR programme, he would have been offered conventional radiation therapy treatment which would have resulted in inferior local control rates compared to surgery. Now, he has a three year local control rate of 85 - 90% based on local NCIS SABR data, which is comparable to surgery. Significantly, this outcome is achieved without any invasive procedures and a solely outpatient treatment modality.

Our 101st patient is Mr Goh, a patient with hepatocellular carcinoma. He was heavily treated with surgery, TACE (transarterial chemoembolisation) and RFA (radiofrequency ablation) previously. He was referred to us for treatment for new hepatomas. Despite having limited liver reserves from previous hepatectomy and local treatment, we were able to treat his new hepatomas with SABR. We expect Mr Goh to have a 90% one year local control rate based on NCIS data of 20 patients treated with SABR to their liver lesions. Liver SABR is a new frontier with promising results which yet may offer another effective modality to patients with hepatocellular carcinoma or metastatic patients with oligometastases to the liver.

Moving forward, in addition to lung SABR, there will be more focus on using SABR to treat other sites like liver and spine. We also hope to improve the average time taken from patient’s consent of treatment to completion of SABR treatment.

* This article was first published in SPARK by NCIS, January 2016 issue.

**Asst Prof Leong Cheng Nang**

Clinical Director & Senior Consultant
Department of Radiation Oncology, NCIS

Asst Prof Leong’s interests are in stereotactic ablative radiotherapy (SABR), thoracic and gastrointestinal malignancy. He received his SABR training in the United States of America under the Ministry of Health Human Manpower Development Program (HMDP) in 2011. Upon his return, he set up the SABR programme at the NCIS. He also organises SABR symposiums and workshops to educate regional radiation oncologists on SABR.
A Holistic Approach to Conquer Myeloma
Multiple myeloma (MM) is a type of bone marrow cancer characterised by the abnormal expansion of malignant plasma cells in the bone marrow. It is the second most common type of blood cancer and afflicts more than 100 patients in Singapore a year. It has rising incidence in Asia, the reason for which is still elusive. Patients tend to be above 55 years of age, and can present in very non-specific manners with fatigue, and bone aches. As these symptoms are rather common in the elderly population, a high index of suspicion is needed for early diagnosis of the condition. Myeloma eventually causes anaemia, lytic bone lesions, which may cause bone pain or pathological fractures, renal impairment and hypercalcaemia. The presence of these features without a clear aetiology should prompt a screen for myeloma to exclude the diagnosis.

The outlook of myeloma patients has changed tremendously in the last decade. Over the last decade, a number of new drugs have been approved for treatment of myeloma. These new treatments are not chemotherapy and have better side-effect profiles. As a result, patients with myeloma are mostly treated in the outpatient setting and have significantly better quality of life even while on treatment as compared to in the past. These drugs are also much more effective compared to chemotherapy with almost 100% of newly diagnosed patients achieving a response and close to 50% achieving complete response. As a result, the average survival of patients has doubled from three to four years previously, compared to seven to eight years, today.

Despite great improvement in treatment, some gaps still remain. With the increase in treatment options, the management of myeloma has also become very complex and confusing for the patients and physicians. The disease is still incurable with resistance being a problem – hence, continued development of potential new therapeutics is critical.

At the National University Cancer Institute, Singapore (NCIS), we take the approach that to further improve on the outcome of patients with MM, we need to take a holistic approach, through optimising current treatment, using resources rationally and providing value to patients, increase access to new drugs as patients relapse, research to find new treatments, and patient support and education to help patients through their journey with myeloma.

Optimising Clinical Care
We lead the development of a consensus guideline for the treatment of myeloma in Singapore. This will facilitate standardised practice and also ensure that expensive drugs are used rationally in patients that will derive the most benefit from it.

To further improve quality of life and treatment for patients, we developed two new programmes that remain the only one of its kind in Singapore. First we started performing outpatient-based stem cell transplant for myeloma patients in 2012. Patients receive the chemotherapy and stem cell infusion in the Cancer Centre and are looked after at home by their family. By doing this, the cost of the procedure is reduced by 30% and the length of hospital stay is reduced by more than 50%. One of the most common treatments for myeloma is Bortezomib, which is given as a subcutaneous injection once a week. We introduced a programme where we gave patients their Bortezomib treatment in the comfort of their own homes to save them travelling time, waiting time, and reduce the risk of infections, at no additional cost to the patient.

To further optimise outcomes, we provide early access to drugs for our patients with a carefully selected portfolio of clinical trials to cover the main indications in myeloma. In the process, our patients have had the opportunity to be treated with drugs that have been approved by the Food and Drug Administration (FDA) in the United States but are not available in Singapore commercially. Over the last five years, the NCIS has become one of the most well-known sites for the conducting of clinical trials in myeloma in the world, culminating this year as one of the top recruiting centres in a trial that led to the approval of a new drug called Carfilzomib.

Research
Patients with high-risk diseases have a survival time of less than
two years even with the current best treatment. Therefore, there is a need to understand the nature of these high-risk diseases and to develop therapeutics effective against these tumours. Another therapeutic problem is drug resistance and relapse. We have made headways over the last few years and some of our discoveries have the potential to be tested in patients.

**Patient Education and Support**

Myeloma patients often feel isolated and confused by the different treatments available to them. They are also worried because they know that they have a disease that is not yet curable and treatment is expensive. It is critical that they have access to a support system of peers as they go through their treatment journey. Also important is the availability of relevant information as well as access to expert opinion. In this regard, we have implemented a few initiatives.

1) Putting in place a navigator who acts as a point of contact and helps to coordinate the needs of our myeloma patients and reduce complexity and confusion to them.

2) Establishing a patient support group comprising of patients and caregivers. The group meets regularly to share their experiences and learn from different experts. Once a year, we will have a larger forum. This allows the patients to feel that they are part of a larger community and not isolated. The patients have been very appreciative and contributed back to the myeloma research by raising about half a million in research funds to aid myeloma research.

3) In addition, to ensure that access to expert and latest information is available and up-to-date, we have set up a website where these information will be disseminated and patients can blog about their experience and ask the doctors about their symptoms. This interactive approach is aimed at reducing anxiety and equipping the patients with enough knowledge to take charge of their illness.

**CONCLUSION**

At the NCIS, we have taken a comprehensive and holistic approach to managing patients with myeloma with the patient at the centre, and clinical, research and educational initiatives focused on them. We hope that this approach towards Total Myeloma Care will provide the framework towards a sustainable strategy for continual improvement in the outcomes of our myeloma patients.
NCIS Health Resource Centre & Patient Support Groups

Beyond just providing clinical care to our patients, the NCIS recognises the emotional distress cancer patients face. We seek to embrace and empower our patients through various supportive care programmes and activities so that they can draw strength and comfort to better cope with their battle against cancer.

Health Resource Centre (HRC)
The HRC is part of our holistic approach in our treatment for cancer patients and their caregivers. We provide an avenue for them to learn more about their conditions and to attend various support programmes which will enable them to better cope with their disease. The HRC is currently home to a resource library shelved with over 900 titles of fiction and non-fiction books.

Our supportive care programmes and activities are designed to provide patients and their families with the necessary information and skills to cope with cancer and the effects of treatment. Some of the programmes that are currently being run at the HRC include cooking demonstrations, yoga classes and educational talks. For the latest information on our supportive care programmes, do visit www.ncis.com.sg.
In Addition

Patient Support Groups
Here at the NCIS, we have a number of support groups which cancer patients and survivors can join. These support group platforms provide a place for them to share common concerns and emotional support. It also gives them an opportunity to connect and interact with others who share similar experiences. Some of our support groups are patient driven while others are facilitated by oncology specialists. Patients are encouraged to share their experiences through regular activities and meetings.

Currently there are nine support groups where patients can find empathy in sharing sessions, interactive group activities, as well as educational talks.
- Acute Leukaemia Warriors Support Group
- Breast Support Group
- Gynaecologic Oncology Patients TEAL Support Group
- Haematopoietic Progenitor Cell Transplantation (HPCT) Support Group
- Lymphoma Support Group
- Multiple Myeloma (MM) Support Group
- Myelodysplastic Syndrome (MDS) Support Group
- NPC oneHeart Support Group
- Sarcoma Support Group

Patients, survivors and caregivers engage in communal drumming during NCIS Celebrates Life - an annual year end party for all our support groups.

Members of the Gynaecologic Oncology Patients TEAL Support Group during an excursion to the River Safari.

Professionals conducting a demonstration during our Look Good Feel Better programme.

Chefs from the Les Amis Group conduct live cooking demonstrations of dishes specially created for cancer patients and survivors.
Your specialty interests are in multiple myeloma and lymphoma. Why these two areas in particular, and did you have any role models in your earlier days as a clinician scientist?

I have always been more interested in malignant haematology compared to benign haematology. Of the malignant haematology, myeloma and lymphoma provide the more interesting challenges due to the heterogeneous ways in which patients present, the diagnostic challenges and the exciting research and drug developments in these diseases. In my earlier days, I looked up to Dr Goh Boon Cher, our current Head in the Department of Haematology-Oncology at NCIS, who was blazing the trails with first in human studies in cancer done in Singapore. I have also been inspired by many scientists who have made seminal discoveries to medicine.

There has been a gradual increase in cancer cases in Singapore since 2010. What do you think are the challenges in encouraging people to go for regular cancer screening programmes, and how can we overcome them?

This is the easiest thing to do to have a major impact yet it is the most challenging as somehow Singaporeans do not go for screening. We are planning to initiate a few programmes, working closely together with primary care physicians, embarking on educational programmes and publicity campaigns with the Health Promotion Board and the Singapore Cancer Society, as well as working with the human resource departments of companies to actively promote screening. We also work with behavioural scientists to see how we can alter behaviour of the population when it comes to screening. It has to be a multi-pronged approach.

How can our local general practitioners (GPs) work together with the NCIS in the fight to bring down cancer cases?

We can definitely work together to identify high-risk patients that should go for screening. GPs can also be our partners in managing patients who have already had their tumours eradicated so that these patients can be monitored mainly in the community. I am very hopeful that there can be close partnerships to ensure that patients have care in the most appropriate setting.
What is the one significant event in your research that has enriched your life?
I think the most enriching thing is when what we discover in our research leads to an impact in our patient’s life. Very often this is most apparent and gratifying in clinical trials which we are conducting that have led to improved patient outcomes with prolonged survival.

After a long day, how do you relax and unwind?
I like to spend time with the family (my wife and three kids), we watch movies or do sports (badminton, bowling) or play board games together. On my own, I like to listen to music (I am a music buff with interests in a broad range of music from classical to jazz to rock so I listen to what my mood dictates) and I read (less time for long novels nowadays so I am reading a lot more comics and graphic novels). I have been collecting comics (not just superhero comics but also others) since my secondary school days.

What are the three most important things to you in your life?
(1) My family, (2) my patients, (3) my colleagues, staff and students

Professor Chng Wee Joo is the Director of the National University Cancer Institute, Singapore (NCIS). He is also the Deputy Director and a Senior Principal Investigator at the Cancer Science Institute (CSI), Singapore, National University of Singapore (NUS). Professor Chng is also a Professor of Medicine at the Yong Loo Lin School of Medicine, NUS. He is the Chairman of the CSI Graduate Studies Committee, and is the President of the Singapore Society of Haematology.

He has a PhD from the NUS and fellowships from the Royal College of Physicians, Edinburgh; Academy of Medicine, Singapore; and the Royal College of Pathologists, UK. He also has a specialist Accreditation in Haematology, Singapore. His research interests focus around multiple myeloma, and the biology and therapeutic practices of haematologic malignancies. He is a member of many international professional committees, such as the American Society of Haematology Scientific Committee on Plasma Cell Neoplasia.

Professor Chng is in the peer review committee of journals such as Blood, Leukaemia, Cancer Research, and Nature Genetics. He is also involved in a number of Grant Review Committees, Conference Organising Committees, Advisory Boards and Steering Committees of global clinical trials. He has authored more than 150 publications in many reputed journals, such as The New England Journal of Medicine. Prof Chng has also authored several book chapters, actively participated in clinical trials and has delivered talks on multiple myeloma in numerous national and international conferences. He has won multiple awards for his research both locally and internationally including the National Medical Research Council Clinician Scientist Award.
UPCOMING EVENTS

9 JUL 2016
Gastroenterology and Hepatology Updates for GPs
University Medicine Cluster
NUHS Tower Block Auditorium, 2pm – 4pm

The Division of Gastroenterology & Hepatology provides a comprehensive array of diagnostic and therapeutic treatment for digestive and liver diseases. Its strengths lie in several key services, notably in viral hepatitis, liver cancer, functional bowel diseases and therapeutic endoscopy. The dedicated facility is equipped with the technology and know-how to provide accurate diagnosis as well as management plans for both common and complicated gastrointestinal, liver and biliary conditions. The division also pride itself as a tertiary referral centre for complex clinical cases and an education hub for patients, nurses, medical students and doctors in the principles and practice of digestive and liver diseases.

30 JUL 2016
Orthopaedics Updates for GPs
University Orthopaedics, Hand and Reconstructive Microsurgery Cluster
NUHS Tower Block Auditorium, 2pm – 4pm

The University Orthopaedics, Hand & Reconstructive Microsurgery Cluster (UOHC) is at the forefront of advanced surgical techniques and it has the largest number of Singaporean patients who have undergone thoracoscopic “keyhole” scoliosis surgery, hip surface replacement, advanced cartilage repair using autologous cartilage implantation or mesenchymal stem cells, and artificial spinal disc replacement.

13 AUG 2016
Urology Updates for GPs
University Surgical Cluster
NUHS Tower Block Auditorium, 2pm – 4pm

The NUH Department of Urology is a well-known provider of one of the most advanced urological services in the region. It focuses on the delivery of specialised medical and surgical care in all major aspects of adult urology. This leading edge is complimented by pioneering research in the field of urological cancers (bladder, kidney and prostate), kidney transplants, treatment of benign prostatic hyperplasia, management of urinary stone conditions and male sexual dysfunction. Their strong research programme is backed by state-of-the-art equipment, which allows patients with complex conditions to be treated with advanced technologies such as minimally-invasive robotic surgery, transurethral needle ablative procedures and flexible ureteroscopy.

Event information listed is correct at time of print. While every attempt will be made to ensure that all events will take place as scheduled, the organisers reserve the rights to make appropriate changes should the need arises. Please refer to our events calendar at www.nuh.com.sg/nuh_gplc for more updates and information.
16 APR 2016
NUHS GP Engagement Event

GPs are important partners in our community, and we would like to do more together with you, said Adjunct Associate Professor Joe Sim, Deputy Chief Executive (Clinical Enterprise), National University Health System (NUHS) and Chief Executive Officer, National University Hospital (NUH), to about 150 GPs attending the NUHS GP Engagement Event on Saturday, 16 April 2016.

In his remarks to our GP partners, Adjunct A/Prof Sim said that we would need a fundamental shift in our approach to ageing and health in order to provide sustainable care for our rapidly ageing population.

Adjunct A/Prof Sim shared that one key thrust would be to transform care delivery from the current model that was built around the hospital to one that is community-based. With this shift, more resources would be channelled to primary care, and GPs could expect an increase in patient load.

To support our GP partners, NUHS would develop primary care networks (PCNs) that would reinforce care partnership with our GP partners, and their patients would have access to nursing, allied health and specialist care, as well as social and community intervention. By improving care delivery, the PCN initiative would also move us closer to our vision of “One Family, One Family Doctor”. Adjunct A/Prof Sim announced that our first PCN would be established in Bukit Panjang, and we would extend this initiative to other areas subsequently.

Our ‘Open Access’ initiative would also allow GPs to directly refer their patients for oesophago-gastro duodenoscopy (OGD) and colonoscopy, which would allow their patients to bypass the need to first see a specialist at the SOC.

Another area for collaboration would be to improve cancer prevention and care in the community. The National University Cancer Institute, Singapore (NCIS) would accredit GP partners to establish Cancer Prevention Care Clinics in the community.

Adjunct A/Prof Sim added that another important shift we need to make would be to move beyond delivering healthcare to maintaining good health, and highlighted the importance of early screening and intervention. To this end, he encouraged GPs to join our Screen for Life@West initiative and Community Health Screening effort.

The event, which was also supported by two national centres of NUHS, namely National University Cancer Institute, Singapore and National University Heart Centre, Singapore, was jointly organised by NUH International and the NUHS Regional Health System Planning Office to thank our GP partners for taking care of our patients in the community.

GPs who are interested in any of the programmes mentioned can contact Ms Kristine Lin at 6772 6752 or gp@nuhs.edu.sg.
At the NUH, we recognise the pivotal role general practitioners (GPs) and family physicians play in providing and ensuring that the general public healthcare is of the highest quality and standard. As such, we believe that through closer partnerships, we can deliver more personalised, comprehensive, and efficient medical care for our mutual patients.

The GPLC aims to build rapport and facilitate collaboration among GPs, family physicians and our specialists. As a central coordinating point, we provide assistance in areas such as patient referrals, continuing medical education (CME) training, and general enquiries about our hospital’s services.

Through building these important platforms of shared care and communication, we hope that our patients will be the greatest beneficiaries.

NUH CME Events

At the NUH, we strive to advance health by integrating excellent clinical care, research and education. As part of our mission, we are committed to provide regular CME events for GPs and family physicians. These events aim to provide the latest and relevant clinical updates practical for your patient care.

Organised jointly by the GPLC and the various clinical departments within NUH, our specialists will present different topics in their own areas of specialities in these monthly symposiums.

For more information on our CME events, you can go to www.nuhcme.com.sg or scan the following QR code.