OHSU Cancer Committee
2010 Annual Report

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Dear Colleagues,

I am delighted to present the 2010 OHSU Cancer Committee Annual Report. As Chair of the Cancer Committee, I have enjoyed the privilege of a front-row seat to impressive growth within the OHSU Knight Cancer Institute—growth that affects all of us in our quest to reduce and eliminate suffering from cancer. This year’s report focuses on liver oncology, one of our many comprehensive programs. As part of our Continuing Medical Education series in April 2010, the OHSU Knight Cancer Institute was honored to host *Progress in the Multidisciplinary Management of Hepatobiliary and Pancreatic Cancer* at the Hotel Vintage Plaza in Portland. As course director, I worked with nine of my expert OHSU colleagues to address the controversy surrounding the appropriate post-operative treatment for pancreatic cancer, and to help participants learn all of the treatment options available to people with liver cancer.

This year, our coordinated care clinics expanded in two critical areas: pancreatic and lung cancer. Patients facing these diseases will continue to have access to some of the best minds in cancer treatment with the added ease of efficient, comprehensive multidisciplinary care. Our vision to provide world-class, compassionate, individualized care for everyone in the Pacific Northwest is enhanced by our growth in the number of multidisciplinary clinics offered.

I am also proud to announce that the OHSU Knight Cancer Institute is using another enhanced tool to treat cancer: hyperthermia treatment. The acquisition of the BSD-500 hyperthermia system allows OHSU radiation oncologists to treat a variety of superficial cancers with high temperatures. Research shows that high temperatures can damage cancer cells and potentially shrink tumors, usually with minimal damage to normal tissue. When hyperthermia treatment is combined with radiation or chemotherapy, the results are dramatic and often vastly exceed the tumor response that would be mediated by chemotherapy or radiation therapy alone.

We were also very pleased this year to initiate Intrabeam therapy for women with breast cancer. This novel therapy provides partial breast irradiation within a single treatment session. This is enormously beneficial for women who want breast-conserving treatment, particularly if they do not live near a radiation treatment facility.

As the OHSU Knight Cancer Institute grows, so does our dedication to collaborate with colleagues across our state and nation to unlock the secrets to defeating cancer. We are encouraged by our successes, and remain grateful to share those victories with you.

Kevin Billingsley, M.D.
Chairman, OHSU Cancer Committee
Hedinger Associate Professor of Surgery and Chief of the Division of Surgical Oncology
OHSU Knight Cancer Institute
My Knight Cancer Story: Anthony Esposito

I was doing yard work when sudden stomach cramps made it impossible for me to bend over. I thought I’d just overdone it a bit, and went it to take a nap. When I woke up, the pain was worse. I drove with my daughter to the emergency room. The pain was so bad, I couldn’t complete the intake paperwork in the waiting room.

Emergency surgery revealed my spleen had ruptured. In removing it, the surgeon noticed a lump on my liver and took a biopsy. I learned over the phone from my doctor that I had liver cancer. He recommended I go to Portland for treatment at the OHSU Knight Cancer Institute.

Kevin Billingsley, M.D., and Jonathan Schwartz, M.D., were extremely patient and helpful in explaining all of my options for surgery and follow-up treatment. They told me that the tumor board, where all OHSU Knight Cancer Institute liver cancer specialists would meet and discuss my case as a team and give me a recommendation, was going to meet at the end of the week, and they would let me know what their recommendation was. The fact that I had a team of specialists working on my case gave me such great confidence. The doctors worked together, focused on my specific situation, and worked with me and my family to make sure we understood all of our options. That allowed me to relax and feel comfortable that the decision we made was the best one for me.

The doctors recommended laparoscopic radiofrequency ablation, a surgical procedure which uses heat energy to destroy the liver tumor. I wasn’t worried about it; I knew it had to be done. I had faith in my doctors and concentrated on going in with a positive attitude. Thankfully, everything went well.

The day after my surgery was my daughter’s birthday, and my doctors knew I was anxious to go home. I was walking the halls for exercise, when Dr. Billingsley came up and said he’d begun the paperwork so I could go home. I was so grateful. I went home with strict orders to take things slowly, especially at work. I listened to my doctors and my body, and within a couple of weeks, I was back to full strength.

I’m now in a clinical trial for a drug which will hopefully keep my cancer from coming back. It’s comforting to know that not only do I have access to cutting-edge care through the clinical trial, but my experience may help someone in the future. It’s a wonderful way to help the doctors who are helping me, as they try to conquer cancer.

My entire experience at the OHSU Knight Cancer Institute was excellent. Everyone was so helpful with information, and they took the time to explain everything to me and my family. The people at the Knight Cancer Institute make you feel like they love their job, and they want to help you. I am so grateful for all they did for me.

To read another inspiring story from an OHSU Knight Cancer Institute liver cancer patient, please visit www.ohsuhealth.com/livercancer.
At the OHSU Knight Cancer Institute, experts gather as a team to provide integrated, multidisciplinary care for patients with liver cancers. Because treatment for liver cancer is very complex, patients benefit most from working with a coordinated team of experts. Hepatologists, interventional radiologists, surgical oncologists, transplant medicine and radiation oncologists all work together to evaluate the cancer and determine the best therapies for patients.

A nurse navigator coordinates appointments and guides patients through all stages of cancer treatment. This service includes scheduling a team of specialists to meet with patients in one or more coordinated sessions and to provide a personalized plan tailored to the individual's specific needs and risks. In addition to access to the latest treatment innovations, patients will also have the opportunity to be evaluated for participation in clinical trials on groundbreaking new therapeutics.

WHAT IS LIVER CANCER?
Liver cancer is increasing in the United States, especially in people with chronic liver diseases. In 2009, approximately 23,000 people were diagnosed with liver cancer in the U.S., and about 18,000 people died from the disease. In Oregon, more people with Asian and Pacific Island heritage get liver cancer and die from this disease.

Primary liver cancer arises from either the cells of the liver or the cells lining the bile duct within the liver. Cancer arising from the bile duct is called cholangiocarcinoma. Cancer arising from the liver itself is called hepatocellular carcinoma (HCC). Most people who get HCC already have a liver disease such as hepatitis B or C or cirrhosis. These conditions lead to chronic liver inflammation that eventually progresses to cirrhosis and can ultimately lead to liver failure. Other liver diseases that may predispose to cirrhosis and liver cancer are hemochromatosis, autoimmune liver disease, fatty liver disease and sclerosing cholangitis.

Secondary liver cancer is cancer that spreads to the liver from another part of the body, such as the prostate, breast or lung.

At the OHSU Knight Cancer Institute, our Liver Cancer Clinic focuses on primary liver tumors with a special focus on HCC, with therapies that represent the complete range of liver tumor treatments available today.
DIAGNOSIS AND STAGING
In addition to a complete medical history and physical examination, diagnostic procedures for HCC may include:

Liver function tests — a series of special blood tests that can determine if the liver is functioning properly.

Abdominal ultrasound (sonography) — a diagnostic imaging technique which uses high-frequency sound waves to create an image of the internal organs. Ultrasounds are used to view internal organs of the abdomen such as the liver, spleen, and kidneys and to assess blood flow through various vessels.

Computed tomography scan (CT or CAT scan) — a diagnostic imaging procedure using a combination of X-rays and computer technology to produce cross-sectional images (often called slices), both horizontally and vertically of the body. A CT scan shows detailed images of any part of the body, including the bones, muscles, fat and organs. CT scans are more detailed than general X-rays.

Hepatic arteriography — X-rays taken after a special substance is injected into the hepatic artery.

Liver biopsy — a procedure in which tissue samples from the liver are removed (with a needle or during surgery) from the body for examination under a microscope.

Magnetic resonance imaging (MRI) — a diagnostic procedure that uses a combination of large magnets, radio frequencies and a computer to produce detailed images of organs and structures within the body.

WHAT ARE THE STAGES OF LIVER CANCER?
When a physician diagnoses liver cancer, the next step is to determine how far the cancer cells have spread (a process called staging). The National Cancer Institute defines the following stages for primary liver cancer:

Localized resectable — Cancer is in the liver only, has not spread and can be removed completely with surgery.

Localized unresectable — Cancer is in the liver only, has not spread but cannot be totally removed.

Advanced — Cancer has spread throughout the liver or to other parts of the body.

Recurrent — Cancer has come back after it was treated.

LIVER RESECTION
By Kevin Billingsley, M.D., chief, Division of Surgical Oncology, co-director, Multidisciplinary Liver Tumor Clinic
Liver resection remains one of the primary treatment modalities for patients with liver cancer. Resection involves the surgical removal of a portion of the liver. Along with liver transplantation, it is one of the only potentially curative treatments for liver cancer.

While the liver is essential for a number of vital functions, removal of a significant portion of the liver is feasible: This remarkable capacity to regenerate is unique to the liver compared to other organs in the body.

The degree and severity of underlying liver disease is very important. Patients with moderate to severe liver disease will not tolerate liver resection, because the liver remnant will not have the capacity to adequately regenerate to replace the lost liver segment. Liver resection in this group of patients usually results in chronic liver failure which can be fatal and can be salvaged only with urgent liver transplantation.

Taking into consideration all of these factors, the liver team recommends resection for only a small percentage of liver tumor patients who are treated at OHSU. Patients deemed inappropriate for resection are referred for alternative treatments including liver transplantation, transarterial chemoembolization, radiation therapy and chemotherapeutic treatment.

For patients who are carefully selected for surgery, OHSU hepatobiliary surgeons are able to offer liver resection with the greatest possible safety. In
Liver resection remains one of the primary treatment modalities for patients with liver cancer.

In some cases, liver resection may be performed using a laparoscopic approach to aid recovery in the postoperative period.

**LIVER TRANSPLANTATION FOR PATIENTS WITH HCC**

*By Susan L. Orloff, M.D., F.A.C.S., chief, Division of Abdominal Organ Transplantation and director, Liver Transplantation*

There are times when HCC cannot easily be removed with a surgical resection, such as when it develops in a damaged (cirrhotic) liver. If a liver is undamaged, up to 75 percent of it can be safely removed during surgery, and the remaining liver will grow back to the original size. If the liver is cirrhotic, surgical removal of the tumor is often not possible, because the remaining liver is also damaged, and does not regenerate nearly as well as a normal liver.

When surgical removal of HCC is not an option because of poor liver function, liver transplant (LT) becomes attractive. With a liver transplant, the cancerous liver can be completely removed, thereby curing the cancer and simultaneously replacing the damaged liver, hence one operation that cures two diseases. Because the cirrhotic liver is removed, the chances of developing a new HCC are dramatically reduced.

Liver transplant is the only available therapy that treats the cancer (by removal) while also profoundly limiting the risk of new liver cancer. Though an excellent option for the right patient, LT is not an option for everyone, for a variety of reasons. In addition, there are not enough donated liver organs to satisfy the need.

The primary problem with using LT to treat HCC is the worry that the cancer may have spread beyond the liver prior to transplant. If the cancer has escaped the liver (or become metastatic), LT will not benefit the patient. Though LT will remove the primary tumor, cancer cells in other parts of the body will not be removed, and will ultimately grow and take the patient’s life.

In fact, medicines used after LT to prevent rejection of the new liver by the patient’s immune system will cause metastatic HCC to grow much more quickly than it might without immune-suppressing medications. Thus, LT for patients with metastatic HCC would cause them to die more quickly than if they had not gotten a transplant.

Metastatic HCC may be difficult to detect before LT. Studies have shown us that the size and number of HCC tumors in the liver correlate well with whether undetectable HCC has escaped the liver. The most commonly used criteria to help us determine if HCC has become metastatic (even if scans do not...
Liver transplant is the only available therapy that treats the cancer (by removal) while also profoundly limiting the risk of new liver cancer.

show it in other parts of the body) are the so-called Milan criteria. These well-validated criteria suggest that if a single HCC tumor is larger than 5 cm (about 2 inches) or three tumors any larger than 3 cm, then it is likely that the HCC has escaped the liver and LT is not a good option.

Most centers, including OHSU, adhere to these criteria, and will not typically transplant patients with HCC that exceeds these sizes. However, some centers have transplanted selected patients with larger tumors where initial treatments (other than LT) directed at the tumor itself are successful in shrinking the cancer (down-staging). OHSU has down-staged selected patients and transplanted them, and will consider this for the right patient.

The other major problem with using LT to treat HCC is that there are simply not enough donor livers available for all the patients who could benefit from transplant. Because of the scarcity of donor livers, transplant centers (including OHSU) are careful to select patients who will survive the LT and have the resources to maintain the rigorous medical regimen needed post-transplant. This means that candidates for LT must not have other serious medical issues (especially significant heart or lung problems), and must have financial and social support resources necessary for success post-transplant. Problems with depression and substance abuse must be adequately treated prior to LT, as active psychiatric and substance abuse problems can easily derail post-transplant care, resulting in the loss of a precious liver.

It is important to receive care from a multidisciplinary team when a patient has HCC. Such a team like the one at OHSU Knight Cancer Institute can help the patient decide if LT would be appropriate, or if one of the other therapies is best. And while the patient with HCC may be undergoing an evaluation for possible LT, he or she is likely to benefit from a number of other different liver-directed therapies in order to give the best chance at long-term survival if LT is not possible. Or, in the case of the patient who is waiting on the LT list, there are a number of possible liver-directed therapies that can be used with the aim of preventing growth of the tumor, to a size or number that would be outside the Milan criteria, and preclude LT. The survival results at OHSU’s liver transplant program are greater than 90 percent at one year, and close to 90 percent at three years.
INTERVENTIONAL RADIOLOGY
By Kenneth J. Kolbeck, M.D., Ph.D., co-director, Multidisciplinary Liver Tumor Clinic

Although liver transplant or resection provide the best statistics for a long term cure, almost 70 percent of patients with HCC are not able to pursue these two treatment options due to other health issues.

Interventional radiology provides an alternative approach to liver cancer treatment with a minimally invasive approach. Using small catheters and needles, treatment options designed to slow progression of the disease can be performed with ¼" long skin incisions and require limited hospital stays (“same day” or overnight). Although there are medical risks with any procedure, most patients do well and go home with a Band-Aid or a small sterile dressing.

In general, patients with outstanding liver function qualify for surgical resection options while patients with mild to moderate liver disease qualify for interventional radiology-based procedures. Patients with severe liver dysfunction have limited treatment options, such as transplant.

Catheter-based procedures utilize the normal flow of blood to help deliver high doses of an agent designed to kill cancer with minimal exposure to the rest of the body, reducing overall side effects. The catheters (Image E – see next page) are inserted in a blood vessel near the hip and follow the inside of the blood vessel through several branch points into the liver’s blood supply—specifically the blood supply to the tumor within the liver. From that point, chemotherapy agents, tumor staining agents, and radioactive beads can be delivered to the blood vessels supplying the tumor. After delivery of the agent, the catheter is removed and pressure applied to help the blood vessel heal. Depending upon the material delivered and symptoms, the patient may go home the same day or spend one night in the hospital. The majority of patients with selective internal radiation treatments go home the same day, while those receiving chemotherapy and tumor-staining agents spend one night in the hospital.

Needle-based procedures use CT, ultrasound or occasionally MRI to guide placement of a treatment device directly into the cancerous tumor while the needles are also small in diameter (Image F – see next page), the treatment zone can be expanded to targets of specific sizes. Depending upon the specific type and location of the cancer within the liver, different forms of energy can be used to heat or freeze the cancer. The extreme temperature change results in tissue death near the needle tip, killing the cancer. The “cook” or “freeze” approach

Figure 4. Liver with multiple tumors, making the patient unsuitable for liver transplant
to tumor treatment results in survival numbers approaching the surgical options described in other sections.

Interventional radiology procedures do not result in a “cure,” primarily because of growth of residual tumor cells after treatment or recurrent disease in new areas of the liver. The goal of interventional radiology procedures is to slow tumor growth, limit the impact on underlying liver function and hopefully prolong survival with minimal impact on the quality of life.

RADIATION THERAPY
By Martin Fuss, M.D., Ph.D., vice chair, Department of Radiation Medicine and director, IGRT Program

Radiation therapy uses high-energy radiation beams that penetrate deep into the body to kill cancer cells and shrink or control the growth of a tumor. Radiation can also be used to relieve symptoms, such as pain caused by the cancer.

While radiation therapy is very effective treatment for many types of cancer, liver tumors are not treated by radiation therapy at most institutions. Radiation treatment for liver tumors is particularly challenging due to their location within an organ that does not have a high tolerance for radiation, and may be permanently damaged by excess radiation doses. Also, the liver, and consequently liver tumors, move with every breath a patient takes during radiation treatments. This tumor motion needs to be accounted for to assure that the target is not missed during radiation delivery. Lastly, liver tumors may look very similar to the healthy tissue surrounding them, making it difficult to visualize them in image-guidance procedures that optimally position a radiation target right before treatment delivery.

On the other hand, smart use of modern radiation technology allows delivering high radiation doses very focally onto small tumors within the liver.

Compressing traditional radiation treatments that span many weeks into only a few days further potentiates the effectiveness of radiation to kill the tumor. Thus, short course, precision radiation treatments become effective in eradicating or ablating small liver tumors, while sparing the normal liver from irreversible radiation damage. At the OHSU Knight Cancer Institute, radiation treatment for liver cancer uses the most advanced techniques to protect healthy liver tissue while killing cancer cells. Most often radiation is prescribed in a multi-modality treatment concept following interventional radiology or surgical procedures. Some of the radiation techniques that help us control cancer include:

- **Stereotactic body radiation therapy (SBRT)** which delivers high-dose radiation treatments in only five treatment sessions.
- **Hypo-fractionated, short-course focused radiation therapy** treatments for liver tumors are delivered over 18 treatment days.
- **Intensity-modulated radiation therapy (IMRT)** a technology that allows to tailor the radiation beam very closely to the outline of a liver tumor.
- **Image-guided radiation therapy (IGRT)** a critical concept used at OHSU for all liver-directed radiation treatments. Image-guidance is used to assess and optimize the location of a liver tumor right before treatment delivery.

To address the challenges associated with radiation treatment of liver cancer, we acquired the only state-of-the-art BrainLAB /Varian Novalis TX linear accelerator in Oregon and southern Washington. In a world-wide unique installation, the Novalis TX unit is combined with a 16-slice in-room big-bore Philips Brilliance CT scanner. This powerful combination of technologies allows the radiation oncologist to
acquire high-resolution imaging of the liver tumor right before the radiation therapy is delivered by IGRT. It also allows us the ability to track changes in breathing-related liver tumor movement on a day-to-day basis.

Under an institutional treatment algorithm for the comprehensive treatment of HCC, precision radiation therapy is used on a case by case basis following transarterial chemoembolization (TACE) to minimize the risk for local tumor recurrence. The recommendation for radiation therapy is made by the OHSU Liver Tumor Board, a panel compromised of hepatologists, surgeons, interventional radiologists, medical oncologists, and radiation oncologists. Encouraging early outcome data presented at the American Society of Clinical Oncology Gastrointestinal Cancers Meeting (ASCO-GI) earlier this year support the safety of adding radiation therapy as a treatment modality for HCC. Preliminary outcomes in patients treated at OHSU Knight Cancer Institute also suggest that local tumor recurrences can be reduced from an expected rate of 30-50 percent to less than 10 percent. These favorable preliminary data serve as the basis for an institutional multi-modality prospective randomized trial assessing the benefit of adding focal radiation therapy to TACE, which is currently under consideration of the OHSU ethics committee.

HEPATOCELLULAR CARCINOMA OUTCOMES ANALYSIS

Recent years have brought increasing awareness of the substantial impact of primary liver cancer (hepatocellular carcinoma, HCC) on the American population. There is substantial evidence that the incidence rate of this disease is increasing. Although this may in part be due to increased surveillance and awareness, it is most likely related to development of liver cancer in individuals that contracted hepatitis C viral infection many years prior to the diagnosis of liver cancer.

In the past 10 years, OHSU has taken an increasingly active role in the treatment of this group of patients. The number of patients treated with HCC has increased to more than 100 new patients annually (Figure 6). The expansion in the clinical volume is partly related to increased incidence, but more likely is associated with the introduction of the OHSU multidisciplinary liver tumor program. This unique service offers comprehensive and coordinated multidisciplinary evaluation and treatment for patients from the entire region with HCC.

Although HCC remains an extraordinarily difficult disease, outcome analysis from patients treated at OHSU indicates that there is cause for cautious optimism for patients with stage I and II disease (Figure 7). OHSU patients with stage I disease have
Figure 7.

**OHSU Hepatocellular Cancer: Five Year Survival**

Source of Data: OHSU Cancer Registry  
Method of Calculation: Observed

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Survival in Months

Figure 8.

**NCDB Hepatocellular Cancer: Five Year Survival**

Source of Data: National Cancer Database (NCDB)  
Method of Calculation: Observed

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Survival in Months
a three-year survival of more than 50 percent. This outcome tracks closely to benchmark outcomes from the National Cancer Data Base which draws patient data from multiple institutions around the country. Stage II patients treated at OHSU have a three-year survival of 50 percent while the three-year survival for the NCDB patients is 38 percent. Patients with early stage disease are treated with a variety of modalities including resection, transplantation, and a full spectrum of catheter based therapies.

Unfortunately, outcomes remain poor and survival is limited for patients with stage III and stage IV disease. The treatment options are limited in this group of patients. For patients with well-preserved liver function, catheter based treatment and sometimes radiation therapy are options. Stage IV patients may be treated with systemic chemotherapy such as sorafenib, but are often best served by palliative (alleviating pain without curing) therapy alone.

RESEARCH AND CLINICAL TRIALS
The OHSU Knight Cancer Institute has more than 650 research scientists, doctors and staff working to treat patients and discover new ways to treat and cure all types of cancer. We are involved in more than 400 clinical trials and studies focusing on cancer treatment, prevention, diagnosis and screening. Clinical trials offer patients with cancer the opportunity for new cures and therapies and an improved quality of life. Our scientists and researchers are exploring promising research on HCC and other primary liver cancers.

Open clinical trials for liver cancer:

Bayer 12414 A Phase III Randomized, Double-Blind, Placebo-Controlled Study of Sorafenib as Adjuvant Treatment for Hepatocellular Carcinoma after Surgical Resection or Local Ablation This study is testing the use of the drug sorafenib for prevention of recurrence after the surgical removal of liver cancer.

Symptoms and Quality of Life in Patients with Advanced Liver Cancer This supportive care study supported by the American Cancer Society plans to provide a comprehensive description of the experience of pain, other symptoms, and quality of life over time in patients with liver cancer.

Transarterial Chemoembolization and Radioembolization for Hepatic Malignancy: The Dotter Experience The purpose of this retrospective study is to review the safety, effectiveness and potential survival benefits of chemoembolization and radioembolization in patients with malignant liver cancer.

Bristol Meyers Squibb CA182-033 5745 A Randomized, Double-Blind, Multi-Center Phase 3 Study of Brivanib versus Sorafenib as First-Line Treatment in Patients with Advanced Hepatocellular Carcinoma This study is being done to compare the effects of brivanib vs. sorafenib on patients with advanced hepatocellular carcinoma (HCC) that have not received previous treatment.

Bristol Meyers Squibb CA182 034A 4881, Double-blind, Multi-center Phase III Study of Brivanib plus Best Supportive Care (BSC) versus Placebo plus BSC in Subjects with Advanced Hepatocellular Carcinoma (HCC) who have Failed or are Intolerant to Sorafenib This study is being done to find out what effects brivanib has on patients with advanced hepatocellular carcinoma (HCC) who have failed or are intolerant to sorafenib.

Oregon Liver Tumor Registry 5222 The Oregon Liver Tumor Registry (OLTR) is being used to address the need for improved treatment and screening methods and to establish a liver specimen bank and epidemiology database for future cancer research including personalized cancer therapies and collaboration.

REFERENCES


# 2009 analytic cases - site and stage distribution

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*Note: Figures above represent 2009 analytic cases only (diagnosed here and/or received part or all first course treatment here). Basal and squamous cell carcinoma of the skin and CIS of the cervix are not collected.*
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