The following three articles refer to the same April 2015 ASA presentation, and the same research. But, more data is offered in the third article.

**Treatment of 200 Locally Advanced (Stage III) Pancreatic Adenocarcinoma Patients with Irreversible Electroporation: Safety and Efficacy**

http://americansurgical.org/meeting/abstracts/2015/13.cgi

Robert CG Martin¹, David Kwon², Sricharan Chalikonda³, Marty Sellars⁴, Eric Kortz⁵, Charles R Scoggins¹, Kevin T Watkins⁶, Kelly M McMasters¹

¹University of Louisville, Louisville, KY; ²Henry Ford Hospital Department of Surgery, Detroit, MI; ³Cleveland Clinic Department of Surgery, Cleveland, OH; ⁴Piedmont Hospital Department of Surgery, Atlanta, GA; ⁵Swedish Medical Center Department of Surgery, Denver, CO; ⁶Cancer Treatment Centers of America, Atlanta, GA

Objectives: Ablative therapies have been increasingly utilized in treatment of locally advanced pancreatic cancer (LAPC). Irreversible Electroporation (IRE) is an energy delivery system, effective in ablating tumors by inducing irreversible cell membrane destruction of cells. We aimed to demonstrate efficacy of treatment with IRE as part of multimodal treatment of LAPC.

Methods: From July 2010 to October 2014, patients with radiographic stage III LAPC were treated with IRE and monitored under a multicenter, prospective IRB-approved registry. Perioperative 90-day outcomes, local failure, and overall survival were recorded and compared to standard of care data for stage III LAPC.

Results: 200 patients with LAPC underwent IRE of tumor (In-Situ, n=150) or IRE with pancreatic ±arterial resection (Margin, n=50). [In-Situ means the use of IRE alone without resection.] All patients underwent induction chemotherapy, with an additional 52% receiving chemo-radiation, for a median of 7 months (range, 5-13) prior to IRE (Figure). IRE was successfully administered to all patients. 19% sustained complications with a median grade of 2(range, 1-3). Median length of stay was 6 days (range, 4-58). With a median follow up of 25 months, 6(3%) had local recurrence. Median overall survival (OS) in both groups was 23.5 months (Figure).

Conclusion: In stage II LAPC, the addition of IRE with established chemotherapy and/or radiation therapy can provide a significant survival advantage. These early outcome metrics and overall survival begin to establish the minimal standards in which to establish future comparative studies.

See charts at http://americansurgical.org/meeting/abstracts/2015/images/g109_1.png
STAR Study Results: New Data Shows Irreversible Electroporation Nearly Doubles Overall Survival of Patients with Locally Advanced Pancreatic Cancer When Added to Standard Therapy

Presented at the American Surgical Association Annual Meeting

SAN DIEGO, PRNewswire April 24, 2015


See the abstract and chart here: http://americansurgical.org/meeting/abstracts/2015/13.cgi

University of Louisville announced today results from the Soft Tissue Ablation Registry (STAR), demonstrating that irreversible electroporation (IRE) with the NanoKnife® System, in combination with chemotherapy, doubled the overall survival rate of locally advanced (Stage III) pancreatic cancer patients to nearly 24 months. The data was presented at the American Surgical Association annual meeting in San Diego. Locally advanced pancreatic cancer is Stage III cancer that has not yet spread.

Pancreatic cancer has one of the highest mortality rates of all cancers and is expected to climb from the fourth leading cause of cancer-related death in the U.S. to the second by 2020. Ninety four percent of pancreatic cancer patients will die within five years of diagnosis, and 74% of patients die within the first year of diagnosis.
"The STAR data adds to the growing body of evidence that IRE ablation may represent a new treatment paradigm for patients with locally advanced pancreatic cancer," said Robert Martin, M.D., Ph.D., F.A.C.S., director of the Division of Surgical Oncology, and Professor, Department of Surgery, University of Louisville, James Graham Brown Cancer Center. "This new analysis of IRE could help change the standard of care for Stage III pancreatic cancer patients whose only treatment options until now were chemotherapy or a combination of chemo-radiation therapy, which will only stabilize the disease and not destroy the tumor. With IRE, these patients now have a surgical treatment option to augment their treatment plan."

The NanoKnife® IRE system is a tool that destroys cancerous cells by subjecting them to a series of short electrical pulses using high-voltage direct current that does not injure surrounding cells, blood vessels and other vital structures. IRE overcomes rapid growth of the tumor by killing all malignant cells at once so they cannot continue to grow and spread. The NanoKnife® IRE system is approved by the U.S. Food and Drug Administration for the surgical ablation of soft tissue. It is not approved for use in specific cancers.

**About STAR.** STAR was a retrospective analysis of IRE performed on 200 consecutive patients diagnosed with locally advanced (Stage III) pancreatic cancer (LAPC) at six centers in the U.S. The centers that collaborated on the study included University of Louisville, Louisville, KY; Henry Ford Hospital, Detroit, MI; Cleveland Clinic, Cleveland, OH; Piedmont Hospital, Atlanta, GA; Swedish Medical Center, Denver, CO; and Cancer Treatment Centers of America, Atlanta, GA.

From July 2010 to October 2014, patients with radiographic Stage III LAPC were treated with IRE and monitored under a multicenter, prospective IRB-approved registry. Perioperative 90-day outcomes, local failure, and overall survival were recorded and compared to standard of care data for Stage III LAPC. All patients underwent induction chemotherapy with 52 percent receiving chemo-radiation, for a median of 7 months (range, 5-13) prior to IRE. IRE was successfully administered to all patients. Nineteen percent sustained complications with a median grade of 2 (range 1-3). Median length of stay was 6 days (range, 4-58) with a median follow-up of 25 months. Six patients (3%) had local recurrence. Median overall survival in both groups was 23.5 months.

**Ablation System May Double Survival in Stage 3 Pancreatic Cancer**

Excitement Tempered With Caution; Selected Patients


Irreversible electroporation, an emerging ablative technique in cancer treatment, may prolong survival in patients with locally advanced pancreatic adenocarcinoma, with the latest survival rates nearly double those of historical controls, according to a new study.
In a study presented at the 2015 annual meeting of the American Surgical Association, surgeons reported that patients treated with irreversible electroporation (IRE), in addition to conventional chemotherapy and radiation therapy, survived for a median of 23 to 28 months after treatment.

The survival rates are more than double those typically expected for patients with stage 3 pancreatic cancer. Most previous studies put median survival for these patients at approximately 11 to 13 months if patients undergo treatment with conventional therapies, the investigators said. Five-year survival is less than 6%.

“These results should emphasize to the greater medical and oncology community that stage 3 pancreatic cancer is a treatable disease and not an immediate death sentence. Clearly, durable overall survival can be obtained with collaborative multidisciplinary care through the use of chemotherapy, IRE and chemoradiation therapy,” said lead author Robert C.G. Martin II, MD, PhD, director of surgical oncology and professor of surgery, University of Louisville, in Kentucky.

Experts caution that the results come from a small number of institutions, and the study was not conducted in a randomized design with a valid comparison arm.

Even so, there is great excitement in the oncology community about the prospect of an ablative technology that can be used with good results on locally advanced pancreatic cancer. Of the 40,000 people in the United States diagnosed with pancreatic cancer annually, only a minority are candidates for surgery. A suitable ablative technique could help control local disease in patients who are ineligible for surgical resection. The thermal ablative techniques used for other cancers, notably liver cancer, are not suitable for pancreatic disease because of widespread damage to tissues beyond the cancer cells.

“What this technique does is offer you an alternative for local control without the morbidity or mortality of complex resection in the select group of patients who are responsive to chemotherapy and have not metastasized, and who have disease that’s amenable to ablation,” said Keith D. Lillemoe, MD, surgeon-in-chief at Massachusetts General Hospital and the W. Gerald Austen Professor of Surgery at Harvard Medical School, both in Boston. “It is a very select group of patients.”

Dr. Lillemoe was not involved with the study and does not personally perform IRE. He does refer patients for the procedure within his institution.

He called the results “encouraging,” but stressed the need for multicenter, randomized trials with long-term follow-up.

“It would be great to be able to say definitively that [IRE] will add to survival. I don’t think we can do that yet, but I do think the door is open to the trials that can make that determination.”

Approved by the FDA under a 510(k) clearance for ablation of soft tissue, IRE is an energy delivery system that ablates tumors by inducing irreversible cell membrane destruction (NanoKnife, Angiodynamics). Clinicians administer high-voltage, nanosecond electrical pulses directly to pathologic tissues by placing minimally invasive electrodes within the
targeted region. The pulses damage the cell membrane porosity, leading to permanent cell death by apoptosis over six to eight weeks, but without causing further damage to surrounding vessels, nerves and neighboring normal tissue.

The system was first reported for use in patients who had locally advanced pancreatic adenocarcinoma in 2009. This is the largest series to date of patients treated with this technology.

In this study, 200 patients with locally advanced pancreatic adenocarcinoma underwent IRE between March 2010 and October 2014. At diagnosis, the cancer was defined as greater than 180-degree encasement of the superior mesenteric artery and/or celiac artery, unreconstructable venous involvement and no evidence of lesions suspicious for metastatic disease.

All patients underwent chemotherapy or chemoradiation or both, according to each institution’s protocol. Approximately four to six weeks after completion of therapy, each patient underwent restaging with a repeat triple-phase computed tomography scan and serum tumor markers. Patients who were free of metastatic disease and did not have significant primary tumor progression were candidates for IRE.

Fifty patients underwent pancreatic resection plus IRE for margin enhancement and 150 patients underwent IRE alone. All patients started with induction chemotherapy, and 52% received chemoradiation therapy for a median of six months (range, five to 13 months) before IRE.

At a median follow-up of 29 months, six patients (3%) experienced a local recurrence. The progression-free interval to local recurrence was a median 10.7 months. One-fourth of patients experienced distant progression, mainly spread to the liver (17%). Median overall survival in the study was 24.9 months, and ranged from 4.9 to 85 (sic) months.

Complications occurred in 37% of the patients and were a median grade of 2. Eleven patients had vascular complications, including deep venous thrombosis, pseudoaneurysm, hepatic arterial thrombosis and nonocclusive super mesenteric vein/portal vein thrombosis. Three patients died within the first 90 days; they had undergone IRE without resection.

This procedure is only indicated in patients who can undergo general endotracheal anesthesia, the investigators noted.

Dr. Martin recommended that surgeons offering IRE or referring patients for the treatment should work with the Americas Hepato-Pancreato-Biliary Association’s collaborative patient safety registry.

Dr. Martin and his co-author, Sricharan Chalikonda, MD, disclosed that they are paid consultants for Angiodynamics. Partial support of the Soft Tissue Ablation Registry came from an unrestricted education grant from Angiodynamics.