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Care That Lasts

In This Issue...

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EDITOR'S NOTE

Dr Chee Cheng Ean
Consultant
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SPARK is our biannual magazine at the National University Cancer Institute, Singapore (NCIS), featuring recent discoveries in cancer research and clinical care, events at the NCIS and the most up-to-date news in the cancer world. We hope that SPARK will continue to provide information on our comprehensive cancer care at the NCIS and allow us to strengthen our ties with our community and institutional partners.

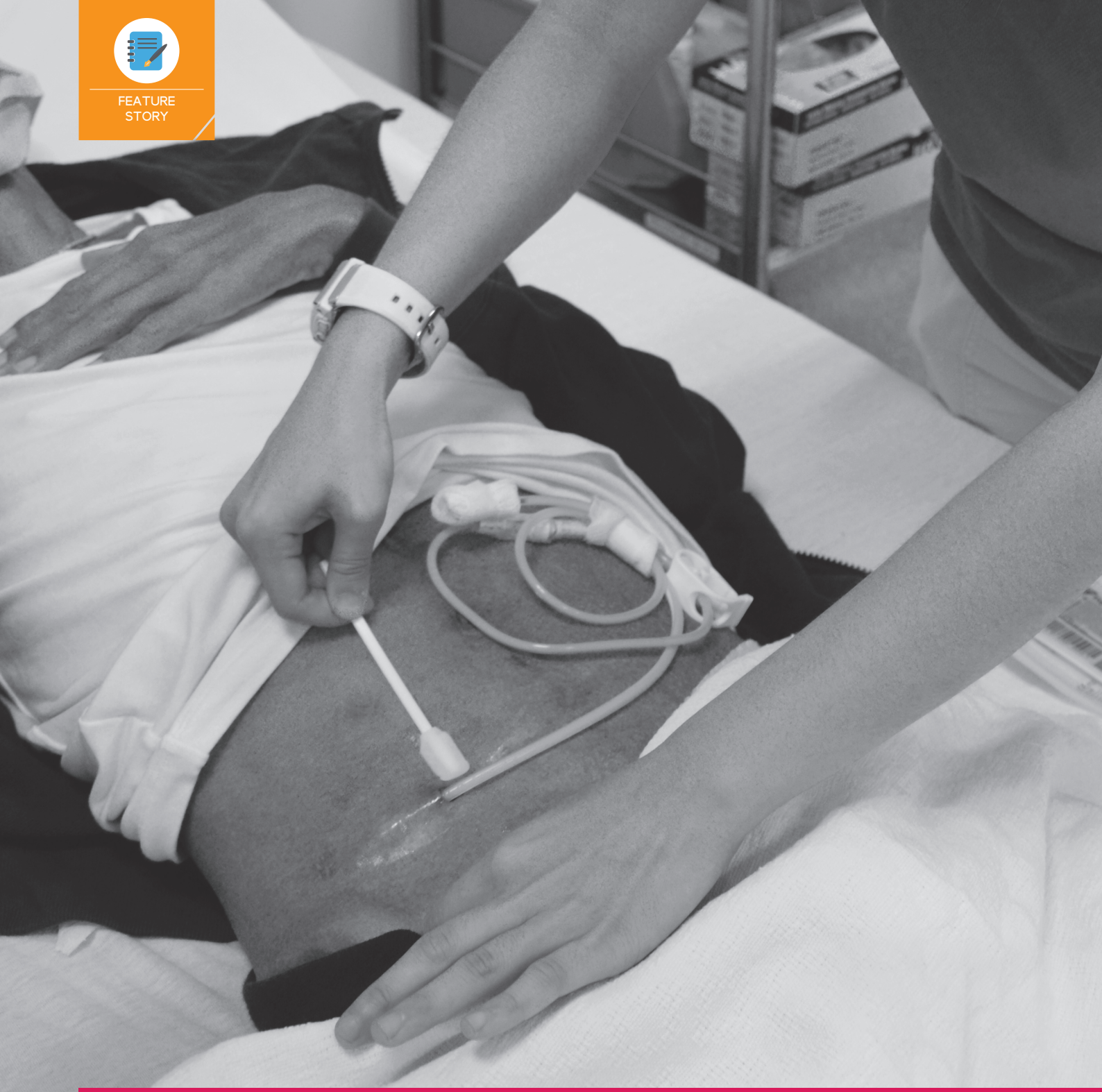
In this second issue, our palliative care team will highlight the oncology long-term catheter service. This service aims to help our palliative care patients, who have recurrent ascites or pleural effusions, to manage their effusions in the comfort of their own homes.

We will also hear from our surgical oncologists with highlights from Colorectal Surgery on HIPEC, Musculoskeletal Surgery on limb salvage and Urology on Prostate Specific Antigen (PSA) screening for prostate cancer.

As we observe Women's Gynaecological Cancer Awareness Month (WGCAM) in July, we also focus on women's cancers in this issue, with a special feature on WGCAM as well as updates on research and clinical trials in breast cancer.

We are now halfway through 2016 but the year ahead remains busy. I hope that you will enjoy reading this issue of SPARK as we continue to improve the lives of our cancer patients.

FEATURE STORY



MANAGEMENT OF MALIGNANT ASCITES IN PALLIATIVE CANCERS

Insertion of tunnelled intra-abdominal catheters

WHAT IS MALIGNANT ASCITES?

Malignant ascites is an abnormal accumulation of fluid in the peritoneal cavity because of cancer. It accounts for around 10 per cent of all ascites and occurs in association with various neoplasms, especially breast, colon, ovarian, pancreas and stomach cancer. It is very common and can present a difficult clinical problem, causing discomfort and distress to many advanced stage patients. In view of their needs, Dr David Tan, Consultant at the Department of Haematology-Oncology, NCIS, spearheaded the Tunnelled Intra-abdominal Catheter project.

PROBLEMS CAUSED BY MALIGNANT ASCITES

Due to the build-up of pressure, malignant ascites can cause various discomforts such as pain from abdominal distension, poor appetite, bowel disturbances or respiratory problems related to diaphragmatic splinting and restricted mobility. Weight gain caused by malignant ascites, may also result in functional problems and issues with self-image and quality of life.

TREATMENT OPTIONS

Malignant ascites can be controlled if the underlying cancer is under control with treatment. However, this is not always possible. Another approach can be via the use of diuretics and procedural draining of the ascites. Most of the time, ascites is recurrent which necessitates repeated drainage for symptom relief. For symptom palliation, the goal is to relieve symptoms.

- ***Medical approach***
  In patients with portal hypertension due to massive liver metastases or cirrhosis with hepatocellular carcinoma, the use of diuretics can be considered. However, in certain tumour groups such as malignant ascites relating to ovarian cancer with carcinomatosis peritoneii, a peritoneal drain will be more useful in addressing the problem.

- ***Procedural approach***
  Case studies suggest that most patients will respond symptomatically to paracentesis (up to 90 per cent), requiring as little as a few litres of fluid to be removed. However, abdominal paracentesis may be required every one to two weeks, depending on the patients' symptom burden.

THE APPROACH TO DRAINAGE:

- ***Short term*** *(hours to days)*
  Bedside abdominal paracentesis is possible but the equipment, nature of drainage or the haemodynamic stability may limit the amount drained. Alternatively, a non-tunnelled abdominal drain (e.g. a Cope-type loop) can be inserted to relieve symptoms and be removed after a few days when drainage volume is reduced. This can also be done at the bedside but is commonly inserted at the National University Hospital's Department of Diagnostic Imaging for oncology patients.

- ***Intermediate term*** *(weeks to months)*
  A non-tunnelled abdominal drain may be used for the short-term, in patients with relatively short prognosis and significant symptom burden. The tube may be left for many weeks until blockage occurs, complications arise, drainage completely dries up, when the patient passes away or when repeated insertion is not suitable. Alternatively, a percutaneous tunnelled abdominal drain, which serves for a longer term placement and usage, can be implanted.

- ***Long term*** *(many months)*
  This approach uses surgical shunting techniques (e.g. Denver-Leveen shunt).

TUNNELLED INTRA-ABDOMINAL CATHETER – CATHETER USED AND HOW IT LOOKS LIKES

The NCIS currently utilises the PleurX system, which is approved by the U.S. Food and Drug Administration (FDA). On the inside, the fenestrated tube contains radiopaque and cuff markings while on the exterior, there is a valve. Its insertion method is percutaneously tunnelled – indwelling. At the NCIS, it is conducted under local anaesthetic (one per cent lignocaine) and abdominal ultrasound guidance at the Diagnostic Imaging Centre.

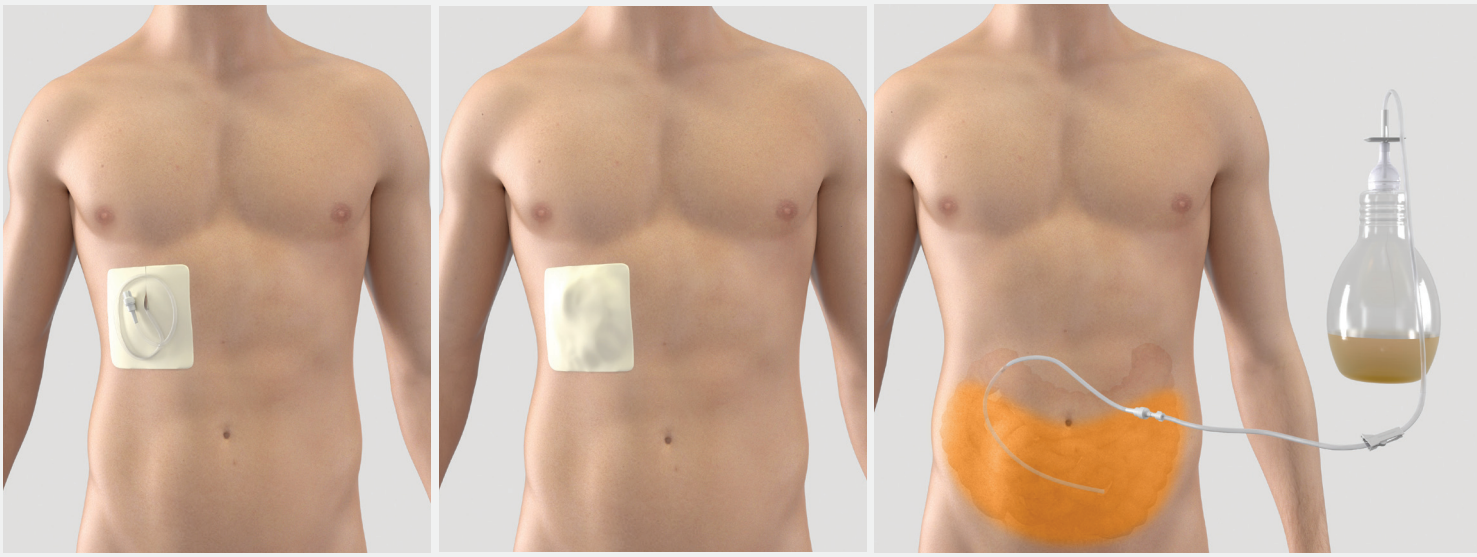
Images are courtesy of Medquest Marketing Pte Ltd

LOCAL ADAPTATIONS – MEANS OF DRAINAGE

In view of the local setting and adaptation, the ascitic fluid is drained by gravity rather than the vacuum system.

Drainage is usually done at home and patients are able to drain according to their comfort level. A smaller volume is recommended as a tunnelled tube will allow patients to drain as per needed. Such frequent drainage may better maintain the haemodynamic stability. Albumin infusion is not required for this unless the rate and volume of drainage is high.

The tube is not connected to any system when not in use, thus allowing patients to continue their daily lifestyle with minor changes (e.g. going back to work with a tunnelled abdominal drain).



Draining of ascitic fluid via a tunnelled tube which allows the patient to drain as required

POTENTIAL BENEFITS

- Effective symptom palliation
- Convenient alternative to repeated drain insertion
- Home management and reduced hospital visits
- Few complications
- Avoidance of associated costs / issues of large volume paracentesis
- Improved quality of life

POTENTIAL RISKS / COMPLICATIONS / ISSUES

- Bleeding
- Perforation
- Infection (e.g. catheter site infection or peritonitis)
- Catheter blockage

Other problems not directly related to the catheter include loculated ascites and unsuccessful drainage. Should significant complications occur, it can be removed.

INDICATIONS FOR TUNNELLED INTRA-ABDOMINAL CATHETER PROCEDURE

- Patients with malignant ascites
- Ascites is unlikely to resolve with anti-cancer treatment i.e. treatment refractory ascites
- Recurrent ascites – Patient has required two or more paracentesis to relieve symptoms within a few weeks (e.g. requiring two or more procedures within six weeks)
- The ascites has not been controlled with spironolactone / furosemide if the main aetiology of the ascites is liver metastases and / or serum-ascitic albumin gradient ⩾11g/l
- Estimated life expectancy is greater than two to three months, but unlikely to be more than a year

Note: As ascites itself implies poor prognosis, selected patients with limited prognosis (but not actively dying) may also be considered for the procedure, so long as the risk and benefits are clearly explained, goals are clearly explored, alternative treatments are offered and there are no significant contraindications.

CONTRAINDICATIONS FOR TUNNELLED INTRA-ABDOMINAL CATHETER PROCEDURE

Relative contraindications

- Chemotherapy carries higher risk of infection
- Hepatorenal syndrome
- Poor social support or circumstances which are likely to compromise the care of PleurX drainage in the community

Absolute contraindications

- Evidence of active infections (focal or systemic)
- Irreversible coagulopathy
- Haemodynamically unstable patients
- Multi-loculated ascites
- Absolute Neutrophil Count <1000/cu mm

CHALLENGES OF PROGNOSTICATION

Prognostication usually poses great challenges. The median survival after a diagnosis of malignancy-related ascites ranges from one to four months, depending on the types of cancer and the patient factors. The catheter is usually placed when active treatment is stopped due to concerns of treatment related infection. However, this usually implies poor prognosis, when the disease no longer responds to treatment and the patient has functionally declined to a very frail state. Therefore, the indication of a "long-term" tube may be questionable.

Prognostication can either be done by a medical oncologist or a palliative care physician and joint discussions will be held if necessary.

The transitional care team at the NCIS

PROGRAMME / SUPPORT SYSTEM

Currently, the primary oncologist will identify suitable patients based on the guidelines available at the NCIS and if necessary, a referral to the palliative care team will be made. Blood tests (FBC, UE's, LFT's, clottings) will be conducted before the procedure, and the patient will be admitted for approximately 24 hours (or less) for insertion, safety monitoring and education of the tube. Thereafter, the patient will be discharged with the help of the transitional care team comprising trained oncology nurses who will conduct home visits intermittently and assist with ascites' drainage depending on the symptoms.

The aim is to support patients and their caregivers and enable them to manage the drainage sessions themselves for a continued period. Patients may also be referred to home hospice services. The goal of transitional care is to transit the patient back to the community and manage any tube related complications. The role of the home hospice team is to provide overall and symptoms support pertaining to progressive advanced cancer. Our cancer hotline, CancerLine *(65) 9722 0569*, managed by our trained oncology nurses, is also offered to patients.

Dr Bernard Wee and his team from the NUH's Department of Diagnostic Imaging

CONCLUSION

As the programme is relatively new, recruitment numbers are still growing. The Tunnelled Intra-abdominal Catheters system has not yet been established in Singapore. While it holds great potential and promise, safety and suitability for full integration in Singapore needs to be ensured. However, the system provides a useful and promising alternative to paracentesis in the management of recurrent symptomatic malignant ascites and the day surgery model is currently being explored by the NCIS.

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Dr Yong graduated from the University of Newcastle-upon-Tyne, UK in 2000. She was trained in Internal Medicine, and subsequently received her postgraduate training in Singapore in Geriatric Medicine and Palliative Care. Awarded by HMDP, she completed her Clinical Fellowship in Palliative Medicine under the University of Alberta, Canada in 2009. As a clinician, her focus is on general palliative care.

Dr David Tan
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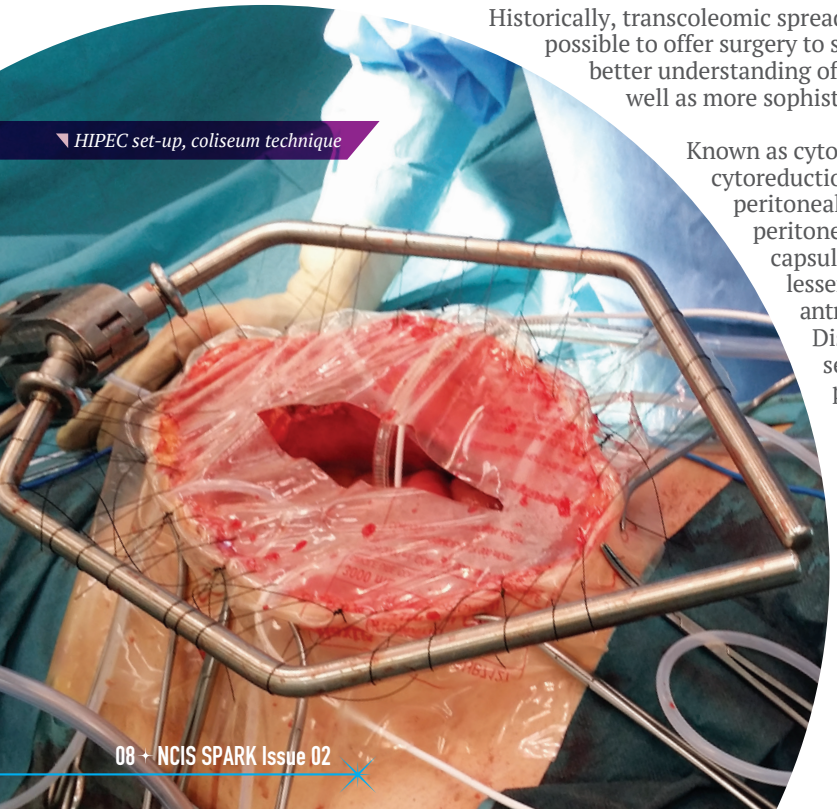
Dr David Tan is a consultant medical oncologist and clinician scientist at the NCIS. He is also an Assistant Professor at the Yong Loo Lin School of Medicine, NUS. Dr Tan graduated with an intercalated BSc in Experimental Pathology and MBBS with Distinction from Guy's, King's and St Thomas' School of Medicine, University of London. He undertook training in internal medicine at Hammersmith, Guy's and St Thomas' Hospitals in London, and obtained his MRCP(UK) in 2005. He was a Cancer Research UK Clinical Research Fellow at the Institute of Cancer Research, London, where he obtained his PhD, and trained in Medical Oncology at the Royal Marsden Hospital, London. He also completed a fellowship in Drug Development and Gynaecologic Oncology at the Princess Margaret Cancer Centre, University of Toronto, before returning to Singapore.

COMBINED TREATMENT FOR PERITONEAL METASTASES FROM COLORECTAL CANCER

The Role of Cytoreductive Surgery (CRS) and Hyperthermic Intra-peritoneal Chemotherapy (HIPEC)

Colorectal cancer is the most common cancer in Singapore. Currently, available screening methods enable the early detection of polyps and cancer, and advances in surgical technology have greatly improved outcomes and survival rates in patients. However, despite these advancements, a significant proportion of patients still present in late stages or have a recurrence of their cancer. To benefit these patients, the Division of Colorectal Surgery at the NCIS and NUH is pushing the boundaries and developing increasingly sophisticated treatment strategies.

Colorectal cancer spreads via lymphatics (approximately 30 to 40 per cent of patients have positive regional lymph nodes at the time of surgery – stage 3 cancer), haematogenic (most commonly leading to liver metastases – stage 4 cancer), or transcoelomic (via the peritoneal cavity – stage 4 cancer) routes.



HIPEC set-up, coliseum technique

Historically, transcoleomic spread had been considered inoperable. However, it is now possible to offer surgery to selected patients due to advances in surgical technology, better understanding of the behaviour and pattern of the spread of the cancer, as well as more sophisticated peri-operative care.

Known as cytoreductive surgery, it aims to achieve the best possible cytoreduction by removing all surgically visible disease present on the peritoneal surfaces. This includes the parietal peritoneum, pelvic peritoneum, peritoneal lining of the diaphragm as well as the liver capsule. Common organs of resection include the greater omentum, lesser omentum, spleen, rectosigmoid colon, ileo-caecal valve, antrum of the stomach, and ovaries and uterus in female patients. Disease on the small bowel and its mesentry can be resected selectively in an attempt to preserve as much small bowel as possible. Invasive nodules through the small bowel require full-thickness resection and repair. The large bowel can potentially be resected in its entirety, leaving the patient with an end-ileostomy.

This surgery requires careful pre-operative assessment with imaging such as CT, MRI and PET scans, to rule out concomitant disease in the liver and thorax, as well as a staging laparoscopy, to adequately assess for the peritoneal cancer index (PCI). The PCI combines size and distribution of the disease and acts as a useful validated prognostic marker. The staging laparoscopy will also determine whether the

Our team at the Division of Colorectal Surgery at the NCIS and NUH

disease is localised in such a way that with removal of the peritoneum and resection of non-essential organs, such as the spleen, a good cytoreductive surgery can be achieved. The main contraindication in most advanced cases is the extensive spread of the cancer to the small bowel and its mesentery.

Cytoreductive surgery is extensive and takes several hours to perform. It requires careful preparation, an open conversation with the patient and between a trained team of surgeons, anaesthetists and theatre staff, as well as post-operative intensive care specialists.

Once the best cytoreduction has been achieved, the patient is prepared for the intra-peritoneal chemotherapy. This requires insertion of inflow and outflow catheters, as well as temperature probes. Meticulous haemostasis is paramount at this stage, as uncontrolled bleeding may require premature termination of the HIPEC. Infusion of the heated chemotherapy agent can be performed with an open or a closed abdomen, taking care not to spill any of the agent. The agent itself is infused at a temperature of approximately 42 degrees Celsius. Depending on the agent, the process takes either 30 minutes (Mitomycin C) or 60 minutes (Oxaliplatin) with concomitant IV injection (Oxaliplatin). Due to the heat, the patient's temperature is monitored closely and he or she can be cooled using a temperature-controlled blanket.

Once the HIPEC has been completed, the abdominal cavity is washed with several litres of water. The in- and outflow catheters remain as drains. If bowel resection has been performed, the bowel ends can be anastomosed.

Post-operatively, the patient will need intensive care unit care, with close monitoring for possible complications.

This advanced form of treatment has dramatically improved survival of patients with peritoneal metastases from colorectal cancer. The median survival of these patients who were traditionally treated with palliative systemic chemotherapy ranges from 13 to 24 months depending on the type of chemotherapy used. However, with the combined treatment of cytoreductive surgery with instillation of hyperthermic intraperitoneal chemotherapy, the median survival has dramatically improved to 22 to 62 months.

The availability of this combined treatment has revolutionised the management of end-stage colorectal cancer, which was once associated with dismal outcomes. At present, HIPEC prolongs survival but does not promise a cure for these patients. However, there are ongoing studies evaluating the use of HIPEC for the prevention and prophylaxis of peritoneal metastases from certain high risk colorectal cancers. We are optimistic about the future of conquering this final frontier in colorectal cancer treatment in the years to come.

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Dr Cheong currently heads the Division of Colorectal Surgery at the NUH. He graduated from the University of Malaya in 1990, obtained his postgraduate qualification from the Royal College of Surgeons of Edinburgh and Royal College of Physicians and Surgeons in 1997, and joined the NUH in 2002.

Dr Bettina Lieske
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Dr Lieske graduated from Friedrich Schiller University in Germany in 2000, obtained her postgraduate qualification from the Royal College of Surgeons of England in 2010 and joined the NUH in 2011.

Together with colleagues in the division of colorectal surgery in the NUH and the NCIS, Dr Cheong and Dr Lieske pushed the boundaries of surgical oncology in colorectal cancer by performing surgery for advanced colorectal cancer using cytoreductive surgery and HIPEC as a treatment offered in the NUH and NCIS.

LIMB SALVAGE IN MUSCULOSKELETAL ONCOLOGY

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

In the last few decades, there have been rapid strides in the evolution of MSO, transforming from a singular orthopaedic surgeon subspecialty to a multi-disciplinary field comprising orthopaedic surgeons, plastic and hand surgeons, paediatric and adult general surgeons, radiologists, radiation oncologists, paediatric and adult medical oncologists, and musculoskeletal pathologists.

RED FLAGS OF MSO

HISTORY	PHYSICAL EXAMINATION
Rapidly growing lesion	General physical examination
Night pain	Lesion is more than 5cm
Constitutional symptoms	Lesion is deeper than the subcutaneous layer
Personal or family history of cancer	Enlarged lymph nodes
Past history of chemotherapy / radiotherapy	Signs of metastases

Previously, MSO treatment was centred on survival (overall and event free survival) as the main measurable outcome, with amputation being the main surgical treatment modality. 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 patients have become significant treatment goals as well.

Limb salvage surgery, also known as limb-sparing surgery, is a highly complex and specialised operation conducted by subspecialty experts in tertiary centres to remove a bone or soft tissue tumour and avoids amputation for patients with malignant tumours affecting the limbs.

With the evolution of MSO as a subspecialty, amputation rates have fallen significantly in most of these tertiary centres. As a surgical fraternity, we continuously push the boundaries of limb salvage surgery as we continue to evolve. Certain 'absolute contraindications' to limb salvage surgery are no longer relevant. For instance, pathological fractures in patients with osteosarcoma are no longer regarded as a contraindication to limb salvage surgery as various studies show that there are no differences in outcomes of limb salvage surgery and amputation, provided that the surgery is carried out by subspecialty experts in tertiary centres and margin control attempts are aggressive.[2,3,4]

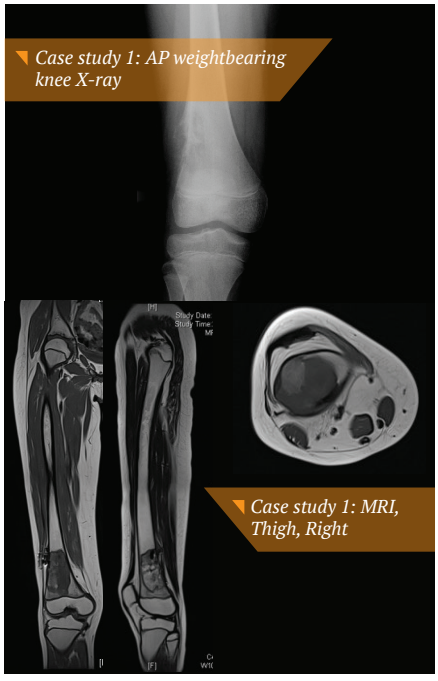
The following case studies illustrate limb salvage surgery in two different paediatric patients with osteosarcoma.

CASE STUDY 1

AKK is an 11-year-old boy who presented with increasing right thigh pain and swelling for two weeks. There was no history of recent leg trauma, constitutional symptoms or similar lumps elsewhere. After preliminary investigations and an open biopsy confirming high grade osteosarcoma, the multi-disciplinary tumour group that conducts weekly meetings came to a consensus for knee joint-sparing surgery, a biological reconstruction using an allograft and preservation of the knee joint. AKK first underwent three months of neoadjuvant chemotherapy followed by restaging imaging.

During preliminary investigations, X-rays 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 showed a 7.8 x 4.9 x 4.6 centimetre (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 physeal plate and there was no involvement of the neurovascular bundle.



Case study 1: AP weightbearing knee X-ray

Case study 1: MRI, Thigh, Right

A whole body bone scan revealed no scintigraphic evidence of bony lesions elsewhere. After chemotherapy, the bony lesion in the distal right femur appeared less intense. A computer topography (CT) scan of the thorax revealed no evidence of pulmonary metastases and no skip lesion was seen elsewhere.

Highly precise preoperative planning and computer guided templating was necessary to obtain an accurately matched structural bone allograft.

A suitable match was found from a 25-year-old donor from the United States. 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.

The right distal femur resection and joint-sparing allograft biological fixation went as planned. Excision 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.

Internal fixation of templated allograft was then carefully conducted using a double plate technique.

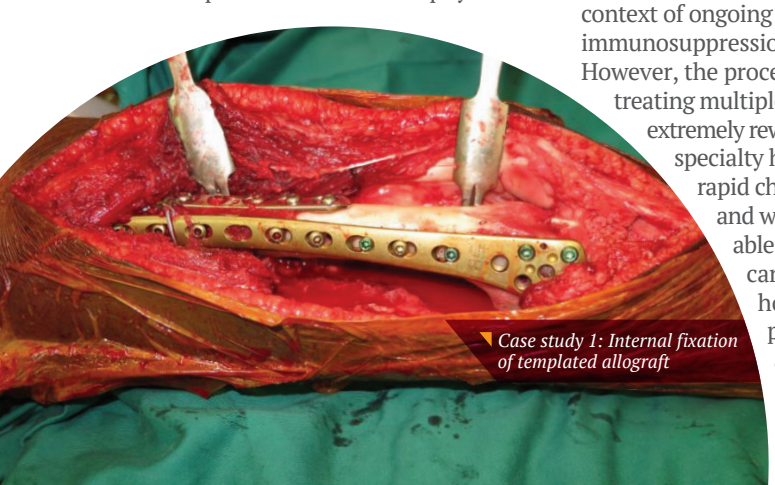
Post operatively, histopathological margins of the resected specimen were confirmed to be negative. AKK recovered well; the distal interface of the host bone allograft has shown good healing. Currently at two months post-surgery and completing adjuvant chemotherapy, he is walking with crutch support and will undergo full weight bearing ambulation in a month's time.

CASE STUDY 2

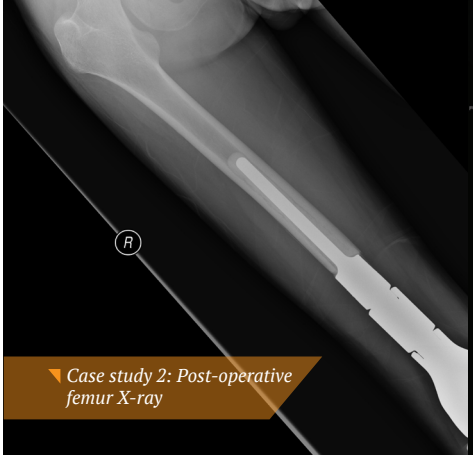
Mr ZBD is a 19-year-old National Serviceman who presented with increasing right knee pain for a month and night pain. A right distal femur confirmed high-grade conventional osteosarcoma. After discussion at the multi-disciplinary tumour board, the decision was made to proceed with distal femur lesion resection and joint replacement using a tumour endoprosthesis as the tumour was adjacent to the joint and joint-sparing surgery would not be possible. Mr ZBD first underwent neoadjuvant chemotherapy followed by restaging imaging.

During preliminary investigations, X-rays revealed a periosteal reaction at the lateral cortex of the diaphyseal region of the right distal femur.

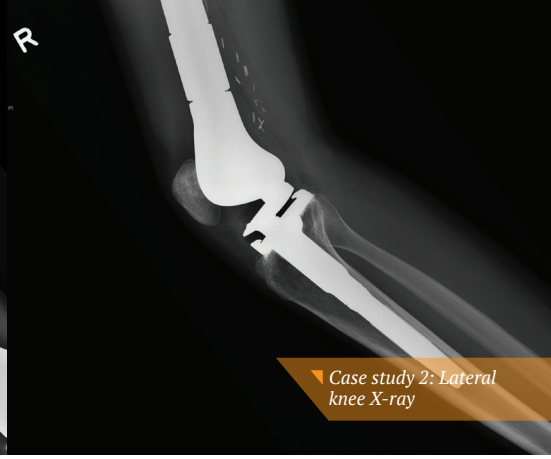
At first, MRI scans of the right thigh and knee showed a destructive lesion in the lateral aspect of the distal metaphysis of the right femur. No fracture, skip lesion or neurovascular involvement was detected. However, the tumour was extremely close to the knee joint. After chemotherapy, the MRI of the right thigh favourably revealed a smaller extraosseous soft tissue component and extent.



Case study 1: Internal fixation of templated allograft



Case study 2: Post-operative femur X-ray



Case study 2: Lateral knee X-ray

The bone scan and CT thorax showed no evidence of distant metastases or skipped lesions. After chemotherapy, the bone scan was less intense.

The operation was performed. Intra-operatively, the neurovascular bundle was found tethered to the femur but was not encased by tumour. Intraoperative frozen section confirmed that all resection margins were clear.

Post-operative imaging showed a stable tumour, endoprosthesis, which 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 at nine months post-surgery. His X-rays done in the clinic earlier this week showed bone growing over the hydroxyapatite coating of the tumour endoprosthesis, suggesting good integration of the prosthesis and host bone junction.

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 is an extremely rewarding one. The MSO specialty has seen massive and 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 help many more patients both locally and internationally.

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Dr Gurpal Singh is a fellowship-trained Orthopaedic surgeon specialising in musculoskeletal oncology and total joint replacement in the NUH. He is also part of the Division of Surgical Oncology (Musculoskeletal Surgery) at the NCIS. Dr Singh's clinical practice consists of musculoskeletal tumours (benign, malignant and metastatic bone disease) with a focus on endoprosthetic reconstruction and limb salvage surgery, as well as primary and revision joint replacement.

His academic interests include osteolysis, periprosthetic tissue responses to wear debris from failed joint replacements, infections and biomaterials in joint replacement. Dr Singh collaborates internationally with a team of musculoskeletal oncologists, arthroplasty surgeons and material scientists from Germany in an effort to continuously improve biomaterials and increase the lifespan of artificial joint prostheses, reduce infection rates and minimise adverse tissue responses from the patient's body.

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TACKLING THE PROBLEMS OF PSA SCREENING

Advances in prostate cancer diagnostics

PROBLEMS OF CURRENT APPROACH TO PROSTATE CANCER DETECTION

Transrectal ultrasound guided biopsy (TRUSB) is the current approach used to detect prostate cancer (PCa) after a suspicious prostate examination or raised prostate specific antigen (PSA). Unfortunately, it is fraught with diagnostic uncertainty. TRUSB is essentially a "blind" systematic sampling of the prostate as the tumours are not visualised on ultrasound, resulting in false negative biopsies (up to 30 per cent) from undersampling or misrepresentation of small low grade lesions as significant cancers.

PSA is not prostate cancer specific. It has a poor specificity (about 25 per cent) for detecting PCa, causing unnecessary biopsies in up to 75 per cent of men. This also brings about unnecessary cost, anxiety and possible morbidity to the patient.

These two issues lead to substantial overdiagnosis and consequently overtreatment of indolent cancers yet still run the risk of underdiagnosis and undertreatment of important cancers. The first issue prompted the United States Preventive Services Task Force (USPTF) to recommend against PSA screening despite high-level evidence that it saves lives and reduces metastatic PCa burden. Abandoning early detection of PCa is clearly not the solution. Instead, the NCIS now has advanced PCa diagnostics to minimise these problems.

ADVANCES IN PROSTATE CANCER BIOMARKERS

p2PSA / PROSTATE HEALTH INDEX TEST

The [-2]proPSA (p2PSA) is the most cancer-specific molecular isoform of free PSA (fPSA). The Prostate Health Index (PHI) is a mathematical formula of three biomarkers – PSA, fPSA and p2PSA. It is used to distinguish PCa from benign prostatic conditions in men aged 50 years and older with a total PSA 2-10 ng/ml, and non-suspicious prostate palpation.

A multi-centre prospective trial with the National University Hospital (NUH) and Tan Tock Seng Hospital validated the PHI in Singaporean men undergoing their first TRUSB for PSA 4-10ng/ml[1]. At a sensitivity of 90 per cent, the specificity of PHI was 58.3 per cent, more than triple the specificity of total PSA at 15.8 per cent, potentially sparing half the cohort from unnecessary biopsies.

Table 1: Interpretation of PHI

PHI range	Probability of cancer	Confidence interval
< 23	8.7%	2.0 - 17.0%
23 - 45	20.6%	17.1 - 24.1%
> 45	43.8%	35.8 - 52.2%

The PHI enables us to risk stratify men with a raised PSA, so that we can better select those more likely to have a positive biopsy. More importantly, a low PHI allows us to reassure men who have had prior negative biopsies but with persistently high PSA that they are at low risk of harbouring significant prostate cancer.

ADVANCES IN PROSTATE CANCER IMAGING

Previously with 1.5T MRI and T2 weighted imaging, only extracapsular extension of prostate cancer could be detected.

Multiparametric MRI (mpMRI) combines multiple functional MRI parameters to the anatomical T2 weighted sequences, and provides the greatest sensitivity and specificity for cancer detection. Combined with an increase in MRI field strength (3T), we are increasingly able to detect anterior and deep central prostate tumours that were previously missed.

Accumulating data shows that while mpMRI cannot detect all prostate cancers, those that it misses are the ones that are unlikely to have an impact on a patient's lifespan. This high negative predictive value may mean that mpMRI could potentially be used to rule out significant disease.

ADVANCES IN PROSTATE BIOPSY – ROBOTIC ASSISTED TRANSPERINEAL MRI FUSION ULTRASOUND GUIDED BIOPSY

With better imaging, we now have the option of a targeted approach to biopsy prostate lesions. The NUH and NCIS have taken advantage of this new approach, using the Mona Lisa® robotic prostate biopsy platform since September 2015.

The prostate MRI performed beforehand is stored in the device, and fused with real-time ultrasound using a digital overlay, enabling the suspicious target lesion(s), previously delineated by a radiologist, to be brought into the aiming mechanism of the ultrasound machine. The fusion results in the creation of a three-dimensional reconstruction of the prostate on which the aiming and tracking of biopsy sites occur (Figures 1 – 3). This is akin to using a GPS to reach your destination rather than driving without directions.

It has the following features:

- Transperineal approach which effectively eliminates the risk of potentially life-threatening post-biopsy sepsis.
- MRI fusion technology allows mapping, targeting and real-time tracking of biopsies of suspicious lesions detected on MRI. This enables us to sample only suspicious lesions seen on MRI, using fewer biopsy cores than current standard biopsy schemes.
- Dual cone concept covers the entire prostate with multiple needles passing through only two perineal skin punctures – compared to multiple perineal skin punctures with standard template grid biopsies.
- For patients without an MRI or one that does not show visible lesions, it provides a very thorough systematic saturation biopsy of the prostate, including the anterior zone, which is notoriously difficult to reach with TRUSB.

However, as this procedure requires patients to undergo general anaesthesia, currently, only men with previous negative TRUSB or contraindications to TRUSB are offered this option.

With MRI guided biopsies, we can confidently biopsy suspicious lesions. For men with low risk prostate cancer on active surveillance, better sampling with the robotic platform allows urologists to more confidently risk stratify them into those who can avoid treatment, or those who need immediate treatment. For men with previous negative TRUSB but persistent suspicion for cancer, the thorough nature of saturation biopsy with this platform allows us to confidently reassure our patients that they do not have significant cancer.

CONCLUSION

The advancements in prostate cancer diagnostics at the NCIS hold great promise in maximising diagnosis of significant PCa, while reducing unnecessary biopsies as well as overdiagnosis and overtreatment of incidental cancers.

Article by
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Consultant
Division of Surgical Oncology (Urology), NCIS

Dr Lincoln Tan is a consultant at the Division of Surgical Oncology (Urology), NCIS. His clinical expertise lies in the minimally invasive treatment of urologic cancers. His research interests lie in prostate cancer biomarkers and image guided biopsy techniques. In 2007, he was a key member of the workgroup appointed by the Ministry of Health to develop the national clinical practice guidelines for prostate cancer screening.

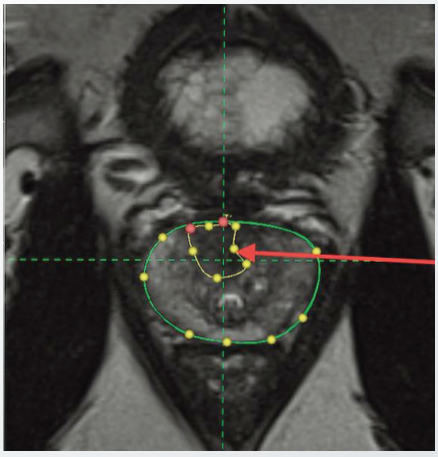

Figure 1: T2 MRI with suspicious lesion marked as target

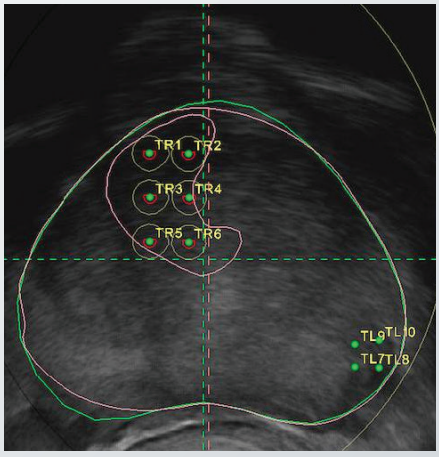

Figure 2: MRI targeted lesions for biopsy fused onto real time transrectal ultrasound image

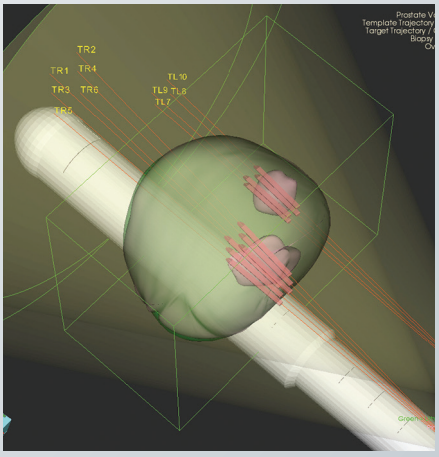

Figure 3: 3D model of MRI-ultrasound fusion, showing targets and biopsy trajectories

Figures 1 – 3 images are courtesy of Biobot Surgical Pte Ltd.

Reference:
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BREAST CANCER
EXPERIMENTAL THERAPEUTICS PROGRAMME

A first-in-man trial of natural killer (NK) cells combined with trastuzumab in HER2+ metastatic breast cancer is currently being conducted. Trastuzumab (Herceptin), a therapeutic monoclonal antibody, is a backbone therapy in HER2+ breast cancer. Apart from inhibiting the HER2 signaling pathway, trastuzumab also induces antibody-directed cell cytotoxicity, although this cell-kill mechanism is minor due to low numbers and weak activity of NK cells in cancer patients. Using a patented technology developed by Professor Dario Campana from the Department of Paediatrics, National University of Singapore, NK cells harvested from patients can be expanded and activated in the laboratory under special culture conditions. These expanded and activated NK cells exert markedly increased cytotoxicity against a variety of cell lines in the laboratory compared to resting NK cells (Figure 1a).

In HER2+ breast cancer cell lines, the addition of trastuzumab further enhanced cell kill by these expanded and activated NK cells. We designed a first-in-man trial of autologous NK cells combined with trastuzumab to test this novel therapeutic approach (Figure 2). Eligible patients are those with metastatic HER2+ breast cancer who have failed at least two lines of anti-HER2 based therapies in the palliative setting. Patients undergo apheresis to harvest NK cells, which are then expanded and activated in culture for 10 to 12 days, before re-infusion into the patient 24 hours after trastuzumab administration. NK cells are kept activated with subcutaneous interleukin-2 injections for six doses, three times per week, starting 24 hours before NK cell infusion.

Thereafter, patients continue on a three-weekly single agent trastuzumab treatment without chemotherapy. Those who achieve sustained stable disease after cycles 4 and 6 receive a second and third NK cell infusion at cycles 6 and 8 respectively. The first three patients received $1x10^6$/kg NK cells with no significant toxicities. The next nine patients were treated at the next dose level of $1x10^7$/kg NK cells, again with no major toxicities. So far, 16 NK cell expansions and infusions have been performed, with three patients receiving a second infusion at cycle 6, and two patients a third infusion at cycle 8. Median NK cell expansion was 337 fold (range 91-478) and comparable to that achieved in healthy donors.

The products contained 81±16% NK cells and were highly cytotoxic (four hour killing of SKBR3 cells, a HER2+ breast cancer cell line, with trastuzumab was 85.8±10.1% at 2:1 effector:target ratio). Median age of the patients was 59, and median lines of prior palliative therapy were six (range two to 13). Treatment was well-tolerated, with the worst toxicity being one case of transient grade 2 thrombocytopenia, and could be safely administered in the outpatient setting. Disease stabilisation was observed in seven out of 11 (64%) evaluable patients, with median progression free survival of 8.5 months in the eight patients who received 10^7/kg NK cells at cycle 1 versus 1.8 months in the three patients who received 10^6/kg NK cells at cycle 1 (Figure 1b).

Expanded and activated NK cells show increased cytotoxicity compared to resting NK cells

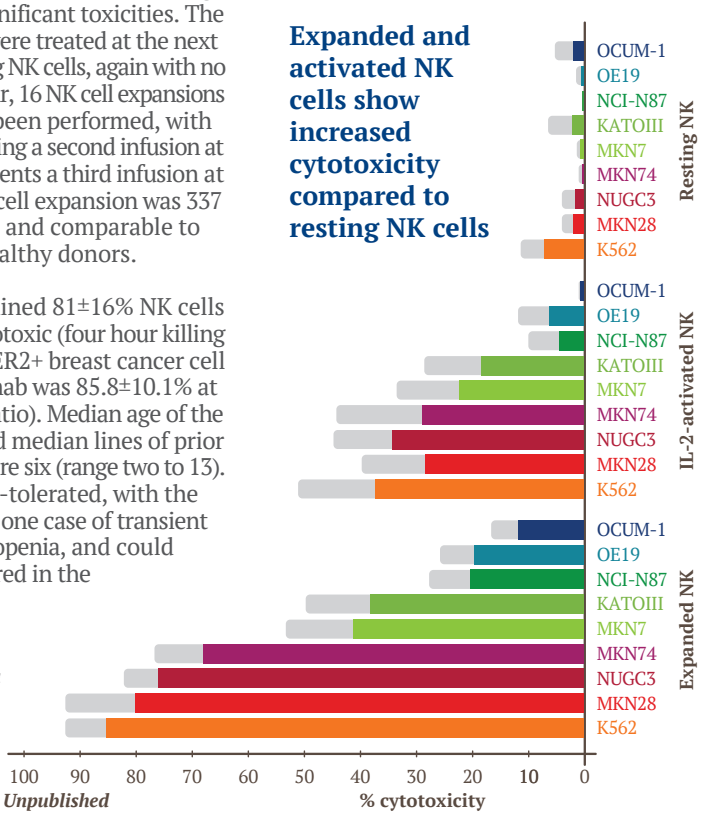


Figure 1a

Kono et al. Unpublished

NK cells + Trastuzumab in HER2+ MBC

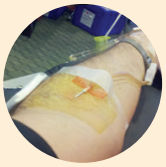
Study Design (First-in-man)

Serial blood sampling for NK cell numbers and ADCC
(pharmacodynamic biomarkers)

- Continue 3-weekly trastuzumab
- Repeat NK cell infusion at cycle 6 and 8 if sustained stable disease at cycle 4 and 6 respectively

Eligible patients: *HER2+ metastatic breast cancer with documented progression*

Apheresis to harvest NK cells



Sufficient for 3-4 expansions

Expansion and activation of NK cells ex vivo x 10-12 days

Trastuzumab followed by NK cell infusion 24 hours later

s/c interleukin 2 x 6 doses to maintain viability of NK cells -Start 24 hours before

Figure 2

Blood taken from patients seven days post-infusion contained NK cells that remained highly cytotoxic against HER2+ breast cancer cell lines. This novel therapeutic strategy is feasible and safe, and resulted in promising disease control in patients with refractory HER2+ breast cancer. Our current plan is to test the safety and efficacy of higher doses of 5-10x10^7/kg NK cells in the next six to twelve patients.

Progression-free survival of refractory HER2+ metastatic breast cancer patients treated with NK cell infusion (n=11)

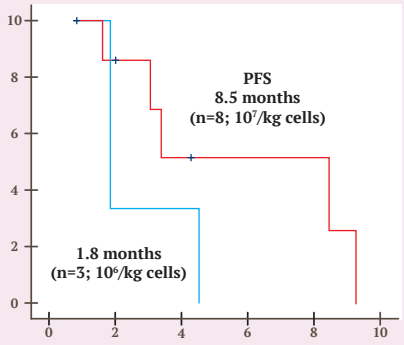


Figure 1b

Article by
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Dr Lee is a Senior Consultant in Medical Oncology and Associate Director of Research at the NCIS. She is also a Senior Principal Investigator at the Cancer Science Institute, Singapore. Her research focuses on breast cancer, pharmacogenetics and cancer genetics, and she has been Principal Investigator of more than 30 industry-sponsored and investigator-initiated breast cancer clinical trials. She directs the NCIS clinical trials unit that supports over 100 Phase I - III therapeutics clinical trials in solid tumours and haematological malignancies. She was awarded the Singapore National Medical Research Council Senior Clinician Scientist Award in 2009 and again in 2015, and has more than 130 peer-reviewed publications.

Pharmacogenetic Study Relevant To Asians: UGT2B17 And Exemestane

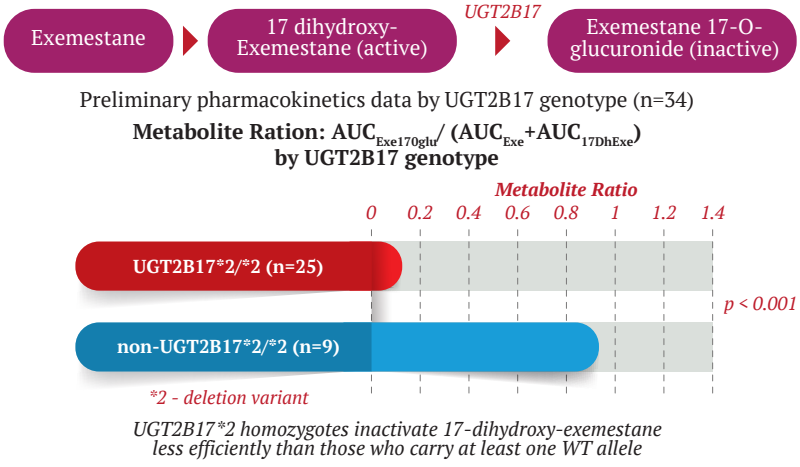
Pharmacogenetics is the study of genetic variants that result in inter-individual or inter-ethnic differences in drug disposition. UGT2B17 is a phase II enzyme involved in glucuronidation, and a deletion variant resulting in reduced enzyme activity has been reported in the UGT2B17 gene which demonstrates interesting inter-ethnic difference. The potential clinical relevance of this inter-ethnic difference was first highlighted in sports medicine in relation to testosterone. Testosterone is converted by UGT2B17 to testosterone glucuronide, and is one of the metabolites that is measured in the urine drug dope test for athletes.

- Swedish investigators previously reported large differences in testosterone excretion between Korean and Swedish men, which were attributed to differences in distribution of the UGT2B17 deletion variant: two-thirds of Korean men were homozygous for the deletion variant, compared to less than 10% of Swedish men. This genetic difference led the lay press to speculate that this 'genetic fluke' may allow certain athletes, i.e., Asian athletes, to evade the drug dope test.

- In 2011, we reported a phase II study of vorinostat, a histone deacetylase inhibitor, in 26 refractory breast cancer patients. Vorinostat is inactivated by UGT2B17, and 72% of our cohort was homozygous for the UGT2B17 deletion variant (UGT2B17 *2/*2). These patients had lower area under the curve (AUC) ratio of vorinostat glucuronide/vorinostat, were exposed to more of the active drug, and were more likely to experience clinical benefit from vorinostat with longer time to progression.

- We are further confirming the clinical relevance of the UGT2B17 deletion variant in our Asian population with exemestane, a steroidal aromatase inhibitor commonly used in hormone receptor positive breast cancer, in a prospective pharmacogenetic study (Figure 3). Exemestane is first converted to an active metabolite, 17-dihydroxy-exemestane, that is then inactivated to exemestane 17-O-glucuronide. Our hypothesis is that patients who are homozygous for the UGT2B17 deletion variant will be exposed to more active drug and therefore derive more clinical benefit.

Pharmacology of Exemestane



*UGT2B17*2 homozygotes inactivate 17-dihydroxy-exemestane less efficiently than those who carry at least one WT allele*

Figure 3

- We have enrolled 62 of the target 110 patients, and preliminary pharmacogenetic/pharmacokinetic data from the first 34 patients showed that those who were homozygous for the UGT2B17 deletion variant indeed had markedly reduced metabolite ratio, confirming our hypothesis that these patients inactivate 17-dihydroxy-exemestane less efficiently than those who carry at least one wildtype allele. We believe this variant, which is common in Asians but rare in Caucasians, may be promising in selecting patients who are most likely to benefit from exemestane in the Asian context.

THE VIRUS THAT CHANGED THE WORLD

Cervical cancer is the second most common cancer in women worldwide. Nearly 85 per cent of incidence is from developing countries where access to cervical cancer screening and prevention are lacking.[1] Majority of women are asymptomatic and present in the late stages where mortality and morbidity from this disease is high.

The discovery of a causal link between Human papillomavirus (HPV) and cervical cancer by Professor Harald Zur Hausen, is considered as one of the most significant discoveries of the 21st century that has led to his Nobel Prize in 2008.[2] This has contributed significantly to our understanding of the pathophysiology of cervical cancer, making total eradication of cervical cancer a realistic possibility.

THE HUMAN PAPILLOMAVIRUS (HPV)

HPV is a double stranded DNA virus which is extremely common worldwide. Transmission is by skin to skin including genital contact; hence those who are sexually active will be infected at some point in their life. Penetrative sex is not a necessity for transmission.[2]

There are more than 100 types of HPV and from these, 14 types are currently recognised to be cancer causing (oncogenic). HPV 16 and 18 are known to cause 70 per cent of cervical cancer. There is also emerging evidence of causal relationship in particular HPV 16, to cancer of the anus, vulva, vagina, penis and oropharynx.

Majority of infection including oncogenic HPV are transient and do not lead to cervical cancer. Approximately 90 per cent of HPV infection clears up within two years. A small proportion of these infections may persist and lead to cervical cancer.[3] Women should be reassured that cervical cancer is an uncommon complication of a very common infection.

SCREENING

Cytology based screening has been the mainstay of cervical cancer screening worldwide for more than 50 years. Countries that adopt an organised cervical screening programme like the United Kingdom, has seen a significant reduction in incidence and mortality from cervical cancer.

The HPV DNA test is a more sensitive method of screening. It provides 60 to 70 per cent greater protection against cervical cancer compared to cytology based screening. A negative HPV DNA test has a significantly lower cumulative incidence rate (CIR) of developing CIN3 or more compared to a negative cytology result (0.3% vs. 0.8%). HPV genotyping also allows for risk stratification in cervical cancer screening leading to better counselling and reassurance for women.[4]

CONCLUSION

Cervical cancer is the only cancer that is preventable. Cervical cancer prevention in this new era must be an all-inclusive package of HPV vaccination and screening. No woman should be burdened with this preventable disease.

Article by
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Dr Ida Ismail-Pratt is a consultant at the Division of Gynaecologic Oncology, NCIS. Apart from being a specialist in obstetrics and gynaecology, she is also a United Kingdom accredited colposcopist working within the NHS Cervical Screening Programme. Her interests are pre-invasive diseases, human papillomavirus, cancer screening and prevention, including a multi-disciplinary approach to care of women with pre-invasive diseases.

HPV VACCINATION

However effective a cervical cancer screening programme is, it will never be able to eradicate cervical cancer entirely on its own. This does not mean cervical cancer screening is not important. Cervical cancer prevention in this new era does not have to rely on cervical cancer screening alone anymore.

The HPV vaccine has been developed as a prophylactic vaccine. It is a viral-like particle, made up of a protein coat with no viral DNA. This allows the vaccine to confer immunity without the ability to infect the host. It has a strong safety profile and to date its most reported adverse effect is pain at the injection site.

There are two HPV vaccines available. Both cover HPV 16 and 18. The quadrivalent vaccine also covers HPV 6 and 11 which causes 90 per cent of genital warts. Both the quadrivalent and bivalent vaccines are extremely effective, giving protection of above 95 per cent.[5,6]

Protection is best if the vaccine is given to women prior to their exposure to HPV infection. Women, who are already exposed to HPV infection e.g sexually active or previous history of CIN, will have limited protection. National school HPV vaccination programme plays a pivotal role in order to ensure this benefit.

Australia was one of the first countries to adopt a school HPV vaccination programme, leading to significant reduction in incidence of CIN3 and above and a near total eradication of genital warts.[7]

Currently, HPV vaccination is available in Singapore and is licensed for women and men between the ages of 9 to 26 years old.

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A DAY IN THE LIFE OF AN ONCOLOGY NURSE

A Beacon of Hope for Cancer Patients

"Nursing has always been my first love."

Yvonne Ng
Assistant Nurse Clinician

In this feature, we delve into the everyday work of Yvonne Ng, Assistant Nurse Clinician at the National University Cancer Institute, Singapore (NCIS).

CAN YOU DESCRIBE A TYPICAL DAY AT WORK?

Having worked in the oncology unit for 13 years, there is not one typical day at the Cancer Centre. Every day, I look forward to the challenges and satisfaction of providing care to my patients, their caregivers, colleagues and the public. My day starts with ensuring the ambulatory centre is organised and ready for patients. Although it may sound mundane, it is an important responsibility of an oncology nurse as it affects the entire patient experience and care team. Meanwhile, I will also plan ahead by examining the patient list and anticipating their needs and treatment-related complications. This is vital, especially for first-time patients and patients undergoing a complex regimen or being administered drugs with the risk of hypersensitivity. This also facilitates in helping patients alleviate their anxiety and keeps us alert for potential emergencies.

After registration, patients are shown to their assigned chemotherapy treatment chair. When I first meet patients, I make it a point to smile and greet them cheerfully to cheer them up. I will also assess their appearance and observe their non-verbal demeanour. For patients with signs of anxiety and apprehension, I will initiate light-hearted conversations to reassure them and put them at ease.

Thereafter, I will conduct a quick and comprehensive assessment of their general condition before preparing to cannulate and set up the intravenous access. This process can be fairly challenging, especially for patients with thrombosed veins. During this, I try to reflect on finding alternative ways to further reduce our patients' anxieties, particularly those who have had unpleasant experiences with pain, uncomfortable side effects from treatment, or difficulties at home.

WHAT ARE SOME NECESSARY SKILLS REQUIRED FOR CHEMOTHERAPY ADMINISTRATION?

Undeniably, knowledge and technical skills are critical to patient safety and quality of care. To maintain competency in them, nurses must undergo training and competency reviews. We also need to keep ourselves updated on the latest chemotherapy regimens and clinical trial guidelines, and acquire skills for new methods in drug delivery. Before any treatment is administered, we need to conduct a comprehensive assessment on patients to establish if they are fit for treatment on that day. This includes ensuring they understand the side effects and self-care methods to carry out at home.

However, I believe an oncology nurse should have more than just clinical knowledge, as the care we provide goes beyond this. We also need to possess compassion, empathy and courage, as cancer is an emotionally demanding disease. I tend to be more patient and understanding towards our patients, as I know their battle with cancer is not easy.

I strongly advocate a holistic approach, where patients' well-being and quality of life are just as important as the treatment itself. Once, I encountered a patient who had a phobia of having a cannula inserted into her. I stayed by her side and held her hand to calm her down until she was mentally and emotionally ready to receive treatment.

DO YOU FIND JOY WORKING WITH CANCER PATIENTS?

Some may perceive working in an oncology unit to be sad, stressful and a place of hopelessness. When I tell my friends and relatives that I specialise in oncology, they will give me a look of sorrow and pity. To me, this is a misconception as I truly find pure joy working in an environment with true courage, selflessness, unconditional love and care. I am constantly awed by the genuine humanity among loved ones, and heartened by strangers bonding and becoming bosom buddies through their cancer journeys.

I had a patient with advanced-stage breast cancer but she was determined and never gave up on treatment. Although it pains me to see her become wheelchair-bound, I witnessed first-hand her family's strong support and her positive disposition through it all. When she passed on, her husband gave me a copy of her memoir, which contains her heartfelt words of gratitude to us (her medical team). This truly touched my heart and made my day.

Although my work can be challenging at times, I derive fulfilment and purpose engaging with patients from all walks of life who cope with their conditions differently. The fighting spirit that they have exhibited during their cancer journeys has given me courage and I have forged close bonds with some of them.

WHAT MAKES YOU PROUD TO BE AN ONCOLOGY NURSE?

Being an oncology nurse is indeed a privilege. As much as I have given, I too have received – gratitude from my patients and their family, admiration from my colleagues and friends, and most of all, the profound and valuable life lessons learnt from my patients. I am a changed person – a better nurse who respects and advocates for my patients, a wiser person in making life decisions, and one who is thankful each day for the lives I have touched and been touched by.

I am proud that I have the courage to nurse, educate and guide my patients during their treatment, while maintaining composure and controlling my emotions when some of them fail to respond to treatment. However, nothing gives me greater job satisfaction than seeing my patients recover and resume their daily lives.

WHAT ARE SOME PERSONAL GOALS AND DREAMS YOU HOPE TO ACHIEVE?

I have already achieved my dream of becoming a nurse! I only wish for good health to continue living my dream and providing good service, I hope to inspire the younger generation of nurses, to let them know that despite the challenges of oncology nursing, one can gain so much gratification and purpose!

Volunteers at the NCIS booth educating members of the public on the importance of breast self-examinations

WORLD CANCER DAY 2016

We Can. I Can.

The National University Cancer Institute, Singapore (NCIS) commemorates World Cancer Day, a global observance on 4 February annually. This year, a one-day event was organised on 20 February 2016 at the Toa Payoh HDB Hub via an inaugural collaboration between the NCIS, Singapore Cancer Society and National Cancer Centre Singapore. The event aimed to generate awareness and educate the public about cancer through educational talks and booths.

The bilingual talks, comprising English and Mandarin sessions, enlightened the audience about cancer prevention. Dr Ida Ismail-Pratt, Consultant, Division of Gynaecologic Oncology, NCIS, touched on the key focus of the event in her talk, women's gynaecological cancers, including breast cancer. Other speakers included Dr Lim Siew Eng, Associate Director (Clinical – Education) and Senior Consultant, Department of Haematology-Oncology, NCIS, and Ms Esther Lin, Senior Dietitian, National University Hospital, who shared on how nutrition correlates with cancer prevention as well as the interlink between Traditional Chinese Medicine (TCM) and cancer.

The educational booths featured breast self-examination demonstrations conducted by the NCIS and interactive educational games about cancer awareness, among others. Participants were also able to collect a Faecal Immunochemical Test (FIT) kit as well as sign up for Pap Smear and mammogram screenings at no cost. The event was supported by the Health Promotion Board, and sponsored by MSD Singapore, Olympus and Yakult.

The event received overwhelming response with close to 1,200 participants and a majority of the talks oversubscribed.

SINGAPORE'S FIRST MUSCULOSKELETAL PUBLIC FORUM

Lumps & Bumps: Is It Cancer?

Sarcoma, a rare but aggressive cancer that affects people across all age groups, currently accounts for one per cent of all cancers and is able to grow at any site in the body, including the muscles, fats or bones in limbs, breasts, head and neck area, uterus, stomach and intestines.

To educate the public on sarcoma, the National University Cancer Institute, Singapore (NCIS) organised Singapore's first-ever Musculoskeletal Public Forum, in collaboration with the KK Women's and Children's Hospital, National Cancer Centre Singapore and Singapore Sarcoma Consortium, on 7 May 2016 at the National University Health System Tower Block Auditorium.

Themed "Lumps & Bumps: Is It Cancer?", the forum commenced with a welcome address by Professor Chng Wee Joo, Director, NCIS, followed by insightful talks by multi-disciplinary and cross-institutional speakers. The speakers from the NCIS included Dr Mark Puhaindran, Senior Consultant, and Dr Gurpal Singh, Consultant, both from the Division of Surgical Oncology (Musculoskeletal Surgery); Dr Choo Bok Ai, Consultant, Department of Radiation Oncology; and Dr Chetan Dhamne, Associate Consultant, Division of Paediatric Haematology-Oncology, who covered a spectrum of topics on Musculoskeletal Cancer such as identifying cancer lumps, the use of radiation, and treatment in adults and children.

Other highlights included sharing sessions by inspirational sarcoma cancer survivors, including a book signing by Ms Tan Ter Cheah, who lost her leg to sarcoma as a child and eventually conquered it. Today, Ms Tan is a successful career woman with two children, and her journey with sarcoma was documented in her autobiography titled "One". The forum also marked the official launch of the first Sarcoma Support Group in Singapore, a milestone which was signified by a cake-cutting ceremony.

The event received positive response, with over 250 participants comprising members of the public, staff, cancer patients, survivors and their caregivers. A participant shared, "This public forum is an eye-opener for those who have not heard of sarcoma. Thumbs up to the organisers!"

SPOTLIGHT

2ND BI-NATIONAL CANCER SYMPOSIUM

Facilitating Cross-Institutional Collaborations

The 2nd Bi-National Cancer Symposium was held at the National University of Singapore (NUS) on 31 March 2016. Jointly organised by the National University Cancer Institute, Singapore (NCIS), NUS, Cancer Science Institute Singapore (CSI) and University of Southern California (USC) Norris Comprehensive Cancer Centre, the symposium aimed to bring together researchers from the NCIS, NUS and USC with complementary knowledge and expertise to exchange ideas, information, and build collaborative ties.

Professor John Wong, Chief Executive, National University Health System (NUHS) and Professor Stephen Gruber, Director, USC, initiated the symposium with a welcome address each. Following this, cross-institutional speakers presented 11 talks on topics spanning across Precision Oncology, Imaging, Genome Instability, ER Stress, Epigenetics and Experimental Therapeutics.

Adjunct Associate Professor Lee Soo Chin, Associate Director (Research) and Senior Consultant, Department of Haematology-Oncology, NCIS, spoke on the NCIS' developmental therapeutics programme for breast cancer and Adjunct Associate Professor Goh Boon Cher, Head and Senior Consultant, Department of Haematology-Oncology, NCIS, shared developmental therapeutics for nasopharyngeal carcinoma. Director and Senior Consultant from the Department of Haematology-Oncology, NCIS, Professor Chng Wee Joo, also presented on the non-canonical role of EzH2 in cancers.

The symposium was well-received with positive feedback from participants. Dr Chee Cheng Ean, Consultant, Department of Haematology-Oncology, NCIS, shared, "This was a great opportunity to establish collaborations with well-established investigators in Gastrointestinal Oncology. I look forward to working with Dr Lenz and Dr Gruber on future research projects." Professor Philip Koeffler, Deputy Director (Research), NCIS, added, "The symposium has launched several cross-Pacific collaborations."

Dr Ivan Tham, Head and Senior Consultant, Department of Radiation Oncology, NCIS, also commented, "It was an eye-opening experience to see so many distinguished faculties from the USC. To me, Professor Conti's insights on cancer imaging were very useful. Evidently, their programme is very well-established and the symposium was an excellent platform to exchange ideas."

NMRC AWARDS 2016

Congratulations to our NCIS Award Winners!

Winners of the NMRC Awards 2016

This year, five doctors from the National University Cancer Institute, Singapore (NCIS) were conferred the National Medical Research Council (NMRC) Awards. The NMRC Awards aim to recognise the outstanding achievements and contributions of clinician scientists and researchers, and support them in developing breakthrough research that yield positive outcomes for patients.

Professor Dario Campana, Mrs Lee Kong Chian Chair in Advanced Cellular Therapy, won the prestigious Singapore Translational Research (STaR) Investigator Award, which includes research funding, salary support and a grant. Professor Campana said, "This award will allow us to continue our research towards developing new immunotherapies for cancer."

Adjunct Associate Professor Lee Soo Chin, Associate Director (Research) and Senior Consultant, and Adjunct Associate Professor Goh Boon Cher, Head and Senior Consultant, both from the Department of Haematology-Oncology, clinched the Clinician Scientist Award (CSA) – Senior Investigator (SI). Comprising the SI level and Investigator level, the CSA provides salary support and a grant.

Dr Ng Chin Hin, Consultant, and Dr Raghav Sundar, Associate Consultant, also from the Department of Haematology-Oncology, achieved the NMRC Research Training Fellowship. The fellowship funds salary and tuition fees for both a local graduate research degree programme, and an overseas research attachment with allowances and benefits.

Dr Sundar said, "It is an honour to be awarded this fellowship, which allows me to pursue my aspiration of becoming a clinician scientist and enables us to bring new ideas from the bench to the bedside to direct patient care."

Dr Ng also shared, "I feel grateful to the NMRC for helping me hone my expertise in early phase clinical trials. This is a niche that is still developing in Singapore and more qualified early phase clinical trialists could render more translational studies. I aim to develop novel combination targeted therapies that is efficacious yet less toxic to our cancer patients."

Congratulations to all the winners as we continue to celebrate excellence in academic medicine!

THE NCIS CANCER FUND
Championing Research For Hope

In 2015, over 300 cancer patients (more than 1,300 cancer patients since 2010) participated in therapeutic clinical trials funded by the National University Cancer Institute, Singapore (NCIS) Cancer Fund. This has created major breakthroughs in cancer research by NCIS clinician scientists and researchers, transforming patient care significantly over the past few years.

For instance, the discovery of genetic changes has enabled the prediction of survival rates in childhood leukaemia patients, resulting in new diagnostic tests to identify patients who need the right treatment earlier. A clinical study on the "YAP" cancer gene[1] found a new aspect of cancer cell behaviour that could potentially uncover novel modalities for cancer treatment. Additionally, the Randomised Clinical Phase II/III Trial for IntraPeritoneal Chemotherapy examines its role in women with epithelial ovarian, fallopian tube or primary peritoneal cancer to improve clinical outcomes. The study has seen positive response with 20 patients recruited thus far, making the NCIS the seventh highest recruiting site out of 57 total international study sites.

Such cancer advancements are only made possible through a concerted team effort by our patients, clinicians, scientists, researchers and donors who shape the future of cancer treatment by exploring multiple possibilities.

Between 2010 to 2015, multiple donations have funded 30 cancer research projects for various cancers including liver, head and neck, lung, breast, blood, colorectal, nasopharyngeal and gynaecological cancers.

Article by
Dr Yong Wei Peng
Associate Director (Research)
& Senior Consultant
Department of Haematology-Oncology, NCIS

Dr Yong Wei Peng is the Associate Director (Research) and Senior Consultant, Department of Haematology-Oncology at the NCIS. He is also a Principal Associate at the Cancer Science Institute, National University of Singapore (NUS). Dr Yong leads the therapeutic arm (NUH module) of the Singapore Gastric Cancer Consortium. The consortium received the prestigious Translational Clinical Research grant in 2007. He is also the Chairman of the National Healthcare Group Domain-Specific Ethics Review Board. His clinical interest is in gastrointestinal cancers and his research interests are pharmacogenetics and epigenetics in cancer.

"FRIENDS OF NCIS"
To express our deepest gratitude to our donors, also known as "Friends of NCIS", a donor board is displayed at our Cancer Centre located at Level 10 of the NUH Medical Centre.

They are also regularly invited for get-togethers with our senior management and staff to find out how their donations have benefited and made a difference in the lives of our cancer patients.

GIVE HOPE, TRANSFORM LIVES
Become a "Friend of NCIS" by funding cutting-edge research at the NCIS and giving hope to our patients, and their families.

Every individual and corporate donation will make a difference to the progress of cancer research and help transform lives.

To make a contribution, please contact ***Ms Chng Li Ming*** at ***(65) 6772 7884*** or ***li_ming_chng@nuhs.edu.sg.*** To find out more about the NCIS Cancer Fund, visit www.ncis.com.sg.

[1]*The "YAP" cancer gene is a potent oncogene that is commonly amplified in liver, breast and pancreatic cancer.*

SATELLITE PHLEBOTOMY @ BOON LAY WELLNESS CENTRE
A Convenient Blood Drawing Service

The National University Cancer Institute, Singapore (NCIS) has commenced satellite phlebotomy services at the Boon Lay Wellness Centre for all our cancer patients from 28 March 2016. The service is administered by our trained oncology home care nurses and targets patients residing in the West of Singapore so as to provide them with greater convenience and reduced waiting and travelling time.

The service is only available from Mondays to Wednesdays between 12.00pm-1.00pm and is strictly by appointment only. Patients who require a blood test may approach our clinic staff or call in to schedule an appointment. The appointment must be scheduled at least one day in advance of the patient's consultation or treatment.

Once the patient has arrived at the centre on his or her scheduled appointment date, our oncology nurse will perform the blood drawing process on the patient. The patient's blood will then be sent back to the National University Hospital for testing and the results will be available to his or her doctor. The doctor will inform the patient of the results during the next consultation session.

Getting There:
Boon Lay Wellness Centre is located at Blk 209 Boon Lay Place #01-239, S640209. It is only a 10-minute walk away from Lakeside MRT Station and is accessible by bus services 99, 240 and 246.

To schedule a new appointment or change an existing appointment, contact ***(65) 6773 7888*** or email ***CancerApptLine@nuhs.edu.sg***.

SUPPLEMENTS

SPECIALIST AND TUMOUR GROUP LISTING

Referral no: (65) 6773 7888
Email: CancerApptLine@nuhs.edu.sg
Website: www.ncis.com.sg

BLOOD CANCERS AND BLOOD DISORDERS

Bone Marrow and Stem Cell Transplant Programme

Haematology-Oncology
Dr Koh Liang Piu (Leader)
Dr Michelle Poon Li Mei
Dr Tan Lip Kun

Radiation Oncology
Dr Balamurugan A Vellayappan
Dr Ivan Tham Weng Keong

Diagnostic Imaging
Dr Khor Lih Kin
Dr Loi Hoi Yin

Coagulation

Haematology-Oncology
Dr Liu Te Chih (Leader)
Dr Lee Shir Ying
Dr Yap Eng Soo

General Haematology

Haematology-Oncology
Dr Liu Te Chih (Leader)
Dr Lee Shir Ying
Dr Ng Chin Hin
Dr Tung Moon Ley

Leukaemia, Myelodysplastic and Myeloproliferative Neoplasms (MDS/MPN)

Haematology-Oncology
Dr Ng Chin Hin (Leader)
Dr Esther Chan Hian Li
Dr Koh Liang Piu
Dr Melissa Ooi Gaik Ming
Dr Tan Lip Kun
Dr Tung Moon Ley

Radiation Oncology
Dr Ivan Tham Weng Keong
Dr Balamurugan A Vellayappan

Diagnostic Imaging
Dr Khor Lih Kin
Dr Loi Hoi Yin

Lymphoma

Haematology-Oncology
Dr Michelle Poon Li Mei (Leader)
Dr Esther Chan Hian Li
Dr Tan Lip Kun

Radiation Oncology
Dr Ivan Tham Weng Keong
Dr Balamurugan A Vellayappan

Diagnostic Imaging
Dr Arvind Kumar Sinha
Dr Khor Lih Kin
Dr Loi Hoi Yin

Multiple Myeloma

Haematology-Oncology
Prof Chng Wee Joo (Leader)
Dr Melissa Ooi Gaik Ming

Radiation Oncology
Dr Ivan Tham Weng Keong
Dr Balamurugan A Vellayappan

Diagnostic Imaging
Dr Arvind Kumar Sinha
Dr Khor Lih Kin
Dr Loi Hoi Yin

BREAST CANCER

Surgical Oncology
Dr Chan Ching Wan (Leader)
A/Prof Mikael Bo Anders Hartman
A/Prof Philip Iau Tsau Choong
Dr Shaik Ahmad Bin Syed Buhari
Dr Tang Siau-Wei

Diagnostic Imaging
A/Prof Quek Swee Tian
Dr Pooja Jagmohan
Dr Jeevesh Kapur
Dr Henry Oscar
Dr Premilla Pillay
Dr Felicity Pool

Pathology
A/Prof Thomas Choudary Putti

Haematology-Oncology
Prof John Wong Eu-Li
Adj A/Prof Lee Soo Chin
Dr Lim Siew Eng
Dr Lim Yi Wan
Dr Tan Sing Huang
Dr Andrea Wong Li Ann

Radiation Oncology
Dr Choo Bok Ai
Dr Koh Wee Yao
Dr Johann Tang I-Hsiung
Dr Balamurugan A Vellayappan

Plastic, Reconstructive & Aesthetic Surgery
Dr Jane Lim
Dr Ong Wei Chen
Dr Yap Yan Lin

COLORECTAL CANCER

Surgical Oncology
Dr Cheong Wai Kit (Leader)
Dr Chong Choon Seng
Dr Ridzuan Farouk
Dr Sharon Koh Zhiling
Dr Lee Kuok Chung
Dr Bettina Lieske
Dr Frances Lim Sheau Huei
Dr Tan Ker Kan

Gastroenterology & Hepatology
Dr David Ong Eng Hui

Diagnostic Imaging
Dr Bertrand Ang Wei Leng
Dr Lynette Teo Li San
Dr Thian Yee Liang

Pathology
Prof Teh Ming
Dr Brendan Pang Nhgee Kheem

Haematology-Oncology
Dr Chee Cheng Ean
Dr Thomas Soh I Peng
Dr Yong Wei Peng

Radiation Oncology
Dr Leong Cheng Nang
Dr Jeremy Tey Chee Seong

GYNAECOLOGIC CANCER

Gynaecologic Oncology
A/Prof Jeffrey Low Jen Hui (Leader)
A/Prof Arunachalam Ilancheran
Dr Ida Ismail-Pratt
Dr Joseph Ng Soon Yau
Dr Pearl Tong

Diagnostic Imaging
Dr Bertrand Ang Wei Leng
Dr Wynne Chua Yuru
Dr Pooja Jagmohan
Dr Khor Lih Kin
Dr Ong Ching Ching
Dr Thian Yee Liang

Pathology
A/Prof Raju Gangaraju Changal
Dr Qasim Ahmed
Dr Diana Lim Gkeok Stzuan

Haematology-Oncology
Dr Lim Siew Eng
Dr Lim Yi Wan
Dr David Tan Shao Peng

Radiation Oncology
Dr Choo Bok Ai
Dr Vicky Koh
Dr Johann Tang I-Hsiung

HEAD & NECK CANCER

Surgical Oncology
A/Prof Thomas Loh Kwok Seng (Leader)
Dr Lim Chwee Ming
Dr Jane Lim
Dr Tan Wee Boon

Diagnostic Imaging
Prof Vincent Chong Fook Hin
Dr Choong Chih Ching
Dr Tan Ai Peng
Dr Eric Ting
Dr Jocelyn Wong Yen Ling

Pathology
A/Prof Fredrik Bengt Petersson

Haematology-Oncology
Adj A/Prof Goh Boon Cher
Dr Tan Chee Seng

Radiation Oncology
Dr Timothy Cheo
Dr Francis Ho
Dr Ivan Tham Weng Keong
Dr Wong Lea Choung

THYROID CANCER

Surgical Oncology
A/Prof Thomas Loh Kwok Seng (Leader)
A/Prof Thirugnanam Agasthian
Dr Lim Chwee Ming
Dr Frances Lim
Dr Ngiam Kee Yuan
Dr Rajeev Parameswaran
Dr Tan Wee Boon

Endocrinology
E/Prof Lim Pin
Dr Chionh Siok Bee
Dr Doddabele S Deepak
Dr Kao Shih Ling
Dr Eric Khoo Yin Hao
Dr Soh Lip Min
Dr Samantha Yang

Diagnostic Imaging
Dr Arvind Kumar Sinha
Dr Khor Lih Kin

Pathology
A/Prof Nga Min En
A/Prof Fredrik Bengt Petersson
Dr Qasim Ahmed

Haematology-Oncology
Adj A/Prof Goh Boon Cher

LIVER, PANCREATIC AND BILARY (HPB) CANCER

Surgical Oncology
Dr Iyer Shridhar Ganpathi (Leader)
Prof Krishnakumar Madhavan
Dr Alfred Kow Wei Chieh

Gastroenterology & Hepatology
Prof Lawrence Ho Khek Yu
Prof Lim Seng Gee
A/Prof Dan Yock Young
Dr Bhavesh Kishor Doshi
Dr Michelle Angela Gowans
Dr Leo Hartono Juanda
Dr Lee Guan Huei
Dr Lee Keat Hong
Dr Lee Yin Mei
Dr Kieron Lim Boon Leng
Dr Low How Cheng
Dr Tan Poh Seng
Dr Thwin Maung Aye

Diagnostic Imaging
E/Prof Lenny Tan
Dr Khor Lih Kin
Dr Stanley Loh Eu Kuang
Dr Neo Wee Thong
Dr Prapul Rajendran
Dr Mangat Kamarjit Singh
Dr Pavel Singh
Dr Thian Yee Liang
Dr Bernard Wee
Dr Yang Cunli

Pathology
Prof Aileen Wee
Dr Pang Yin Huei
Dr Benjamin Wong Pak Kwong

Haematology-Oncology
Dr Chee Cheng Ean
Dr Thomas Soh I Peng
Dr Yong Wei Peng

Radiation Oncology
Dr Francis Ho
Dr Leong Cheng Nang
Dr Jeremy Tey Chee Seong

LUNG/THORACIC CANCER

Haematology-Oncology
Dr Ross Soo (Leader)
Adj A/Prof Goh Boon Cher
Dr Chin Tan Min
Dr Tan Chee Seng
Dr Alvin Wong Seng Cheong

Surgical Oncology
A/Prof John Tam Kit Chung
A/Prof Thirugnanam Agasthian

Respiratory & Critical Care Medicine
Prof Lim Tow Keang
A/Prof Lee Pyng
Dr Adrian Kee
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Diagnostic Imaging
Dr Arvind Kumar Sinha
Dr Anil Gopinathan
Dr Loi Hoi Yin
Dr Lynette Teo Li San

Pathology
Dr Seet Ju Ee

Radiation Oncology
Dr Koh Wee Yao
Dr Leong Cheng Nang
Dr Ivan Tham Weng Keong

PROSTATE/UROLOGY CANCER

Surgical Oncology
Prof Kesavan Esuvaranathan (Leader)
A/Prof Edmund Chiong
Dr David Terrence Consigliere
Dr Lincoln Tan Guan Lim
Dr Tiong Ho Yee

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Dr Bertrand Ang Wei Leng
Dr Wynne Chua Yuru
Dr Edwin Siew Poh Yiew

Pathology
Prof Teh Ming
Dr Thomas Paulaj Thamboo

Haematology-Oncology
Prof John Wong Eu-Li
Dr Alvin Wong Seng Cheong

Radiation Oncology
Dr David Chia
Dr Keith Lim Hsiu Chin
Dr Jeremy Tey Chee Seong

UPPER GASTROINTESTINAL CANCER

Surgical Oncology
A/Prof Jimmy So Bok Yan (Leader)
E/Prof Ti Thiow Kong
Dr Asim Shabbir

Gastroenterology & Hepatology
Prof Lawrence Ho Khek Yu
A/Prof Yeoh Khay Guan
Dr Lim Li Lin
Dr David Ong Eng Hui

Diagnostic Imaging
Dr Prapul Rajendran
Dr Pavel Singh
Dr Bernard Wee
Dr Yang Cunli
Dr Yeong Kuan Yuen

Pathology
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Dr Brendan Pang Nghee Kheem
Dr Benjamin Wong Pak Kwong

Haematology-Oncology
Dr Chee Cheng Ean
Dr Thomas Soh I Peng
Dr Yong Wei Peng

Radiation Oncology
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Dr Kimpo Miriam
Dr Tan Poh Lin
Dr Mariflor Villegas
Dr Frances Yeap

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Dr Johann Tang I-Hsiung

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Dr Ooi Kiat Huat
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Dr Jamie Zhou

Radiation Oncology
Dr Wong Lea Choung

Psychological Medicine
A/Prof Rathi Mahendran
Dr Terence Leong Sun Chee

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Haematology-Oncology
Adj A/Prof Goh Boon Cher (Leader)
Prof Chng Wee Joo
Adj A/Prof Lee Soo Chin
Dr Chee Cheng Ean
Dr Ross Soo
Dr David Tan
Dr Andrea Wong
Dr Yong Wei Peng

EVERY PERSON MATTERS

With the patient at the heart of all our programmes, we bring professionals across multi-disciplines including doctors, surgeons, nurses, medical professionals, pharmacists and rehabilitative therapists to provide a broad spectrum of cancer care and management, from screening and early diagnosis to treatment and long-term care.

National University Cancer Institute, Singapore
A member of the NUHS

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