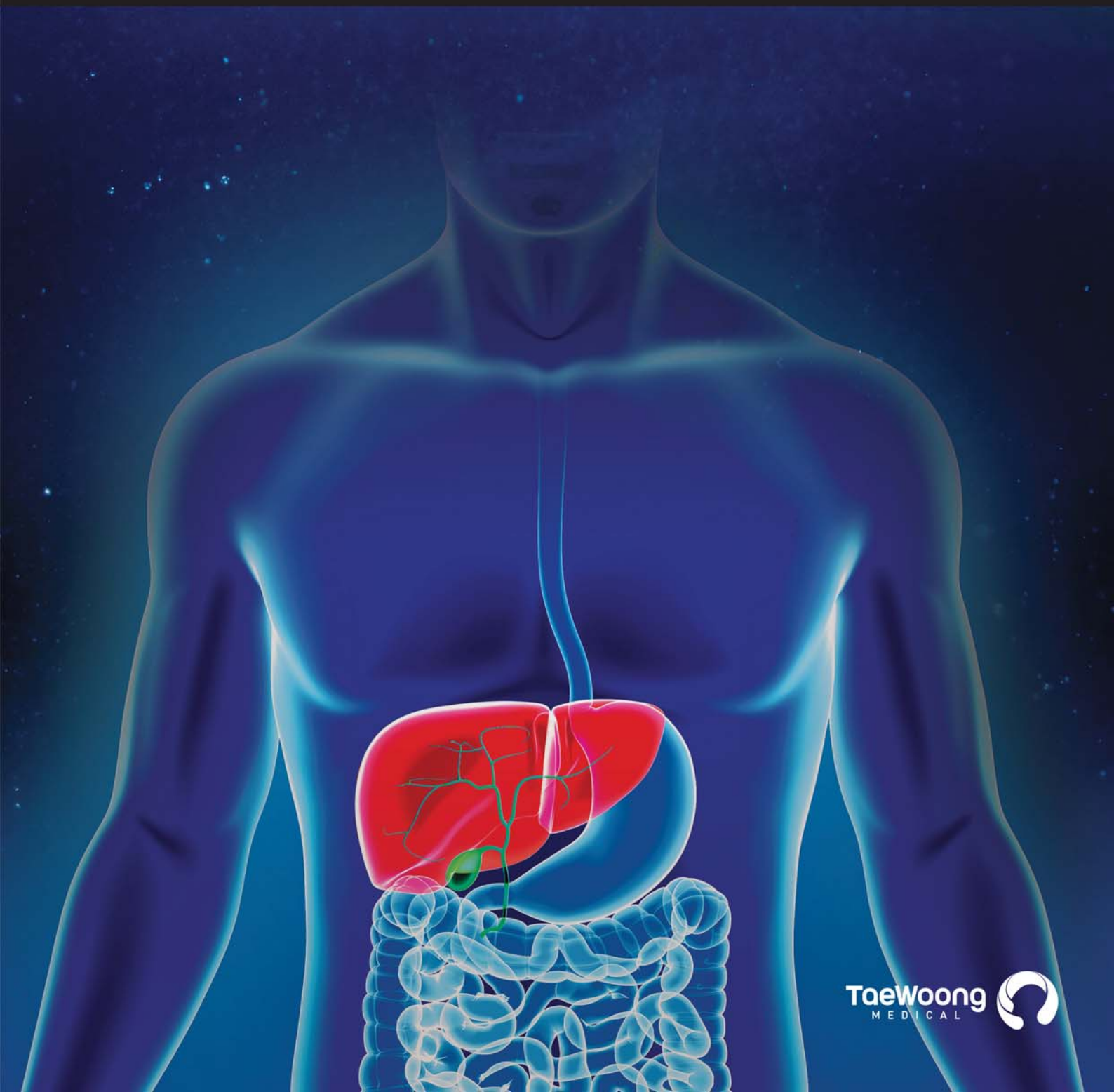
A TAEWOONG MEDICAL NEWSLETTER

OCT 2018 / ISSUE 9

CONNECT

WE CONNECT YOUR LIFE



A LOOK INTO TAEWOONG MEDICAL PERFORMANCE IN 2018

20th Dusseldorf International Endoscopy Symposium

Feb 2-3, 2018 / Dusseldorf, Germany

This symposium is one of the largest local conferences in Germany and is attended by about 5,000 doctors from neighboring countries. It was our 4th exhibition this year and meaningful lectures and live demonstrations related to RFA products were held. Prof. Reddy gave a lecture on "Endoluminal Tumor Ablation: When and how?" for ELRA™. We hope it was helpful for those who have been interested in our RFA products. The next symposium will be held in Feb 8th-9th 2019.

ESGE Days 2018

April 19-21, 2018 / Budapest, Hungary

ESGE Days was held for the first time in Budapest, Hungary by Thierry Ponchon. During the exhibition, we met many doctors who were interested in our products and many lectures related to our products were done. The next congress will be held in April 4th-6th 2019 and we hope to meet more doctors in Prague, Czech Republic.

The 5th Master Course of EUS-guided RFA EUSRA™ Training

April 24-25, 2018 / Marseille, France

The 5th Master Course of EUS-guided RFA EUSRA™ Training was held in Nord Hospital, Marseille, France. 15 doctors from 8 countries attended this workshop and Prof. Barthet prepared 4 live cases related with adenocarcinoma, PNET, IPMN, and MCN. Prof. Barthet also gave a lecture and an in-vivo animal test with the EUSRA™. The purpose of this training was to provide an in-depth understanding of the EUSRA™ procedure. The next workshop will be held in November 20th-21st, Marseille, France.

Digestive Disease Week 2018

June 2-5, 2018 / Washington D.C, USA

DDW 2018 was held in Walter E. Washington Convention Center and Taewoong Medical participated in the exhibition with its main products. During the exhibition, the SPAXUS™ stent for LAMS and RFA devices such as EUSRA™ and ELRA™ received extensive attention. The 13th Taewoong Medical Dinner Party was held at the National Park major league baseball stadium. We had an unforgettable time with our customers this year and promise to hold an even better event next year. See you in San Diego in 2019.

IDEN 2018

June 30-July 01, 2018 / Seoul, Korea

International Digestive Endoscopy Network (IDEN) is held every year in Seoul by the international gastrointestinal endoscopy society. Many doctors visited Seoul to attend the IDEN conference and we had a factory tour with our customers who visited Seoul before the start of the IDEN conference. Many customers told us that it was a great opportunity to see the headquarter office and see the production process of the Niti-S stent in person. The next IDEN will be held in June 13th-15th, 2019 in Seoul, Korea.

ENDO LIVE 2018

May 16-18, 2018 / Rome, Italy

ENDO LIVE which is one of the biggest Italian local congress was held in Catholic University Rome, Italy. We participated in this exhibition with our distributor. There were some lectures and liver demonstration with EUSRA™ by Prof. Marc Giovannini and ELRA™ by Prof. Reddy. More and more doctors were interested in our RFA products. Taewoong Medical will do our best to present our products in more countries in the future.

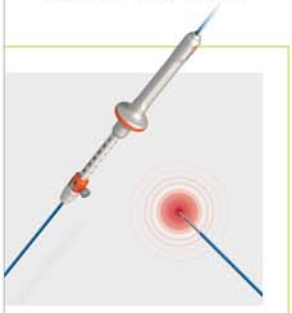
PRODUCT NEWS

FDA approved in USA

EUSRA™

DWD Medical, the Taewoong US office, announced that EUSRA™ electrode has received 510(k) clearance from the U.S Food and Drug Administration (FDA). EUSRA™ is an electrode for an endoscopic ultrasound-guided radio-frequency ablation in pancreatic tumors. The official launching of EUSRA™ will be at ACG (American College of Gastroenterology) 2018 October 5-10, in Philadelphia. DWD Medical sees a near-term market opportunity of about $63 million a year in sales of EUSRA™ in the US.

"Available in the US"



EUSRA™ electrode

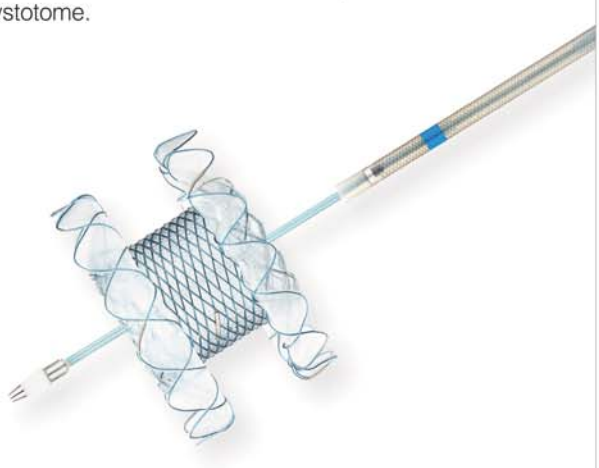
VIVA Combo™ RFA generator

KFDA approved in KOREA

HOT SPAXUS™

The electrocautery-enhanced LAMS

HOT SPAXUS™ was approved by KFDA (Korea Food and Drug Administration) in Sep 2018. The newly applied electrocautery tip at the distal tip of the delivery system facilitates are ONE-STEP procedure of stent deployment. The electrocautery tip makes the procedure simple, quick and easier as the stenting procedure can be done without additional devices such as puncture needle and cystotome.



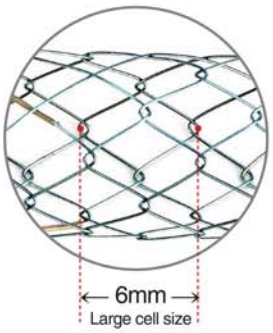
NEWLY RELEASED IN 2018

CHANGES AND ADDITIONS

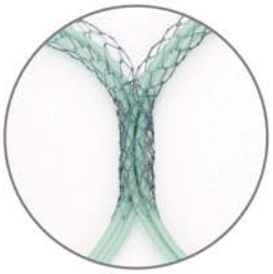
LCD™ Biliary Stent

The 7Fr delivery system has been available since February 2018. This new thinner delivery system facilitates easy access to the hilar obstruction lesion while enabling smoother deployment.

Not only has the delivery system evolved, but also the stent itself. While keeping the 8Fr LCD™ Stent's advantage of the Large Cell Design along with low axial force, an Adjustable Vertical Axis (blue line in the picture) which can be easily moved aside during the stent-in-stent procedure for the second stenting while enhancing stent kinking resistance has been added.



The conventional LCD™ stents on the 8Fr delivery system is still available.



The adjustable vertical axis

GIOBOR™ Biliary Stent

The GIOBOR™ Stent which is specially designed for Hepatico-Gastrostomy is now 70% covered to minimize the bile leakage in the peritoneal cavity.

The long covered portion prevents bile leakage between the left hepatic duct and the stomach. The short bare portion avoids the blockage of the side branches in the hepatic duct and prevents migration.

NEW PRODUCTS

Biliary

S Flare type

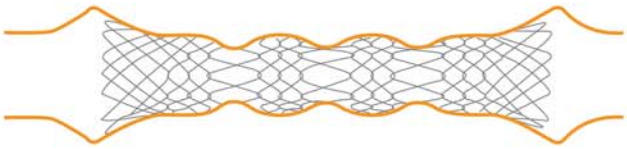
The Biliary S Flare type is a new S-type covered stent with flares at both tips which prevent migration. Flares on both ends have been added to the design in order to decrease the migration rates which have been a long time problem for biliary covered stents. The larger flare with a dramatic angle is placed outside the papilla while the smaller flared end is positioned inside the biliary tract to prevent migration.

Conventional S-type

New S-type

BUMPY™ String type

The BUMPY™ stent with irregular cell sizes now comes with a 10cm platinum string. This long radiopaque string aids for easy removal in high-up anastomotic strictures after liver transplantation.



Irregular cell size

Esophageal

CONIO™ II type

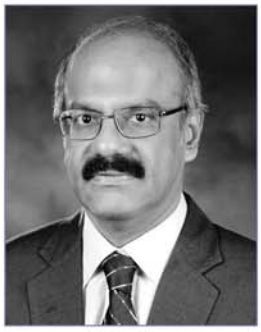
The CONIO™ II type is a fully covered stent for upper esophageal strictures. Unlike the conventional CONIO™, CONIO™ II has a D-type weaved body to improve conformability as well as a double anti-migration layer with holes prevents migration.

DUAL™ type

The Esophageal DUAL™ is a dumbbell-shaped stent indicated for malignant esophageal strictures. Both heads with silicone coating prevent migration and the body with DUAL™ construction enables the stent to conform to the esophagus movement.

Endoscopic drainage of pancreatic fluid collections by use of a novel biflanged stent with electrocautery-enhanced delivery system

Sundeep Lakhtakia, Zaheer Nabi, Jong Ho Moon, Rajesh Gupta, Radhika Chavan, Jahangeer Basha, Nageshwar Reddy
[VideoGIE. 2018 Jul 27;3(9):284-288]



D. Nageshwar Reddy
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AIM

The aim of this study was to evaluate the feasibility and safety of a novel BFMS with electrocautery-enhanced delivery system (EC-BFMS).

METHODS

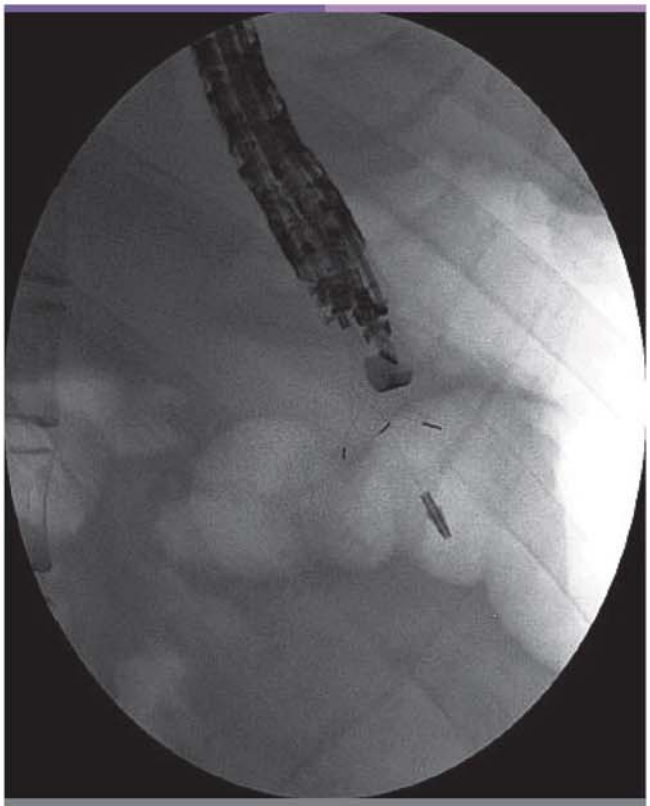
Five patients with symptomatic PFCs undergoing drainage with the EC-BFMS were included in the analysis. The data were extracted from a prospectively collected database and analyzed retrospectively.

DRAINAGE TECHNIQUE

All the PFC were drained under EUS guidance after thorough assessment and choice of an appropriate site for drainage. The standard sequence of steps for EUS-guided drainage of PFCs with conventional BFMSs are (1) puncture of the PFC with a 19-gauge needle, (2) coiling of a guidewire inside the PFC, (3) creation of a cystogastric fistula by use of a 6F cystotome over the guidewire, (4) dilation of the fistula with a small-caliber balloon, and (5) deployment of the stent under EUS, fluoroscopic, and endoscopic guidance. The important differences in drainage technique when the EC-BFMS was used are as follows. First, the cyst wall was punctured either with a 19-gauge regular FNA needle or directly with the electrocautery-enabled stent assembly with a free-hand technique, depending on the operator's preference. Second, steps 3 and 4, including the use of a cystotome and balloon for creating a cystogastric tract were omitted. Third, the guidewire was not coiled in all cases, and the decision to coil the guidewire inside the cyst cavity was left to the endoscopist's discretion. Technical success was defined as successful deployment of the EC-BFMS. Clinical success was defined as resolution of symptoms along with >50% reduction in the size of the PFC cavity. All intraprocedural and postprocedural adverse events were recorded.

POSTPROCEDURE FOLLOW-UP

All the patients were followed up clinically and radiologically. If clinical symptoms persisted at 48 to 72 hours, a nasocystic drainage tube was placed for flushing with diluted hydrogen peroxide and saline solution. Subsequently, direct endoscopic drainage was considered for patients with persistent symptoms. The stents were removed about 4 weeks after initial placement. MRCP, endoscopic retrograde pancreatography, or both were performed before removal of the stents to delineate pancreatic ductal anatomy. A pancreatic ductal stent was placed in case a ductal stricture or leak was demonstrated.



Entire drainage procedure performed in a single step: cyst wall puncture with the electrocautery-enabled stent delivery system followed by deployemtn of stent.

ELECTROCAUTERY-ENHANCED BFMS

The EC-BFMS (Hot NAGI™) device is a through-the-scope BFMS delivery system (10F) (**Fig. 1**). The delivery system has a conical hollow stiff metallic tip, which is connected by an internal fine wire to the connector hub handle. The tip enables passage of the stent assembly without any dilation of the tract. This allows the operator to place the stent directly without intervening steps like guidewire placement, passage of a cystotome to create a fistula, or balloon dilation to allow passage of a stent assembly. The BFMS is a conventional fully covered metal stent made of nitinol with flared ends and covered with silicone membrane. The EC-BFMS is available in 2 lengths (20, 30 mm) and 4 diameters (10,12,14,16 mm). The stent flanges measure 26 mm in diameter. The recommended settings on an electrosurgical generator are 80 to 120 watts on pure cut mode.

RESULTS

A total of 5 patients, all men (median age, 31 years; range, 18-39 years), underwent EUS-guided drainage of PFCs by use of an EC-BFMS equipped with an electrocautery-enhanced delivery system. Technical success was achieved in all the patients. The median size of fluid collections was 9.8 cm (range, 7.7-17 cm). The mean wall thickness of the PFCs at point of entry was 4.38±1.02 mm (range, 3.2-5.6 mm). In 2 cases, a 16x30mm stent was used; in the other 3 cases, a 16x20mm stent was used.

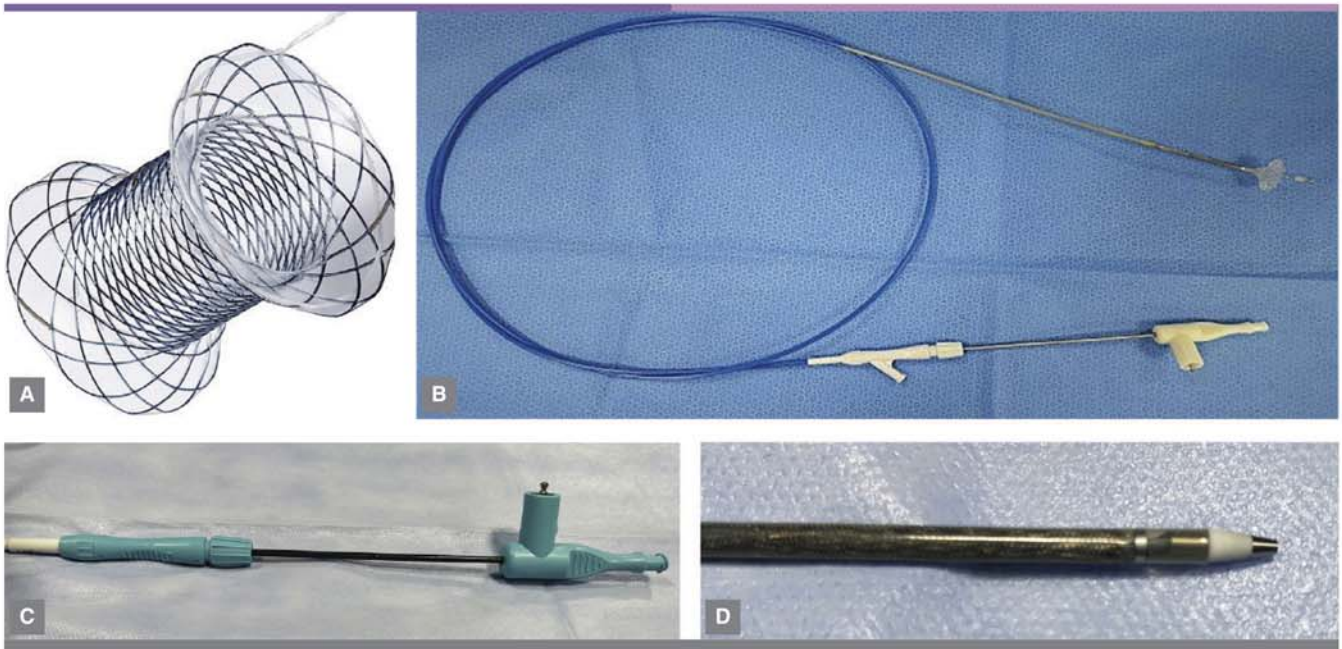


Figure 1. Components of electrocautery-enhanced stent delivery system. **A,** Novel biflanged metal stent. **B,** Electrocautery-enhanced stent delivery system. **C,** Magnified view of electrocautery plug. **D,** Electrocautery-enabled tip of catheter.

CONCLUSIONS

Endoscopic drainage of PFCs is feasible and safe by use of a novel biflanged metal stent with an electrocautery-enhanced delivery system. Larger studies are required to establish the utility of this novel stent delivery system for drainage of PFCs.

The success of KAFFES™ stent insertions for post liver transplant anastomotic strictures

Warner B., Harrison P., Devlin J., Reffitt D., El-Sherif Y., Khorsandi S., Prachalias A., Cortes Cerisuelo M., Menon K., Jassem W., Srinivasan P., Vilca-Melendez H., Heneghan M., Heaton N., Joshi D.
Institute of Liver Studies, King's College Hospital, London
[British Society of Gastroenterology Annual Meeting, Liverpool, 4th-7th June 2018]

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BACKGROUND

Anastomotic strictures (AS) are isolated, short-length strictures, affecting 4-9% of patients post liver transplantation, which if untreated, ultimately lead to graft failure. Endoscopic stenting has historically been with plastic stents (PS). However, AS frequently recur, and patients require multiple procedures. Niti-S Kaffes stent are the new type of covered metal stent that have an anti-migration waist, short stent length and long retrieval wires deployed within the duodenum (**Figure 1**). Previous randomised trials have highlighted their success with resolving AS compared to PS.[1]

METHODS

To examine outcomes in patients with AS, we compared a recent cohort of patients treated using KS with a historical cohort of patients who received PS. KS were inserted in patients with duct-to-duct anastomoses and reassessed 10-12 weeks after, to determine stricture resolution. Sphincterotomies and dilatations were performed at the endoscopist's discretion. Independent variables were analysed for significance using the Independent samples t-test on SPSS.

RESULTS

Analysis of both groups are shown in **Table 1**. AS resolved after one deployment of KS in 14 out of 16 patients (88%) compared to 26 out of 69 patients (38%) after their first PS. There were no complications, including stent migration, after KS compared to 6 (8.4%) in the PS group (3 cholangitis, 2 pancreatitis, and 1 bleeding). Following initial ERCP, PS patients required more ERCPs (mean 2.71 vs 1.13 more; $p<0.01$) and 32% required biliary reconstruction.

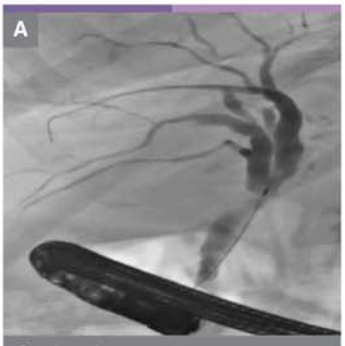
CONCLUSIONS

Our data indicate that the KS is a promising method for managing post transplant AS because the majority of strictures are treated by deployment of a single stent at first ERCP.

Table 1. Shows the analysis of both KS and PS groups, along with complication and stricture resolution rates

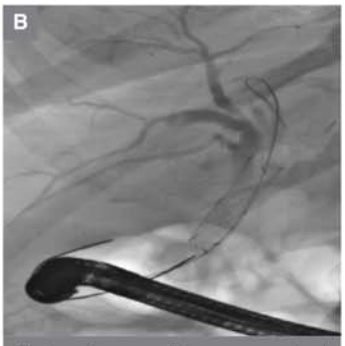
	Kaffes stent	Plastic stent
No. inserted	22	69
No. removed	16	69
Stricture resolution (%)	14 (88%)	26 (38%)
Complications (%)	0	6 (8,4%)
Need for biliary reconstruction	0%	32%
Mean age (Years)	55	51
Females (%)	12 (55%)	20 (29%)
DBD (%)	11 (50%)	47 (68%)
DCD (%)	11 (50%)	22 (32%)
CIT (Hours) (±SD)	9.6 (±3.3)	8.9 (±3.1)

Figure 1. Shows the KAFFES™ stent with its long retrieval wires



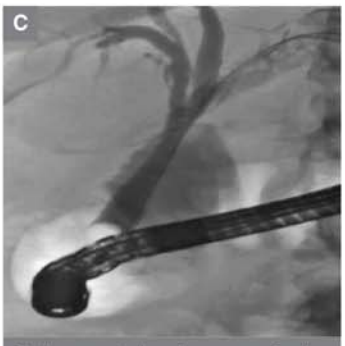
A

Cholangiogram shows an anastomotic stricture persisting despite previous plastic stenting



B

Cholangiogram of the same patient at Kaffes stent insertion



C

Balloon cholangiogram of the same patient 4 months later after KAFFES™ stent removal, showing complete stricture resolution

A new designed biliary covered SEMS to prevent stent migration: A preliminary report

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[DDW 2018 Abastract]

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Camposampiero, Padova, Italy

AIMS

Evaluation of migration rate, and efficacy of a new type of biliary covered stent, with large flange on both proximal than distal end to prevent prosthesis migration [Niti-S™ Biliary Covered Stent (Flare Type)]. The stents have 4, 6, 8 or 10 cm in length with a body diameter of 10 mm the proximal flange is dilated up to 12 mm. to prevent distal migration. The distal flange is dilated up to 16 mm. to avoid proximal migration.

METHODS

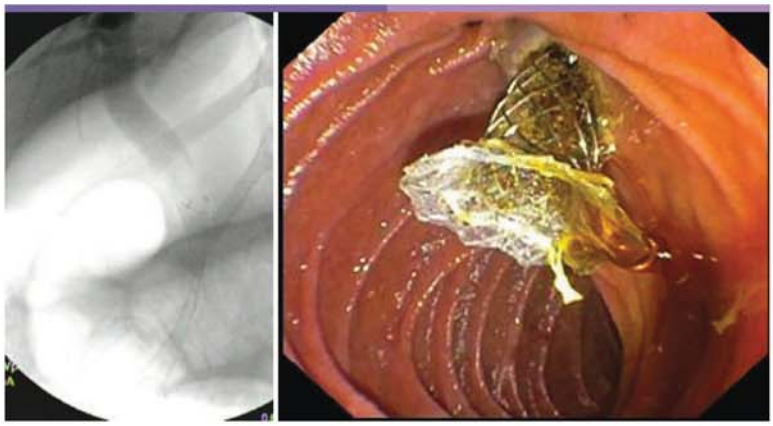
We have treated with the news device 7 patients with biliary duct stricture due to advanced pancreatic cancer. All the patients received a routine sphincterotomy prior stent insertion. The stent has been selected in accordance with stricture length. The day after the insertion we check serum level of bilirubin and pancreatic amylase. The same parameters have been recorded at first, third and sixth month. The stents have been checked at first, third and sixth month since insertion time using abdomen X-ray film to assess stent patency and absence of migration.

RESULTS

We report a 100% of success rate on stent insertion. Bilirubin serum level has decreased within 6 days to normality. In 1 of 7 patients we recorded a peak of serum amylase up to 350 U/L, returned to normal level within three days, with no clinical signs of pancreatitis. No bleeding or any other complication related to the SEMS has been recorded. We did not suffer any both proximal than distal migration along the three months observation.

CONCLUSIONS

These newly designed biliary covered SEMS to prevent migration look to be an effective and secure device on this preliminary report. More data will be recorded in future.



Novel temperature-controlled RFA probe for treatment of blocked metal biliary stents in patients with pancreaticobiliary cancers: initial experience

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INTRODUCTION

Survival is limited in patients with PB tumors and continues to be poor inspite of chemotherapy and/or radiotherapy. Palliative endoscopic biliary stenting to relieve obstruction and maintain biliary flow is the mainstay intervention in management of these patients. However stents can become blocked resulting in repeated admissions and procedure-related morbidity and mortality. RFA may reduce tumor volume prior to biliary stenting or can be used to ablate ingrowth of tumor in previously placed stents. We describe the first UK experience with use of this endoluminal RFA probe in a series of patients for treatment of blocked metal biliary stents.

Fig 1. ELRA™ catheter - 18mm

Fig 2. VIVA combo™ generator

PATIENTS AND METHODS

This study was done between July 2016 and April 2017. As this was the first RFA probe used in the unit, the patients were considered for RFA treatment after careful discussion among the pancreatobiliary multidisciplinary team. Stricture diameter was measured by study of the cholangiographic images pre- and post-treatment by JSL&MKN.

RFA TECHNIQUE

The RFA probe used in the patients was the ELRA™ (EndoLuminal Radiofrequency Ablation) electrode (Taewoong Medical, South Korea; ▶**Fig.1**). The length of the probe is 18mm, diameter 7 Fr, ablation depth 4mm and it has multiple bipolar electrodes which provide linear ablation and therefore there is no need for ground pads. The VIVA (Taewoong Medical, South Korea ▶**Fig.2**) combo™ generator is versatile and the settings include power (range 0 watts to 200 watts), and temperature (range 5°C to 95°C) and time (range 10 seconds to 10 minutes). The target area was identified during ERCP (▶**Fig.3a**). The VIVA combo™-generator (▶**Fig.2**) was set to 2-minute duration, maximum temperature of 80°C and a power of 10 watts and then connected to the 18-mm ELRA™ catheter (▶**Fig.1**). The "Start" button of the VIVA combo™-generator was pressed and the current was delivered.

This feature is unique to this probe and potentially safe for the patient as compared to the commonly used probes because with the latter it is impossible to know if the current is being delivered to the malignant tissue alone. Once the 2 minutes were over; the ELRA™ probe was removed and the stricture reassessed with a repeat cholangiogram (▶**Fig.3c**). The procedure was repeated if there was partial resolution of the stricture or the stricture was longer than 2cm. At the end of the procedure a biliary stent (metal or plastic)was inserted through the indwelling metal stent.

RESULTS

Seven patients (4 male; 3 female) had nine procedures performed during the study period. Demographic and clinical details are depicted in ▶**Table1**. Two patients were admitted with cholangitis due to blocked stents and the other five patients had worsening obstructive liver function tests prior to RFA. Five of seven patients (71%) required the standard protocol for ablative therapy (i.e., 2 minutes at 10 watts and 80°C. Two patients required the treatment

Fig 3. Cholangiogram of patients treated with RFA. **a.** Cholangiogram prior to RFA treatment. **b.** Cholangiogram showing the RFA probe across the stricture. **c.** Cholangiogram of a patient following successful RFA treatment; successful stricture resolution.

to be repeated, one because response was suboptimal and the other because of a stricture >2cm. Additional biliary stents were inserted in five of seven patients (71%) (2 plastic & 3 self-expandable metal stents) to maintain biliary drainage. The two patients who did not have additional stents inserted did not require repeat procedures. Antibiotics were given pre- and post-procedure. Mean stricture diameter prior to RFA was 1.13mm (standard deviation 0.54) and 4.42mm (standard deviation 1.54) following RFA (P<0.0001). There were no immediate procedure-related complications.

Table 1. Demographics and clinical details

Age	Sex	Type of tumor	Stricture length	Stricture diameter pre-RFA (mm)	Stricture diameter post-RFA (mm)	Bilirubin pre-procedure	Bilirubin post-procedure	Outcome
74	F	Gallbladder cancer	15mm	1.55	3.79	129	43	Alive
69	F	Pancreatic cancer	25mm	1.2	4.48	4	6	Alive
63	M	Hilar cholangiocarcinoma	20mm	1.29	6.26	231	265	Died
62	M	Distal cholangiocarcinoma	20mm	1.33	3.57	66	18	Died
70	F	Pancreatic cancer	20mm	2.04	6.15	114	81	Alive
82	M	Hilar cholangiocarcinoma	15mm	0.30	2.34	90	86	Alive
56	M	Colorectal cancer metastasis	15mm	1.28	5.21	208	173	Died

DISCUSSION

Our first experience using this new temperature-controlled RFA probe showed successful biliary metal stent occlusion treatment with no procedure-related complications. These data are promising especially since >50% of stents are occluded within 6 months . RFA creates an electrical circuit by using an alternating current which causes protein denaturation and coagulative necrosis. Because of the poor electrical conductivity of tissues, the closest areas to the electrode experience the highest current and temperature, whereas tissues farther away are heated by thermal conduction (i.e., in these regions, the heat may not be sufficiently high to cause necrosis) . Therefore, a key limitation is the extent of coagulation produced by RFA, which is often insufficient to cover the tumor volume. During the coagulation induced by RFA, tissue may become dehydrated and charred. As a result, the current stops, leading to a rise in impedance, which limits the volume of tissue successfully ablated. One of the ways to get around this is by delivering pulsed RFA. The commonly used probe in routine clinical practice is the Habib EndoHPB. Advantages include that it can be used with a range of commonly available generators and it allows partial destruction of the tumor prior to stent insertion and also to clear obstructed metal stents. However, there are potential drawbacks. While applying RFA under fluoroscopic control, it is difficult to predict for certain if the entire current is being delivered. It is not clear if adequate temperature and wattage is being applied to the malignant tissue as the energy settings are preset. One of the reasons for this could be that the energy settings have been extrapolated from either in vivo animal model or ex vivo human studies without considering delayed necrosis and heat-sink effects in vivo . This may also result in complications due to inadvertent high temperatures, charring of tissue and shorter current flow, leading to suboptimal response.

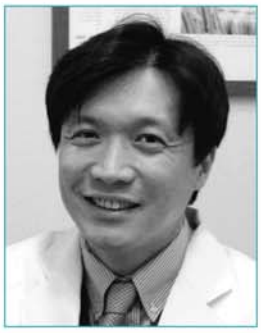
We hypothesize that the patient who died 8 weeks after the first procedure had a rapidly growing and aggressive tumor that resulted in recurrent stent blockages. One of the advantages of using this device is the ease of assembly. In addition, the generator only delivered current when there was good tissue contact with the probe.

CONCLUSIONS

In conclusion, this novel temperature-controlled endoluminal radiofrequency ablation probe seems to be safe and effective in ablating malignant tissue ingrowth in blocked metal biliary stents (secondary RFA). However, larger randomized controlled studies using this probe are required to establish survival benefit and efficacy.

This article has been summarized based off of the original article.

Efficacy of endobiliary radiofrequency ablation for malignant distal biliary obstruction: Multicenter experience of temperature controlled radiofrequency ablation



Eui Joo Kim, Jae Hee Cho, Yun Nah Lee, Seok Jeong, Young Koog Cheon, Se Woo Park, and Min Kyu Jung

Jae Hee, Cho
Division of Gastroenterology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Republic of Korea

BACKGROUND

Endobiliary radiofrequency ablation (EB-RFA) is an endoscopic local treatment modality in patients with malignant biliary tract obstruction (MBTO). It may provide improvement of stent patency and patient survival, however, hyperthermic injury can induce serious complications such as perforation, bleeding and stricture. We aimed to evaluate the clinical outcomes of EB-RFA in patients with distal MBTO.

METHODS

Total 43 patients who underwent temperature controlled EB-RFA (7-10 W, target temperature 80°C, 120 seconds) were retrospectively collected from six academic medical centers. All patients had unresectable distal MBTOs including 28 CBD cancer, 11 pancreatic cancer and 4 GB cancer. After EB-RFA, biliary drainage was maintained by placing a covered/uncovered self-expanding metallic stent (SEMS) or plastic stent. The duration of stent patency was defined as the period between the date of EB-RFA and the date of reintervention or death. Stent patency, patient survival and EB-RFA related adverse events were analyzed.

RESULTS

Temperature controlled EB-RFA was safely performed in all patients without technical difficulties. The median length of MBTO was 22 mm (range: 12-50), and EB-RFA was followed by placement of biliary stents; 15 uncovered SEMS, 26 covered SEMS and two plastic stents. There were 18 (41.9%) patients who required reintervention during follow-up period. The median durations of stent patency were 173 days for uncovered SEMS group and 203 days for covered SEMS group (P = 0.119; **Table 1**). In patients with biliary tract cancer (4 GB cancer, 28 CBD cancer), the median durations of stent patency were estimated to be 173 days and 323 days for uncovered SEMS group and for covered SEMS group, respectively (P = 0.075). The median overall survival was estimated to be 449 days. The median overall survivals were 630 days and 191 days for biliary tract cancer and for pancreatic cancer, respectively (P < 0.001; **fig. 1**). Total incidence of adverse events after procedure was 18.6% (8/43; 5 pancreatitis, 1 cholangitis with cholecystitis and 2 cholecystitis), and there was no major complication such as perforation and hemobilia.

Table 1. Overall survival and stent patency

	Biliary tract cancer (n=32)	Pancreatic cancer (n=11)	P
Overall Survival, median (95% CI), d*	630 (457 - 803)	191 (128 - 254)	< 0.001
Stent patency, median (95% CI), d*	203 (74 - 332)	148 (100 - 196)	0.109
Stent occlusion, n (%)	17 (53.1)	1 (9.1)	0.014
Overgrowth	4 (12.5)	0 (0)	
Ingrowth	11 (34.4)	1 (9.1)	
Migration	0 (0)	0 (0)	
Sludge	2 (6.3)	0 (0)	
Occlusion free survival, median (95% CI), d*	268 (23 - 513)	NA	0.217

Estimated by Kaplan-Meier method

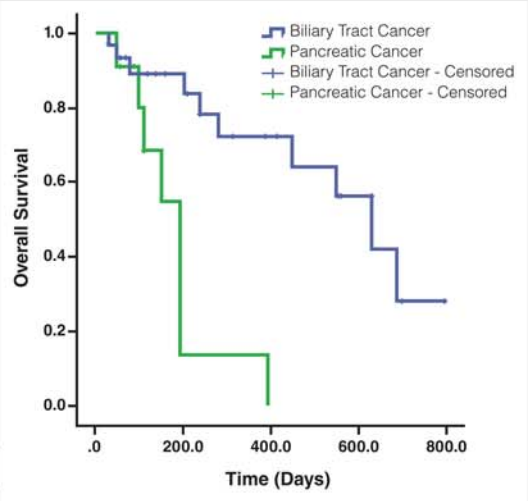


Fig 1. Overall survival curve

CONCLUSION

EB-RFA is a safe and effective adjunctive local therapy in patents with distal MBTO. Distal MBTO caused by biliary tract cancer including GB cancer and CBD cancer might be an adequate indication for EB-RFA in terms of stent patency and overall survival. Further prospective randomized studies are warranted to confirm the survival benefit of EB-RFA.

This article will soon be published.

EUS-guided Radiofrequency Ablation (EUS-RFA) of Solid Pancreatic Neoplasm Using an 18-gauge Needle Electrode: Feasibility, Safety, and Technical Success

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INTRODUCTION

Despite the progress in research, pancreatic cancer (PDAC) remains one of the most aggressive tumors, along with a poor prognosis. Some studies demonstrate that thermal ablation can induce an immune response towards the tumor, determined by the release of necrotic cell content in the extracellular space that stimulate the host's antitumor immunity. Moreover, a recent study documented increased blood flow around the ablated area.

Endoscopic ultrasound (EUS) represents the perfect tool to guide local treatment of pancreatic lesions, as it provides real-time visualization of the procedure with high-resolution images of the pancreas and surrounding structures. A specifically designed needle tip electrode for performing EUS-RFA (EUSRA™ RF Electrode, STARmed, Korea) was used for the first time in 2012. This study aimed to evaluate the feasibility, safety, and technical success of pancreatic EUS-RFA performed in a single center.

METHODS

Indications for EUS-RFA include: a) a cyto/histological diagnosis of PDAC, which was non-resectable and had no metastases after first line chemotherapy and/or radiotherapy (stage III); b) a solid pancreatic lesion that was resectable but not suitable for surgery or chemotherapy due to the patient's comorbidities. Contraindications were poor performance status, extension of necrosis into the tumor, coagulation disorders, and no informed consent given.

EUS-RFA TECHNIQUE

All procedures were started with a preset radiofrequency power of 30W. The slowly increasing hyperechoic zone was easily visualized during EUS examination. The radiofrequency generator was stopped if the hyperechoic area sufficiently covered the tumor, or a few seconds after there was an increase in the value of the impedance indicated by the generator. If necessary, the procedure was repeated by reinserting the needle in another part of the lesion until obtaining the largest possible ablation of the tumor. In particular, if a not ablated, large (>3cm) portion of tumor was clearly visible after the first RFA application, the needle was reinserted specifically targeting that area to perform a second ablation. Procedures were performed leaving a "security ring" of at least 5mm at the periphery of the tumor in order to avoid thermal injuries of the nearby structures.

EUS-RFA TECHNIQUE

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RESULTS

Data from 9 consecutive patients (6 males, mean age 67 years) with a diagnosis of locally advanced PDAC in 8 cases, and pancreatic head metastasis from renal clear cell carcinoma in 1 patient (not suitable for resection or chemotherapy due to chronic renal failure) were collected. One PDAC patient was excluded because of the presence of a large necrotic area inside the tumor, which was detected during EUS as a fluid portion with

avascular pattern after contrast injection (Sonovue, Bracco, Milan, Italy). EUS-RFA was feasible in all the 8 remaining patients. Tumors were located in the pancreas head (3), body (3), and uncinate process (2). One patient with pancreatic head cancer underwent EUS-RFA with a previously placed plastic biliary stent. Mean tumor size was 36 mm (range 22-67 mm). Procedures were performed from the stomach, the duodenal bulb, and the second portion of the duodenum in 4, 2, and 2 patients, respectively. No technical difficulty in inserting the needle was recorded even for those lesions ablated with the scope in a torque position. The mean time of a single RFA application was 58 seconds, with a mean number of applications of 1.5 (range 1-3). An ablated area in the tumor was obtained in all patients. At post-procedure CECT (both at one day and one month) the mean volume of thermo-lesions was 3.75㎤ (range 0.72-12.6 ㎤), corresponding to a mean of 30% tumor mass (range 5.8-73.5 %). Three patients experienced mild abdominal pain after the procedure, which was managed conservatively with NSAIDs administration. No major adverse events such as pancreatitis, bleeding, duodenal or biliary injury, infection or perforation, or procedure-related mortality was observed in a mean follow-up of 4.3 months (range 1-8 months).

DISCUSSION

The optimal thermal kinetic characteristics of the pancreas are not yet determined, so there is no standardized protocol for pancreatic RFA.

The needle temperature is affected by the energy used, which determines the ablation volume reached. In previous studies, 50 W was employed for 10/15 seconds, and the procedure was repeated by reinserting the electrode in different zones until the hyperechoic area sufficiently covered the tumor. In this study, a slightly different technical approach was used: the electrode was positioned in the middle of the tumor and a lower radiofrequency power (30 W) was applied. The time of the procedure was not determined in advance and the procedure was stopped after noting the rise in impedance and its stabilization. The sudden increase of impedance expresses the dehydration of the tissue when the thermal diffusion reaches the largest area. We believe that a lower wattage, applied for a longer time can result in a greater but slower diffusion of thermal damage. This should result in longer applications of radiofrequency energy (on average, 50 s/application), which could reduce the number of applications (in our series, 1.5 on average), and avoid the need to relocate the electrode several times inside the tumor. This technique is based on the so-called “thermal diffusivity effect”, which is related to thermal neoplastic conductibility: heat spreads inside the neoplastic mass, and not outside of it, making the procedure safer. EUS-RFA of pancreatic neoplasms aims to reduce the mass , to improve the vascularity in the residual mass and to stimulate a systemic immune response that acts against the tumor , thus facilitating the efficacy of chemo(radio) therapy. The timing of EUS-RFA during the multimodality treatment approach remains to be established .

Technique, safety, and feasibility of EUS-guided radiofrequency ablation in unresectable pancreatic cancer

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BACKGROUND

Pancreatic ductal adenocarcinoma (PDAC) is the seventh leading cause of cancer death in the world with the lowest survival rate among major cancers. Despite advancements in the multimodal approach, surgical resection still represents the only potentially curative treatment. Nevertheless, more than 80% of patients are not suitable for surgery either for local vessels involvement or distant metastases. Aim of the present study was to evaluate the feasibility and safety of EUS-guided RFA in patients affected by unresectable pancreatic cancer.

STUDY DESIGN AND INCLUSION CRITERIA

Consecutive patients with unresectable non-metastatic PDAC who presented with stable disease or down-sizing without down-staging after systemic chemotherapy were prospectively included. According to our protocol, when a biliary or duodenal metal stent was present, the stent was removed before RFA to avoid thermal injuries and replaced after the procedure.

PERIOPERATIVE MANAGEMENT

Before the procedure, each patient underwent routine blood tests, ECG, and chest X-Ray. Patients received broad spectrum antibiotics, somatostatin analogues (octreotide), and thromboprophylaxis with low molecular weight heparin.

EUS-GUIDED RFA TECHNIQUE

The operative needle was a novel monopolar 18 guage RFA electrode 140cm long (EUSRA™) with a sharp conical 1cm tip for energy delivery. The needle is associated with an internal cooling system connected via a pump to an external cold saline solution source (0°C) that prevents the charring of the tip and improves the ablation accuracy. The electrode was placed under EUS guidance into the target lesion through the duodenal or gastric wall using color-Doppler to avoid interposing vessels. Energy was set at 30W for lesions larger than 3cm and at 20W for smaller lesions, according to our experience in open surgery.

PRIMARY ENDPOINTS

As primary endpoints, we prospectively evaluated feasibility and safety of the EUS-guided RFA. Feasibility was defined as the successfully placement of the needle within the pancreatic lesion with safe margins from the surrounding vital structures in order to avoid potential thermal injuries.

SECONDARY ENDPOINTS

As secondary endpoint, we evaluated the presence of necrosis within the neoplastic tissue as effect of the ablative procedure. Based on our surgical experience, the effects of RFA ablation cannot be fully confirmed with the 1 week post operative CT scan since the necrotizing process is still in progress.

RESULTS

From Feb 2016 to Oct 2016, a total of 10 patients (7 males and 3 females) with unresectable PDAC were recruited and enrolled. All patients underwent neoadjuvant systemic chemotherapy and five underwent additional external radiation therapy. Median time between the beginning of oncological treatments and the RFA procedure was 8 months (range 5-30). Five patients experienced a partial response with reduction in size of the tumor after the oncological treatment while the other 5 patients had stable disease. Pre-procedure radiological characteristics of the lesion, technical parameters of the EUS-guided RFA, and post procedural radiological results at 7 and 30 days are detailed in.

This article has been summarized based off of the original article.

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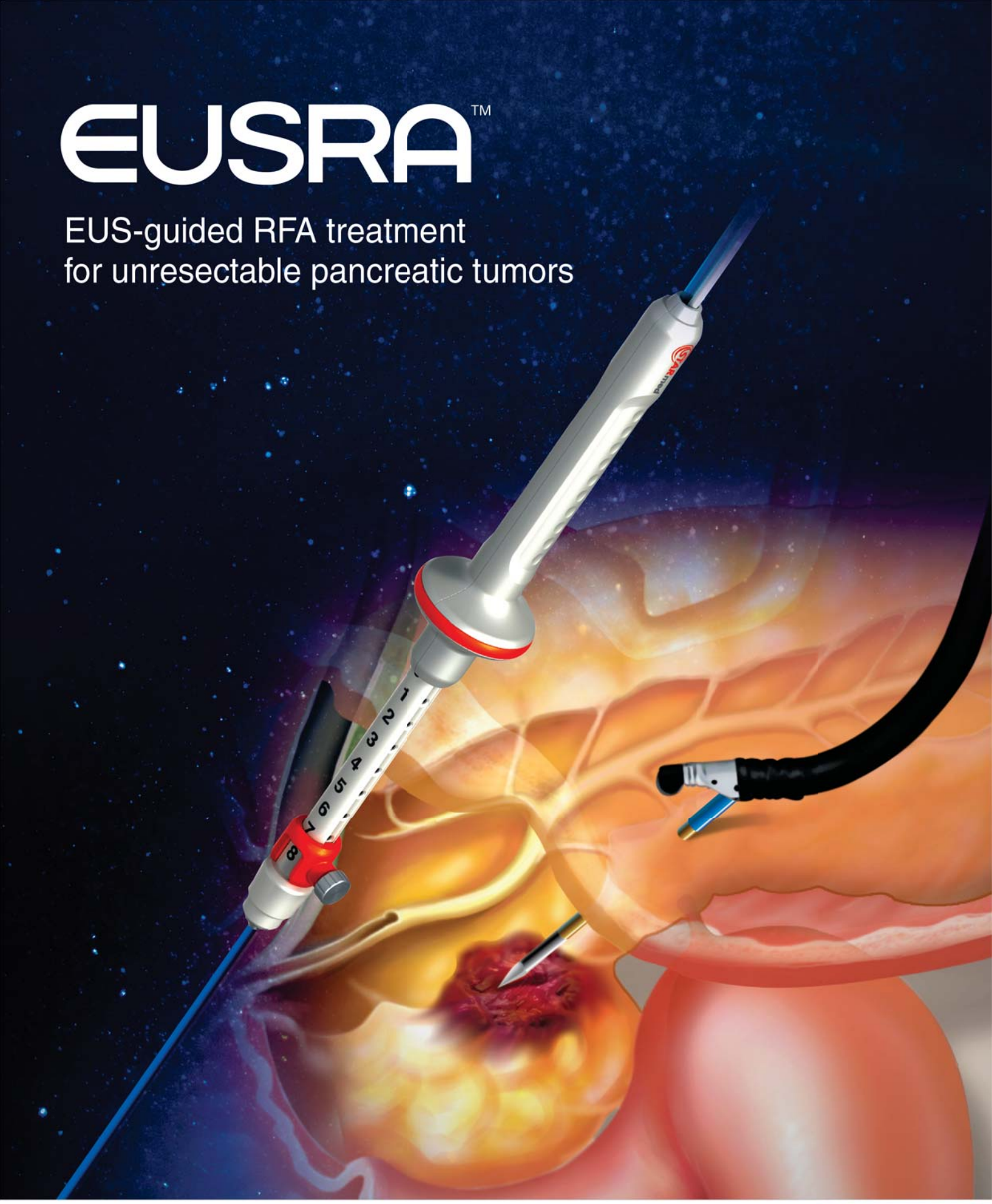
EUS-guided RFA treatment for unresectable pancreatic tumors



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