

NanoKnife System

Experience in HPB Surgery

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

AUTHORS

Robert CG Martin¹, David Kwon^{*2}, Sricharan Chalikonda^{*3}, Marty Sellars^{*4}, Eric Kortz^{*5}, Charles R Scoggins¹, Kevin T Watkins^{*6}, Kelly M McMasters¹

AFFILIATIONS

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). 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).

CONCLUSIONS

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.

**Robert CG Martin is a consultant for AngioDynamics.*

The link to the abstract on the American Association of Surgery website <http://meeting.americansurgical.org/abstracts/2015/13.cgi>



Borderline and Locally Advanced Pancreatic Adenocarcinoma Margin Accentuation with Intraoperative Irreversible Electroporation.

AUTHORS

Kwon D¹, McFarland K¹, Velanovich V², Martin RC 2nd^{3*}

AFFILIATIONS

¹Department of Surgery, Henry Ford Hospital, Detroit, MI; ²Department of Surgery, The University of South Florida, Tampa, FL. ³Division of Surgical Oncology, Department of Surgery and James Graham Brown Cancer Center, University of Louisville School of Medicine, Louisville, KY. Electronic address: Robert.martin@louisville.edu.

Surgery. 2014 Oct;156(4):910-20. doi: 10.1016/j.surg.2014.06.058.

INTRODUCTION

Complete tumor extirpation (R0 resection) remains the best possibility for long-term survival in patients with pancreatic adenocarcinoma. Unfortunately, approximately 80% of patients are not amenable to resection at diagnosis either because of metastatic (40%) or locally advanced disease (40%). Recent reports of irreversible electroporation (IRE), a high-voltage, short-pulse, cellular energy ablation device, have shown the modality to be safe and potentially beneficial to prognosis. IRE to augment/accentuate the margin during pancreatic resection for certain locally advanced pancreatic cancers has not been reported.

METHODS

Patients with locally advanced/borderline resectable pancreatic cancer who underwent pancreatectomy with margin accentuation with IRE were followed in a prospective, institutional review board-approved database from July 2010 to January 2013. Data regarding local recurrence, margin status, and survival were evaluated.

RESULTS

A total of 48 patients with locally advanced pancreatic/borderline cancers underwent pancreatectomy, including pancreatoduodenectomy (58%), subtotal pancreatectomy (35%), distal pancreatectomy (4%), and total pancreatectomy (4%), with IRE margin accentuation of the superior mesenteric artery and/or the anterior margin of the aorta. Most patients had undergone induction therapy with 33 patients (69%) receiving chemoradiation therapy and 18 patients chemotherapy for a median of 6 months (range, 4-13) before resection. A majority (54%) required vascular resection. A total of 9 patients (19%), sustained 21 complications with a median grade of 2 (range, 1-3), with a median duration of stay of 7 days (range, 4-58). With median follow-up of 24 months, 3 (6%) have local recurrence, with a median survival of 22.4 months.

CONCLUSIONS

Simultaneous intraoperative IRE and pancreatectomy can provide an adjunct to resection in patients with locally advanced disease. Long-term follow-up has demonstrated a small local recurrence rate that is lower than expected. Continued optimization in multimodality therapy and consideration of appropriate patients could translate into a larger subset that could be treated effectively

**Robert C Martin is a consultant for AngioDynamics. All other authors have nothing to declare. Partial support of the Soft Tissue Ablation Registry has come from an unrestricted educational grant from AngioDynamics.*

The link to the article on PubMed at <http://www.ncbi.nlm.nih.gov/pubmed/25239345>

Irreversible Electroporation of Locally Advanced Pancreatic Head Adenocarcinoma

AUTHORS

Martin RC¹

AFFILIATIONS

¹University of Louisville, Louisville, KY, USA, Robert.Martin@louisville.edu.

J Gastrointest Surg. 2013 Oct;17(10):1850-6. doi: 10.1007/s11605-013-2309-z. Epub 2013 Aug 9.

ABSTRACT

Irreversible electroporation of locally advanced pancreatic adenocarcinoma has been used to palliate appropriate patients with locally advanced pancreatic adenocarcinoma. The setting was at a university tertiary care center. Subjects are patients with locally advanced pancreatic adenocarcinoma who have undergone appropriate induction chemotherapy for at least 3 to 4 months in duration. Technique of open irreversible electroporation of locally advanced pancreatic adenocarcinoma is described. The technique of open irreversible electroporation with continuous intraoperative ultrasound imaging and consideration of intraoperative navigational system is described. Irreversible electroporation of locally advanced pancreatic adenocarcinoma is feasible for locally advanced unresectable pancreatic cancer.

**Robert C Martin is a consultant for AngioDynamics.*

The link to the article on PubMed at <http://www.ncbi.nlm.nih.gov/pubmed/23929188>

Irreversible Electroporation in Locally Advanced Pancreatic Cancer: Potential Improved Overall Survival.

AUTHORS

Martin RC II¹, McFarland K, Ellis S, Velanovich V.*

AFFILIATIONS

¹Division of Surgical Oncology, Department of Surgery and James Graham Brown Cancer Center, University of Louisville School of Medicine, Louisville, KY, USA, Robert.Martin@louisville.edu.

Ann Surg Oncol. 2013 Dec;20 Suppl 3:S443-9. doi: 10.1245/s10434-012-2736-1. Epub 2012 Nov 6.

BACKGROUND

Locally advanced unresectable pancreatic adenocarcinoma (LAC) is characterized by poor survival despite chemotherapy and conventional radiation therapy. We have recently reported on the safety of using irreversible electroporation (IRE) for the management of LAC. The purpose of this study was to evaluate the overall survival in patients with LAC treated with IRE.

METHODS

A prospective, multi-institutional evaluation of 54 patients who underwent IRE for unresectable pancreatic cancer from December 2009 to October 2010 was evaluated for overall survival and propensity matched to 85 matched stage III patients treated with standard therapy defined as chemotherapy and radiation therapy alone.

RESULTS

A total of 54 LAC patients have undergone IRE successfully, with 21 women, 23 men (median age, 61 (range, 45-80) years). Thirty-five patients had pancreatic head primary and 19 had body tumors; 19 patients underwent margin accentuation with IRE and 35 underwent in situ IRE. Forty-nine (90 %) patients had pre-IRE chemotherapy alone or chemoradiation therapy for a median duration 5 months. Forty (73%) patients underwent post-IRE chemotherapy or chemoradiation. The 90 day mortality in the IRE patients was 1 (2 %). In a comparison of IRE patients to standard therapy, we have seen an improvement in local progression-free survival (14 vs. 6 months, $p = 0.01$), distant progression-free survival (15 vs. 9 months, $p = 0.02$), and overall survival (20 vs. 13 months, $p = 0.03$).

CONCLUSIONS

IRE ablation of locally advanced pancreatic tumors remains safe and in the appropriate patient who has undergone standard induction therapy for a minimum of 4 months can achieve greater local palliation and potential improved overall survival compared with standard chemoradiation-chemotherapy treatments. Validation of these early results will need to be validated in the current multi-institutional Phase 2 IDE study.

**Robert CG Martin is a consultant for AngioDynamics. All other authors have nothing to declare. Partial support of the Soft Tissue Ablation Registry has come from an unrestricted educational grant from AngioDynamics.*

The link to the article on PubMed at <http://www.ncbi.nlm.nih.gov/pubmed/23128941>

Evaluation of Thermal Injury to Liver, Pancreas and Kidney During Irreversible Electroporation in an In Vivo Experimental Model

AUTHORS

E. M. Dunki-Jacobs, P. Philips and R. C. G. Martin II*

AFFILIATIONS

¹Division of Surgical Oncology, Department of Surgery, University of Louisville, Louisville, Kentucky, USA

BJS. 2014 Jun 24;101(9):1113-21. DOI: 10.1002/bjs.9536

BACKGROUND

Irreversible electroporation (IRE) is a new technique for tumour cell ablation that is reported to involve non-thermal-based energy using high voltage at short microsecond pulse lengths. In vivo assessment of the thermal energy generated during IRE has not been performed. Thermal injury can be predicted using a critical temperature model. The aim of this study was to assess the potential for thermal injury during IRE in an in vivo porcine model.

METHODS

In vivo continuous temperature assessments of 86 different IRE procedures were performed on porcine liver, pancreas, kidney and retroperitoneal tissue. Tissue temperature was measured continuously throughout IRE by means of two thermocouples placed at set distances (0.5 cm or less, and 1 cm) from the IRE probes within the treatment field. Thermal injury was defined as a tissue temperature of 54°C lasting at least 10 s. Tissue type, pulse length, probe exposure length, number of probes and retreatment were evaluated for associations with thermal injury. In addition, IRE ablation was performed with metal clips or metal stents within the ablation field to determine their effect on thermal injury.

RESULTS

An increase in tissue temperature above the animals' baseline temperature (median 36.0°C) was generated during IRE in all tissues studied, with the greatest increase found at the thermocouple placed within 0.5 cm in all instances. On univariable and multivariable analysis, ablation in kidney tissue (maximum temperature 62.8°C), ablation with a pulse length setting of 100 μ s (maximum 54.7°C), probe exposure of at least 3.0 cm (maximum 52.0°C) and ablation with metal within the ablation field (maximum 65.3°C) were all associated with a significant risk of thermal injury.

CONCLUSIONS

IRE can generate thermal energy, and even thermal injury, based on tissue type, probe exposure lengths, pulse lengths and proximity to metal. Awareness of probe placement regarding proximity to critical structures as well as probe exposure length and pulse length are necessary to ensure safety and prevent thermal injury. A probe exposure of 2.5 cm or less for liver IRE, and 1.5 cm or less for pancreas, with maximum pulse length of 90 μ s will result in safe and non-thermal energy delivery with spacing of 1.5–2.3 cm between probe pairs.

*R.C.G.M. is a consultant for AngioDynamics. The authors declare no other conflict of interest.

Link to the abstract on *BJS* at <http://www.bjs.co.uk/details/article/6418171/Evaluation-of-thermal-injury-to-liver-pancreas-and-kidney-during-irreversible-el.html>

Evaluation of Resistance as a Measure of Successful Tumor Ablation During Irreversible Electroporation of the Pancreas

AUTHORS:

Erik M Dunki-Jacobs, MD, Prejesh Philips, MD, Robert CG Martin II, MD, PhD, FACS*

AFFILIATIONS

From the Department of Surgery, Division of Surgical Oncology, University of Louisville, Louisville, KY

J Am Coll Surg. 2013 Feb;218(2):179-187. DOI: <http://dx.doi.org/10.1016/j.jamcollsurg.2013.10.013>

BACKGROUND

Intraoperative evaluation of successful pancreatic tumor ablation using irreversible electroporation (IRE) is difficult secondary to lack of visual confirmation. The IRE generator provides feedback by reporting current (amperage), which can be used to calculate changes in tumor tissue resistance. The purpose of the study was to determine if resistance can be used to predict successful tumor ablation during IRE for pancreatic cancers.

STUDY DESIGN

All patients undergoing pancreatic IRE from March 2010 to December 2012 were evaluated using a prospective database. Intraoperative information, including change in tumor resistance during ablation and slope of the resistance curve, were used to evaluate effectiveness of tumor ablation in terms of local failure or recurrence (LFR) and disease-free survival (DFS).

RESULTS

A total of 65 patients underwent IRE for locally advanced pancreatic cancer. Median follow-up was 23 months. Local failure or recurrence was seen in 17 patients at 3, 6, or 9 months post IRE. Change in tumor tissue resistance and the slope of the resistance curve were both significant in predicting LFR ($p = 0.02$ and $p = 0.01$, respectively). The median local disease-free survival was 5.5 months in patients who had recurrence compared with 12.6 months in patients who did not recur ($p = 0.03$). Neither mean change in tumor tissue resistance nor the slope of the resistance curve significantly predicted overall DFS.

CONCLUSIONS

Mean change in tumor tissue resistance and the slope of the resistance curve could be used intraoperatively to assess successful tumor ablation during IRE. Larger sample size and longer follow-up are needed to determine if these parameters can be used to predict DFS.

**Dr Martin received an unrestricted education grant from AngioDynamics; the company had no access or ability to review or influence any of the data presented here. All other authors had nothing to disclose*

Link to the article at <http://www.journalacs.org/article/S1072-7515%2813%2901173-3/abstract>

About AngioDynamics

AngioDynamics, Inc. is a leading provider of innovative, minimally invasive medical devices used by professional healthcare providers for vascular access, surgery, peripheral vascular disease and oncology. AngioDynamics' diverse product lines include market-leading ablation systems, vascular access products, angiographic products and accessories, angioplasty products, drainage products, thrombolytic products and venous products. More information is available at www.angiodynamics.com.



International > Haaksbergweg 75 (Margriettoren), 1101 BR, Amsterdam Z-O > The Netherlands
tel: +31 (0)20 753 2949 > fax: +31 (0)20 753 2939

www.angiodynamics.com

AngioDynamics, the AngioDynamics logo, NanoKnife and NanoKnife logo are trademarks and/or registered trademarks of AngioDynamics, Inc., an affiliate or a subsidiary.
©2015 AngioDynamics, Inc MLC 653 A4 Rev A 04/15