Journal of
Family Practice Oncology

Issue Number 26, Spring 2016 | www.fpon.ca

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Changing outlooks on metastatic cancer – hope for long term cancer control

Gillian lives a full life 11 years after a diagnosis of metastatic breast cancer.

By many physicians' estimations, Gillian should not have survived the high risk HER2+ breast cancer she was diagnosed with in 2003. She had a mastectomy in her 30s followed by high dose chemotherapy and radiation. Then, eight months later, she was admitted to hospital on oxygen and narcotics, with rapid escalation of pain throughout her skeleton. Her bone marrow was packed with breast cancer cells that were behaving like an acute leukemia, and were easily visible on peripheral blood smear. The cancer cells also filled her pulmonary capillaries leading to significant hypoxia.

BC Cancer Agency Medical Oncologist, Dr. Lee Ann Martin, treated Gillian with further chemotherapy plus Trastuzumab (Herceptin®), a targeted antibody therapy that became available for management of HER2+ breast cancer. Within weeks her pain disappeared, her breathing returned to normal and she went home to her young family and back to her career. She has remained on Herceptin® for more than 11 years, receiving this monoclonal antibody every three weeks.

"Targeted therapies are changing how we think about metastatic cancers particularly breast, lung, gastrointestinal and blood cancers," notes Dr. Martin. "Special tests determine if a patient has one of the subtypes that can benefit hugely from targeted therapy and support the oncologist's decision regarding whether a treatment is likely to improve a patient's quality of life and even their expected survival."

continued on page 2

Palliative care posters and patient information cards for your office

Increasing understanding and promoting the benefits of the early adoption of palliative care are the aims of two new resources for family physicians' offices throughout BC and the Yukon. Thanks to a collaborative effort between the Family Practice Oncology Network and the BC Cancer Agency's Pain and Symptom Management/Palliative Care Program, copies of a newly developed poster and patient information card are available at no cost. Two copies of the information card are enclosed.

"One of the biggest barriers to receiving good quality palliative care is the erroneous belief that palliative care is only for end-of-life care," notes Dr. Pippa Hawley, Medical Leader of the Agency's Pain & Symptom Management/Palliative Care Program. These materials feature the new "Bow Tie" visual showing how a palliative approach to care is now considered appropriate for people living with serious illness irrespective of prognosis. This approach can be helpful right from the time of diagnosis and whether such patients expect to get better eventually or not. Much (if not all) of the early palliative approach to care, such as excellent symptom control, advance care planning discussions, and access to programs and services, can readily be accomplished in a family practice setting."

Contact Lindsay Muldoe to request copies, lmuldoe@bccancer.bc.ca

Tribute to Dr. Phil White, longtime Network Chair and Medical Director

Dr. Phil White was a driving in force in advancing cancer care at the community level.

The Family Practice Oncology Network lost one of its most passionate and dedicated supporters this past December when Dr. Phil White passed away from pancreatic cancer. Dr. White was one of the Network's original chairs leading its governing Council and serving as Medical Director since its establishment in 2002.

Under his leadership, the Network developed its internationally renowned General Practitioner in Oncology Training Program; its nationally accredited Oncology CME Webcast Program offered in partnership with the University of British Columbia's Division of Continuing Professional Development (UBC CPD), this Journal of Family Practice Oncology, its annually sold-out Family Practice Oncology CME Day; and again with UBC CPD, its series of community cancer workshops for family physicians. Dr. White also led the development and publication of a collection of cancer care guidelines customized specifically for family physicians the most recent being the newly published Upper Gastrointestinal Cancer Guidelines (see page 11).

Dr. White truly believed in the Network's rationale of supporting family physicians to strengthen their oncology skills and knowledge, and to take on a greater role in caring for their cancer patients.

Along with his Agency role with, Dr. White was also a highly regarded family physician in Kelowna and Chief of Staff at Kelowna General Hospital from 1983 to 2001. He was also an active member of the Doctors of BC, a board member of Ovarian Cancer Canada and took part enthusiastically in many other initiatives dedicated to improving primary care oncology. We miss him very much and extend our condolences to his family and friends.

Changing outlooks on metastatic cancer continued from page 1

"The Trastuzumab antibody, for example, was one of the first applications of a means to target specific cancer cells and direct the body's own immune system to destroy these cells without significantly affecting the rest of the body's tissues. With such developments, a diagnosis of widely disseminated metastatic cancer may no longer lead to the pronouncement 'You have only a few weeks or months to live'."

"There are still subtypes where we have not yet found that crucial target, but our expertise and development of new agents is expanding rapidly, meaning that a given patient's prognosis may exceed months or years beyond previous expectations. Such developments can enable long term cancer control; hence, re-categorizing some types of cancer as a chronic disease."

"I knew Gillian's response could be remarkable, but we had no idea just how well it was going to work both for her and for others in the same situation. All cancer centres around the world now have cohorts of patients with advanced metastatic HER2+ breast cancer living 10 years and more. Since 2005, we now administer Herceptin® in the adjuvant (post surgical) setting combined with chemotherapy leading to an increase in curative outcomes."

Gillian's View

I want to share my story as I have lived longer than anyone expected and enjoy an excellent quality of life. My children were in grades four and six when I was first diagnosed and my goal then was to see them both graduate. Thanks to Herceptin®, my diligent care team, and great support from my family, I made it! My new goal is to see my grandchildren.

I encourage family physicians to change their perception of metastatic cancer patients. Please don't regard our cases as hopeless because many are not. Herceptin® was an absolute miracle for me.

I've had a few scares along the way, including removal and treatment of a brain metastasis, but my health has been stable now for nine years. My family physician addresses any new developments promptly and never hesitates to refer to a specialist. The big strength of everyone who works with me is that they follow-up on any changes immediately taking me at my word whenever I tell them that 'something is not right'. Patient intuition is important.

Even when I was very sick, Dr. Martin remained positive and optimistic. When I asked about the cancer recurring, she simply replied "If it does, we will treat it and continue to treat it". I knew she would never give up and that's the approach I hope all physicians will take. Metastatic cancer is not necessarily a death sentence. In many cases, there is good reason for hope. I am living proof.

Contact Dr. Lee Ann Martin at lmartin@bccancer.bc.ca

Personalized care for the oncology patient

By Dr. Howard Lim, Medical Oncologist, BC Cancer Agency Vancouver Centre

Cancer is a disease of alterations within a person's genome leading to unregulated growth. By understanding these growth pathways, it is plausible to use this information to select drugs that may be beneficial. Chemotherapy in general is therapy that targets various growth mechanisms and oncologists have been using personalized care for over a decade. An early example is the use of Tamoxifen in estrogen receptor positive breast cancer to block the action of estrogen promoting growth. With the advances in gene sequencing technology, genomic tumor profiling has become more accessible. However, the information gained from these platforms still remains largely experimental and invalidated.

Dr. Howard Lim's 2015 Family Practice Oncology CME Day presentation, Personalized Onco-Genomics Explained, is available at www.fpon.ca

The technology has advanced through the use of gene sequencing technology. Many clinical and consumer based tests use panels which target specific mutations. This provides limited information but in a quick and reliable means. Whole genome sequencing is more involved looking at the entire genome instead of a specific area. While it provides more information, it takes more time to analyze the data. It also yields variants that may not yet be described with unknown significance.

The hope is to gain a detailed understanding of the pathways that may drive a cancer's growth leading to biomarkers which aid in treatment decisions (predictive factors) or a person's survival with the disease (prognostic factors). The research community has continued to provide newer and novel markers that are being validated prospectively in clinical trials. These assays are then used to determine if a person's cancer will respond to treatment. In addition, more efficient means of determining familial risk for developing cancer based on hereditary panels can result in counseling of prophylactic strategies.

The caveat to this explosion of bioinformatics is that the majority of discoveries largely remain invalidated. Mutations or expression of one particular pathway may prove to be predictive in one tumor site but does not hold true in another. The site of disease biopsy is also key, as the metastatic lesion may have a different profile from primary tissue.

Another unfortunate consequence has led to commercial products direct to consumer for genetic testing. This is done largely out of context to a patient's history, and the report is generated and left to the unsuspecting physician to interpret. The disease process is made up of both genetic and environmental risks, and genomic information obtained without the proper context tends to be confusing and misleading for both physician and patient. Given that most of this data is largely experimental and should be analyzed in the context of a person's disease process, the use of consumer testing should be discouraged at present.

Efforts to validate markers for therapeutics should be done in the context of clinical trials and are largely hypothesis generating. While the thought of personalized medicine based on sequencing looks to be attainable, it should be done with an extensive discussion with patients about the pitfalls of using non-validated markers.

As we continue to understand more about tumor biology, more therapies will be developed and treatments tailored for patients. This learning has extended beyond the oncology arena and will affect other areas of medicine, likely leading to a paradigm shift in how we treat patients in the future.

Contact Dr. Howard Lim at *hlim@bccancer.bc.ca*

Congratulations 2015 Terry Fox medal winners

The Family Practice Oncology Network was delighted, when late last year, one its founding members received the 2015 Doctors of BC Terry Fox Medal. Dr. Judith Pike, recently retired long-serving General Practitioner in Oncology (GPO) at the BC Cancer Agency Vancouver Centre, was awarded the medal for her efforts in establishing our highly regarded GPO Training Program. Dr. John Hay, recently retired Radiation Oncologist at the BC Cancer Agency Vancouver Centre, also received the medal for his leading contributions to Canadian radiation oncology. The awards were presented at the Terry Fox Institute Research Day in Vancouver. Congratulations to both winners!

Dr. Malcolm Moore, President of the BC Cancer Agency (left), and Dr. Bill Cavers, past President of the Doctors of BC (right), presented the 2015 Terry Fox Medals to Drs. Judith Pike and John Hay.

Full service family physician boosts oncology care in Powell River

Powell River General Practitioner in Oncology (GPO), Dr. Stephen Burns, has a very fulfilling professional life. He has practiced as a full service family physician in the community since 1994, operating a busy family practice, including obstetrics, usually with a family practice resident working alongside. He also works part-time in Powell River General Hospital's Emergency Ward plus works as a GPO two mornings a week supporting the lead Internist. When this Internist is away, often for several months at a time, this latter role extends up to five mornings a week.

GPO, Dr. Stephen Burns (far right) is part of the oncology team in Powell River that ensures cancer care expertise is always available in this community. Left to right are Dr. Blake Hoffert, Janet White (nurse) and Chensey Martinig (secretary).

"I've always had an interest in oncology," notes Dr. Burns, "and when I heard there was a need for some extra help in our community back in 2012, I jumped right in."

"Internist, Dr. Blake Hoffert, was the driving force in establishing our oncology clinic almost 20 years ago. Now we have space in the hospital, trained chemotherapy nurses, a specialized pharmacist, a 5-chair chemotherapy room, and a waiting room. Previously, we provided very little chemotherapy in Powell River and it was a 'hodge-podge' operation at best. There is a real benefit to the community in having more that one physician with oncology skills as that allows for continuity for patients. We arrange our schedules so that there is always someone available."

"The GPO role is a rewarding, interesting part of my work. Most patients are uplifting and determined and it is always encouraging to see how strong people are in dealing with serious illness. Even in the short time that I've been doing this work, there has been an explosion of new treatments. It's an exciting time to gain expertise and be involved in oncology care."

"I also serve as an oncology resource for family physicians in our area having facilitated community cancer workshops on colon screening and advanced cancers as part of the joint Network/UBC Division of Continuing Professional Development series."

"Overall, I found the GPO Training Program well organized and worthwhile. The linkages established with the Vancouver Cancer Centre oncologists are most helpful, and the ongoing CME opportunities such as the annual conference and the monthly Webcasts are great resources for learning and keeping up to date."

Contact Dr. Stephen Burns at burnsuitz@shaw.ca

Dr. Catherine Clelland – appointed Interim Medical Director for Family Practice Oncology Network

Dr. Catherine Clelland, long-time Council member of the Family Practice Oncology Network, accepted the BC Cancer Agency appointment in February to serve as the Network's Interim Medical Director. She takes on the role following the death last December of one the Network's original chairs and initial Medical Director, Dr. Phil White. Dr. Clelland will lead the Network's participation in the search for a permanent Medical Director and in its preliminary planning to support the Agency's growing emphasis on the importance of family practice within the cancer care continuum.

Dr. Catherine Clelland will lead the Family Practice Oncology Network through an important transition.

Dr. Clelland completed her medical training at the University of Alberta and her Family Medicine residency at the Misericordia Hospital in Edmonton. She practiced full service family medicine in BC beginning in 1986 first in Prince George, then Kelowna and finally in Coquitlam. She joined the Board of the Society of General Practitioners of BC in 1997, was president in 2002/03 and subsequently was Executive Director from 2004 – 2013. Dr. Clelland also currently works as a consultant to the GP Services Committee, provides Billing and Practice Management Seminars to residents and practicing family physicians, maintains a focused practice in primary obstetrics and is Head of the Department of Family Practice at Royal Columbian Hospital.

Contact Dr. Catherine Clelland at cathy.clelland@bccancer.bc.ca

Cutaneous melanoma: a brief overview of management with an introduction to immune checkpoint inhibition

By Dr. Sanjay Rao, Medical Oncologist, Sindi Ahluwalia Hawkins Centre for the Southern Interior

While cutaneous melanoma is projected to comprise 3.4% of new cancer diagnoses in Canada in 2015, that figure rises to 6% in the 30-49 age group and 8% in the 15-29 age group[1]. Age-standardized incidence rates have risen steadily in Canada from 1992-2014[2].

Past research has suggested that the incidence rate was rising fastest among young adults[3]; however, research published in 2015[4,5] suggests that incidence rates in this population are now decreasing in some parts of the world, possibly as a result of efforts aimed at raising awareness and promoting prevention.

Management of Resectable Non-Metastatic Melanoma

Early detection is vital to curative management of melanoma; patients with thin (<0.75 mm Breslow thickness) non-ulcerated melanomas, without evidence of mitotic figures, may have 12-year survival rates exceeding 90%[6].

For resectable melanomas not meeting the above criteria, management beyond wide resection may vary from center to center. Some sources suggest at least discussion of sentinel lymph node biopsy (SLNB) for any invasive melanoma of Breslow thickness 0.75 mm or more[7], although that cut-off is not used in the current BC Cancer Agency guidelines.

SLNB itself serves primarily to provide additional prognostic information and to possibly to guide subsequent treatment; there does not appear to be a survival benefit to SLNB.

Historically, a positive SLNB has led to discussion of complete dissection of the involved node basin(s). However, this procedure has also not demonstrated a survival benefit, and may be associated with potential post-operative morbidity, such as chronic lymphedema.

Options for adjuvant therapy for patients after resection of higher-risk melanoma remain suboptimal, but may include irradiation of resected lymph node basins and adjuvant interferon. The true benefit of adjuvant interferon is uncertain, the treatment lasts one year, and toxicity can be significant. Participation in clinical trials is highly recommended for this patient group.

Management of Unresectable Advanced and Metastatic Melanoma

Significant advances have been made in the management of unresectable advanced and metastatic melanoma. Until recently, these patients had very poor prognoses—median survival was typically quoted at 6 months—and treatment options were limited and largely ineffective[8].

In the past two years, both molecularly targeted therapy and immune checkpoint inhibition (anti-PD-1 and anti-CTLA4 antibodies) have produced marked improvements in response rates and long-term outcomes, compared to previously available therapies.

Molecularly Targeted Therapy

Combination BRAF+MEK inhibition in patients whose tumors harbor a mutant BRAF gene produces an objective response rate (ORR) of approximately 65%, median progression-free survival of approximately 1 year, and median overall survival (mOS) of approximately 2 years[9]; while patients often relapse due to the development of various tumor resistance mechanisms, long periods of disease response and even durable remission have been reported.

Immune Checkpoint Inhibition

Blockade of certain T-cell—tumor interactions, and the resultant reactivation of cell-mediated cytotoxicity, has produced unprecedented survival benefits in advanced, unresectable melanoma (and, though beyond the scope of this article, promising results in advanced non-small cell lung cancer, renal cell carcinoma, and potentially other malignancies). Immune checkpoint inhibitors such as the anti-PD-1 antibodies nivolumab and pembrolizumab, and the anti-CTLA4 antibody ipilimumab, are rapidly entering clinical practice.

In advanced melanoma, single-agent nivolumab has produced an ORR of 40% in previously untreated patients; mOS has yet to be reached[10], and extrapolation of available data suggests that the durable remission rate may be approaching 40%[11]. Combination nivolumab+ipilimumab therapy has produced ORRs of 55-70%, with mOS data immature[12]. However, extrapolations of early-phase trial data suggest that the durable remission rate may reach or exceed 60%[13].

View the full webcast of this topic at www.fpon.ca – Continuing Medical Education

Although the availability of effective new therapies is cause for excitement, there must also be an awareness of the potential for a broad range of significant—even life-threatening or fatal—immune-related toxicities (irAEs) associated with these agents. For example, although single-agent nivolumab is quite well tolerated, with a low risk of grade 3 or higher toxicity, patients must report—and health practitioners must be aware of—even mild toxicity. Seemingly innocuous findings or symptoms may herald more serious subsequent toxicity. Typical irAEs include diarrhea/colitis, pneumonitis, rash, and endocrinopathy, though renal, neurological, and many other manifestations have been reported.

Combined nivolumab+ipilimumab therapy is associated with a risk of serious (grade 3 or greater) irAE of 50% or more. Multidisciplinary care, parenteral steroids and other immunosuppression, hospitalization, and permanent discontinuation of antibody therapy may be required to manage these toxicities.

See references on page 13

Contact Dr. Sanjay Rao at srao@bccancer.bc.ca

Ovarian cancer: an update for primary care practitioners

By Dr. Anna Tinker, MD, FRCPC, Medical Oncologist, BC Cancer Agency, Vancouver Centre, Clinical Associate Professor, Department of Medicine, University of British Columbia

Ovarian cancer is the 7th most common cause of cancer-related death in women (lifetime risk: 1/70). Most GPs will encounter a case of ovarian cancer once every 8-10 years.

Presentation /Initial Evaluation

Symptoms: persistence/worsening of abdominal cramping, bloating, and changes in bowel and bladder function.

View the full webcast of this topic at www.fpon.ca – Continuing Medical Education

Physical examination: abdominal and pelvic masses, ascites, peripheral lymphadenopathy and pleural effusions.

Laboratory evaluation: CBC, Cr, LFTs, electrolytes and tumour markers (CA125, CA15-3, CA19-9, and CEA). The CA125 is the most commonly elevated marker. The CEA should be normal in most cases of ovarian cancer. Tumour markers are not sufficient to establish the diagnosis.

The optimal imaging modality is a computed tomography scan of the chest abdomen and pelvis. Initial assessment by ultrasound and X-ray is often insufficient.

Biopsy or Surgery

It is safe to biopsy if there is wide spread disease (even pelvic masses). A core biopsy is always preferred over a fine needle aspirate.

Pelvis confined disease should not be biopsied. Evaluation by a Gynecologist or a Gynecologic Oncologist is required.

Dr. Anna Tinker

All cases of suspected/diagnosed ovarian cancer should be reviewed by a Gynecologic Oncologist. The treatment prescribed will depend on the distribution of disease.

Ovarian Cancer Screening

Screening by pelvic and transvaginal ultrasound and serum CA125 measurements do not work. Survival is not improved in screened populations. High false-positive rates lead to unnecessary investigations and surgeries. Screening for ovarian cancer, even in high risk women, is not endorsed by any major cancer group in Canada, the US or Europe.

BRCA1/2 Germline Mutations

The BCCA Hereditary Cancer Program offers BRCA1/2 testing to all women diagnosed with a non-mucinous ovarian cancer, as there is a 20% risk of carrying a BRCA mutation. Testing of first degree relatives takes place only if the index case is positive.

Prevention

BRCA mutation carriers are offered surgical prophylaxis by bilateral salpingo-oopherectomy, reducing the risk of ovarian cancer by ~85%.

Opportunistic salpingectomy at the time of surgery for benign indications (e.g. hysterectomy) is a population-based strategy supported by the SOG of Canada and the American Congress of Obstetricians and Gynecologists (based on expert opinion).

Treatment and Prognosis

Despite treatment with chemotherapy and surgery, most women diagnosed with advanced ovarian cancer will experience a recurrence. The median survival is ~3 yrs. Patients with early stage disease have a better prognosis. Platinum-based therapies are the mainstay of treatment. Ovarian cancer clinical trials are an active area of clinical research.

Contact Dr. Anna Tinker at atinker@bccancer.bc.ca

Oncology CME events of note for 2016

Here are several upcoming oncology CME events key for your calendar.

- First is the May 28 Oncology Education Day at Surrey Memorial Hospital presented by the BC Cancer Agency and Fraser Health Authority. The event includes a plethora of practical topics from the principles of oncology, through to presentations on the most prevalent cancers and a debate on PSA screening. Full details and registration via www.fpon.ca – Upcoming Events.
- Next is the highly acclaimed Canadian Association of General Practitioners in Oncology's (CAGPO) annual conference being held in Vancouver for the first time, September 29 – October 2 at the Four Seasons Hotel. The event focuses on continuing medical education needs of GPOs, but has much to offer primary care practitioners who care for cancer patients. Among the agenda items are new and practice changing developments in the management of melanoma, breast, lung, pancreatic and ovarian cancer plus monitoring and managing side-effects of some of the new targeted therapies. Full details and registration at www.cagpo-annual-conference.ca
- BC Children's Hospital is then hosting its Pediatric Oncology/Hematology Conference in Vancouver on October 27 – 28. All primary care providers are welcome. Contact Paulina Chen, ppchen@cw.bc.ca, for details.
- Finally, our very own Family Practice Oncology CME Day will be held November 19 in Vancouver. Conference planners are busy developing an agenda which will address the most topical oncology learning needs of family physicians and primary care providers. Full details will be distributed in the coming months and via www.fpon.ca. Hope to see you there!

Ovarian cancer symptom management

Problem	Approach
Chemotherapy Induced Nausea and Vomiting	Characteristics/Symptoms: Onset within 1 week of chemotherapy without signs of bowel obstruction. DDx: Bowel obstruction, metabolic abnormalities, CNS metastases. Investigations: CBC, electrolytes (including Ca2+ and Mg2+), serum glucose, Cr, LFTS. Abdominal X-ray to r/o bowel obstruction +/- head CT to r/o brain metastases. Treatment: Ondansetron 8 mg PO TID, Dexamethasone 4 mg PO BID, Prochorperazine 10 mg PO QID prn, Aprepitant, and olanzapine to prevent nausea with future treatment. *See the Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting on the BCCA website: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCNAUSEA_Protocol_1Mar2012.pdf
Malignant partial or complete bowel obstruction	Characteristics/Symptoms: Persistent nausea, vomiting, abdominal distension, pain, obstipation. DDx: ileus, benign causes (e.g. adhesions), post chemotherapy emesis. Investigations: Abdominal x-ray (air-fluid levels and distended bowel). CT scan (determine if multi- or unifocal obstruction). Management: Complete obstruction: hospitalize, IV hydration, bowel rest (NPO), N/G suction, Dexamethasone (e.g. 4-8 mg PO/IV BID). Surgical review for bypass options. Palliative venting gastrostomies if needed. Partial obstruction: outpatient if hydration can be maintained. Low fiber diet, dexamethasone, and gentle laxatives. Otherwise, as per complete obstruction.
Malignant effusions	Characteristics/Symptoms: Ascites: abdominal distension, early satiety, urinary frequency, weight gain, SOB. Pleural Effusions: dyspnea. DDx: Ascites: Bowel obstruction, CHF, cirrhosis. Pleural effusion: Pulmonary embolus, pneumonia/empyema, CHF, tumour, diaphragmatic paralysis. Investigations: Abdominal ultrasound, chest-Xray (decubitus views), pulmonary CT angiogram. Diagnostic paracentesis (serum: ascites/albumin-gradient should be <11 if related to malignancy). Diagnostic thoracentesis: exudative malignant effusion, fluid cytology. Management: Ascites: paracentesis: short term (<6 weeks): pigtail drain: refractory ascites may require long term indwelling catheter (>6 weeks): pleurX drain. Pleural effusions: thoracentesis. Refractory effusions managed by pleurX drainage (rarely pleurodesis). Malignant effusions (without contributing CHF or cirrhosis) are refractory to diuretics.
Lymphedema	Characteristics/Symptoms: Uni- or bi-lateral lower limb edema. Associated with inguinal, pelvic or retroperitoneal lymphadenopathy, refractory ascites, or prior pelvic lymph node dissection and/or radiation. DDx: DVT (especially if unilateral), CHF, cirrhosis, cellulitis. Investigations: Doppler ultrasound (especially if unilateral), CT of abdomen and pelvis. Management: Refractory to diuretics unless CHF or cirrhosis are contributing factors. May improve with effective chemotherapy. Supportive management: compression stockings/bandaging, physiotherapy, lymphapress, lymphatic drainage. The BC Lymphedema Association website lists service providers.
Cancer related hydronephrosis	Characteristics/Symptoms: Unilateral hydronephrosis often asymptomatic, but back pain, pyelonephritis, or decline in renal function can occur. DDx: Renal stones, post surgical scarring, bladder tumours. Investigations: CBC, Cr, BUN, Ca2+, KUB, renal ultrasound or CT scan of abdomen and pelvis. Management: Unilateral hydronephrosis, not causing pain or renal impairment, can be observed. Stents and nephrostomy tubes bypass the obstruction but can be associated with morbidity.
CNS metastases	Characteristics/Symptoms: Headaches, nausea and vomiting, vision changes, ataxia, hemiplegia, altered speech, seizures. DDx: stroke, metabolic aberrations (hyponatremia, hypercalcemia, hyper/hypo-glycemia), infection (sepsis, meningitis, encephalitis). Investigations: CBC, Cr, BUN, Ca2+, electrolytes, serum glucose, CT or MRI of brain +/- spine. Management: Steroids to control intracranial/paraspinal swelling (Dexamethasone 8 mg PO BID), urgent referral to Radiation Oncology, as all cases of spinal cord compression are emergent.

Breast reconstruction and the general practitioner

By Dr. Sheina Macadam, Plastic and Reconstructive Surgeon, Vancouver

Dr. Sheina Macadam

Breast reconstruction rates are increasing but still less than half of women who undergo mastectomy will have reconstruction. This is due to several factors: proximity of the patient to a plastic surgeon, the referring doctor's knowledge of who is eligible for breast reconstruction, and logistical issues such as timing. In order to increase a patient's chance of having breast reconstruction, the general practitioner can take a number of steps at the time of diagnosis:

1. Encourage the patient to request a consultation with a plastic surgeon before any surgery or treatment is administered – radiation and/or surgery prior to reconstruction may affect the result.
2. Ensure expedient referral to the general surgeon and oncologist so that there will be time to consult with a plastic surgeon.
3. Encourage patients who smoke to stop. Complication rates increase in patients who smoke.
4. Refer the patient to educational material so she will have a working knowledge of breast reconstruction options before she sees the plastic surgeon (http://breastreconstruction.vch.ca).
5. Know that the only contraindications for reconstruction include BMI >35, active smoking and a comorbidity that would preclude a long general anaesthetic.

If possible, patients should be offered breast reconstruction at the same time as mastectomy (*immediate reconstruction*) or at the very least be offered consultation with a plastic surgeon prior to mastectomy. In this way the patient is given the choice not to have to live with a mastectomy defect which can lead to depressive reactions.

Reconstruction can be *autologous* (using a patient's own tissue) or *alloplastic* (using implants). Autologous reconstruction employs tissue from the abdomen, buttock, back or thighs to recreate the breast. Initially, autologous breast reconstruction began with movement of tissue still attached to its blood supply and would sacrifice functional muscles. In order to reduce the risks of problems associated with muscle sacrifice, surgeons now perform these surgeries with no muscle attached and this is known as *perforator flap* surgery. If a patient decides to have autologous reconstruction she will:

1. Likely have a long-lasting, natural result and high satisfaction with the outcome.
2. Have a recovery period of 6 weeks to 2 months.
3. Need to have enough tissue to reconstruct a breast and will have additional scars elsewhere on the body.

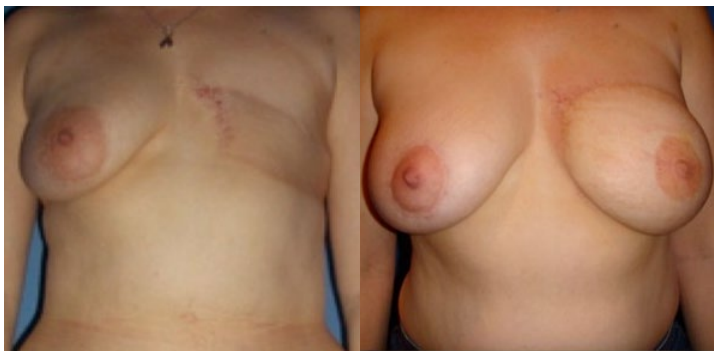
Alloplastic reconstruction can be performed in one or two stages. Two-stage surgery involves initial placement of a tissue expander under the pectoral muscle, a 3-4 month period of stretching, and then a second surgery to replace the tissue expander with an implant. One-stage surgery involves placement of the final implant and a piece of cadaveric skin inside the breast at the time of mastectomy. Only certain types of patients are candidates for one-stage surgery.

If a woman undergoes implant reconstruction she:

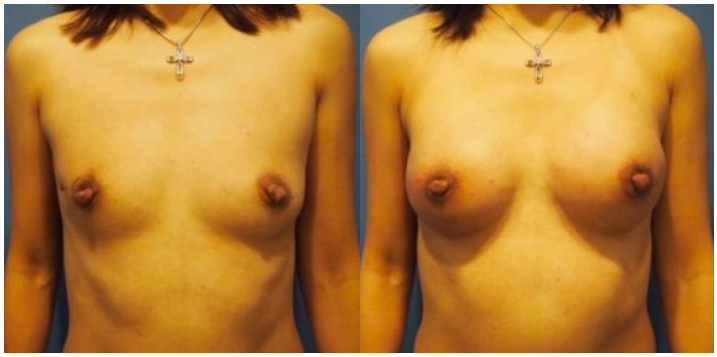
1. May require more surgeries during her lifetime, as the result with implants does not always last over the long term.
2. Will have breasts that feel like implants, not tissue.
3. Will attain reconstruction with surgery that is shorter and less invasive than autologous reconstruction.

Overall, patients who undergo breast reconstruction tend to have improved satisfaction and quality of life compared to those who live with a mastectomy defect. General practitioners see the patient at a critical time in the breast cancer journey and this is the time where awareness of breast reconstruction can be raised.

Contact Dr. Sheina Macadam at drsamacadam@gmail.com.



42 year-old patient 5'3" and 140lbs. This patient underwent delayed left breast reconstruction using a deep inferior epigastric perforator (DIEP) flap, nipple reconstruction and tattoo. She also required a right mastopexy. The post-operative photo is one year post-reconstruction.



40 year-old patient 5'4" and 105lbs. This patient underwent bilateral mastectomies with immediate reconstruction using Alloderm and round silicone gel implants (305g).

Breast imaging conundrums

By Dr. Peggy Yen, Diagnostic Radiologist and Dr. Christine Wilson, Diagnostic Radiologist and Past Medical Director, Screening Mammography Program, BC Cancer Agency

The goal of the Screening Mammography Program is the early detection of breast cancer when treatment is more likely to be successful. The guideline changes[1] in the past year mean that there needs to be an increased vigilance and awareness of the screening process on the part of the caring physician.

Dr. Peggy Yen

The screening program is aimed at asymptomatic women without a history of breast cancer or breast implants and the frequency with which women may attend is determined by whether she has had a first degree relative (mother/sister/daughter) with breast cancer. Women with such a family history may attend annually. All others may attend biennially. Higher risk women, including those who have a genetic mutation (BRCA 1 or 2), are screened by the Hereditary Cancer Program, and qualify for closer imaging surveillance which includes yearly MRI and mammography annually. Women who have received mantle radiation also qualify for this annual screening.

Women with breast symptoms are not eligible for screening and should present to their family physician for referral to a diagnostic centre since the imaging investigation is tailored to the presentation. Some common presentation includes:

- Palpable mass: Diagnostic workup including mammography and ultrasound. A negative diagnostic workup has a 99.7% negative predictive value and only a 0.3% estimated cancer rate[2].
- Nipple discharge: Diagnostic work up and if the symptoms includes spontaneous, single duct clear or bloody discharge, ultrasound +/- a galactogram can be performed.
- Nipple changes: if there is no mass, mammography should be performed if it is not up to date. If findings are highly suspicious, a diagnostic work up can be requested with consideration of a surgical consultation.

Breast screening with mammography is the only method proven to reduce breast cancer mortality[3]. However, it is recognized that the primary limitation of full-field digital mammography is that of overlapping dense breast tissue which can decrease visibility of malignant lesions. Breast density is categorized into quartiles and the sensitivity of mammography for cancer detection is negatively correlated with increasing density[5]. Breast ultrasound can be considered as a supplement, but not a replacement in breast screening though it is currently not included in the MSP coverage and there is a recognized higher false positive rate[6]. There are no studies supporting the use of thermography either alone or as an adjunct for the detection of breast cancer[4].

View the full webcast of this topic at www.fpon.ca – Continuing Medical Education

Male breast disease comprises a wide spectrum of benign and malignant processes but is often under recognized owing in part to its rarity and also to a lack of awareness[7]. Male breast cancers represent only 1% of all breast cancers[1] and despite the anatomical differences between male and females, male breast malignancies are histologically similar to those encountered in the female breast. Men present symptomatically and the initial imaging evaluation is that of a diagnostic mammography with sonography reserved for cases where the mammographic appearance is not typical for gynecomastia.

See references on page 13

Contact Dr. Peggy Yen at peggy.yen@cw.bc.ca

Managing venous thromboembolism in cancer patients

By Dr. Erica A. Peterson, Clinical Hematologist, Vancouver General Hospital and University of British Columbia.

Venous thromboembolism (VTE) is a common complication of cancer, with incidence rates by cancer type ranging from 8.2 to 19.2% in large database studies.[1] The development of VTE in cancer patients is associated with poor clinical outcomes and a high burden on the health care system. VTE is an independent predictor of mortality irrespective of cancer stage and is the second leading cause of death in cancer outpatients receiving chemotherapy.[2,3] Furthermore, anticoagulant-related bleeding and recurrent VTE are more commonly observed in cancer patients.[2,4] Finally, VTE may cause disruptions in cancer treatment, negatively affecting cancer outcomes.

Dr. Erica Peterson

Despite the high incidence of cancer-associated VTE, routine outpatient thromboprophylaxis is not recommended as VTE risk in the general cancer population is heterogeneous and not uniformly high enough to justify primary thromboprophylaxis for all patients.[5] Selected high-risk patients may benefit from thromboprophylaxis and this can be considered in consultation with the treating oncologist.[5] All cancer patients should be educated on the signs and symptoms of deep vein thrombosis and pulmonary embolism.

All major consensus guidelines recommend single agent low molecular weight heparin (LMWH) for treatment of cancer-associated VTE.[5,6] This recommendation is based on

continued on page 10

Restructuring of the British Columbia Cancer Agency

By Dr. Malcolm Moore

In March of 2016 I announced a reorganization of the leadership structure at both the provincial office and the regional cancer centres. I would like to describe why the Agency needed to change, and what this will mean for the Family Practice Oncology Network (FPON) and Primary Care Physicians in BC.

Dr. Malcolm Moore

BCCA needs to become a Cancer Control Agency which is defined as one that attempts to reduce the impact of cancer on all citizens of BC and provides care and support for patients all along the cancer continuum from cancer prevention, screening, diagnosis, treatment, to survivorship and end-of-life care. At present BCCA directly provides all radiation therapy in the province; 100% of PET scans, and 60% of the systemic therapy, but many other important elements of cancer control are delivered by Regional Health Authorities, Primary Care Providers and others partners such as volunteer societies, and public health. Thus to have a truly patient-centred approach to Cancer Control requires integration and coordination of all Cancer Services delivered by all the different care and support providers in the province. This overall coordination of the system is a role that BCCA has been asked to take on, and to do it effectively, we need strong representation from all the Regional Health Authorities and Primary Care. This was one of the key drivers of the reorganization which will better position BCCA to work effectively with others to develop standards and coordinate care.

You are all aware of the multiple important roles the Primary Care Physician plays in Cancer Control including health promotion, cancer screening, support during diagnosis and treatment and involvement in ongoing care for cancer survivors as well as palliative support for those who are not cured with therapy. This aligns with our goal to provide care and support close to home whenever possible. In the reorganization, Primary Care, represented by FPON, will sit on the Cancer Clinical Council with all the other key specialties – Medical Oncology, Pathology, Radiation Oncology, Surgical Oncology – reporting to the VP of Clinical Programs and Quality. We will ask FPON to expand its scope and consider how best to involve Primary Care in all aspects of Cancer Control from Prevention to Survivorship and End-of-Life Care. This enhanced role will include current priorities such as education and GPO training, but also development of standards, care pathways, communication and appropriate support, around all components of the Cancer Journey for Primary Care Physicians in BC.

It is an exciting time and there are great opportunities to work together to integrate the health system in BC to enhance the patient experience, and improve outcomes. FPON will play an important role in the Cancer Control System in BC going forward, and I look forward to working with and meeting many of you.

Contact Dr. Malcolm Moore at malcolm.moore@bccancer.bc.ca

Managing venous thromboembolism continued from page 9

data from open label trials comparing LMWH with vitamin K antagonists (e.g. warfarin). Meta-analysis of these studies demonstrated that LMWH is associated with a significant reduction in recurrent VTE (RR 0.59, 95%CI 0.44-0.78) with no increase in major bleeding (RR 0.96, 95%CI 0.65-1.42) or mortality (RR 1.00, 95%CI 0.88-1.33).[6] In addition to improved efficacy, LMWH has other advantages over warfarin including stable pharmacokinetics in patients with chemotherapy-associated nausea and decreased oral intake, a short half-life which allows interruption for bleeding, thrombocytopenia and procedures, and a lack of drug interactions. Qualitative studies have shown that patients are accepting of LMWH injections, as they prefer safety, efficacy, and a lack of interaction with their cancer treatment over the route of administration.[7]

Direct oral anticoagulants (DOACs) targeting thrombin (dabigatran) and factor Xa (rivaroxaban and apixaban) have recently been approved in Canada for VTE treatment. In non-cancer patients, DOACs are non-inferior to warfarin for the prevention of recurrent venous thromboembolism, with a similar or reduced risk of major bleeding.[8-11] Oral administration with fixed dosing, minimal drug interactions, and lack of monitoring make these agents an attractive option for cancer-associated VTE. However, their use is premature due to a lack cancer-specific data, absence of studies comparing DOACs against the current standard of care (LMWH), unreliable administration and absorption in patients with nausea and vomiting, mucosal erosion, possible drug interactions with chemotherapy, and the high incidence of renal and hepatic dysfunction in cancer patients. Studies comparing DOACs and LMWH in cancer-associated VTE are currently ongoing and should definitively answer this question.

Although recurrent VTE despite adequate anticoagulation can occur in cancer patients, limited evidence exists for management of anticoagulation failure. Expert opinion recommends a transition to LMWH in patients with recurrent VTE on warfarin. Patients who experience a recurrence on LMWH can be managed with a 25% dose escalation once non-compliance and heparin-induced thrombocytopenia have been excluded.[12]

Online resource for management of VTE:

www.thrombosiscanada.ca
(Thrombosis Canada website)

www.thrombosisbc.ca
(VGH Thrombosis clinic website)

References available with online edition at www.fpon.ca

Contact Dr. Erica Peterson at epeterson2@bccancer.bc.ca

A primer for well differentiated thyroid cancer

By Dr. Jonn Wu, Radiation Oncologist, BC Cancer Agency Vancouver Centre

The incidence of thyroid cancer has been increasing faster than any other malignancy; fortunately, most thyroid cancers are considered "well differentiated" (papillary and follicular carcinomas) with excellent survival rates. Many patients with metastatic disease may live with their disease for many years or decades. Less than 10% of thyroid cancers are medullary thyroid or anaplastic carcinomas with much poorer outcomes. The focus of this article and accompanying webcast is "well differentiated" disease.

Dr. Jonn Wu

Most patients present with a palpable neck mass and slow rate of growth, without any other associated symptoms. Persistent or suspicious masses should undergo ultrasound and/or fine needle aspiration biopsy. Once confirmed, surgery is the primary therapy; the recommended procedures include unilateral lobectomy and isthmusectomy for smaller tumours or total thyroidectomy. Patients with invasion of neck structures such as the esophagus, trachea, or strap muscles should have a more extensive resection. A neck dissection may be required if cervical lymphadenopathy is present.

A number of staging systems can be used to estimate the risk of recurrence and/or disease-specific survival, including TNM, AGES, and AMES. The BCCA Head & Neck Tumour Group routinely use the Metastases, Age, Completeness of Resection, Invasion, Size (MACIS) nomogram, in addition to histopathological factors to determine if adjuvant therapy is indicated.

Adjuvant treatments include orally administered radioactive iodine (131-Iodine) and external beam radiation therapy (EBRT). Radioiodine can be used for ablation of residual thyroid tissue, treatment of microscopic or macroscopic disease, and imaging of persistent disease. Radioiodine uptake is improved with stimulation by thyroid stimulating hormone (TSH); in BC, we use recombinant human TSH (thyrotropin alpha) to avoid thyroxine withdrawal and clinical hypothyroidism. For non-iodine avid or persistent (unresectable) disease, EBRT can be given daily over 5 to 6 weeks.

View the full webcast of this topic at www.fpon.ca – Continuing Medical Education

Thyroid cancer patients require replacement thyroxine to avoid hypothyroidism and to minimize TSH stimulation of tumor growth. FreeT4 (FT4) target goal is the upper limit of normal to suppress TSH to 0.1-1.0mU/L. Follow-up includes blood tests (FT4, TSH, Thyroglobulin [Tg] and anti-Tg antibodies) every 3-6 months and physical examination every 6-12 months. In the absence of antibodies, Tg can be a useful tumour marker. Occasionally, ultrasound or other imaging may be required. Surgery is the primary modality for locoregional recurrence, followed by radioiodine and/or EBRT. If necessary, conventional chemotherapies and newer systemic therapies (tyrosine kinase inhibitors) might be useful for metastatic disease.

Contact Dr. Jonn Wu at jonnwu@bccancer.bc.ca

New upper gastrointestinal guidelines for primary care

The Family Practice Oncology Network recently published two new primary care guidelines for Upper Gastrointestinal Cancers. The first covers cancers of the esophagus and stomach while the second focuses on the duodenum, pancreas and extrahepatic biliary tract. These guidelines outline recommendations for prevention, screening, diagnosis, treatment and follow-up and were developed using a systematic guideline adaptation approach.

Both are based on the most recent BC Cancer Agency Gastrointestinal Cancer Clinical Practice Guidelines and their recommendations reflect a review and evaluation of clinical evidence published since the BCCA Guidelines' development, including expert clinical opinion and external review. The Working Group responsible included practicing family physicians, specialists in gastroenterology, general surgery and oncology.

"Our goal in developing these guidelines is to provide brief, practical and easy-to-follow advice for family physicians and other primary care providers to enable effective patient care," noted the Network's Acting Medical Director, Dr. Catherine Clelland. "The intention is to improve early detection of these cancers resulting in improved patient outcomes, patient experience and quality of care. The guidelines support both practitioner and patient understanding of the spectrum of cancers in the upper GI tract, and outline recommended approaches to the investigation and management of the problem from the time of presentation to post treatment survivorship, including advance care planning."

Download these guidelines customized for family physicians at www.fpon.ca

These new guidelines join those already developed by the Network in partnership with the BC Guidelines Protocols Advisory Committee (GPAC) including the three part Palliative Care Guidelines (now being updated) and the Female Genital Tract Cancer Guidelines. The Network also contributed to GPAC guidelines on Breast and Colorectal Cancer.

Visit www.fpon.ca for full details and guideline access.

Myelodysplastic syndrome: a primary care perspective

By Dr. Thomas J. Nevill, Clinical Director, Leukemia/BMT Program of British Columbia

Background

Dr. Tom Nevill

Myelodysplastic syndrome (MDS) is a clonal bone marrow stem cell disorder that typically presents with pancytopenia. However, patients may have unilineage involvement and MDS should be considered in an anemic patient in whom history, physical examination and routine blood work do not reveal a clear explanation for the low hemoglobin. MDS has an incidence of ~36 new cases/million/year, is more frequent in men, and median age at diagnosis is 65-70 years. MDS is the most common marrow failure syndrome, but its features overlap with a number of related conditions including acute myelogenous leukemia (AML), aplastic anemia and myeloproliferative neoplasms (MPNs).

View the full webcast of this topic at www.fpon.ca – Continuing Medical Education

Pathogenesis

MDS can, rarely, be a familial disorder or can be due to exposure to cytotoxic drugs and/or radiation. However, more than 90% of cases are idiopathic or "primary" MDS. Primary MDS may result from some degree of genetic loading, but the key to its development is cumulative exposures to environmental toxins. The most important modifiable risk factor is cigarette smoking although the odds ratio for developing MDS is higher with chronic exposure to gasoline, oil, exhaust, benzene, pesticides and fertilizers. At risk professions include healthcare professionals, painters, construction workers, gas/oil refinery workers, heavy machine operators, pulp and paper workers, agricultural workers and automotive/rail/dockyard workers.

Prognosis

MDS is a heterogeneous disease with a highly variable prognosis. Its name is derived from the abnormal ("dysplastic") appearance of red cells, neutrophils and platelets in the blood and bone marrow. A characteristic feature of MDS cells are genetic/chromosomal abnormalities found on analysis of cultured bone marrow metaphases. Some abnormalities are associated with a favorable prognosis. [e.g., absence of the long arm of chromosome 5 or "del(5q)"] while others are known to be unfavorable (e.g. monosomy 7). Chromosome analysis is the most important prognostic feature in MDS and it is mandatory that the test be done at the time of diagnosis. In combination with the percentage of blast cells in the marrow and the number of cell lines affected by the disease, an international prognostic (IPSS) score can be calculated to estimate survival times and to guide therapy.

Therapies

The mainstay of MDS treatment remains "best supportive care" – blood product transfusion and antimicrobials when infections occur. Patients with low-risk MDS may respond to Erythropoietin (Eprex®) or Lenalidomide (Revlimid®). Hypocellular MDS patients may improve with immunosuppressive therapy (Cyclosporine and ATGAM®). For individuals <70 years of age with higher-risk MDS, the treatment of choice is allogeneic stem cell transplantation (SCT), the only curative therapy available. For advanced MDS patients ineligible for SCT, Azacitidine (Vidaza®) has been shown to prolong survival and improve quality of life compared to best supportive care.

Contact Dr. Tom Nevill at TNevill@bccancer.bc.ca

Next GPO training course begins September 12, 2016

The GPO Training Program is an eight-week course offering rural family physicians and newly hired Agency GPOs and Nurse Practitioners the opportunity to strengthen their oncology skills and knowledge. The program covers BC and the Yukon and includes a two-week introductory module held twice yearly at the Vancouver Cancer Centre followed by six weeks of flexibly scheduled clinical rotation at the Centre where participants' patients are referred. The program is accredited by the College of Family Physicians of Canada and eligible physicians will receive a stipend and have their expenses covered. Full details at www.fpon.ca

FAMILY PRACTICE ONCOLOGY NETWORK CHAIRS

NETWORK COUNCIL INTERIM CHAIR
Dr. Catherine Clelland – Port Coquitlam
cathy.clelland@bccancer.bc.ca

CONTINUING MEDICAL EDUCATION
Dr. Raziya Mia – Abbotsford
604.851.4710 ext. 644744
rmia@bccancer.bc.ca

GUIDELINES AND PROTOCOLS
Dr. Catherine Clelland
cathy.clelland@bccancer.bc.ca

GPO TRAINING PROGRAM
Dr. Bob Newman – Sechelt
604.885.2667
drbobnewman@gmail.com

FOR MORE INFORMATION

To learn more about the Family Practice Oncology Network or become involved please contact:
Jennifer Wolfe
Tel. 604.219.9579
email: jennifer.wolfe@bccancer.bc.ca

Visit the Network Website: www.fpon.ca

ISSN 2369-4165 (Print)
ISSN 2369-4173 (Online)
Key title:
Journal of family practice oncology

Publications Mail Agreement Number 41172510

Return all undeliverable Canadian Addresses to
BC Cancer Agency
600 West 10th Ave, Vancouver, BC
V5Z 4E6

Cutaneous melanoma continued from page 5

References

1. Canadian Cancer Society 2015 http://www.cancer.ca/~/media/cancer.ca/CW/publications/Canadian%20Cancer%20Statistics/Canadian-Cancer-Statistics-2015-EN.pdf (p. 30), accessed January 17, 2016
2. Canadian Cancer Society 2015 http://www.cancer.ca/~/media/cancer.ca/CW/publications/Canadian%20Cancer%20Statistics/Canadian-Cancer-Statistics-2015-EN.pdf (p. 26), accessed January 17, 2016.
3. Reed KB, Mayo Clin Proc. 2012 Apr;87(4):328-34. doi: 10.1016/j.mayocp.2012.01.010

4, 5. Wallingford SC et al., Int J Cancer. 2015 Nov 1;137(9):2227-33. doi: 10.1002/ijc.29598. Epub 2015 May 29
Campbell LA et al., J Pediatr. 2015 Jun;166(6):1505-13. doi: 10.1016/j.jpeds.2015.02.050. Epub 2015 Apr 9.

6. Mariuchi A, JCO August 10, 2014 vol. 32 no. 23 2479-2485
7. NCCN Melanoma Guideline, http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf (p. 11), accessed January 17, 2016.
8. Korn EL., J Clin Oncol 26:527-53.
9. Long GV, Lancet Volume 386, No. 9992, p444–451, 1 August 2015
10. Robert C et al. N Engl J Med. 2015 Jan 22;372(4):320-30
11. Hodi FS, et al. Pigment Cell Melanoma Res. 2014;27:1199
12. Larkin J et al. N Engl J Med, May 2015. epub ahead of print
13. Kluger H et al., SMR 2014 (conference proceeding).

Breast imaging conundrums continued from page 9

References

1. Screening Mammography Program. BC Cancer Agency 2015. Available at: http://www.screeningbc.ca/Breast/ForHealthProfessionals (accessed January 2016).
2. Chan CH, Coopey SB, Freer PE et al. False-negative rate of combined mammography and ultrasound for women with palpable breast masses. Breast Cancer Res Treat. 2015; 153:699-702.
3. Independent UKPoBCS. The benefits and harms of breast cancer screening: an independent review. Lancet 2012 Nov 17;380(9855):1778e86.
4. Breast thermography: Society of breast imaging position paper. Society of Breast Imaging 2011. Available at https://www.sbi-online.org/RESOURCES/PolicyPositionStatements/Breast_Thermography.aspx (accessed March 2016).
5. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology. 2002 Oct; 225(1):165-75.
6. Weigert J and Steenbergen S. The Connecticut experiments second year: Ultrasound in the screening of women with dense breasts. 2015; 21:175-180
7. Gethins M. Breast cancer in men. J Natl Cancer Inst. 2012;104(6):436-8.