Anesth Pain Med. 2015 June; 5(3): e22786. DOI: 10.5812/aapm.22786

Published online 2015 April 20. **Research Article**

Intra - operative Anesthesia Management in Patients Undergoing Surgical Irreversible Electroporation of the Pancreas, Liver, Kidney, and Retroperitoneal Tumors

Robert CG. Martin [1,2,*]; Eric Schwartz [1]; JoAnn Adams [3]; Ian Farah [3]; Brian M Derhake [3]

[1]Division of Surgical Oncology, University of Louisville School of Medicine, Louisville, USA
[2]James Graham Brown Cancer Center, Louisville, USA
[3]Department of Anesthesiology, University of Louisville School of Medicine, Louisville, USA

*Corresponding author: Robert CG. Martin, Division of Surgical Oncology, University of Louisville School of Medicine, Louisville, USA. Tel: +1-5026293355, Fax: +1-5026293030, E-mail: robert.martin@louisville.edu

Received: August 15, 2014; **Revised:** September 14, 2014; **Accepted:** October 13, 2014

Background: Irreversible electroporation (IRE) is a relatively new approach to the management of multiple types of locally advanced soft tissue tumors. Unique peri-procedural anesthetic management is needed in the safe and effective delivery of this therapy.
Objectives: This study analyzed IRE therapy in relation to anesthetic management for our initial cohort and then established and validated a set of best practical guidelines for general anesthesia in patients undergoing IRE for abdominal tumors.
Patients and Methods: An IRB-approved prospective data collection outcome protocol was utilized. This study was broken up into two cohorts as follows: the initial 38 patients (pts) undergoing IRE in which anesthetic management was not defined or optimized and then a 40-pt validation cohort to establish the most efficacious anesthetic protocols.
Results: During IRE delivery, a deeper neuromuscular blockade is required to ensure that all retroperitoneal muscle excitation was minimized. In the initial 38-pt cohort, attempts to treat hypertension (median SBP 190, range 185–215 and median diastolic 98, range 91–115) were made with various types of anti-hypertensives with minimal-to-insufficient effects. The established inhalation was sevoflurane with an approximate median dose of 8.0 volume percentage. Analgesic management of continuous remifentanil was utilized with epidural management, which optimized HTN and tolerance to IRE therapy.
Conclusions: Anesthetic management for IRE of soft tissue deviates from standard anesthetic medical therapy in regards to depth of neuromuscular blockade and analgesic management during IRE energy delivery. However, minor modifications in anesthesia management allow for a safe and efficient patient procedure.

Keywords: Anesthetic; Electroporation; Tumors

1. Background

Irreversible electroporation (IRE) is a relatively new approach to the management of multiple types of locally advanced soft tissue tumors. Its current use has been in the therapy of locally advanced tumors that have had poor response or recurrence to traditional chemotherapy or radiation therapy (1-3). This method exposes cells to high-field electrical pulses for a short duration of microseconds to milliseconds to irreversibly damage cell membranes (4, 5). IRE is especially promising in the management of pancreatic carcinomas, which have an extremely poor prognosis, with a 5-year survival rate of 5%, and, of which, 30–40% were unresectable at the time of diagnosis (1). The use of IRE has developed over (roughly) the past decade and is currently evolving data regarding the techniques efficacy to improve overall survival (OS) and disease free survival. In addition to these studies regarding the long-term outcomes with IRE therapy, there remains little information regarding the anesthetic management of patients undergoing IRE. The use of general anesthesia is required for IRE therapy because the pulse lengths required for the energy with currently approved devices. However, there remains unique peri-procedural management considerations needed in the safe and effective delivery of this therapy. This management is in relation to the depth of neuromuscular blockade (NMB), pain management, hypertension management, and, rarely, cardiac arrhythmia. It has been demonstrated that electrocardiogram synchronization is an absolute requirement to minimize risks of arrhythmias induced by high voltage and high amperage therapy. With these unique management concerns, there remains a need for optimal anesthesia protocols to allow for safe, effective, and successful treatments.

2. Objectives

This study analyzed IRE therapy in relation to anesthetic management for our initial cohort and then established and validated best practice guidelines for

general anesthesia in patients undergoing IRE for abdominal tumors.

3. Patients and Methods

An IRB-approved prospective data collection outcome protocol was utilized to capture all patients who were undergoing irreversible electroporation through either an open, laparoscopic, or percutaneous approach at the University of Louisville Hospital. Prior publications have established optimal patient selection for patients undergoing IRE of locally advanced soft tissue tumors within the liver or the pancreas (2, 4-7). In short, these patients needed to have appropriate-sized tumors, which have a clearly understood underlying biology to ensure that a local electroporation technique is optimal for tumor control, patient quality of life, and enhanced disease-free survival. In the initiation of our IRE program, optimal anesthetic management had not been defined and with the only absolute requirement for cardiac synchronization (AccuSync® 72 ECG Trigger Monitor, http://www.accusync.com/accuSync72.html) to prevent any type of cardiac arrhythmia. Thus, this study was broken up into two cohorts as follows: the initial 38 patients in which anesthetic management was not defined nor optimized to establish the most efficacious anesthetic protocols for induction, management, peri-electroporation management, and optimal post-electroporation management for the safety and efficacy to deliver this novel energy therapy. All anesthetic management was recorded prospectively and each case that followed this initial cohort was evaluated for effectiveness of NMB, hypertensive, cardiac irritability, and other intraoperative hemodynamic parameters. We established abnormalities for all parameters for the following: heart rate above 110 beats per minute was defined as abnormal since IRE delivery cannot occur with that degree of tachycardia as well as we were not comfortable with that degree of heart rate. Neuromuscular blockade of > 0 twitches was defined as abnormal since this created too much movement for the target organ because the surrounding muscle contract and the needles were not anchored, which could lead to malposition leading to reduced efficacy. Blood pressure with systolic > 140 and diastolic > 88 prior to initiation of IRE energy delivery was defined as abnormal since this commonly led to significant hypertension, which is defined as SBP > 180 and DBP of > 100 in some cases within this initial cohort. From this initial cohort, as presented below, a validation cohort (another 40 patients treated consecutively) was included utilizing established anesthetic protocols that were generated from the initial cohort of patients. This validation protocol was reviewed on a case-by-case basis to further confirm anesthetic quality, optimization from an operating surgeon and anesthesia provider or anesthesiologist perspective. The quality parameters were evaluated based on the effectiveness and efficiency of NMB; the effectiveness and efficiency of analgesic management to reduce significant hypertensive episodes; and the effectiveness and efficiency of post-procedural anesthetic awakening following effective electroporation.

3.1. Surgical Management

Our operative approach has been presented previously, but in short, the access for open IRE was performed through a superior midline incision 5. A superior midline incision was utilized based on the planned needle placement performed most commonly through a caudal-to-cranial approach. The abdomen is thoroughly examined to rule out any type of occult solid organ liver metastases as well as peritoneal or mesenteric metastases. Only after there was no evidence of metastatic disease confirmed and local advancement was confirmed, an in situ IRE was then planned. Following appropriate needle placement and ultrasound confirmation of appropriate spacing, those spacing measurements are entered into the energy unit's software, which allows for optimal voltage and pulse length delivery. Standard default voltage of 1500 volts per cm is initiated with a planned delivery of 90 pulses and a pulse width of 70–90 microseconds. Twenty pulses are delivered initially and then delivery is halted to assess the underlying amperage draw to establish optimal voltage and pulse widths. Once effective current delivery has been confirmed between all pairs, the needles are pulled back to an appropriate distance such that there is no overlapping treatment performed. Sequential pullbacks are performed to obtain adequate margins superiorly and inferiorly. Following treatment, a prophylactic gastro-jejunostomy is commonly performed in conjunction with a jejunal feeding tube. An abdominal drain is usually not placed in patients who only undergo in situ IRE. The postoperative management of these patients is standard and follows guidelines for any type of pancreatic resection. The return of GI function and the length of stay remain approximately 6–10 days.

4. Results

An initial cohort of 38 patients was followed prospectively with all anesthetic management recorded as well as hemodynamic parameters. This initial cohort of patients was made up predominantly of patients with borderline resectable or locally advanced pancreatic cancers (n = 34) with the remaining cohort being within the liver and a single patient undergoing electroporation within the pelvis. Table 1 presents the initial hemodynamic parameters including heart rate, blood pressure, and time of procedure as well as temperature ranges, which demonstrates significant variability predominantly in heart rate as well as blood pressure during irreversible electroporation therapy.

Table 1. Summary of Vital Signs and Operation Times for Patients [a]

Cancer Location	Low HR	High HR	Median HR	Low SBP, mm Hg	High SBP, mm Hg	Median SBP, mm Hg	Low DBP, mm Hg	High DBP, mm Hg	Median DBP, mm Hg	OR Time, h	High Temp, °C	Low Temp, °C
Pancreas	55	90	72.5	108	170	125	60	90	70	6:12	38.5	35.5
Pancreas	50	110	85	85	195	112	40	90	55	4:56	38.1	36
Pancreas	60	95	75	85	158	115	50	85	65	3:53	37.6	36.6
Pancreas	65	112	90	90	140	110	50	75	60	5:31	37.3	36
Pancreas	65	100	90	80	180	110	45	90	70	4:21	37.3	36.4
Liver	60	110	75	100	142	112	48	88	70	3:30	36.7	36
Pancreas	50	105	80	90	145	110	50	85	62	4:03	36	35.1
Pancreas	40	120	90	78	160	110	40	78	60	3:38	38.1	36.2
Pancreas	40	90	75	85	160	115	42	80	60	4:37	38.2	36.1
Pancreas	70	105	85	90	170	135	58	110	85	2:21	39	36.5
Pelvis	55	95	60	88	150	108	45	85	55	2:29	36.4	36
Pancreas	52	85	65	90	172	110	55	90	70	4:00	36.4	35.9
Colon	55	90	65	90	138	110	45	82	60	3:42	37.2	34.8
Pancreas	60	90	80	92	138	115	50	70	60	3:16	37.4	35.9
Liver	70	85	80	100	140	125	70	100	80	1:43	36.6	36
Pancreas	60	120	87.5	70	180	120	35	100	70	4:14	36.6	36
Colon	55	65	60	90	140	118	55	75	65	2:04	36.7	36.4
Pancreas	65	90	82	80	170	115	45	85	60	4:47	37.6	36.3
Pancreas	60	85	78	85	130	100	45	70	55	4:41	37.8	36.2
Pancreas	75	95	85	100	160	128	50	100	62	3:09	36.7	35.8
Pancreas	60	90	75	90	150	110	50	102	70	3:17	38	36.4
Pancreas	80	105	90	100	140	120	55	88	75	3:58	37.5	36.6
Pancreas	55	95	78	108	175	131	60	105	80	3:05	37.1	35.9
Pancreas	65	95	75	88	140	110	50	88	60	3:00	36.5	35.1
Pancreas	50	90	67.5	98	140	110	48	80	60	2:29	37.2	35
Pancreas	60	95	80	80	122	100	38	78	58	2:08	37.3	36.6
Pancreas	50	95	73.5	85	160	120	45	85	65	4:13	37.7	35.9
Pancreas	52	100	70	85	172	115	55	95	65	6:14	36.9	36.1
Pancreas	50	80	70	95	170	118	50	110	65	4:42	37.8	36.1
Pancreas	75	105	90	100	168	120	50	92	70	4:21	36.8	35.4
Pancreas	60	90	75	95	148	115	45	88	68	2:09	36.4	36
Pancreas	65	90	80	95	175	110	45	105	65	5:07	36.5	35.9
Pancreas	70	100	85	82	140	110	45	80	65	4:07	36.9	36.6
Pancreas	70	95	82	90	180	115	50	110	60	5:50	37.3	36.4
Pancreas	80	115	95	80	140	103.5	52	90	62	2:20	37.6	36.4
Pancreas	70	105	85	78	150	108	42	95	65	5:11	38.4	36.4
Pancreas	60	95	75	102	150	115	45	88	65	4:20	37.2	34.8
Pancreas	62	95	85	92	140	108	45	70	58	5:36	37.6	36.5
Median	60	95	80	90	150	113.5	49	88	65		37.3	36
Mean	60.4	96.6	78.7	90.0	155.2	114.3	48.6	88.9	65.0		37.3	36.0

[a] Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, operation room; HR, heart rate.

All patients received general anesthetic with propofol induction and oxygen maintenance. Two patients were maintained with desflurane, four with isoflurane, and 29 with sevoflurane. One patient received a mixture of isoflurane and sevoflurane and one patient received desflurane, isoflurane, and sevoflurane. Additionally, five patients received additional anesthesia support with ketamine. Patients received several opioid regiments, all of which included fentanyl. Nondepolarizing NMB was used for all patients. Either vecuronium or rocuronium was used as the NMB for these procedures. Vitals were recorded for all patients throughout the procedure. Surgery times ranged from 103–374 minutes with a median time of 242 minutes. An example patient who underwent irreversible electroporation of a locally advanced pancreatic cancer with an in situ technique demonstrated anesthetic medication management from induction therapy to recovery room delivery as well as the medications and time intervals that were administered. The irreversible electroporation in this patient (Table 2) was initiated at 8:45 AM and then completed at 10:10 AM, clearly demonstrating a significant increase in dosing of the vecuronium utilized as well as the fentanyl.

Table 3 presents a summary of the various types of anesthetic medications and dosages utilized for this initial cohort of 38 patients, which clearly demonstrates a wide range of analgesics and anti-hypertensives as the most variable in this cohort. We also evaluated all other parameters of these patients such as age, diagnosis, prior induction therapy, prior surgery, history of hypertension, prior radiation, current analgesic use, and location of lesion and did not find any other predictive factors that lead to hemodynamic or neuromuscular blockade abnormalities as defined above within our methods.

4.1. Neuromuscular Blockade Management

After review of these 38 patients on a case-by-case basis, it became clear that the type of NMB, whether vecuronium or rocuronium, was insignificant and just as effective. However, during the irreversible electroporation delivery, a deeper NMB is required to ensure that any and all retroperitoneal muscle excitation is minimized. The successful and safe delivery of IRE energy demands complete neuromuscular blockade verified by 0 of 4 on a four-train twitch monitor. The reason for this degree of deep NMB is that the electroporation needles do not have an anchoring device and, thus, there is an inherent need to avoid any type of organ movement during IRE delivery. Since a median number of four electroporation needles are needed to deliver irreversible electroporation effectively, any moderate-to-significant retroperitoneal or diaphragmatic excitation can lead to the target organ moving between 3.0 and 5.0 cm in a cranial-caudal fashion, which potentially could enhance the underlying needle trauma. Therefore, the deep level of NMB is necessary to safely deliver the irreversible electroporation and minimize any and all needle trauma.

4.2. Analgesic and Hypertension Management

Another unique aspect of irreversible electroporation is the rapid hypertension that occurs even with deep anesthetic management and deep NMB. In the initial 38-patient cohort, attempts to treat this hypertension (median systolic BP 190, range 185–215 and median diastolic 98, range 91–115) were attempted with various types of anti-hypertensives (Table 3) with minimal-to-insufficient effects. It became evident that larger doses of the analgesic utilized, most commonly fentanyl, would provide far more effective management of these inevitable hypertensive episodes. This led to significant amounts of fentanyl utilized with a median dosage of 500 μg, which was effective in managing the retroperitoneal pain. However, this led to prolonged anesthetic management and subsequent prolonged inhalation support with a post-incisional closure extubation median time of 48 minutes with a range of 25–69 minutes. This decreased the overall efficiency of patient extubation and, consequently, room turnover. It was only after establishing analgesic use was the most effective management to control this retroperitoneal pain and subsequent hypertension that a switch to remifentanil in the last five patients of this 38-patient cohort was evaluated. From this initial evaluation, a second validation cohort of 30 patients was evaluated. Of these, 25 underwent irreversible electroporation of locally advanced pancreatic cancer and five patients underwent irreversible electroporation of either the liver or retroperitoneum. The established inhalation anesthetic was sevoflurane with an approximate median amount of 2% of inhalational agent. Analgesic management of remifentanil was accomplished as a continuous infusion initiating approximately 10 minutes before irreversible electroporation and then stopping five minutes after the irreversible electroporation with the supplementation of epidural management, which was initiated post-electroporation and prior to extubation. The titration of the remifentanil drip can be predicted by monitoring the patient during the initial 20-pulse delivery. NMB utilized were vecuronium and rocuronium with established vasopressors (phenylephrine) being utilized in only 10 of the 30 patients in this validation cohort. This regimen led to a limited number of hypertensive episodes (n = 4) for which patients needed supplemental nitroglycerine on top of the remifentanil. This regimen of sevoflurane, epidural management, and remifentanil led to far more efficient NMB management as well as a reduction in hypertension, which did not require at any time for the energy delivery to be aborted. Furthermore, the regimen and reduction in hypertension reduced the overall IRE delivery time by a median of 30 minutes with a range of 12–40 minutes in comparison to the initial evaluation cohort. This validation management led to a significant reduction in post-incisional closure extubation to a median time of eight minutes with a range of 3–19 minutes, which was significantly less than what was seen in the initial evaluation patient cohort.

Table 2. Anesthetic Management and Dosing Schedule from Induction to Extubation During Irreversible Electroporation of the Pancreas

	Time																														
	Preoperation	7:30	7:35	7:40	7:55	8:05	8:15	8:20	8:30	8:35	8:45	9:00	9:35	10:00	10:10	10:20	10:30	10:35	10:45	11:00	11:20	11:50	12:15	12:25	12:30	12:35	12:40	12:45		12:55
Isoflurane, %					1		1			1.4	1	0.8	1.3	1.4		1.4		1.6	1.2	1.1	1.1	1.1			1			Completion of operation		
Midazolam, mg	2																														
Fentanyl, µg		100	50				100					100	50		50					50											
lidocaine			90																												
Propofol, mg			100																												
Vecuronium, µg			10							3			4		2		1				2										
Neosynephrine, µg				200		100																									
Neosynephrine gtt, µg						100	100			150																					
Neostig, mg																										2					
Robinul, mg																											0.3				
Zofran, mg																								4							
Toradol, mg																								30							
Dilaudid, mg																												1		1	
Phenylephrine, µg																100	150						200				175	50		117

Table 3. Summary of Select Medications and Doses Used During Procedures

Drug	Median Dose	Mean Dose	Median Number of Doses	Median Interval, min
General Anesthetics [a]				
Desflurane (n = 3), %	4.5	5.2	11	16
Sevoflurane (n = 31), %	8.0 volume	8.0 volume	14	17
Isoflurane (n = 6), %	2.8	2.8	13	16
Propofol (n = 36), mg	160	202.8	1	0
Narcotics				
Fentanyl (n = 36), μg	500	493.1	5	36.5
Dilaudid (n = 11), μg	2	1.8	2	10
Morphine (n = 6), mg	10	9.7	2	45
Epidural Fentanyl (n = 6), μg	150	158.3	1.5	22.5
Hydromorphone (n = 6), mg	1.5	1.8	1.5	16.5
Remifentanil, μg (n = 5), mg	100	280.2	1	0
Epidural Dilaudid (n = 1), ml/min	20	20	2	95
Neuromuscular Blockade				
Vecuronium, μg (n = 24), mg	16.5	14.1	4	34
Rocuronium (n = 26), mg	60	77.4	2	26
Succinylcholine (n = 1), mg	100	100	1	n/a
BP support meds				
phenylephrine (n = 20), mg	600	696.8	6	25
epinephrine (n = 1), mg	1.1	1.1	2	75
phenylephrine gtt, μg (n = 3), μg	210	245	3	15
Antihypertensives				
Nitroglycerine (n = 3), mg	0.4	0.5	2	10
Esmolol (n = 7), mg	22	31.7	2	10
Metoprolol (n = 5), mg	1	3.6	1	0
Labetalol (n = 4), mg	10	9	2	15
Hydralazine (n = 1), mg	10	10	2	45
Other Meds				
Lidocaine (n = 20), mg	85	78.2	1	0
Zofran (n = 28), mg	4	4.5	1	0
Ephedrine (n = 14), mg	10	19	2	7.5
Versed (n = 30), mg	2	2.6	1	0
Neostigmine (n = 26), mg	3	3.5	1	0
Glycopyrrolate (n = 29), mg	0.6	0.7	1	0

[a] Data presented as (%).

5. Discussion

IRE for ablation of locally advanced soft tissue tumors has been demonstrated to have acceptable efficacy in a small number of centers that embarked on IRE use approximately 5 years ago. Recent reports from our institution have demonstrated that this therapy does spare surrounding tissues and allows for effective therapy when needing to treat around vital ducts and major vessels. As we have reported, the IRE procedure does require a general anesthetic with adequate neuromuscular blockade. Ball et al. (3) first reported that anesthetic management with the predominant use of IRE being a percutaneous approach via CT guidance. Their report was presented before the absolute requirement of cardiac synchronization was in place; cardiac dysrhythmias that they reported have been corrected with a 0% incidence of cardiac arrhythmias in our prior reports as well as in this current study. A smaller series from Trabold et al. (8) also confirmed the recent results from Ball et al. (3) as well as our study. From Ball et al., we herein present many of the anesthetic challenges that they reported have indeed been corrected. The cardiac synchronization device is accurate and incredibly conservative such that if the ECG signal is not adequate and consistent, then the IRE energy will not be delivered (3). This conservative filter can lead to inefficient energy delivery such that IRE energy will not be delivered at each cardiac pulse, but it has translated into 0% cardiac arrhythmias. Given these recent changes to

require ECG synchronization for all IRE deliveries except for the prostate with the combination of cardioprotective anesthetic agent delivery now allows for an exceedingly safe energy device (9). This has been further confirmed by a recent publication from our group in which 107 consecutive patients from 7 institutions with tumors that had vascular invasion treated with IRE from May 2010 to January 2012 and none of these patients had cardiac complications (9). Additionally, all of these patients were able to undergo successful IRE energy delivery (9). Intra-procedural IRE pain management has now been optimized with this report by our institution with the early use of remifentanil and with consideration for epidural management. This pain management algorithm now controls all hypertensive episodes such that the IRE energy can be delivered efficiently and safely with little to no delay in incisional closure extubation. From this study, (more importantly) from the validation group, and other publications regarding optimal anesthetic management (10), we have created an optimal anesthetic algorithm for IRE of all intra-thoracic and intra-abdominal electroporation (Box 1). These results and algorithms allowed us to demonstrate the safety and efficacy of this device in the pancreas (1, 11), liver (2, 6), and any type of soft tissue (7, 10) with vascular invasion of vital structures.

Box 1. Optimal Anesthetic Preferences for Irreversible Electroporation of the Intra-Thoracic or Intra-Abdominal Soft Tissue

Set up
1) Arterial-line or non-invasive equivalent monitoring that allows for continuous real-time, beat-to-beat information on cardiac output (co), blood pressure (bp), and other hemodynamic parameters calibrated hemodynamic parameters (cardiac output, stroke volume, systemic vascular resistance, and stroke volume variation).
2) Fluid warmer
3) Remifentanil drip
4) Train-of-four monitoring
5) Try to limit IV fluids to less than 700 cc prior to ablation/resection if the operation includes liver resection
Nitroglycerine drip
Esmolol
2-4 Units pack red blood cells
After Induction:
1) Place A-line or equivalent non-invasive monitoring device
2) Place 2 peripheral IV lines-18 Gauge or larger
3) Place nasogastric tube
4) Upper and lower body forced-air warmers
5) Try to limit IV fluids to less than 700 cc prior to ablation/resection if the operation includes liver resection
(likely normovolemia after the liver portion of the case is completed)
expect low urine output with fluid limitations and bowel preparation
6) Change monitor heart rate source to A-line
Ablation interference with EKG waveform will cause false audible alarming.
7) Start epidural upon arrival to operating room (if bag is available)
8) Start remifentanil at a very low dose (e.g. 0.05-0.1 µg/kg/min), somewhat early in the case, once otherwise settled, to help estimate patient response
When Probes are placed for Ablation:
(remember, often only 5 minutes between the start of probe placement and potential start of ablation)
Ensure zero twitches on TOF
Titrate remifentanil gtt up to approximately 0.5-1 µg/kg/min
Give epidural PCA bolus (if possible)
Increase anesthetic agent, often up to 1.4 %, just before ablation
Have Esmolol/NTG ready (instead of or in conjunction with increased %)

In conclusion, the anesthetic management for IRE of soft tissue does deviate from standard anesthetic medical therapy in regards to the depth of NMB and analgesic management during IRE energy delivery. However, minor modifications and changes in the types of therapy allow for safe and efficient patient management.

Funding/Support

This study was supported by Division of Surgical Oncology University of Louisville

References

1. Martin II RCG, McFarland K, Ellis S, Velanovich V. Irreversible electroporation in locally advanced pancreatic cancer: potential improved overall survival. *Ann Surg Oncol.* 2013;**20**(3):443–9.
2. Cannon R, Ellis S, Hayes D, Narayanan G, Martin R2. Safety and early efficacy of irreversible electroporation for hepatic tumors in proximity to vital structures. *J Surg Oncol.* 2013;**107**(5):544–9.
3. Ball C, Thomson KR, Kavnoudias H. Irreversible electroporation: a new challenge in "out of operating theater" anesthesia. *Anesth Analg.* 2010;**110**(5):1305–9.
4. Dunki-Jacobs EM, Philips P, Martin R2. Evaluation of resistance as a measure of successful tumor ablation during irreversible electroporation of the pancreas. *J Am Coll Surg.* 2014;**218**(2):179–87.
5. Martin RCG. Irreversible Electroporation of Locally Advanced Pancreatic Head Adenocarcinoma. *J Gastrointest Surg.* 2013;**17**(10):1850–6.
6. Martin RCG. Irreversible Electroporation: a Novel Option for Treatment of Hepatic Metastases. *Curr Colorectal Cancer Rep.* 2013;**9**(2):191–7.
7. Philips P, Hays D, Martin RC. Irreversible electroporation ablation (IRE) of unresectable soft tissue tumors: learning curve

evaluation in the first 150 patients treated. *PLoS One*. 2013;**8**(11).
8. Trabold B, Wiggermann P, Akyol D, Jung EM, Niessen C, Stroszczynski C, et al. Anesthesia for irreversible electroporation of hepatic malignant tumors. *J Clin Anesth*. 2013;**25**(5):430–1.
9. Imantalab V, Seddighi Nejad A, Mir Mansouri A, Sadeghi Meibodi A, Haghighi M, Dadkhah H, et al. A comparative study of cardioprotective effect of three anesthetic agents by measuring serum level of troponin-T after coronary artery bypass grafting. *Int Cardiovasc Res J*. 2012;**6**(3):70–4.
10. Dunki-Jacobs EM, Philips P, Scoggins CR, McMasters KM, Martin R2. Stroke volume variation in hepatic resection: a replacement for standard central venous pressure monitoring. *Ann Surg Oncol*. 2014;**21**(2):473–8.
11. Martin R2, McFarland K, Ellis S, Velanovich V. Irreversible electroporation therapy in the management of locally advanced pancreatic adenocarcinoma. *J Am Coll Surg*. 2012;**215**(3):361–9.