Translational Research in Endoscopy: The New Paradigm

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Reseaches

- basic research
- ex-vivo animal experiment
- in-vivo animal experiment
- human trial
Carcinogenesis Study after Oxysterol Treatment

University of Washington
Seattle Experience
Diff-Quick Staining after Oxysterol Tx
DAPI nucleus staining

Control

Oxysterol
Cell culture & molecular biology

- interesting
- time consuming
- needs continuous fund
- clinical applicability?
Animal Experiment of HIFU: Limitations & Potential Complications

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Division of Gastroenterology, Asan Medical Center University of Ulsan College of Medicine
High Intensity Focused Ultrasound (HIFU)

- ultrasound energy: extra-corporeal application
- totally non-invasive
- therapeutic potentials
Pretx imaging
Tx dose: 750~1250J
Automatic & manual
Pig model for HIFU

- large abdominal organs
- similar anatomy to human
- difficult to manipulate
- expensive
50/F  Pancreatic SPN (Bx proven)
Unmet needs

- find out during clinical practice
- discussion with experts
- review of literature
- discussion with engineers & mechanics
Modification of RF electrodes

- Multiprong arrays
- Bipolar arrays
- Internally cooling electrodes
- Cluster RF
- Pulsed RF

(Goldberg SN et al Gastrointest Endosc 1999)
(Rhim H, Dodd GD J Clin Ultrasound 1999)
Radiofrequency ablation:
From ex vivo to in vivo animal

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EUS-guided RFA
EUSRA (Starmed Co, Seoul, Korea)
EUS-RFA needle
Ex vivo study
Target: Liver muscle
Needle: 17, 18 G
Work time: 6 min
RF power: 80W, 50W

1) 17G, 6min, 80W
2) 18G, 6min, 50W

Ex vivo
18G needle image
Post Tx ablation size
Ex vivo test

- Bovine liver
- A 18 Gauge 1cm exposed electrode
- Power : 50 watts
- Water flow : 30ml/min

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
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<tbody>
<tr>
<td>A</td>
<td>2 Min</td>
</tr>
<tr>
<td>B</td>
<td>4 Min</td>
</tr>
<tr>
<td>C</td>
<td>6 Min</td>
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<tr>
<td>D</td>
<td>8 Min</td>
</tr>
<tr>
<td>E</td>
<td>10 Min</td>
</tr>
<tr>
<td>F</td>
<td>12 Min</td>
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</table>
EUSRA RFA ex vivo data

Group A: 30watt, 6min
Group B: 50watt, 6min
Group C: 80watt, 6min
Group D: 30watt, 12min
Group E: 50watt, 12min
Group F: 80watt, 12min
EUSRA RFA ex vivo data

summation of ablation zone for large tumor ablation

10mm, 50watt, 10sec*9

중단면

횡단면
EUS-RFA needle
In vivo animal study
EUS-guided RFA image
Animal study

Liver

- 18G needle, 6min, 50W
- 18G needle, 12min, 80W (Max)

Pancreas

18G needle, 6min, 50W
Ultrasound image
Liver, 18G, 6min, 50W
Post Tx ablation image & size
18G, 6min, 50W

1.1cm
Post Tx ablation image
18G, 6min, 50W
Post Tx ablation size
18G, 6min, 50W

24cm
Scope이 지나간 stomach wall image

liver

Panc.
EUS-guided radiofrequency ablation of porcine pancreas

Hong Jun Kim, Dong Wan Seo, Su Hui Kim¹, Choong Heon Ryu, Sang Soo Lee, Sung-Koo Lee, Myung-Hwan Kim

Department of Internal Medicine, Asan Medical Center, ¹Asan Institute for Life Sciences, University of Ulsan College of Medicine, Seoul, Korea
Factors affecting efficacy of EUS–RFA

- **Length** of delivery system
- **Thickness** of electrode
- **Length** of exposed electrode
Needle electrode assembly

- **18-gauge RFA electrode** (STARmed, Korea)
  - Total length: 150 cm
  - Exposed electrode + delivery system
  - Exposed electrode length: 1 cm
  - Echogenic
  - Needle-shaped
  - Cooling system: 30 ml/min

- **VIVA RF system** (STARmed, Korea)
EUS-guided RFA in animal model
On day 7 after EUS–RFA

1. Laparotomy

2. Body weight and performance

3. Laboratory tests
RESULTS

Baseline characteristics

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<th>Mean ± S.D</th>
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<tr>
<td>Body weight (kg)</td>
<td>34.6 ± 1.6</td>
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<tr>
<td>Serum AST (U/L)</td>
<td>86.3 ± 50.0</td>
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<tr>
<td>Serum ALT (U/L)</td>
<td>23.3 ± 4.9</td>
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<tr>
<td>Serum amylase (U/L)</td>
<td>3005.0 ± 367.7</td>
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<tr>
<td>Serum lipase (U/L)</td>
<td>15.5 ± 2.1</td>
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## Size of ablated lesions

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<tr>
<td><strong>Diameter</strong> of RFA lesion (mm) - <strong>EUS</strong></td>
<td>14.5 ± 1.5</td>
</tr>
<tr>
<td><strong>Diameter</strong> of RFA lesion (mm) - <strong>laparotomy</strong></td>
<td>23.0 ± 6.9</td>
</tr>
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</table>
Gross pathology

- Ablated lesion was demarcated from normal parenchyma by fibrous wall.
Histopathological examination

Specimen from a histopathological examination (H&E, orig. mag. ×40)
Specimen from a histopathological examination (H&E, orig. mag. ×200)
Complications

- No signs of distress
- No significant changes of body weight
- Fibrosis or adhesion in 3 pigs

- Retroperitoneal fibrosis
- Adhesion to the stomach wall
- Adhesion to the bowel

Adhesion to the stomach wall

Adhesion to the bowel
SUMMARY

- Technically feasible to perform EUS-guided RFA of porcine pancreas
- Successful formation of ablated lesion about 23 mm in diameter
- No significant complication
- Fibrosis and adhesion in 3 pigs
- No signs of distress and no abnormal laboratory findings in all pigs
CONCLUSION

- EUS-guided RFA of porcine pancreas was feasible and effective.

- We could make ablated lesion about 23 mm in diameter without significant complication.

- Application of EUS-RFA to the human pancreatic lesion can be possible.
EUS-guided RFA

NEW METHODS: Experimental Endoscopy

EUS-guided radiofrequency ablation of the porcine pancreas

Hong Jun Kim, MD,¹ Dong-Wan Seo, MD, PhD,¹ Aizan Hassanuddin, MMed, MRCP,¹ Su-Hui Kim,² Hee Jung Chae,³ Ji Woong Jang, MD,¹ Do Hyun Park, MD, PhD,¹ Sang Soo Lee, MD, PhD,¹ Sung-Koo Lee, MD, PhD,¹ Myung-Hwan Kim, MD, PhD¹

Seoul, Korea

(Gastrointest Endosc 2012;76:1039-43)
Complications

Perinephric fibrosis

Perigastric adhesion

(Gastrointest Endosc 2012;76:1039-43)
EUS-guided RFA: ascites model
EUS-RFA human application
Pancreatic cancer
EUS-RFA of PCa: Human trial

IRB approved inclusion criteria

- histologically confirmed PCa
- advanced & unresectable case
- failure to chemotherapy: PD
M/66 Pancreas head cancer  
Metal stent guided SBRT (26Gy/4 Fr)  
GT chemotherapy #4

Op tried but failed d/t omental seeding  
-> 2\textsuperscript{nd} line CTx #3 (Folfox) -> disease progression
EUS-RFA of Pca: Human case 3

50W, 10 sec
continuous mode
x 8 times
EUS-RFA of PCa: Human case 3

1 day after EUS-RFA
EUS-RFA of PCa: Human case 3

1 day after EUS-RFA

2 month after EUS-RFA
EUS-RFA for pancreatic cancer

NEW METHODS

Initial experience of EUS-guided radiofrequency ablation of unresectable pancreatic cancer

Tae Jun Song, MD, PhD,1 Dong Wan Seo, MD, PhD,1 Sundeep Lakhtakia, MD, PhD,2 Nageshwar Reddy, MD, PhD,2 Dong Wook Oh, MD,1 Do Hyun Park, MD, PhD,1 Sang Soo Lee, MD, PhD,1 Sung Koo Lee, MD, PhD,1 Myung-Hwan Kim, MD, PhD1

Seoul, South Korea

Conclusions: EUS-RFA could be a technically feasible and safe option for patients with unresectable pancreatic cancer.

(Song TJ et al. Gastrointest Endosc 2016;83:440-3)
Thickness of needle design
EUS-RFA for Benign Pancreatic Tumor
F/69, Pancreatic neuroendocrine tumor

A CT scan demonstrated a well-enhanced pancreatic body tumor
## Baseline characteristics and outcomes (n=10)

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<th>No.</th>
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<th>Sex</th>
<th>Symptom</th>
<th>Dx</th>
<th>site</th>
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Endoscopic ultrasound-guided radiofrequency ablation for management of benign solid pancreatic tumors

(J-H Choi et al. *Endoscopy* 2018)

**Conclusions** EUS-RFA may be a safe and potentially effective treatment option in selected patients with benign solid pancreatic tumors. Multiple sessions may be required if there is a remnant tumor, and adverse events must be carefully monitored.
Potential complications of EUS-guided RFA

- Pancreatitis
- MPD stricture
- Perforation
- Bleeding
- RFA: Pancreas is close to many vital organs
Translational Research in Endoscopy

- large animal model: pig or dog
- dedicated endoscopy for animal
- research assistant team
- continuous funds application
Translational Research in Endoscopy

Our passion is most Important !!!

- continuous funds application
Thank you very much