<table>
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<th>Name of Study</th>
<th>Researchers</th>
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<td>(OPAR) Once-a-day partial breast irradiation: A feasibility study</td>
<td>Co-Principal Investigators: D. Kim &amp; T. Whelan</td>
<td>(OPAR) Once-a-day partial breast irradiation: A feasibility study</td>
<td>Funded 2011 Study recruited completed; analysis to follow</td>
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<td>Co-Investigators: J. Wright, J. Sussman, B. Strang, H. Reiter, S. Voruganti, G. Okawara, I. Dayes, J. Julian</td>
<td>Approximately two thirds of women with early breast cancer undergo breast conservation surgery (BCS). It is standard practice to administer radiation to the breast, called whole breast irradiation (WBI) after surgery to reduce the chances of recurrent cancer in the breast. WBI usually is given in daily treatments (fractions) and takes 3 to 4 weeks to complete. Currently researchers at the Juravinski Cancer Centre are leading a national multicentre clinical trial which is comparing a novel breast radiation regimen consisting of two treatments a day for 5 days delivered to the part of the breast where the surgery was performed (called partial breast irradiation) with the standard longer treatment WBI in women with early breast cancer who have undergone BCS. The shorter treatment has the potential to be more convenient for patients. However early results show that there is more scarring and thickening of the skin of the breast. Investigators are evaluating once-a-day partial breast radiation treatment over five days using 3D conformal radiation therapy following BCS. Limiting radiation to a smaller volume of the breast (partial breast irradiation) can reduce the</td>
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short and long term side effects of radiation without sacrificing tumor control and shorten the total duration of treatment (treatments over five days compared to the traditional three to five weeks of radiotherapy). With successful completion of the pilot study, once-a-day partial breast radiotherapy will be studied further in a large multi-centre randomized trial. All 60 patients have been recruited.

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<th><strong>(UPTAKE) Understanding predictive testing attitudes in BRCA1/2 Kindreds</strong></th>
<th>Co-Principal Investigators: K. Bell &amp; L. Learn Co-Investigators: L. Bordeleau, K. Zbuk</th>
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| **(UPTAKE) Understanding predictive testing attitudes in BRCA1/2 Kindreds** | Hereditary breast cancer accounts for 5-10% of all breast cancer diagnoses and is primarily caused by changes (mutations) in two genes called BRCA1 and BRCA2. Female relatives found to carry a familial BRCA1/2 mutation are at high risk to develop breast and ovarian cancers. Male relatives are at increased risk to develop male breast cancer and prostate cancer. These individuals form a uniquely high risk population that would benefit significantly from cancer prevention and early detection initiatives. However, the number of family members of BRCA1/2 who take advantage of predictive BRCA1/2 genetic testing is lower than expected.

The UPTAKE study used a questionnaire-based survey to examine the uptake of predictive genetic testing within close relatives of BRCA1/2 carriers. The goal was to identify potential facilitators and barriers to the communication of their results.

Funded 2009 Study Completed + Reported
process that might impact an individual's choice to consider predictive genetic testing. Participants were also asked to identify services or resources that might help in the risk communication process within their family. This information will then be used to develop tools and/or counseling strategies that could be used to better inform and educate unaffected, high-risk women and men of the health benefits of BRCA1/2 genetic testing.

Summary of Results: 141 questionnaires were returned. Overall, 83% of family relatives were informed about the participant’s BRCA1/2 status. Of the living, informed family relatives, 62% did not have genetic testing; 10% of these family relatives reportedly had concerns about insurance/employment discrimination. Women are more likely to access predictive genetic testing in our population. Cancer status, socioeconomic status, age and gender of the participant did not appear to be associated with different levels of genetic testing uptake among their family relatives. However, a trend was observed between participant distress in communication and lower uptake of predictive genetic testing among family relatives. About 25% of participants report a desire for more help in discussing BRCA status with family, particularly with their children as this appeared to be associated with the most distress. All
participants reported a high level of interest in all suggested interventions.

Conclusion: Communication of BRCA mutation status is high among family members, however, the resulting uptake in predictive genetic testing is less than anticipated. Possible factors identified include gender, insurance concerns and distress in communication of genetic risk information. This patient population appears highly motivated to take advantage of clinic-based interventions to assist in family communication.

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<td>Historically clinic-pathologic features such as tumor size, axillary lymph nodes involved with cancer, tumor grade, and hormone receptor status have been used to determine the prognosis of a patient with early breast cancer who has undergone surgery. During the last five years, a fourth factor, HER2 has been added to the routine reporting of the pathology of a new breast cancer. Patients with a breast cancer that over-expresses HER2 have a worse prognosis than those without over-expression. Based on these factors the risk of recurrence and survival can be estimated and a decision for adjuvant systemic therapy e.g. chemotherapy, tamoxifen, or aromatase inhibitor is made.</td>
<td>Funded 2011 Study completed pending publishing.</td>
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Unfortunately, many patients are over-treated because their tumor is intrinsically not sensitive to the treatments or despite the clinic-pathologic features the tumor has a very indolent natural history.

In recent years there has been much excitement about personalized medicine and the ability to tailor therapy to the molecular characteristics of a tumor, and avoid treatment in patients in whom it will not work. Research examining breast cancer genes has shown that breast cancer can be classified into subtypes. Estrogen receptor positive breast cancers can be divided into Luminal A and Luminal B types. Estrogen receptor negative cancers can be divided into the HER2 overexpressing, normal breast-like and the basal-like. This molecular classification of breast tumors was subsequently shown to have prognostic significance with Luminal A type tumors displaying an excellent prognosis whereas HER2 overexpressing and basal-like tumors having a particularly poor prognosis.

Breast cancers that are estrogen receptor negative, progesterone receptor negative, and HER2 negative, called triple negative, are associated with a particularly bad prognosis and are thought to belong predominantly of the basal-like subclass. Patients with triple negative tumors tend to receive aggressive adjuvant
However from clinical experience not all of these breast cancers are associated with a poor prognosis, and hence some patients are being over-treated.

It is now possible to sequence the genes in a cancer and to identify those changes specifically related to the cancer. In this study frozen tumor samples from women with triple negative (TN) breast cancer were retrieved from the Ontario Tumor Bank and sequenced for mutations. We identified a cohort of 10 women with basal-like/TN breast tumours and retrieved tumour and normal fresh frozen tissue. These women had been followed for four years, being assessed for breast cancer recurrence both in the breast and elsewhere in the body. RNA and DNA were successfully extracted from the 10 fresh frozen breast tumours and paired normal samples from the same woman. The RNA was stored for potential later use, whereas the DNA extracted was exom-enriched and PE sequenced on Illumina GAIi. This part of the study was conducted as a strategic collaboration with the Genome Technologies Platform (GTP) of the OICR and the whole genome analysis was conducted at the MaRS Institute in Toronto.

Variants detected in both the tumour and paired normal DNA were eliminated from further analysis as they likely represent common
variants and single nucleotide polymorphism (SNPs) specific to the individual. The remaining variants represent the somatic alteration specific to the tumour and represent the variants of interest in our study.

At the time of study completion three of the 10 women whose tumours had been sequenced had suffered a systemic relapse and/or had passed away from breast cancer. These three samples represented the ‘poor prognosis’ group. The remaining seven women were alive and well and their tumours represented the ‘good prognosis’ group for comparison. A number of mutated genes were identified that were unique to either the ‘poor’ or ‘good prognosis’ group and in addition a number of mutated genes common to both groups were identified.

Confirmation of these results is being conducted using alternate sequencing techniques with subsequent validation planned in a larger patient cohort of triple negative breast cancers.

| Evaluation of Cosmetic outcome in a randomized trial of Hypofractionated Radiotherapy for Early Breast Cancer | Principal Investigator: T. Whelan  
Study Completed, results pending. | Women who undergo lumpectomy receive breast radiation after surgery to lower the risk of recurrent cancer in the breast. Sometimes |
radiation can cause excessive fibrosis (scarring and thickening) of the skin of the breast which leads to a poor cosmetic result. Usually breast radiation is administered daily over about 4 weeks. Shorter courses of radiation in which a larger dose is delivered each day are being evaluated in clinical trials. However, it is possible that such radiation regimens can lead to excessive fibrosis.

There are various methods used in clinical trials to assess cosmetic outcome in women who had radiation after lumpectomy. All of them have limitations including validity and reproducibility. The breast cancer radiation oncology research team has obtained software from researchers in Portugal that can measure the cosmetic result following radiation using a digitized photograph of the breast. Drs. Dayes, Whelan, and Theberge from Quebec City conducted a pilot study to compare the cosmetic outcome using this software with the usual physician assessment.

The ability to measure the cosmetic outcome in clinical trials of breast irradiation following lumpectomy is important in order to be able to weigh the advantages and disadvantages of different radiation regimens. However measuring the cosmetic outcome is a labor intensive and expensive process, particularly as large numbers of patients are usually required. It is hoped that
**THORN: Clinical utility of a Novel Molecular Breast Imaging Gamma Camera**

Co-Principal Investigators: G. Pond & K. Gulenchyn & L. Bordeleau, J. Valliant

**THORN: Clinical utility of a Novel Molecular Breast Imaging Gamma Camera**

Imaging of the breast is an important tool in the early detection, diagnosis and monitoring of response to treatment in breast cancer. Mammography has been the gold standard for detection of breast cancer for many years. Mammographic findings are based on anatomic changes in the breast and detection is based on differences in density of normal and abnormal tissues. However, the ability of mammography to correctly spot cancer varies from greater than 80% in women over the age of 50 to 68% for women 40 to 44 years of age. This difference is due to increased breast density in younger women. Ultrasound (US) uses high-frequency sound waves to create a picture of an area of interest. It is most frequently used to direct biopsy and to determine whether a lump is solid or cystic. Magnetic Resonance Imaging (MRI) uses magnetic fields to produce detailed cross-sectional images providing very good soft tissue contrast. MRI of the breast is now used in addition to mammography, as a test in high risk women for detection of breast cancer. In addition, MRI is increasingly being used prior to

Funded 2010 Study Accrual Complete; analysis is pending
breast cancer surgery to assess the extent of tumor.

Another imaging method is to use a substance with attached radioactivity and inject it into patients. This substance is taken up preferentially by cancer cells and can then be photographed. A novel compact gamma imaging system, developed by General Electric, can be used to photograph a radioactive substance taken up by breast cancer cells. This new camera is positioned close to the breast so that, in most cases, all breast tissue is within 5 cm of the detector. Most recently, dual detector systems have been introduced, further reducing the lesion to detector distance and improving the image. This modern technology, called Molecular Breast Imaging (MBI), has the potential to detect breast cancer in difficult situations (e.g. dense breasts), to measure the response of breast tumors to treatment, to measure blood flow within tumors, and to determine whether drugs can penetrate into tumors.

Dr. G. Pond, an OCOG biostatistician, lead the multidisciplinary team (J Valiant, head of the Centre for Probe Development and Commercialization (CPDC), at McMaster; K Gulenchyn, head of Nuclear Medicine at HHS; and L. Bordeleau, medical oncologist at the JCC who specializes in hereditary cancers) in the
THORN trial. In the THORN trial the goal was to study the feasibility and safety of the MBI Gamma Camera, and to explore the ability of this camera to detect early breast cancer in women at high risk of developing breast cancer (e.g. BRCA1/2 carriers). These women presently undergo annual MRI and as part of the study, underwent MRI and MBI at baseline and again at 12 months. 42 women participated in this study.

Identifying risk factors for Locoregional Recurrence following Postmastectomy Radiotherapy in Breast Cancer Patients

Co-Principal Investigators: L. Chang & D. Kim
Co-Investigators: C.Gu, J. Julian, I. Dayes, H. Reiter, B. Strang, J. Wright, T. Whelan

Identifying risk factors for Locoregional Recurrence following Postmastectomy Radiotherapy in Breast Cancer Patients

Funded 2011
Study Completed

Approximately 30% of women who present with early breast cancer undergo mastectomy. The results of randomized clinical trials have shown that post mastectomy radiotherapy (PMRT) (radiation to the chest wall, nodes in the neck and nodes under the arm) reduces the risk of local (chest wall) and regional (nodes of the neck and under the arm) recurrence and possibly improves survival. Recurrence under the arm can be particularly symptomatic with swelling of the arm and pain from invasion of the nerves, which can have a devastating impact on quality of life.

Unfortunately, even with PMRT, some patients remain at an increased risk of recurrence and it is not clear why these patients are more likely to recur.

In the current study led by a radiation oncology resident, Dr. Lynn Chang, a historical cohort
study was performed to identify tumor and patient factors which predict for local regional recurrence following PMRT. The records of the Juravinski Cancer Centre were searched to identify patients who received PMRT between January 1997 and December 2008. Information regarding the patient and their breast cancer disease factors, such as tumor size, estrogen receptor status, number of lymph nodes involved, etc., were collected. The goal was to identify patients who had a local regional recurrence after receiving PMRT, to determine if there were any specific risk factors associated with recurrence. If such risk factors can be identified, there is the potential to perform further research evaluating novel radiation regimens in patients with this type of breast cancer.

800 patients were identified as eligible for this study. The research team collected the study specified information from the case records of these patients and has identified those who have had a local regional breast cancer recurrence. A biostatistician has analyzed the data and results have been presented nationally. The results showed that patients with lymphovascular invasion positive or hormone (estrogen/progesterone) receptor negative disease appear to be at higher risk of locoregional recurrence despite PMRT and may
| Phase II study of Acupuncture-like Transcutaneous Stimulation (ALTENS) in the management of Vasomotor Symptoms induced by Breast Cancer Treatments | Co- Principals: R. Wong & M. Forbes  
Co-Investigators: M. Levine, S. Sagar, J. Hayward | Phase II study of Acupuncture-like Transcutaneous Stimulation (ALTENS) in the management of Vasomotor Symptoms induced by Breast Cancer Treatments  
After menopause many women experience hot flashes that are bothersome and at time debilitating. Using hormone replacement therapy is not an option for women with breast cancer because it can increase the risk for breast cancer recurrence or the formation of a new breast cancer. Although there are medications (e.g. Effexor XR, Gabapentin, Dixarit) that can reduce hot flashes, they often have side effects. As such, women often prefer to use lifestyle interventions to ease hot flashes. Scientific studies have shown that acupuncture can have some benefit in relieving hot flashes, but is often costly and difficult to obtain skilled services. In addition, some women do not like the needle penetration associated with acupuncture. For this reason, Dr. Raimond Wong and Margaret Forbes RN(EC) developed a clinical study to find out whether a non-needle treatment using acupuncture-like transcutaneous electrical stimulation (ALTENS) is an effective way of reducing hot flashes in women with breast cancer. Using a randomized method, eligible women with breast cancer received either a standard lifestyle intervention (education and counseling) or twelve ALTENS treatments. | Funded 2010  
Study Accrual completed |
treatments in addition to the standard lifestyle intervention. Results to follow completion of study.

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<th>CABOT - Determining the cardiac biomarker profile in Breast Cancer patients receiving adjuvant trastuzumab therapy</th>
<th>Principal Investigator: B. Dhesy</th>
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<td>Doxorubicin is a chemotherapy drug used commonly in women who have undergone surgery for breast cancer to prevent recurrent cancer. Although it is a very effective agent in fighting breast cancer, it can cause permanent damage to the muscle of the heart. Approximately 25% of breast cancers overexpress a gene called HER2 neu. As a result of this change the cancer is more aggressive than a cancer which has the normal amount of this gene. There is a drug called trastuzumab which is very effective in targeting and killing cancers which overexpress HER2 neu. Unfortunately this drug can cross react with the heart tissue and damage the heart. Currently women with breast cancer who receive doxorubicin followed by trastuzumab are monitored by nuclear cardiac imaging. However such testing is not very good at assessing cardiac damage.</td>
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<td>Dr. Dhesy and colleagues are conducting a study to evaluate whether blood tests called cardiac biomarkers (troponins and pro-brain natriuretic peptide) are able to detect cardiac damage.</td>
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<td>Funded 2010 Study Open to Accrual 10 participants still required.</td>
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peptides) which are sensitive to very small amounts of heart muscle injury can detect very early damage to heart muscle in patients receiving doxorubicin and trastuzumab. If this were to be the case, then these drugs could be discontinued before there was any permanent damage to the heart.

The study started to recruit patients in July 2010 and to date 15/25 patients have been recruited.

**CD200 in Human Breast Cancer**

Co-Principal Investigators: D.A. Clark & B. Dhesy
Co-Investigator: J. Ramsay

It has been recognized that an established tumor is able to shut down immune rejection cells so they can’t work. A molecule called CD200 appears to be very important in this shut down process. CD200 is expressed on stem cells. All tissues in the body develop from stem cells. When a genetic change occurs in a stem cell, it may become malignant and give rise to a collection of more developed cells recognized as a cancer, and many of these cells do not express CD200. However, as long as CD200 is present, the stem cell can evade rejection. Chemotherapy is most effective when aided by an immune response, but killing the last cell requires eradicating cancer stem cells. Over time, more and more genetic changes in stem cells enable the tumor to metastasize to different organs, and resist chemotherapy. In this project, tumor tissues removed at surgery are stained for CD200⁺ cells, to see if tumors with a large
percentage of these cells are more aggressive. CD200\(^+\) cells can also protect CD200\(^-\) tumor cells from rejection by releasing CD200 in soluble form into surrounding tissues and the bloodstream. Investigators expect to find more CD200 in the blood when there are more CD200\(^+\) cells in the tumor. Eventually, we hope to predict which women will benefit most from a new monoclonal antibody to human CD200.

**Antineoplastic activity of Vitamin D and melatonin: A clinical trial**

**Principal Investigator:** P. Rana & P. Muti  
**Co-Investigators:** N. Hodgson, P. Lovrics, B. Heller

We plan to study whether Vitamin D and melatonin can reduce the growth of cancer cells in women with breast cancer. Studies using cell cultures and animals have shown that Vitamin D can reduce the spread of cancer. Studies in people have shown that exposure to sun and eating foods containing high levels of Vitamin D can protect against cancer. Your body secretes a natural hormone called melatonin usually during the night while you sleep. Researchers have noticed that an increase in melatonin levels appears to lower the risk of getting cancer. Women with cancer proven by breast biopsy who are planned for surgery will be included. We want to see if treatment with Vitamin D (2000 IU daily), or melatonin (20mg daily), or both pills, reduces the growth of cancer cells when compared to women who are treated with sugar pills. All women will receive identical appearing

**Funded 2013 Study to open soon**
pills for approximately four weeks. We will measure a tumour protein called Ki67 in the biopsy and in the tumour removed at surgery. Ki67 provides information on how rapidly the cancer grows. The reduction in the Ki67 levels between the biopsy and surgery will be compared between the four groups. The protocol has received ethics approval.

**Young Women with Breast Cancer Experiences and Needs**

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<th>Principal Investigator: N. Hodgson &amp; P. Rana</th>
<th><strong>Young Women with Breast Cancer Experiences and Needs</strong></th>
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<td>Co-Investigators: J. Sussman, G. Pond, L. Bordeleau, S. Mukherjee, M. Forbes, K. Madde</td>
<td>Breast cancer in young women is a distinct entity with its own challenges. Young women with breast cancer can experience similar physical and emotional issues as older women with breast cancer, e.g. nausea, vomiting, hair loss, altered body image and uncertainty about the future. In addition, they can experience unique problems including: premature treatment-induced menopause, infertility, strain in relationships and decisions for bilateral mastectomy (or not). This proposal examines these issues and experiences which are often sources of distress in young women with breast cancer. The primary aim is to explore the unique physical and psychosocial needs of young women (&lt;40 years) with breast cancer in LHIN 4. The study has two parts. In Phase 1, found focus groups of 4-8 women with breast cancer &lt;40 years will be conducted to learn about the treatment experience, decisions during treatment, needs during and after treatment and supports sought and received.</td>
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Funded 2013 Study to open soon
Based on Phase 1, an instrument will be constructed with items that reflect themes identified in the focus groups. This instrument will then be completed by approximately 60 young women with breast cancer who are within the first 12 weeks of diagnosis. It will describe the care that is being provided to these women and where gaps exist. It will help inform us on the development of the best strategies to improve the care and experience of these women.