

IOERT

Intraoperative Electron-beam Radiation Therapy

Joel Tepper, MD – Former Chairman, Radiation Oncology;
Former President of ASTRO

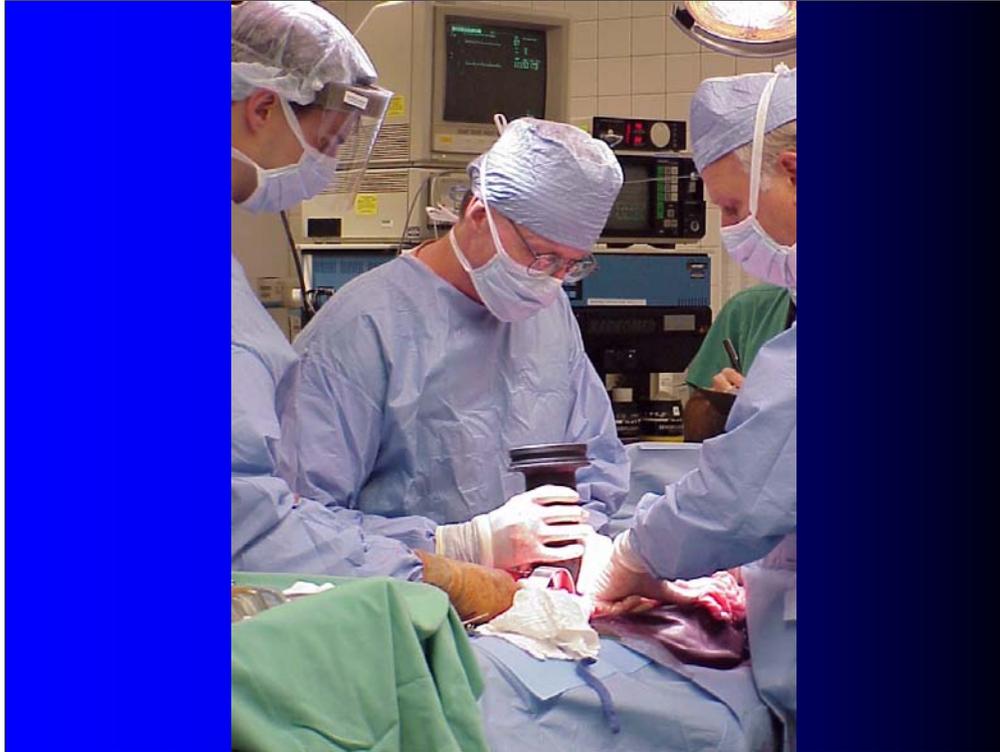
Benjamin Calvo, MD – Chief, Division of Surgical Oncology
& Endocrine Surgery

University of North Carolina

Good Morning. I am Dr. Joel Tepper, a radiation oncologist and former Chairman of Radiation Oncology at the University of North Carolina School of Medicine in Chapel Hill, North Carolina, and a former President of the American Society of Therapeutic Radiation Oncologists, or ASTRO.

Today I would like to briefly describe a treatment procedure called IntraOperative Electron-beam Radiation Therapy (or “IOERT”) that we are fortunate to have at our hospital and which is used at several other university hospitals in the U.S. This treatment is for cancer patients undergoing surgery to remove malignant tumors.

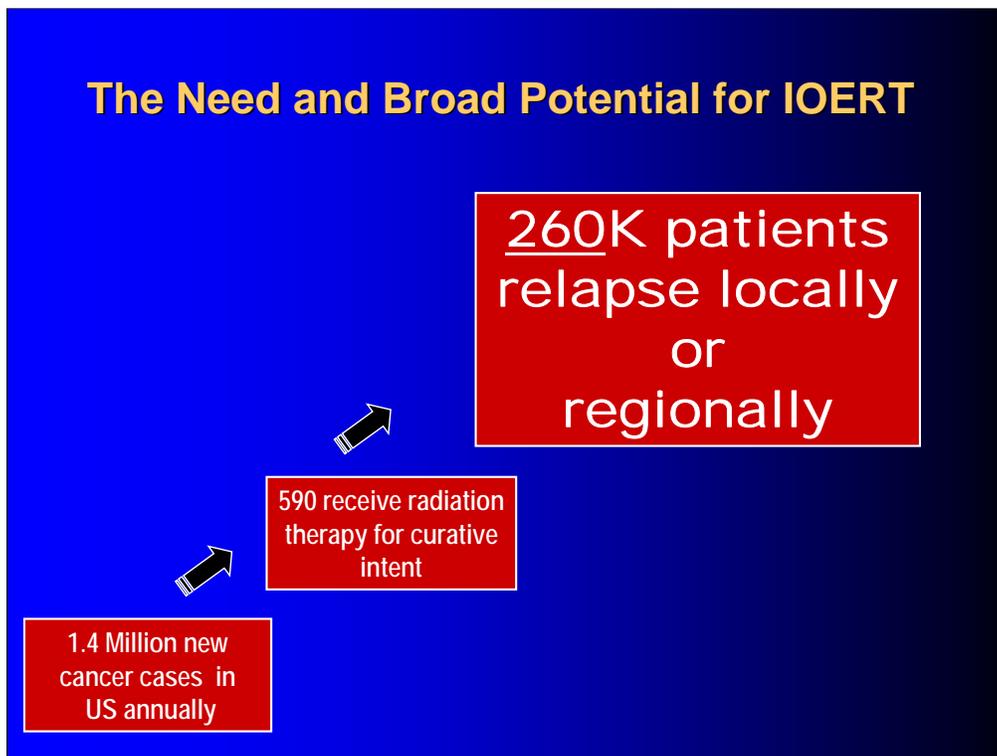
I will tell you about this technique, why we are glad to have it at our institution, and the technology that we have at our institution that makes IOERT practical to deliver. My colleague, Dr. Calvo, will discuss some of the clinical results and show you how this technology is actually used at UNC.



Every year in the U.S. approximately 700,000 patients undergo surgery to remove all or part of a malignant tumor. Either prior to the surgery, or after the surgery, many cancer patients will also receive a 5-8 week course of conventional external beam radiation therapy, and sometimes also a course of chemotherapy.

If the radiation is given before the surgery, the idea is to shrink the tumor and to make it easier for the surgeon to operate and remove the cancer. If the radiation is given after the surgery, we are trying to destroy any remaining tumor cells and to prevent recurrence of the disease.

The Need and Broad Potential for IOERT



In spite of the great improvements that have been made in cancer surgical techniques and in the improvements available with modern external beam radiation treatment units, unfortunately, the recurrence rates are still higher than we would like them to be.

Approximately 1.4 million new cancer cases are diagnosed each year in the U.S. Of these about 590,000 are treated with external beam radiation with curative intent, but almost half of those patients suffer a relapse either locally or regionally.

We are always searching for ways to improve these results. IOERT may be one of the answers for the patients whose tumors are surgically resected.

What is Intraoperative Electron Beam Radiation Therapy (IOERT)?



Intraoperative Electron Beam Radiation Therapy is the application of radiation directly to the residual tumor or tumor bed during cancer surgery

IOERT allows the radiation oncologist to deliver a powerful dose of radiation at the time of surgery to any microscopic or residual tumor that may still be present after the surgeon has removed all of the tumor that he can see.

“IOERT is focal radiation therapy, where you have direct visualization of the tumor or tumor bed which thus allows the radiation oncologist to exclude sensitive normal tissues from the field of radiation and thus avoid potential morbidity to those tissues. IOERT allows for the delivery of a higher dose of radiation therapy and thus the potential for increased tumor control.”

Biological Model Prediction

If the total dose of radiation is increased safely:

- The tumor recurrence rate would decrease
- The long-term survival rate would increase

Biological models suggest that a single dose of IOERT is equivalent to several weeks of conventional radiation treatments. The higher the dose that is safely delivered to the patient, the higher the chances are of decreasing tumor recurrence and the better the chance of increasing patient survival.

These are the goals of all cancer treatments.

Radiation oncologists cannot safely increase the dose with conventional external beam radiation therapy alone.

IOERT Benefits

- Critical structures that limit the total dose given can be temporarily moved or protected from irradiations.
- Patients with advanced disease can safely receive a higher dose of radiation.
- Residual tumor and tumor bed can be irradiated without irradiating sensitive skin.
- Higher doses can be delivered in fewer treatments in a shorter period of time, likely replacing two weeks of conventional external beam radiation therapy.

What are the benefits to the patient of delivering IOERT?

- (1) While the surgical wound is still open, critical structures such as nerve bundles and large blood vessels and other sensitive structures which limit the amount of radiation that can be delivered safely to a patient are temporarily moved out of the way.
- (2) It is possible that microscopic disease can be released by tumor resection. If this occurs, immediate irradiation of these cells can reduce the chance that these cells can re-implant or move around through the lymphatic system.
- (3) If a patient receives IOERT, several weeks of conventional radiation treatment can be eliminated. This may be a more convenient treatment for the patient and, in some cases can provide the additional radiation at just the right time so that the overall cancer treatment of the patient is more effective.

IOERT with Conventional Equipment Using Patient Transportation

- Remove malignancy in operating room
- Temporarily close or cover the surgical wound
- Move the patient with all monitoring and anesthesia equipment
 - Out of Operating Room
 - Down an elevator
 - Into radiation oncology treatment bunker
- Reopen surgical wound
- Treat with electron radiation from conventional accelerator
- Return to operating room
- Complete the surgery and close surgical wound

Clearly, IOERT has great potential benefit to any major cancer program. Before telling you how we deliver IOERT at the University of North Carolina, let me try to explain how some other hospitals have tried to deliver IOERT.

Because conventional linear accelerators are very heavy (20,000 pounds) and require tons of shielding to protect surrounding areas, very few centers have linear accelerators to administer radiation therapy in operating rooms. They are forced to go to extreme measures to deliver IOERT.

After tumor resection the patients are removed from the operating room still on the operation table and still connected to all of the monitoring and anesthesia equipment. They are then transported with all the equipment down an elevator and through corridors to the Radiation Therapy Department where they are treated with a conventional linear accelerator.

In most institutions the patients are then transported back to the operating room for closure of the surgical wound. This procedure is difficult and risky, but the results prove beneficial for the patients. For several types of tumors at various anatomical sites, the recurrence rates significantly decrease, and survival rates significantly increase.

This procedure, which I used to do 25 years ago at Massachusetts General Hospital, tied up the conventional linear accelerator and the OR for 1-2 hours. Very few hospitals can do IOERT this way any longer, because both the surgery and radiation departments are just too busy to have such a major interruption to their daily routines.

Mobile IOERT Approach

- IOERT dedicated, self-shielded, mobile, electron linear accelerator available when needed in a standard operating room
- In use at several hospitals in the U.S. and abroad
- Requesting new ICD-9 III Procedure Code 17.10 for this new approach.



More recently, companies have designed self-shielded Electron Linear Accelerators dedicated to IOERT use and have installed them directly in ordinary operating rooms. This eliminated the problems outlined with the previous approaches.

This new technology provides IOERT treatment at 1/8 of the weight of conventional units, and requires no shielding during its use. Because the accelerator is light and mobile, it can be shared among a hospital's existing operating rooms.

92.25 is an old code that is used for conventional external beam radiation therapy delivered by treatment units located in the radiation therapy department. The code that we are requesting is for IntraOperative Radiation Therapy which is very different and is beneficial to patients in that it delivers a much higher dose of radiation through the surgical opening to patients while they are in the operating room by a specially designed IOERT accelerator

Mobile IOERT Equipment



Now let me explain how the mobile IOERT system works.

Clinical Applications of IOERT



Now I would like to introduce my colleague, Dr. Ben Calvo, Division of Surgical Oncology & Endocrine Surgery at UNC who will tell you about some of the clinical results using IOERT to treat cancer at our University.

Good Morning. I will be discussing selected clinical results using IOERT and showing you an example of how IOERT with mobile technology works. Despite the improved clinical results with IOERT that I will show you, as the head of a busy surgical oncology division I am not certain we would ever have considered adding IOERT to our cancer program if we had to transport the patient out of the operating room environment. IOERT just isn't practical to do unless the IOERT unit is in the surgery department.

Breadth of IOERT Clinical Applications

- Locally advanced and recurrent rectal
- Locally advanced and recurrent GYN
- Pancreatic
- Gastric
- Bladder
- Soft tissue, bone and retroperitoneal sarcomas
- Head and Neck
- Hepatobiliary
- Esophageal
- Central Nervous System Tumors
- Breast*
- Lung*
- Prostate*

* Early research shows promise

These are some of the cancers that have been treated with IOERT. In most published studies, the use of IOERT in the treatment of these cancers results in an increase in local control, and for many sites, also an improvement in survival. Hospitals tend to specialize in just a few of these areas, depending on the specialty interests of their surgeons and radiation oncologists.

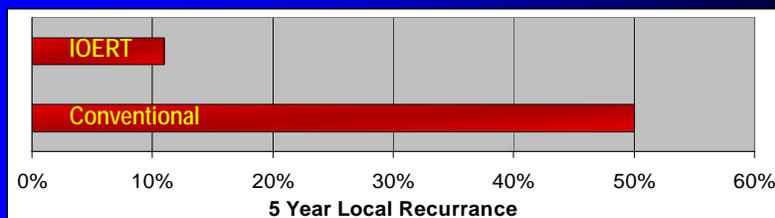
Speaking on behalf of the clinical community, we have used IOERT to treat locally advanced rectal cancer, recurrent rectal cancer, recurrent gynecological cancer, sarcomas, pancreatic cancer, head & neck, bladder and early stage breast cancer. I have personal experience with breast, head and neck, and rectal cancer treatment delivery.

We have presented some of our experiences with IOERT at various scientific meetings, and recently published the innovative IOERT technique we have developed for treating early stage breast cancer.

As the Chief of the Division of Surgical Oncology & Endocrine Surgery, I can tell you that we are very pleased to have IOERT at our institution to offer our patients. We have had this capability at UNC for approximately five years. While we are still accumulating our own data at the various sites I mentioned, I would like to share with you some of the results of published studies on IOERT from some other institutions so that you can see why we are so glad to have this treatment option available.

Locally Advanced Rectal Cancer

IOERT Decreases Recurrence



Colorectal cancer is the third leading cancer in both men and women. Fortunately, when it is detected early the patients have an excellent chance of being cured. Unfortunately, not all patients have early stage disease at the time of diagnosis. The more advanced the disease, the more difficult the treatment and the worse the prognosis.

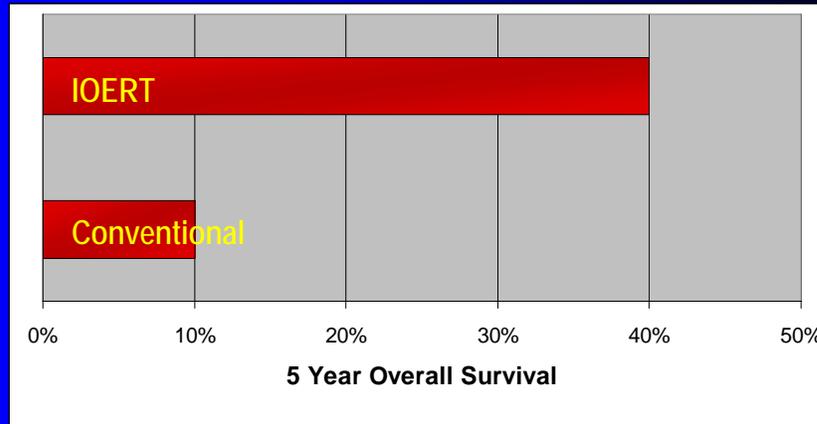
For patients with locally advanced rectal cancer, the treatment strategy is to give the patient pre-operative radiation and chemotherapy in an attempt to shrink the tumor and make the tumor more amenable to surgery. If the surgeon can achieve a total resection, the patients have up to a 40% chance of surviving 5 years. But in these advanced rectal cancer patients, more than half of the patients will have the tumor grow back, in spite of this aggressive treatment with surgery, radiation and chemotherapy.

If the tumor recurs in a rectal cancer patient, the patient will need more surgery, more hospitalization, more radiation and much more medical care. The prognosis for recurrent rectal cancer patients is not good.

However, if IOERT is added, survival is improved to about 60%. Very importantly, the tumor will recur in only 10% of the patients. Having a technique that can reduce recurrences is a real benefit to the patient.

Saving Lives – Recurrent Rectal Cancer

IOERT Increases Survival



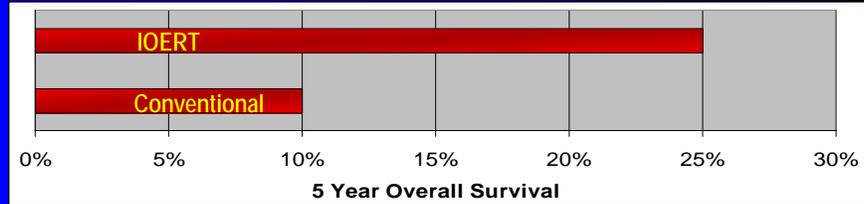
If the oncologist is presented with a recurrent rectal cancer, the prognosis for most patients is indeed grim. The 5-year survival is less than 10% with the best surgical and conventional external beam radiation therapy approaches.

However, if you also give IOERT to the patient, the survival is increased to as much as 40%.

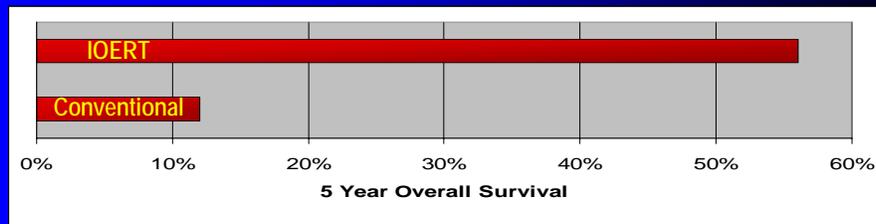
With advanced and recurrent disease, IOERT is a powerful weapon we can use in the battle to help these cancer patients.

Saving Lives -- Head and Neck Cancer

IOERT Increases Survival for Locally Recurrent Head & Neck Cancer



IOERT Increases Survival for Locally Advanced Head & Neck Cancer



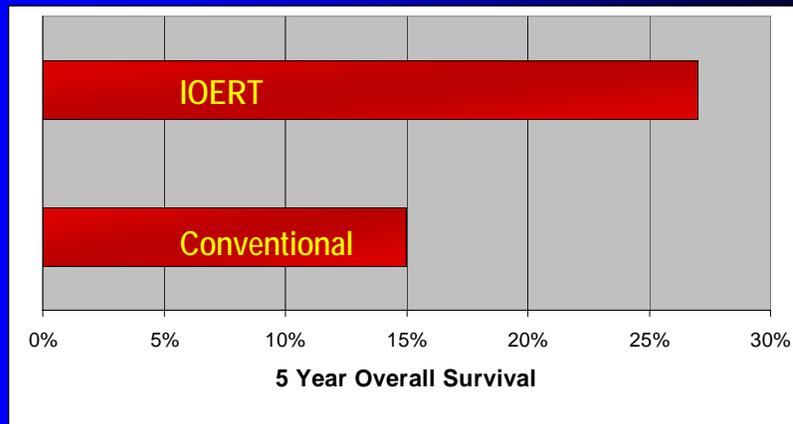
Locally advanced and recurrent head and neck cancers are difficult diseases to treat because the tumors are close to and sometimes involve critical normal structures.

The best treatment option for these patients is to combine aggressive surgery with precise radiation. However, because there are so many critical normal structures in this part of the body, it is very difficult to always give sufficient dose to the tumor or residual tumor to achieve tumor control or a cure.

With IOERT, critical structures are moved out of the way or protected, and a precision dose of radiation is delivered. In combination with the best conventional external beam radiation techniques, excellent results are being reported for patients who also receive IOERT.

Saving Lives -- Pancreatic Cancer

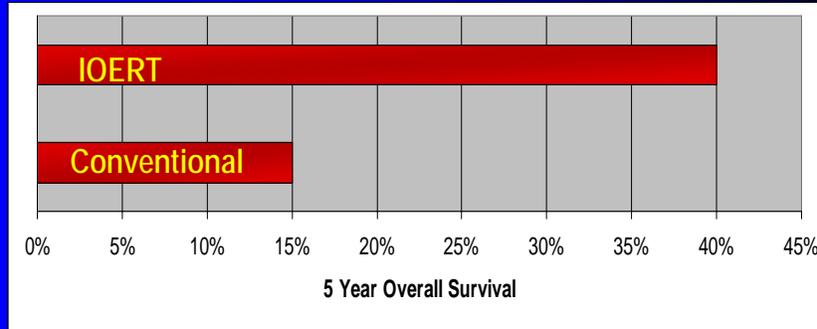
Operable Pancreatic Cancer



Each year more than 31,000 Americans will die from pancreatic cancer. It is one of the most deadly of cancers with only 3% of patients achieving a 5-year survival. About 25% of pancreatic cancer patients have tumors that are operable, and this group of patients has a better outcome than those whose cancers are inoperable. Today, with modern chemotherapy and modern radiation techniques, combined with a successful operation, 5-year survivals of 10-20% have been reported. If IOERT is added during surgery, survival rates of 25 to 30% have been reported. Most operable pancreatic cancer patients will die of metastatic disease, so we clearly need better chemotherapy to improve the results. But, those patients that get IOERT have more than 70% local control compared to only 30-40% local control for patients that are treated without IOERT. With pancreatic cancer, if one can achieve local control, patients will have less pain than those who do not achieve local control. So, even for patients that do not survive, IOERT may improve the quality of their life.

For inoperable pancreatic cancer, the story is even more grim. More than 50% of the patients will die in the first year and very few survive as long as even three years, no matter how they are treated. With IOERT, though, there are some long-term survivors. One U.S. study of 150 inoperable pancreatic cancer patients who received IOERT had eight long-term survivors, one as long as 8 years. And several studies show that IOERT will increase local control and reduce pain, thereby improving the quality of life for these patients in this disease.

Saving Lives – Lung Cancer



Stage IIIA Non-small Cell Lung Cancer

Lung cancer is a major killer. It is the leading cause of cancer death in men and the second leading cause of death in women. Because of the difficulty in doing IOERT before mobile IOERT technology became available, there is very limited data upon which to draw definitive conclusions.

However, the few published results on the use of IOERT at this tumor site have shown promising results. As more operating room based IOERT units become available, this is clearly a site that would be interesting to conduct additional studies to determine the role of IOERT in the treatment of this disease.

IOERT – Advantages and Benefits

Patient Benefits:

- Markedly improved local tumor control
- Significantly extended long term survival for many patients
- Reduced pain and suffering
- More rapid return to better quality of life by often eliminating of pre/post operative external beam radiation treatments

Made possible by IOERT Advantages:

- Directly destroys residual tumor cells left behind after surgery
- Earliest possible start of post surgical radiation treatment
- Substantially increases the effective dose of radiation to the tumor bed
- Normal critical tissues surrounding the tumor can be displaced and protected

In summary, the advantages of IOERT have been clearly demonstrated at more than 30 hospitals in the U.S.:

- It helps destroy residual microscopic disease.
- Together with the multi-week course of radiation given as an outpatient, IOERT increases the total dose of radiation delivered.
- And it does this without compromising the nearby critical structures

The clinical benefits to the patients are many:

- Most important – It can increase long-term survival
- Also, it improves local control (and therefore decreases pain and suffering) even when long-term survival cannot be increased because the disease has already begun to spread to other parts of the body.
- In many cases IOERT eliminates at least part of the multi-week course of outpatient radiation treatments.

Approximate Annual Provider Costs*

Total annual cost per hospital**	\$642,000
Total cost per patient	\$6,420

*Based on 100 patients per year.

** Annual costs include the costs of the linear accelerator at a 5 year amortization rate, service contract, physics, therapists, OR time, disposables, and miscellaneous costs.

Shown here are some of the costs for mobile IOERT which are currently not reimbursed to the hospital by CMS.

This analysis is based on 100 patients per year for one hospital. The annual costs of purchasing and maintaining and using the mobile linear accelerator is about \$642,000. The cost per patient, then, is \$6,420.

These costs include the purchase of the equipment and maintenance. It also includes the costs of physics, therapists, disposables, increased OR time, and miscellaneous expenses.