Irreversible Electroporation for the Ablation of Liver Tumors

Are We There Yet?

Kevin P. Charpentier, MD

Objective: To explore irreversible electroporation (IRE) as a novel, non-thermal form of tissue ablation using high-voltage electrical current to induce pores in the lipid bilayer of cells, resulting in cell death.

Data Sources: PubMed searches were performed using the keywords electroporation, IRE, and ablation. The abstracts for the 2012 meetings of both the American Hepato-Pancreato-Biliary Association and the Society for Interventional Radiology were also searched. All articles and abstracts with any reference to electroporation were identified and reviewed.

Study Selection: All studies and abstracts pertaining to electroporation.

Data Extraction: All data pertaining to the safety and efficacy of IRE were extracted from preclinical and clinical studies. Preclinical data detailing the theory and design of IRE systems were also extracted.

Data Synthesis: Preclinical studies have suggested that IRE may have advantages over conventional forms of thermal tumor ablation including no heat sink effect and preservation of the acellular elements of tissue, resulting in less unwanted collateral damage. The early clinical experience with IRE demonstrates safety for the ablation of human liver tumors. Short-term data regarding oncologic outcome is now emerging and appears encouraging.

Conclusion: Irreversible electroporation is likely to fill a niche void for the ablation of small liver tumors abutting a major vascular structure and for ablation of tumors abutting a major portal pedicle where heat sink and collateral damage must be avoided for maximum efficacy and safety. Studies are still needed to define the short-term and long-term oncologic efficacy of IRE.


Metastatic colorectal cancer (MCRC) represents the most common indication for liver resection.1,2 Five-year survival may be as high as 60% following liver resection for MCRC.3,5 Unfortunately, only 10% to 20% of patients with MCRC are candidates for potentially curative liver resection.2 Improved survival and quality of life have been reported in patients with unresectable MCRC treated with radiofrequency ablation (RFA) compared with patients treated with chemotherapy alone.4,6-9 Thermal ablation in the future liver remnant may also be used in combination with surgical resection to get more patients to a potentially curative resection when all sites of disease are not amenable to surgical resection alone.4,10 Ablation alone or in combination with resection has been reported for the treatment of liver metastases from various primary tumor sites including breast,11-15 testicular,12 neuroendocrine,12 and renal,11,13 as well as melanoma11,13 and sarcoma11,13,16 Thermal ablation has also proven effective for the treatment of primary liver cancer. The pathologic complete response rate of RFA for the treatment of small (<3 cm) hepatocellular carcinoma (HCC) in selected patients is approximately 65%.17,18 The results of microwave ablation and RFA for the treatment of HCC appear equivalent.19

See Invited Critique at end of article

Several significant limitations exist with thermal ablation. First, optimal results with thermal ablation are achieved for the treatment of small tumors (<3 cm).20 Complete pathologic response rates following RFA fall to 10% to 25% when tumor size exceeds 3 cm.17,18 Berber et al17 reported an improvement in median survival following RFA for the treatment of unresectable MCRC when treating tumors less than
Siperstein et al also showed a trend toward improved median survival following RFA of unresectable hepatic metastases less than 3 cm vs those greater than 3 cm (28 months vs 20 months, respectively).

Second, thermal ablation relies on the ability to heat the target tissue to 60°C for instantaneous cell death. The inability to reach the target temperature for effective ablation of tumors abutting a large vein (heat sink) represents another major limitation of thermal ablation. Tumors adjacent to the hepatic veins, large portal veins, and inferior vena cava are at greatest risk for incomplete tumor necrosis and local recurrence owing to heat sink (Figure 1).

Finally, thermal ablation carries a risk for collateral damage to normal structures adjacent to the desired zone of ablation (Figure 2).

METHODS

PubMed searches were performed using the keywords electroporation, IRE, and ablation. All articles with any reference to electroporation were identified and reviewed from PubMed as well as the abstracts for the 2012 meetings of the American Hepato-Pancreato-Biliary Association and the Society for Interventional Radiology. All data pertaining to the safety and efficacy of IRE were extracted from preclinical and clinical studies, and preclinical data detailing the theory and design of IRE systems were also extracted.

RESULTS

ELECTROPORATION

Breakdown of the cell membrane owing to an induced electric field was first described in the 1970s. Electroporation can be applied in either a reversible (RE) or an irreversible manner (IRE), depending on the strength and duration of the electrical field. Pulses of direct current are delivered to tissue in rapid, short intervals (milliseconds), permeabilizing the lipid bilayer of the cell membrane.

REVERSIBLE ELECTROPORATION

When the electrical field strength is below a critical threshold or when the electrical field is turned off prior to achieving a critical pore radius, the process is reversible. Reversible electroporation has been used to promote uptake of chemotherapy into tumor cells—electrochemotherapy. Studies have shown that RE in combination with bleomycin therapy is safe and improves outcomes for the treatment of squamous cell carcinoma of the head and neck when compared with bleomycin therapy alone.

IRREVERSIBLE ELECTROPORATION

Preclinical Data

Irreversible electroporation uses higher voltage direct current to overcome the ability of the cell membrane to seal, resulting in cell death. Electron microscopy reveals that the pore size is larger following IRE of hepatocytes compared with RE. Davalos et al introduced the concept of nonthermal tissue ablation using IRE. They showed that IRE could be used to ablate substantial volumes of liver tissue without undesirable thermal effects.

The application of 1500 V/cm in sets of 10 pulses of 300 microseconds produces complete ablation of hepatocarcinoma cells in vitro. Delivering the electrical energy in multiple pulses is more effective for tumor cell ablation than delivering the same energy in a single pulse.
To my knowledge, the first description of liver ablation in vivo using IRE was reported by Rubinsky et al\textsuperscript{41} in 2007. They reported their results creating 35 ablations in 14 swine livers. They varied the electrode configuration between 2 and 4 electrodes, with varying electric pulse parameters. All 14 animals survived to the designated time (24 hours to 14 days). Reversible, chemical paralysis was shown to be necessary to control unwanted, muscular contractions. The ablation zones were well demarcated and extended to a predicted electrical field magnitude of 600 V/cm. Histologic analysis showed hemorrhagic necrosis of the hepatocytes with preservation of the bile ducts within the zone of ablation. Hepatocytes immediately adjacent to central veins were ablated, suggesting that IRE is not affected by heat sink.

The design of the first IRE system approved for clinical use was reported in 2007.\textsuperscript{42} Using this system, Lee et al\textsuperscript{43} created ablations in swine liver up to 6 cm in maximal dimension with preservation of the portal structures and no evidence of heat sink. Bcl-2 oncoprotein staining was noted in all of the ablation zones but not detected in normal hepatic tissue, suggesting apoptosis as a possible mechanism of cell death.

Our group performed 16 liver ablations in 8 swine using 2 monopolar electrodes spaced 2 cm apart.\textsuperscript{44} Treatments included 90 pulses of 2500 to 3000 V/cm with a pulse length of 100 microseconds. Pulses were delivered in groups of 10, with a 250-microsecond pause between grouped pulses. Using this technique, we were able to create elliptical ablations ranging from 2.3 cm to 3.3 cm × 1.5 cm. Hemorrhagic necrosis of the hepatocytes was noted in the zone of ablation (Figure 3). Liver tissue immediately adjacent to the hepatic veins was ablated with no evidence of heat sink (Figure 4).

In addition, we performed 4 ablations across a portal pedicle in the liver hilum. Treatments included 90 pulses of 3000 V/cm, with a pulse length of 100 microseconds and a 2-cm exposed length of the active portion of the electrodes. Pulses were delivered in groups of 10 with a 250-microsecond pause between grouped pulses. This resulted in an elliptical ablation measuring a mean (SD) 4.45 (0.07) cm × 1.8 (0) cm. The hepatic artery, portal vein, and bile duct within the ablation zone were relatively preserved and appeared to be more resistant to the effects of IRE, as previously described (Figure 5).

Irreversible electroporation has also been shown to be safe and effective for the ablation of extrahepatic tissues including of the prostate,\textsuperscript{45} carotid artery,\textsuperscript{46} atrial appendage,\textsuperscript{47} pancreas,\textsuperscript{48,49} small bowel,\textsuperscript{50} kidney,\textsuperscript{51,52} and lung.\textsuperscript{54,55} These studies showed similar findings to those described previously with effective ablation of the target tissue, lack of heat sink, and preservation of critical structures in and around the zone of ablation such as nerve tissue for prostate IRE, renal pelvis during kidney IRE, and duodenal and vascular preservation following IRE of the pancreatic head.

Defining Ablation

While the effects of thermal ablation are evident immediately, the zone of ablation following IRE is not immediately evident owing to the mechanism of cell death. Triphenyltetrazolium chloride staining is able to predict the
zone of ablation as early as 15 minutes following IRE (Figure 6). Ultrasonography and magnetic resonance imaging have also been reported to accurately predict the zone of ablation following IRE.

Preclinical Oncologic Data

The experience treating cancer cells with IRE is growing. Al-Sakere et al reported complete regression in 12 of 13 cutaneous tumors implanted in mice with IRE.

Guo et al created hepatomas in 30 Sprague-Dawley rats. Animals were either treated by IRE using 8 100-microsecond pulses of 2500 V/cm or served as control subjects. Nine of 10 animals treated with IRE and euthanized 7 to 15 days after treatment had a pathologic complete response.

Other groups have reported the ability of IRE to ablate prostate cancer cells in vitro, breast cancer cells in vitro, breast orthotopically implanted in nude mice in vivo, and pancreas ductal adenocarcinoma in vivo in a mouse model.

Safety

To my knowledge, the first prospective study of IRE for the treatment of human tumors was designed as an ablation followed by resection trial in 6 patients with renal tumors. No clinically significant electrocardiographic, hemodynamic, or serum biologic changes were noted during or following IRE. One patient in the series had a transient, self-limiting supraventricular arrhythmia.

The first article detailing IRE in human liver was a retrospective report detailing the complications encountered while performing 28 IRE ablations in 21 patients. Seventeen procedures treated liver tumors, 8 renal tumors, and 3 lung tumors. In this study, complications included transient systolic hypertension in all patients, muscular contractions in inadequately paralyzed patients, postoperative pain following 13 procedures (46%), acid-base disturbances following 4 procedures (14%), and pneumothorax related to electrode placement in 3 procedures (11%). Ventricular tachycardia occurred during 7 procedures (25%). In 4 of these 7 cases, the arrhythmia was as-
sociated with markedly decreased blood pressure. In a follow-up article, the authors reported only 2 episodes of arrhythmia in 30 patients using electrocardiogram synchronization of the IRE treatment—supraventricular tachycardia (n=1) and atrial fibrillation (n=1).67

Mali et al68 reported on the effects of electroporation on the function of the heart in human patients. Fourteen patients were treated with electrochemotherapy. In this series, voltages for electrochemotherapy ranged from 680 to 960 V/cm compared with the 2500 to 3000 V/cm typically used for liver IRE. No pathologic morphologic changes of the electrocardiogram in any of the patients treated were reported. The authors suggested an algorithm for cardiac synchronization with electroporation that may improve its safety.

In a subsequent study, Deodhar et al69 reported improved safety with IRE with the use of cardiac synchronization in a swine model. All of the 7 ablations performed within 1.7 cm of the heart without electrocardiogram synchronization resulted in a severe, life-threatening arrhythmia compared with no serious arrhythmias in 12 ablations performed within 1.7 cm of the heart but with cardiac synchronization. No serious arrhythmias occurred in either the synchronized or unsynchronized group when the electrode was positioned more than 1.7 cm from the heart; however, unsynchronized ablations still had a higher incidence of minor, self-limiting arrhythmias compared with synchronized ablations (2/11 and 0/7, respectively). The distance of 1.7 cm was modeled to predict an electrical field strength of 100 V/cm, which is less than the threshold to achieve RE. They concluded that the risk for cardiac arrhythmia during IRE is directly related to the distance of the electrode from the heart and that serious arrhythmias can be avoided with cardiac synchronization.

In the last 2 years, a growing volume of experience with IRE for ablation of human tumors has been reported in abstract form. Four abstracts presented at the 2012 meeting of the Society for Interventional Radiology detailed the experience and safety of IRE for the ablation of 158 tumors in 106 patients (Table 1 and Table 2).70-73 A multi-institutional, voluntary tumor treatment registry has been established for IRE. Data from the registry was presented at the national meeting of the American Hepato-Pancreato-Biliary Association in March 2012. This experience had considerable overlap with the data presented at the Society for Interventional Radiology’s 2012 meeting and detailed a similar safety profile for IRE of the liver in humans.74

Irreversible electroporation appears to be finding a niche for ablation of small tumors (<3 cm) abutting large vessels or other critical structures where either heat sink or collateral damage are a concern. Narayanan et al75 reported narrowing or thrombosis in only 3 of 84 vessels in close proximity to the ablation.

A recent case report describes IRE for the treatment of unresectable MCRC abutting a portal pedicle, validating our group’s preclinical experience showing the safety of IRE for liver ablations across the porta hepatis.44,76

Oncologic Efficacy

The most important study to date regarding IRE for liver tumors is a well-designed, prospective, multicenter study to evaluate the safety and efficacy of IRE as first-line treatment in biopsy-proven, early-stage HCC (clinicaltrials

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**Table 1. Early, Retrospective Experience With Irreversible Electroporation of the Liver and Pancreas Presented in Abstract Form**

<table>
<thead>
<tr>
<th>Study</th>
<th>Liver Patients</th>
<th>Pancreas Patients</th>
<th>Lung Patients</th>
<th>Other Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narayanan et al70</td>
<td>0</td>
<td>8 (8)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bagla et al71</td>
<td>0</td>
<td>4 (7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Narayanan et al72</td>
<td>49 (76)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hays et al73</td>
<td>33a</td>
<td>1a</td>
<td>12a</td>
<td>4a</td>
</tr>
</tbody>
</table>

a Some patients treated at more than 1 site.

**Table 2. Safety of Irreversible Electroporation in the Early Experience With Ablation of Human Liver and Pancreas Tumors**

<table>
<thead>
<tr>
<th>Study</th>
<th>Pneumothorax</th>
<th>Hypertension</th>
<th>Arrhythmia</th>
<th>Pancreatitis</th>
<th>Other/Self-limiting</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narayanan et al70</td>
<td>1/8</td>
<td>NR</td>
<td>NR</td>
<td>1/8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bagla et al71</td>
<td>0</td>
<td>7/7</td>
<td>0</td>
<td>NR</td>
<td>1/7</td>
<td>0</td>
</tr>
<tr>
<td>Narayanan et al72</td>
<td>6/49</td>
<td>NR</td>
<td>2/49a</td>
<td>NR</td>
<td>2/49</td>
<td>NR</td>
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<tr>
<td>Hays et al73</td>
<td>7/50</td>
<td>1/50</td>
<td>0</td>
<td>NR</td>
<td>2/50</td>
<td>NR</td>
</tr>
</tbody>
</table>

Abbreviation: NR, not reported.
a Self-limiting.
cioni et al\textsuperscript{77} reported a complete response in 23 of 29 tu-
ciples, Au et al\textsuperscript{80} demonstrated successful gene transfer in
tion zone and normal liver. Capitalizing on this prin-
troporate the cell membrane is lost.
reversible form of electroporation. When the field strength
falls to less than 100 V/cm, the ability to reliably elec-
able to establish the efficacy of IRE
for the treatment of human liver tumors before proceeding
with head to head studies of IRE vs microwave ab-
Electrical field strength diminishes with increasing dis-
ence of new technology into surgical practice.
motes the interests of innovators, patients, and early adopt-
ers—the early adopters. More data are emerging to sup-
cers—either the length and/or quality of life for their patients.
At times, physician motives for using innovative tech-
ology, the so-called learning curve. Physicians also have
_pagebreak_ a vested interest in new technologies that can improve
either the length and/or quality of life for their patients.
and financial interest in seeing their products developed. Patients have
vested interest in new technologies that could improve
the length and/or quality of life; however, this is
trumped by their desire for safety and autonomy during
the phase of innovation and early adoption of new tech-
nology, the so-called learning curve. Physicians also have
a vested interest in new technologies that can improve
either the length and/or quality of life for their patients.

**FUTURE DIRECTIONS**

Additional data are needed to establish the efficacy of IRE
for the treatment of human liver tumors before proceeding
with head to head studies of IRE vs microwave ab-
lation and/or RFA.

**THE NANOKNIFE SYSTEM**

The only system currently available for clinical use is the
NanoKnife (AngioDynamics), which has received 510(k)
approval for soft-tissue ablation and has not received any
tissue-specific indications. The Federal Food and Drug Ad-
ministration has granted an investigational device exemp-
tion to study IRE for the treatment of prostate cancer and is
currently reviewing another investigational device ex-
emption application to study NanoKnife for the treatment of
locally advanced, unresectable pancreatic cancer.

Irreversible electroporation can be performed using a
percutaneous, laparoscopic, or open surgical tech-
nique.\textsuperscript{43,72} Tumor size and configuration can be pro-
grammed into the NanoKnife system, which then gen-
erates a treatment plan. The treatment plan is displayed
on the computer interface and can be modified by the
user to optimize accuracy and efficacy. Up to 6 elec-
trodes (19 gauge) can be positioned around the tumor
with image guidance depending on the size and shape of
the tumor before delivering the treatment.

The list price for NanoKnife is $395 000 but center-
specific pricing may vary significantly. Electrodes cost
from $1000 to $2000 per piece; therefore, the cost per
case varies on the number of electrodes used. Na-
noKnife is approved by the Federal Food and Drug Ad-
ministration for soft-tissue ablation; therefore, in some
cases, generic ablation codes may be reimbursed.

**LESSONS LEARNED FROM THE ADOPTION
OF NEW TECHNOLOGIES**

The introduction of novel medical technology is a com-
plex process with multiple competing interests. Innova-
tors and corporations have an intellectual and financial
interest in seeing their products developed. Patients have
vested interest in new technologies that could improve
the length and/or quality of life; however, this is
trumped by their desire for safety and autonomy during
the phase of innovation and early adoption of new tech-
nology, the so-called learning curve. Physicians also have
a vested interest in new technologies that can improve
either the length and/or quality of life for their patients.
At times, physician motives for using innovative tech-
nologies have been questioned, with some citing con-
cerns of conflicts of interest and with potential second-
ary gains being academic development or financial gain.
Strasberg and other members of the Balliol Collabora-
tion have published a series of articles highlighting the
potential pitfalls and conflicts of interest that can occur
during the adoption of new technology.\textsuperscript{82-85} Through the
IDEAL model (Innovation, Development, Exploration,
Assessment, and Long-term study) recommendations,
they went on to suggest a framework through which surgical
innovation may be developed that protects and pro-
motes the interests of innovators, patients, and early adopt-
ers of new technology into surgical practice.

Based on the IDEAL model recommendations, IRE is
in Stage 2a development (Table 3). The data support-
ing the proof of concept for ablation of liver tumors with
IRE is robust. The early innovators have published sev-
eral case series describing the safety and technical suc-
cesses of the procedure, as detailed previously. Now, we
are seeing IRE use expanding out to a wider range of users—
the early adopters. More data are emerging to sup-
port safety, and prospective data are just now emerging
to establish early efficacy of IRE for liver tumor abla-
tion. A prospective, voluntary database for IRE of hu-
man tumors is established, and we are beginning to see
Irreversible electroporation is a novel, nonthermal method for tumor ablation. The early clinical and preclinical experiences with IRE establish its safety for liver tumor ablation when electrocardiogram synchronization is used and when the treatment is delivered in properly selected patients and by someone with experience and expertise in image-guided tumor ablation. Irreversible electroporation is likely to find a niche for the ablation of large hepatic veins, or portal structures where conventional thermal techniques for ablation of colorectal cancer metastases to the liver are limited owing to heat sink and/or concerns regarding collateral damage. Further study is needed to establish the oncologic efficacy for IRE in the treatment of primary and metastatic liver cancer.

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CONCLUSIONS

Conflicts of Interest Disclosures: Dr Charpentier serves on the data safety monitoring board for ONC-204, a trial of NanoKnife for the treatment of locally advanced, unresectable pancreatic cancer. He has also previously received a research grant from AngioDynamics.

REFERENCES


Table 3. Stages of Surgical Innovation: The IDEAL Model

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Number and types of patients</th>
<th>Number and types of surgeons</th>
<th>Output</th>
<th>Intervention</th>
<th>Method</th>
<th>Outcomes</th>
<th>Ethical approval</th>
<th>Examples</th>
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</thead>
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<tr>
<td>Purpose</td>
<td>Proof of concept</td>
<td>Single digit, highly selected</td>
<td>Description</td>
<td>Evolving</td>
<td>Prospective development studies</td>
<td>Proof of concept</td>
<td>Sometimes NOTES video</td>
<td>Yes</td>
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<tr>
<td>Number of patients</td>
<td>Few; selected</td>
<td>Very few, innovators</td>
<td>Development</td>
<td>Evolving</td>
<td>Research database; explanatory or feasibility RCT (efficacy trial); diseased based (diagnostic)</td>
<td>Mainly safety; technical and procedural success</td>
<td>Yes</td>
<td>Italian D2 gastrectomy study</td>
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<tr>
<td>Number of surgeons</td>
<td>Few; innovators and some early adopters</td>
<td>Description</td>
<td>Exploration</td>
<td>Evolving</td>
<td>RCT with or without additions/modifications; alternative designs</td>
<td>Safety; clinical outcomes (specific and graded); short-term outcomes; patient-centered (reported) outcomes; feasibility outcomes</td>
<td>Yes</td>
<td>Swedish obese patients study</td>
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<td>Output</td>
<td>Description</td>
<td>Measurement; comparison</td>
<td>Assessment</td>
<td>Exploring</td>
<td>Registry; routine database (eg, SCOAP, STS, NSQIP); rare case reports</td>
<td>Clinical outcomes (specific and graded); middle-term and long-term outcomes; patient-centered (reported) outcomes; cost-effectiveness</td>
<td>Rare events</td>
<td>No</td>
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<tr>
<td>Intervention</td>
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<td>Procedure refinement; community learning</td>
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<tr>
<td>Method</td>
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<td>Prospective development studies</td>
<td>Assessment</td>
<td>Production</td>
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<tr>
<td>Purpose</td>
<td>Learning</td>
<td>Many; may expand to mixed; broadening indication</td>
<td>3: Assessment</td>
<td>Many; expanded indications (well defined)</td>
<td>All eligible</td>
<td>RCT with or without additions/modifications; alternative designs</td>
<td>Clinical outcomes (specific and graded); middle-term and long-term outcomes; patient-centered (reported) outcomes; cost-effectiveness</td>
<td>Rare events; long-term outcomes; quality assurance</td>
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<tr>
<td>Number of patients</td>
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<td>All eligible</td>
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<td>All eligible</td>
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</tr>
</tbody>
</table>

Abbreviations: IDEAL, Innovation, Development, Exploration, Assessment, and Long-term study; NOTES, natural orifice translumenal endoscopic surgery; NSQIP, National Surgical Quality Improvement Program; RCT, randomized controlled trial; SCOAP, Surgical Clinical Outcomes Assessment Program; STS, Society of Thoracic Surgeons.

Adapted with permission from Elsevier.
Another Club in the Bag

In the event that you have had any difficulty keeping up with the near explosion of new technologies and techniques that continue to rapidly change the nature of hepatobiliary surgery, in this article, Kevin P. Charpentier, MD, has graciously provided a timely, comprehensive, and thoughtful review of yet another new treatment option. With the increasing incidence of primary hepatic malignancies, such as hepatocellular carcinoma and cholangiocarcinoma, as well as a host of secondary tumors, including colorectal and neuroendocrine tumors, there is certainly a need for new options. Improvements in imaging, surgical tools and techniques, catheter-based treatments, and ablative technologies have all converged to expand the locoregional treatment alternatives. Indeed, the concepts of unresectable and untreatable tumors are undergoing continuous redefinition. With more on the horizon, irreversible electroporation (IRE) represents one relatively new such modality. I may be horrible at golf, but I do understand the concept: choose the best club based on where the ball lies. Unfortunately, relative to critical anatomy, sometimes tumors in the liver lie in very unfortunate locations. In this article, Charpentier gives us a perspective on soft-tissue tumor ablation, explains the underlying mechanisms, and describes the role potentially filled by IRE. I especially appreciated learning about the IDEAL (Innovation, Development, Exploration, Assessment, and Long-term study) framework for assessing surgical innovation and the place currently held by the IRE technology. In its current state, IRE is costly and indicated for a relatively small niche, but it certainly has promise for an expanded role as more is learned. To answer Charpentier’s question, I doubt whether we are there yet; however, as we play the course, it certainly cannot hurt to have a new, albeit expensive, club in the bag.

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