

THE ROLE OF MINIMALLY INVASIVE SURGERY IN THE MANAGEMENT OF GYNAECOLOGIC CANCERS

by Dr Felix Chan

Surgery plays an important role in the management of gynaecological malignancies. The role of minimally invasive surgery in the management of these cancers continues to expand.

CERVICAL CANCER

Radical vaginal trachelectomy with laparoscopic pelvic lymphadenectomy has emerged as a safe, reasonable option for women with early-stage cervical cancer who desire fertility preservation.¹

Similarly, laparoscopically assisted radical vaginal hysterectomy has been systemically described as feasible and can be offered to women with early-stage cervical cancer who do not desire future childbearing.²

ENDOMETRIAL CANCER

In the treatment of early stage endometrial cancer, the surgical approach of laparoscopic hysterectomy, peritoneal washings, and pelvic and para-aortic node dissection, with or without an omentectomy, is being compared with the same surgery via laparotomy.³ Large case series and randomised controlled trials are emerging in Australia and international centres showing safety, comparable long term survival with reduced hospital stay and better quality of life. Endemic obesity continues to be the leading cause for endometrial cancer. Laparoscopic treatment reduces the analgesic requirement, hospital stay, wound and respiratory complication.

OVARIAN CANCER

In ovarian cancer, minimally invasive surgery has been incorporated to manage early-stage, advanced-stage, and recurrent disease, as well as second-look procedures. Hand assisted laparoscopy has been described managing larger volume primary and recurrent gynaecological cancers.⁴

Intraperitoneal chemotherapy has shown improvement in disease free intervals for patients with optimally debulked epithelial ovarian cancer. A port and flexible catheter can be inserted using laparoscopic guidance to ensure proper placement. Adhesions can be divided to promote even distribution of a peritoneal chemotherapy agent.

Extraperitoneal laparoscopy for para-aortic and pelvic lymph node dissections has been

shown to yield adequate nodal counts and to be safe and feasible in the management of gynaecological cancers.⁵

OTHER APPLICATIONS

Ovaries can be transposed to the upper abdomen in patients with advanced cervical cancer receiving chemo-radiotherapy, to preserve ovarian function, especially in younger patients. The ovaries are separated from the uterine body with their blood supply transposed above the pelvic brim to avoid the potential harmful effect of scattered radiation.

Oocytes preservation is performed with operative laparoscopic wedge resection of the ovary. This opens the options for young patients to preserve their oocytes before receiving potential long term side effects from chemotherapy and radiotherapy. Successful pregnancy has been reported through surrogate mothers. The procedure can be carried out as a day procedure without a significant delay in cancer treatment.

FOR PATIENT SELECTION

Operative laparoscopy has been used as a means of determining a patient's eligibility for pelvic exenteration for recurrent cervical cancer. It has proven to be a valuable step in the work up and management of patients with locally recurrent cervical cancer. This helps to prevent unnecessary laparotomies, and associated reduction in morbidity and a shorter postoperative stay. Appropriate palliation care can also be carried out. The use of a PET scan helps to further refine the selection process.⁶

Laparoscopic assisted ileostomy and colostomy have also been seen to palliate symptoms of entero and or colonic vaginal fistula. This helps to improve a patient's quality of life with reduction in pain, the length of hospital stay and to avoid the risk of a laparotomy.

Laparoscopy is now frequently used to assess the aetiology for patient with ascites. If a patient presents with radiological evidence of ascites after a detailed history, physical examination, laboratory tests, and a pan-endoscopy, an operative laparoscopy can help to obtain tissue to confirm the diagnosis. Omental, peritoneal, nodal biopsy and drainage of ascitic fluid can be performed as a day procedure.

Risk reduction surgery for familial cancer syndrome can be carried out laparoscopically for peritoneal washing, removal of fallopian tubes, ovaries, and uterus with the added benefit of being minimally invasive. This increases the therapeutic benefit of the surgery with minimal disruption of a patient's quality of life. Detailed histological analysis on a collected specimen is used to exclude occult cancer. Rapid development of molecular biology and improved understanding of familial cancer syndrome and prophylactic surgery has become an important, integral treatment option after expert counselling.

Prospective studies are in progress to look at the expanding role of minimally invasive surgery and open surgery.

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ACUPUNCTURE IN CANCER CARE

by Dr Byeongsang Oh

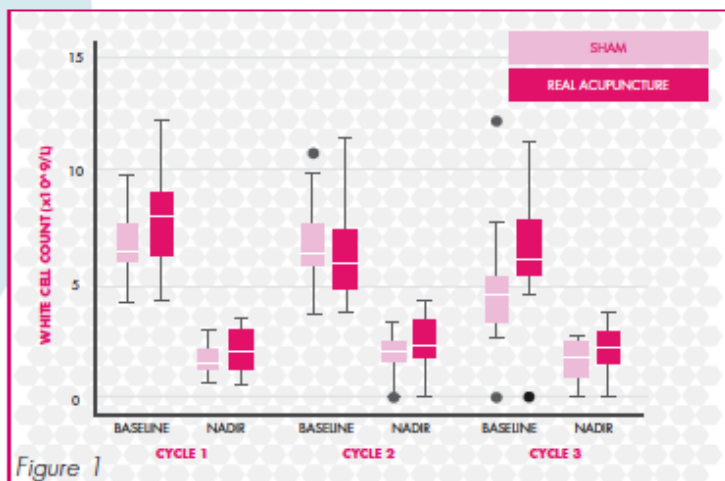


Figure 1

The incidence of cancer worldwide has risen over the past decade. Medical progress has ensured a multitude of therapies are available for cancer. However, some treatments have significant side effects and many cancer related symptoms are difficult to manage. Acupuncture and complementary and alternative medicine (CAM) therapies are widely used by cancer patients both in Australia and abroad.^{1,4} It has been reported that 20-84% of cancer patients use some form of CAM therapies.⁵⁻⁸ The use of acupuncture specifically has increased substantially in Western countries. According to a recent survey by the American Hospital Association (AHA 2008), up to 72% hospitals including the Memorial Sloan-Kettering Cancer Center (MSKC), Dana-Farber Cancer Institute (DFCI) and MD Anderson Cancer Center were offering evidence-based CAM therapies including acupuncture after research, and 84%

of hospitals indicated patients demand as the primary rationale for offering acupuncture and CAM services.

Recently, concurrent use of CAM therapies, especially acupuncture, has gained increasing popularity in relieving some side effects. Acupuncture is a safe, virtually painless and effective form of Traditional Chinese Medicine that has been practiced for thousands of years in Eastern countries (China, Japan and Korea). Acupuncture involves the stimulation of specific points on the body with fine, disposable needles or finger pressure. It works through the body's nervous system and other mechanisms to relieve many physical ailments and emotional problems.

Recent scientific research with advanced technologies proposed that acupuncture produces its effects through regulating the

nervous system, thus aiding the activity of biochemical agents including endorphins and immune system cells at specific sites in the body. In addition, studies have shown that acupuncture may alter brain chemistry by changing the release of neurotransmitters and neurohormones and thus, affecting parts of the central nervous system related to sensation and involuntary body functions, such as immune reactions and processes that regulate a person's blood pressure, blood flow, and body temperature.⁹

Studies suggest that acupuncture can improve low back pain,¹⁰ be used for symptomatic treatment of osteoarthritis of the knee,¹¹ and effectively manage a range of psychoneurological issues.¹² Specifically in relation to cancer, emerging evidence from randomised clinical trials have shown that acupuncture can provide important symptom benefits and reduce side effects commonly experienced by cancer patients. Studies using acupuncture have suggested that acupuncture may have the potential to effectively manage depression,¹³ chemotherapy-induced nausea and vomiting,¹⁴ chemotherapy-related neutropenia,¹⁵ chemotherapy-related hot flushes,^{16,17} cancer fatigue,¹⁸ cancer treatment related pain including joint pain,^{19,20} radiation-induced xerostomia,¹⁵ and overall well-being.²¹ Our recent acupuncture study on female breast cancer patients conducted at the Sydney Cancer Center, RPAH also found that acupuncture has a potential to improve chemotherapy induced nausea and vomiting, white blood cell count and neutrophil count. (Figure 1&2) Furthermore, acupuncture is increasingly becoming incorporated into standard care, being included in a variety of oncology clinics and hospices in the UK²² and USA.²³⁻²⁵ In Australia, the Sydney Adventist Hospital was one of the first hospitals to recognise the importance of acupuncture and CAM therapies in cancer care and introduced acupuncture services in 2010.

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References available on request.

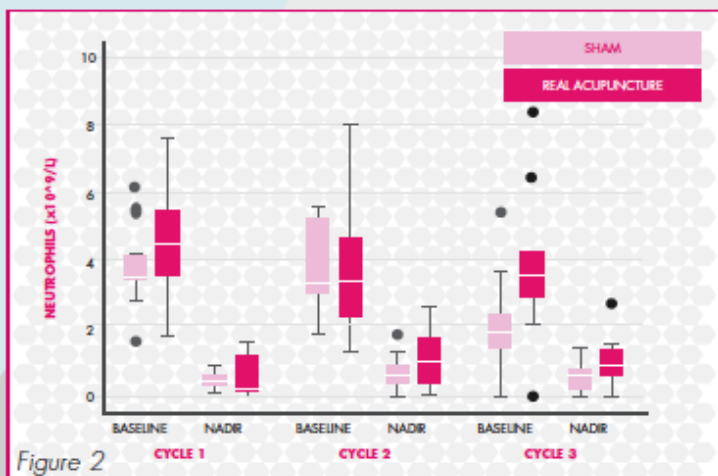


Figure 2



DR
BYEONGSANG
OH

Dr Oh established the Australian Integrative Medicine Services (AIMS) at Sydney Adventist Hospital and Royal North Shore Hospital, and specialises in integrative oncology (acupuncture, Medical Qigong and a Complementary and Alternative Medicine consultation service).

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CASTRATE RESISTANT PROSTATE CANCER PROGRESS TO 2011

by A/Prof Gavin Marx

Prostate cancer is a significant problem in Australia with more than 18,000 new cases diagnosed and approximately 3,000 deaths per annum. Although there remains some debate regarding the role of screening, PSA detection has increased the number of new diagnoses.

Treatment options at diagnosis are dependent on a number of factors: extent of localised disease, gleason grade, presence of metastases, Prostate Specific Antigen (PSA), co-morbidities and patient preferences. Depending on these factors treatment options would include active surveillance, a radiotherapeutic approach or a surgical approach. Initial treatment for those patients with relapsed or metastatic disease would include hormonal manipulation through androgen deprivation. These strategies may involve LHRH agonists, orchidectomy, anti androgen therapy, combined androgen deprivation, intermittent androgen deprivation or androgen withdrawal therapy. As outlined in Figure 1, some patients will become resistant to castrate levels of testosterone. This paper outlines the progress in systemic treatment options for these patients with castrate resistant prostate cancer (CRPC).

Castrate resistant prostate cancer (CRPC) consists of a heterogeneous group of patients, ranging from patients with asymptomatic biochemical progression

only, to patients with high volume metastatic disease involving the bone and viscera.¹ The ideal timing for commencement of cytotoxics remains somewhat controversial.² Early palliative care intervention, local radiation therapy and appropriate utilisation of bisphosphonates are important modalities that need to be incorporated into the multidisciplinary approach to this disease.

Not all patients with CRPC require systemic therapy. Consideration of extent of disease, presence of metastases (particularly visceral), PSA doubling time, gleason score, presence of systemic symptoms, competing co-morbidities and patient preference will influence the decisions regarding timing and systemic chemotherapy options (REF APJOH).

Historically, the median survival for CRPC was 10-12 months. The management of CRPC has dramatically changed since 2004 when it was recognised that cytotoxics can improve survival. Docetaxel (Taxotere) has emerged as the standard first line chemotherapy for CRPC since 2004, based on two phase III studies demonstrating a survival benefit.^{3, 4} In the landmark TAX-327 trial,³ 1006 men with chemotherapy-naïve metastatic CRPC (either asymptomatic or symptomatic) were randomised to three treatment arms: docetaxel 3 weekly vs. docetaxel weekly vs. mitoxantrone. This study demonstrated

improved survival in patients treated with the 3 weekly docetaxel regimen. In the most recent update,⁸ the survival benefit of 3 weekly docetaxel has persisted to over 19 months with a 3 year survival rate of 18%. Furthermore, it provided PSA, quality of life and symptom control benefits.

Despite first line docetaxel chemotherapy providing a modest overall survival benefit, the prognosis of patients with CRPC remains limited. In 2010, three randomised control trials have demonstrated survival benefits in the second line, post docetaxel setting. Interestingly, these have been utilising 3 different modalities: cytotoxic (Cabazitaxel),⁹ hormonal (Abiraterone)¹⁰ and immune-therapy (Sipuleucel-T)¹¹.

CABAZITAXEL

The TROPIC trial evaluated the role of cabazitaxel, a semi-synthetic taxane developed to overcome the emergence of taxane resistance, versus mitoxantrone in the second line setting. Seven hundred and fifty five patients were randomised in a multicentre international trial of carbazitaxel versus mitoxantrone. The groups were well matched and approximately 75% of patients in each arm had relapsed within 3 months of completing docetaxel therapy. There was a significant improvement in overall survival (15.1 months versus 12.7 months, $p < 0.0001$). Response rate and PSA response also reached statistical significance. The main toxicities were fatigue, myelosuppression (including febrile neutropenia) and diarrhoea.⁹

SIPULEUCEL-T

The IMPACT trial evaluated the role of immunotherapy in asymptomatic or minimally symptomatic metastatic CRPC. Patients were randomised in a 2:1 ratio to Sipuleucel-T versus placebo 2 weekly for 3 episodes. Sipuleucel-T is a novel cell-based vaccine composed of autologous antigen-presenting peripheral blood mononuclear cells that have been exposed to a

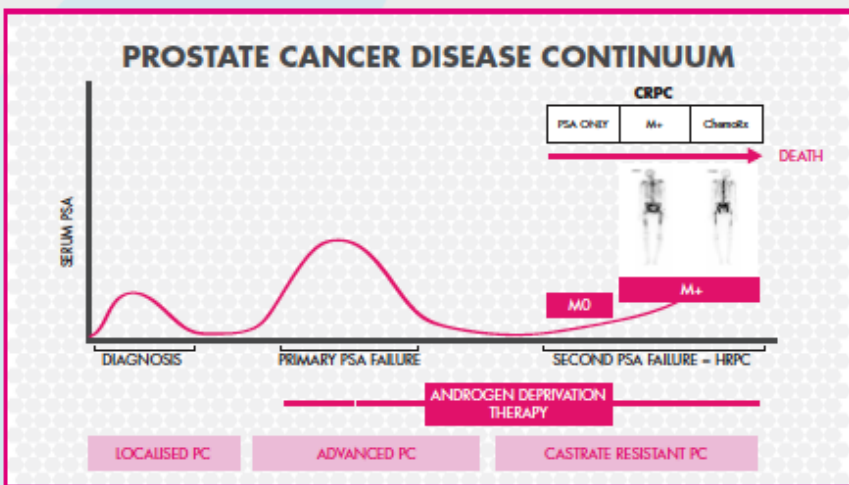


Figure 1. Prostate Cancer Disease Continuum



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recombinant protein consisting of granulocyte-macrophage, colony-stimulating factor fused to prostatic-acid phosphatase, a protein expressed by prostate cancer cells. Upon administration, the vaccine may stimulate an antitumor T-cell response against tumour cells. The results confirmed an improvement in the primary endpoint of overall survival (25.8 months versus 21.7 months). This study is the first positive study for immune based therapy in CRPC and may have a role in second line therapy in the future.¹¹ This agent has recently been approved by the FDA. Although the costs of this agent may be prohibitive, this is an important trial that highlights a proof of principle potential benefits with immune modulated therapy in this setting.

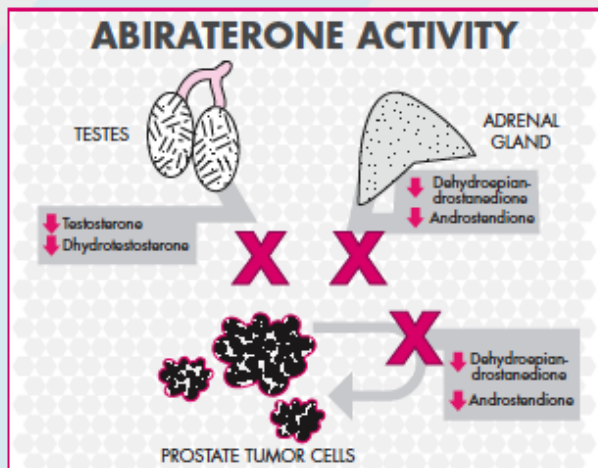
ABIRATERONE ACETATE

Ongoing research into the biology and mechanisms of resistance at the androgen receptor level in CRPC has resulted in an improvement in our understanding of this complex process. A number of contributing factors have been identified including; non-gonadal sources of androgens, androgen receptor over-expression, mutation, and activation by coactivators. These pathways and factors are potential targets for therapeutic interventions. Studies involving agents targeting the androgen receptor in CRPC have recently been completed or are nearing completion. Abiraterone acetate, an oral,

potent irreversible inhibitor of CYP17 has been evaluated in the second line setting. Importantly this agent provides potent inhibition of testosterone production in the testes, adrenals and intra-tumoral. These data have recently been published in abstract form demonstrating a survival and PSA benefit compared with placebo.¹⁰

Despite significant progress in the last few years with CRPC, the outcomes still remain poor. Identification of factors and biomarkers that predict which patients will most likely need and benefit from a particular treatment modality is needed. Ongoing research in the setting of CRPC to optimise treatment options, with the objectives of survival prolongation, improvement in quality of life and pain management, and appropriate patient selection is ongoing. Improved understanding of the mechanisms and biology of androgen resistance has proven important in the development of novel treatment options and clinical trial design. Continued inclusion and support for well designed clinical trials remains an important approach to further improve the outcomes for patients with CRPC. A focus on selection and utilisation of appropriate biomarkers as predictors of response is required in future trials to better aid physicians in the most clinically relevant treatment option for our patients with CRPC.

References available on request.



NEWS FROM THE SAN

The Sydney Adventist Hospital Clinical School of The University

of Sydney was opened on February 9 by Her Excellency Marie Bashir AC CVO, Governor of NSW and Chancellor of The University of Sydney. It is the first fully-fledged private hospital clinical school in NSW offering training for future doctors, physiotherapists, pharmacists and other health professionals. The opening was attended by over 250 guests.

12 stage one medical students, 28 new physiotherapy students, 20 pharmacy students, and 2 health informatics students will undertake clinical training at the SAH Clinical School in 2011.

SAN CANCER SUPPORT GROUPS

San Cancer Support Groups and resources are available free to any cancer patients, irrespective of where their treatment is provided.

- **Bowel Cancer Group** - 10am Thurs (alternate weeks)
- **Breast Cancer Group (women)** - 1pm Tues
- **General Group** - 10am Wed
- **Carcinoid Group** - 1:30pm 3rd Thurs
- **Gynaecological Group (women)** - 10am 3rd Monday
- **Look Good / Feel Better Workshops** 10am Tues (4 - 6 weekly)
- **Lung Cancer Group** - 10am Thurs (alternate weeks)
- **Meditation/Relaxation** - 10am Thurs, Support Group follows at 11am
- **Prostate Cancer Group** - 2.30pm 2nd Monday or 7pm 4th Monday
- **Stoma Group** - 10am 1st Wed

San Cancer Support ph: 9487 9061

NEWLY ACCREDITED DOCTORS

- | | |
|--|---|
| Dr Shawn Li – Anaesthesia | Dr Cindy Pan – Surgical Assistant |
| Dr Andrew Fong – Radiation Oncology | Dr Rajesh Bedi – Surgical Assistant |
| Dr Luke Timmermans – Surgical Assistant | Dr Shyan Goh – Surgical Assistant |
| Dr Jenny Yang – Surgical Assistant | Dr Bruce Greig – Surgical Assistant |
| Dr Fiona Pearce – Surgical Assistant | Dr Chung Kwun Won – Surgical Assistant |