

# Translational Research in Endoscopy: The New Paradigm

Dong Wan Seo

Department of Gastroenterology, Asan Medical  
Center, University of Ulsan College of Medicine

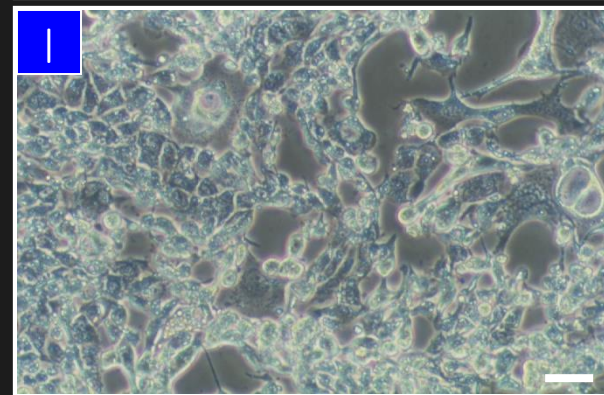
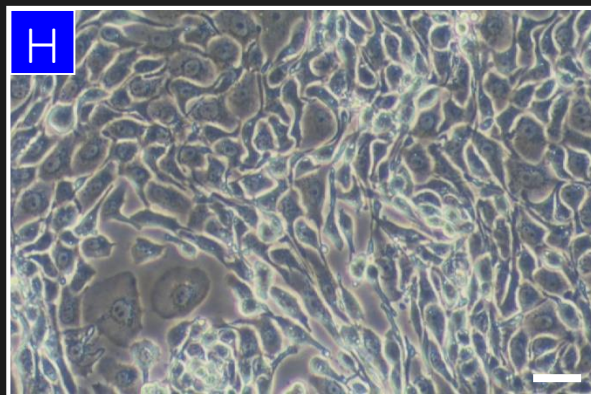
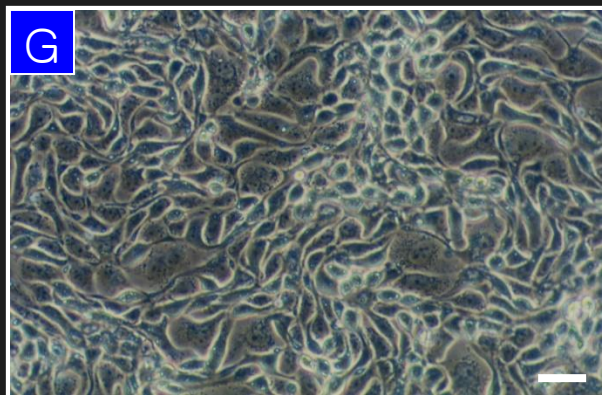
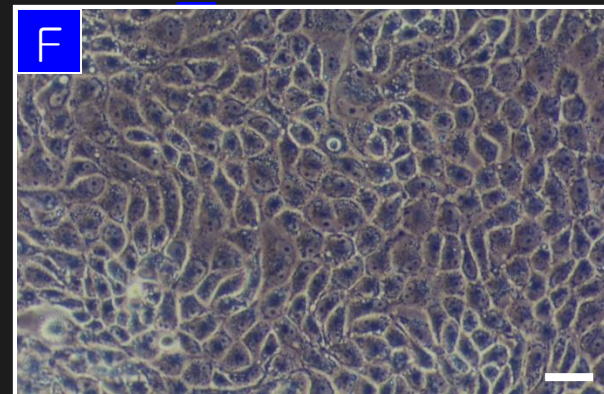
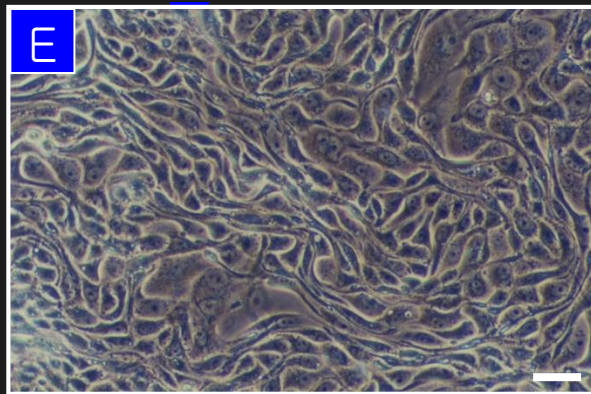
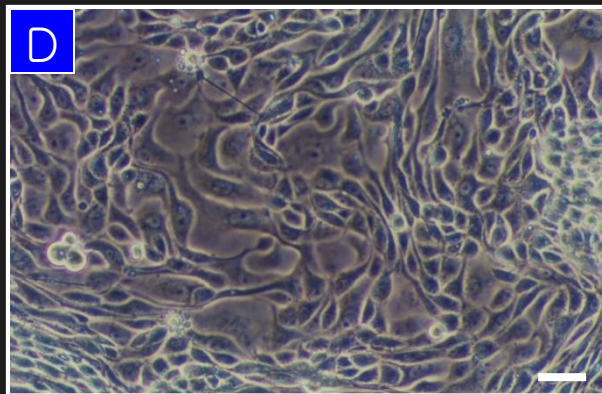
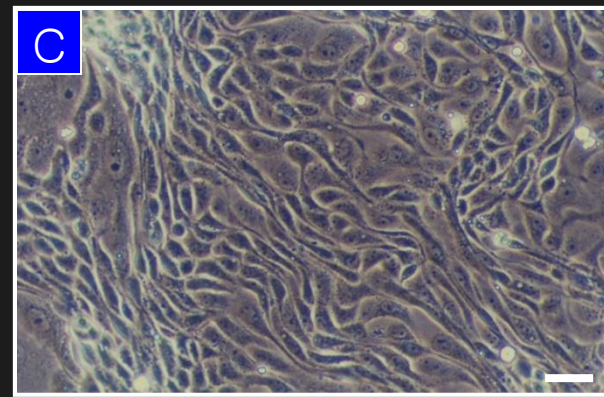
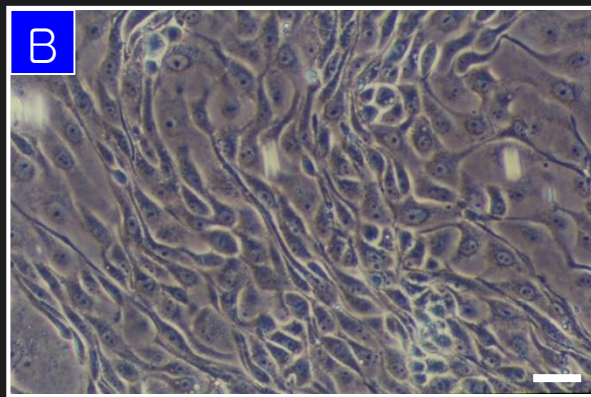
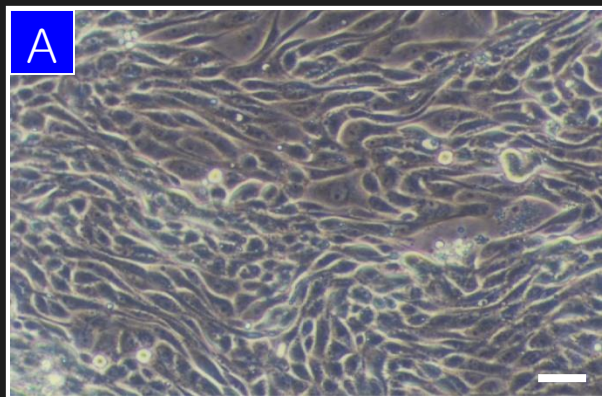
# Researches

- basic research
- ex-vivo animal experiment
- in-vivo animal experiment
- human trial

# Carcinogenesis Study after Oxysterol Treatment

University of Washington  
Seattle Experience





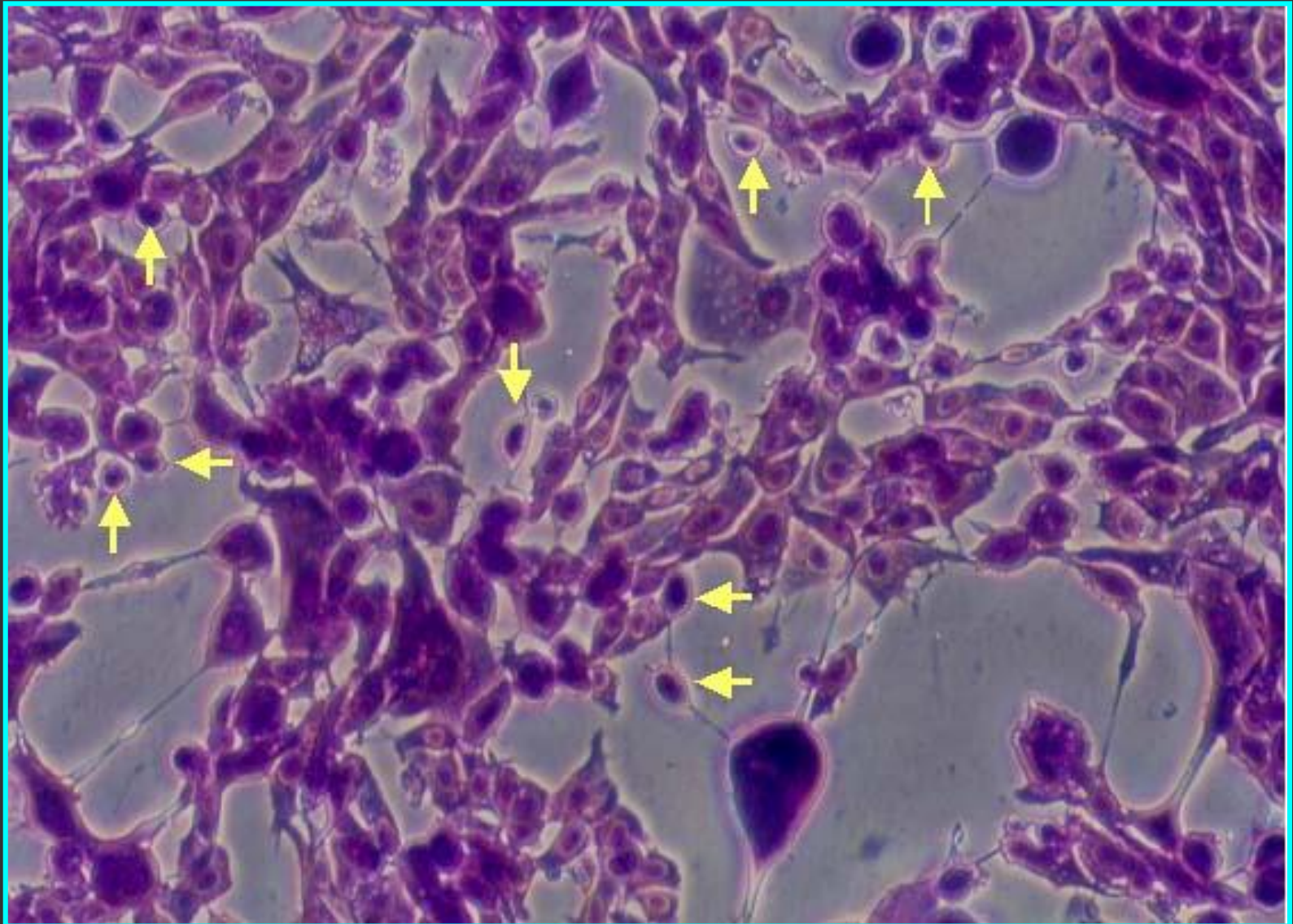
6 hr

24 hr

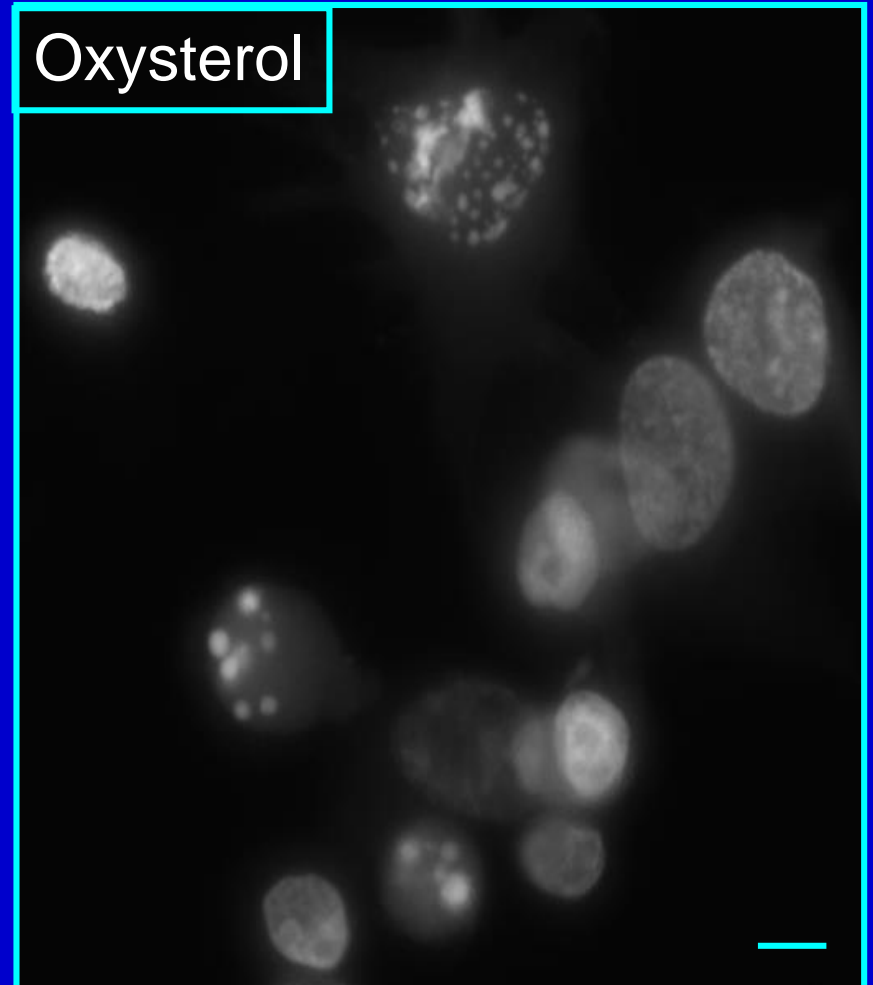
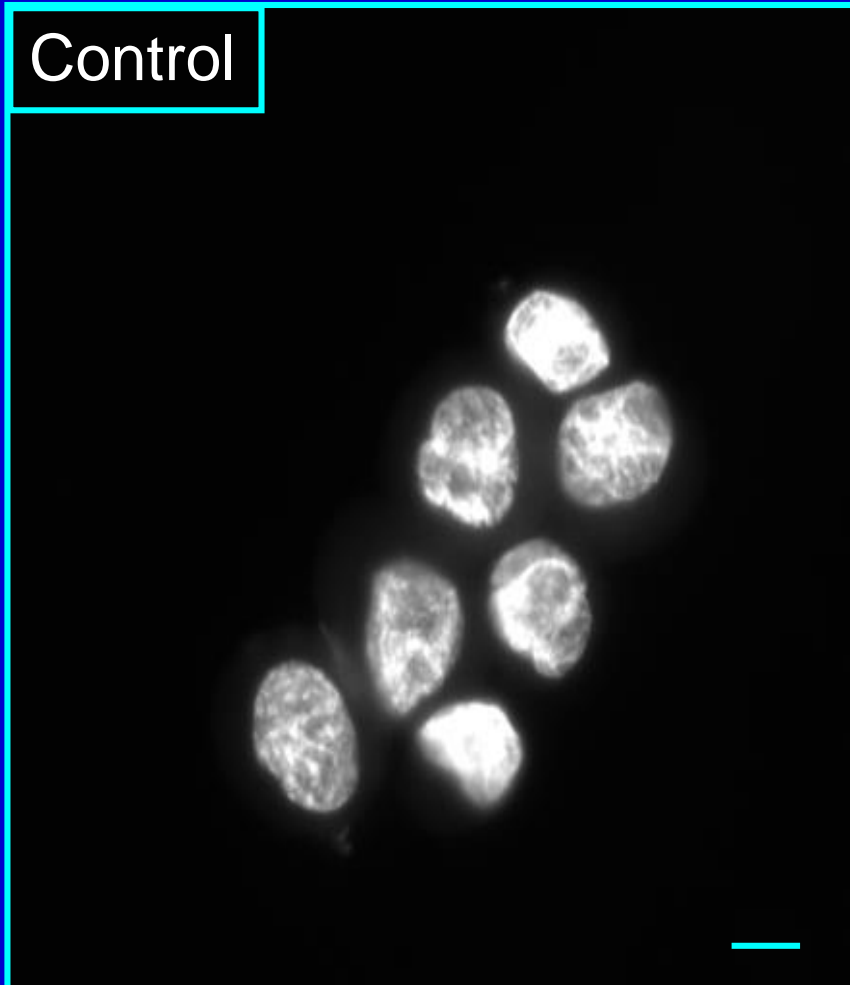
48 hr



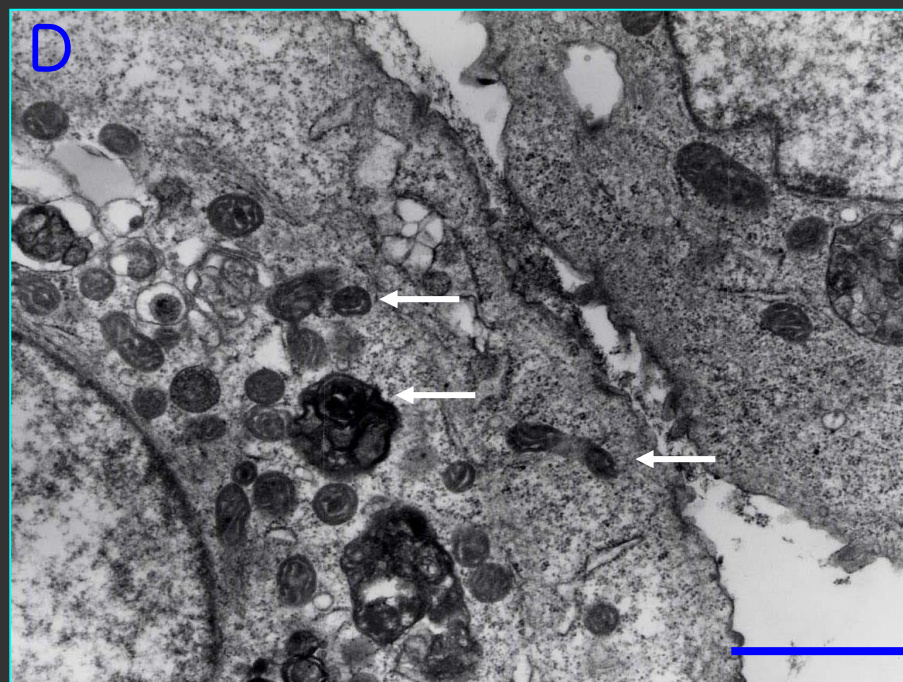
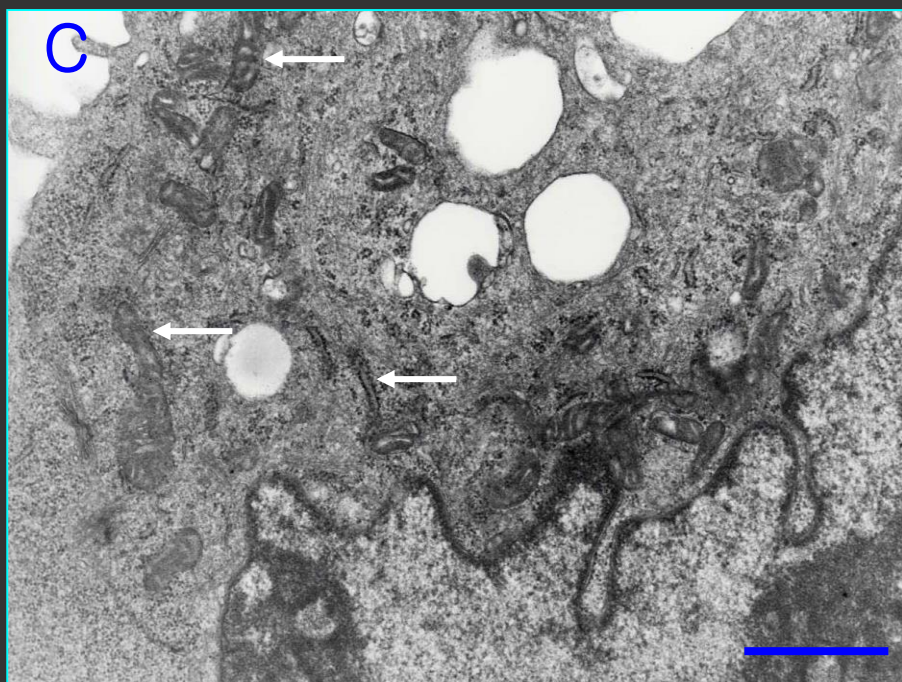
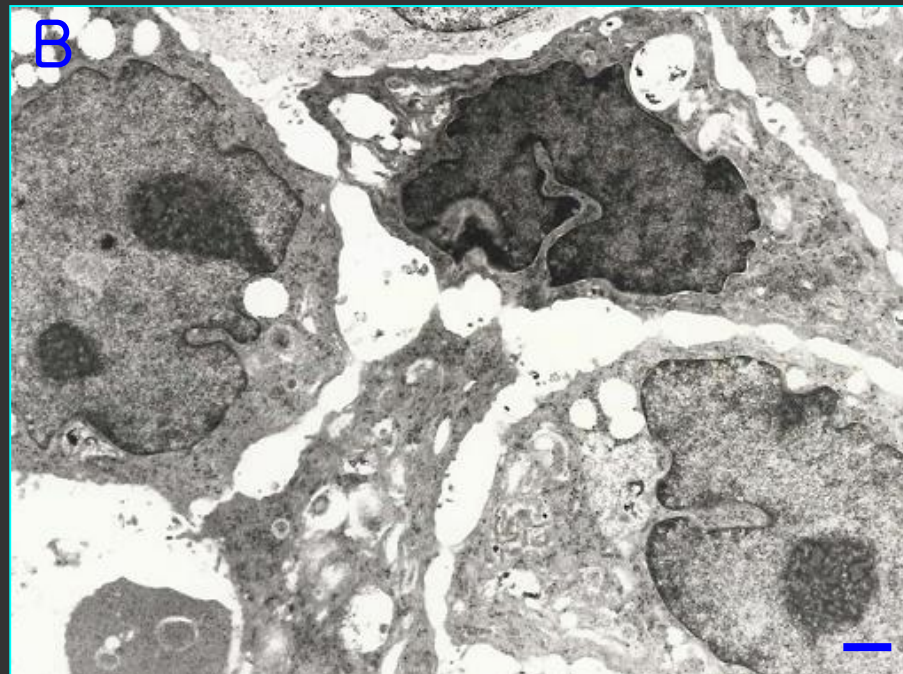
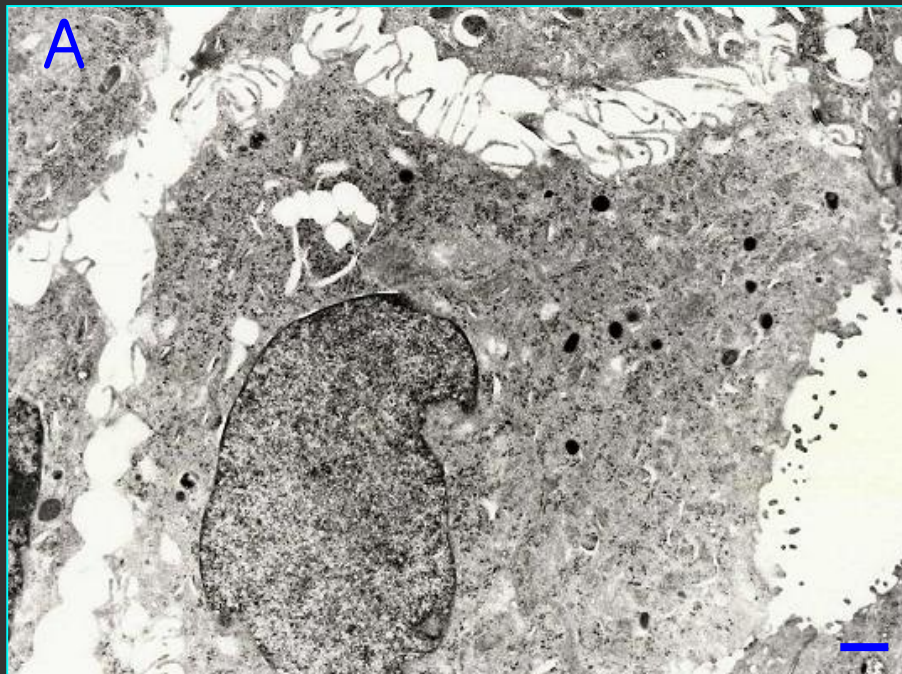
# Diff-Quick Staining after Oxysterol Tx



# DAPI nucleus staining









# Cell culture & molecular biology

---

- interesting
- time consuming
- needs continuous fund
- clinical applicability ?

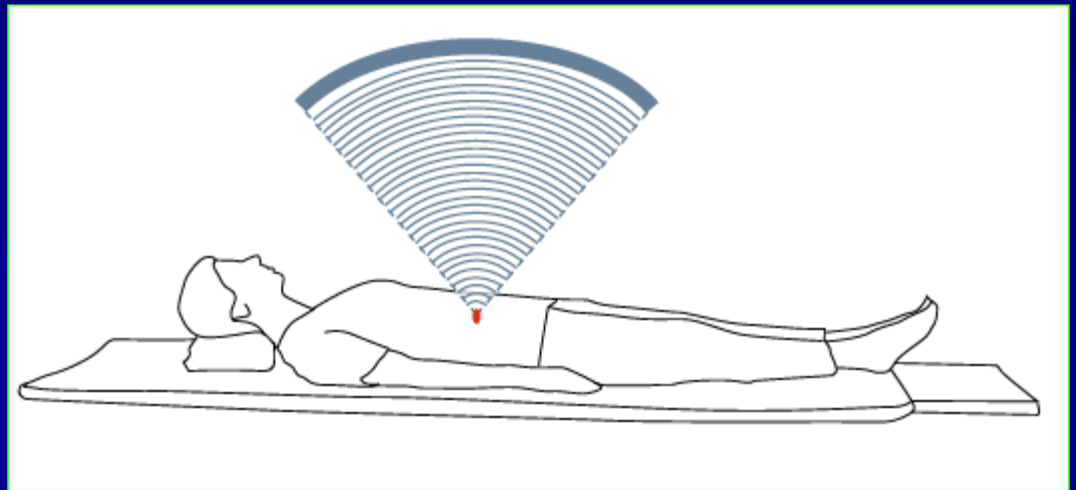
# Animal Experiment of HIFU : Limitations & Potential Complications

Dong Wan Seo

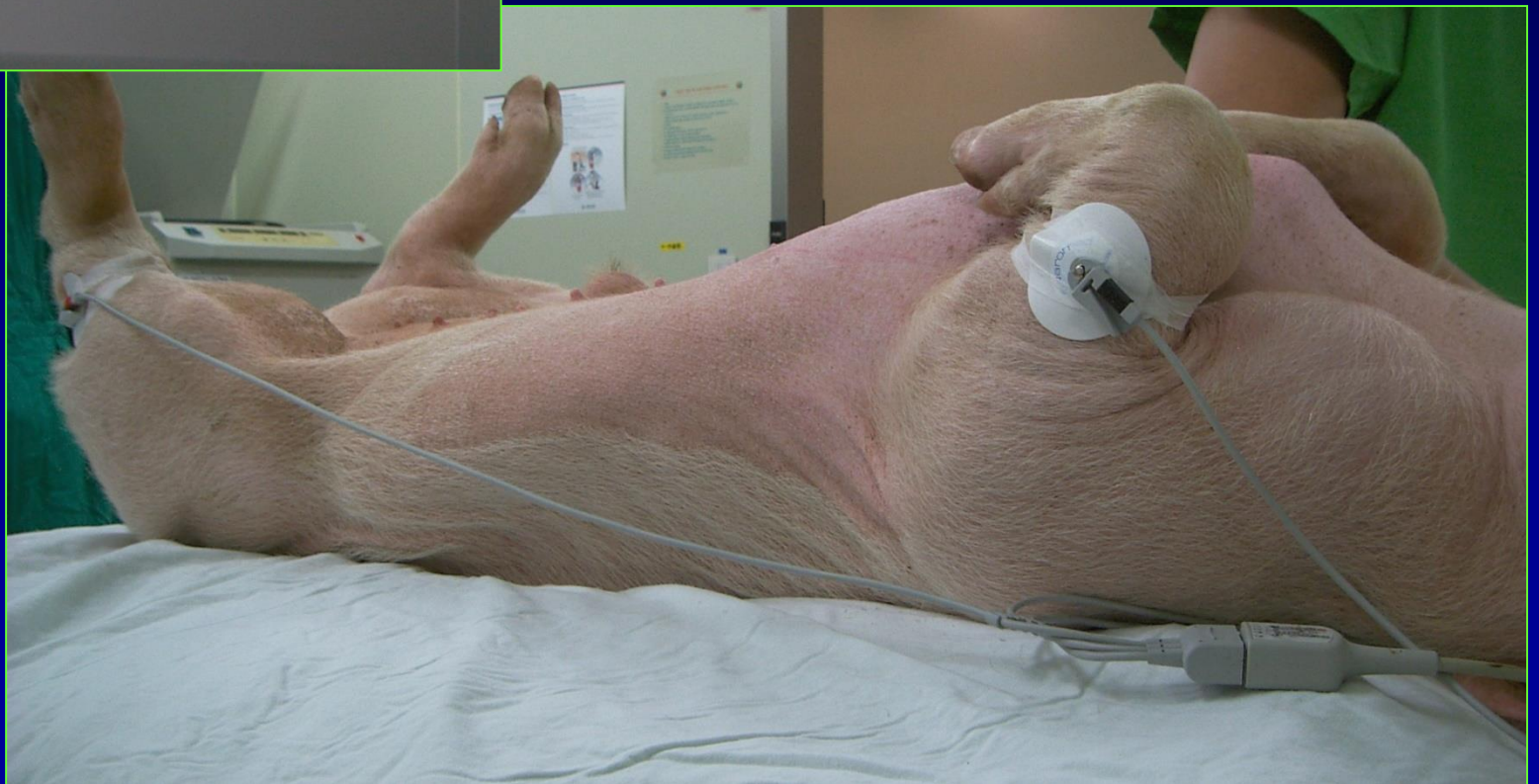
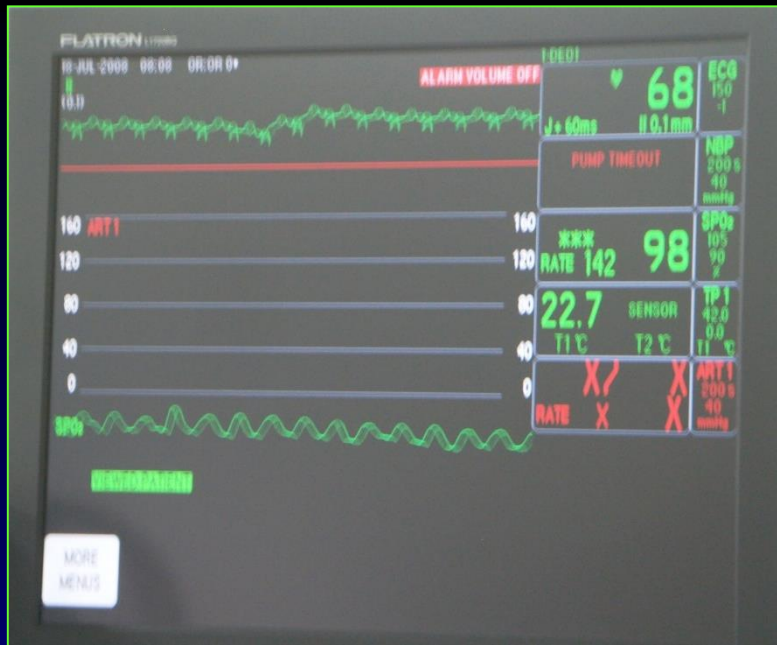
Division of Gastroenterology, Asan Medical  
Center University of Ulsan College of Medicine

# High Intensity Focused Ultrasound (HIFU)

- ultrasound energy: extra-corporeal application
- totally non-invasive
- therapeutic potentials

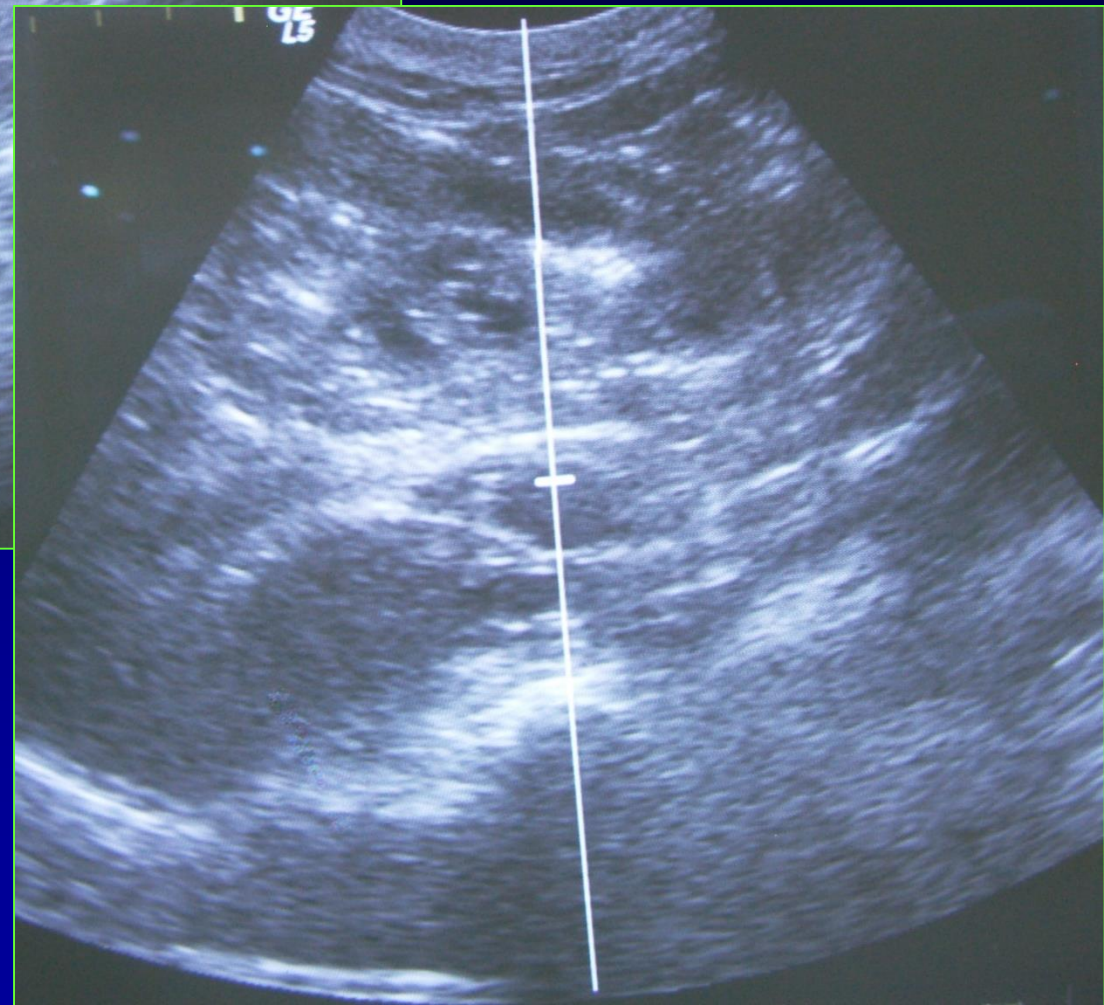
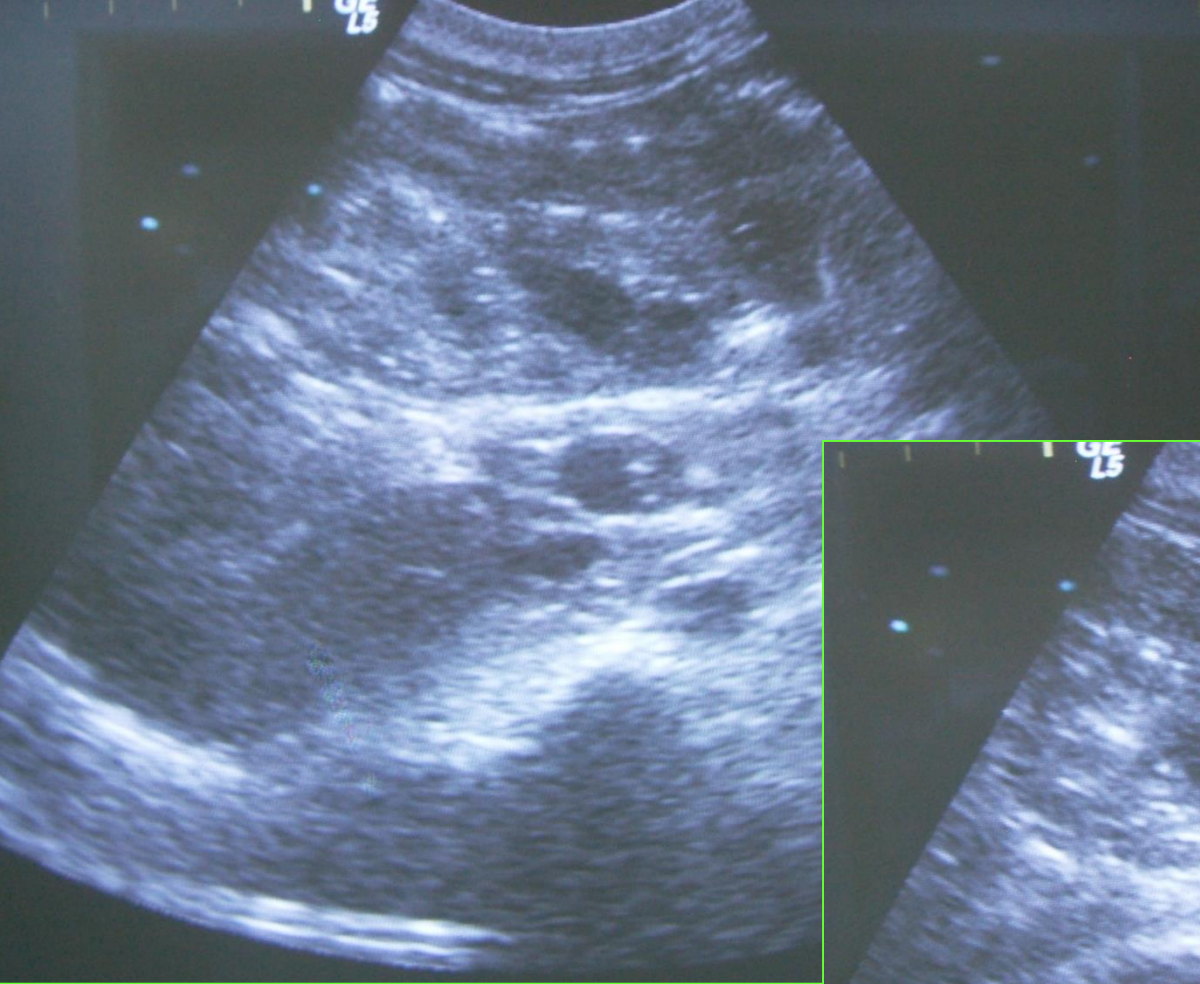












Pretx imaging

Tx dose: 750~1250J

Automatic & manual

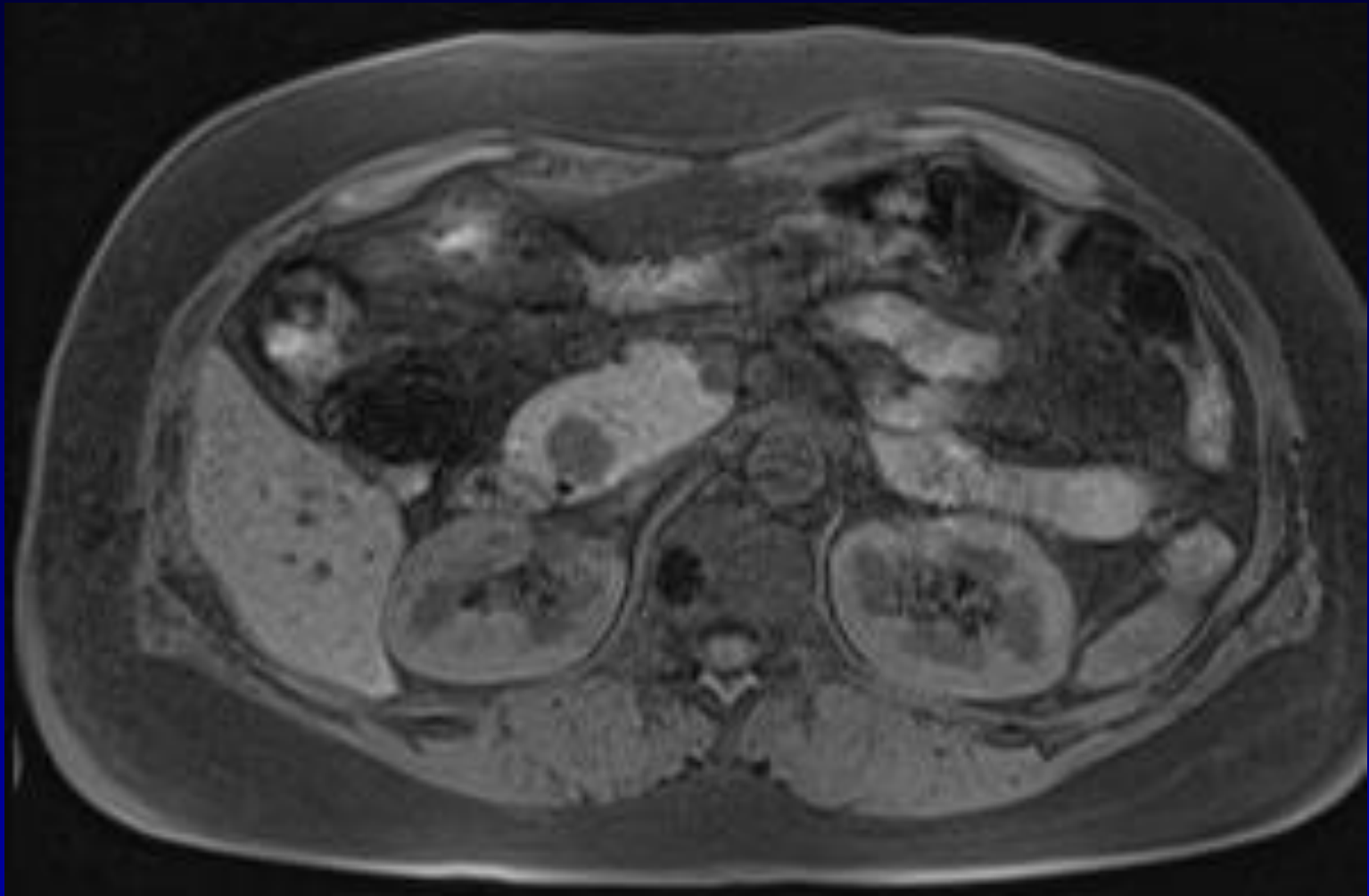


# Pig model for HIFU

---

- large abdominal organs
- similar anatomy to human
- difficult to manipulate
- expensive

50/F Pancreatic SPN (Bx proven)



# Unmet needs

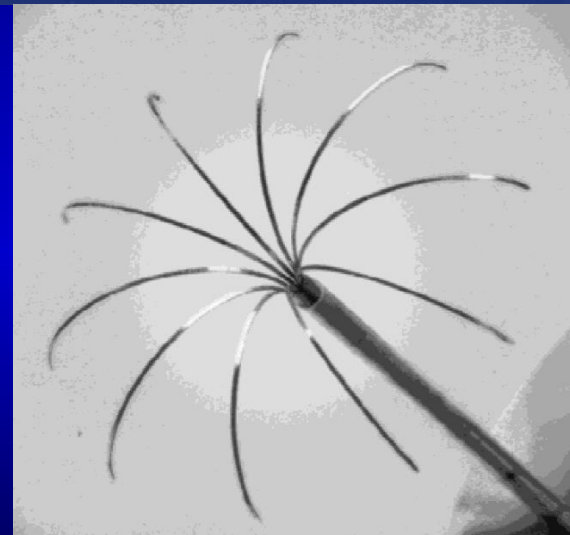
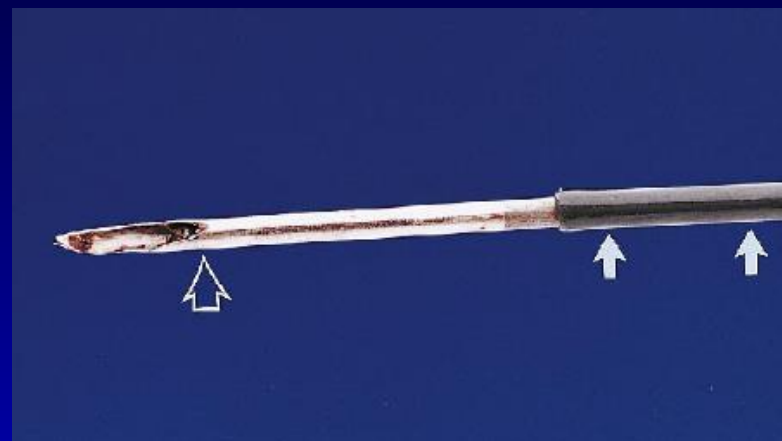
---

- 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

Dong Wan Seo

Department of Gastroenterology, Asan Medical  
Center, University of Ulsan College of Medicine

# EUS-guided RFA

EUSRA (Starmed Co, Seoul, Korea)





# EUS-RFA needle Ex vivo study

# *Ex vivo*

Target : Liver muscle

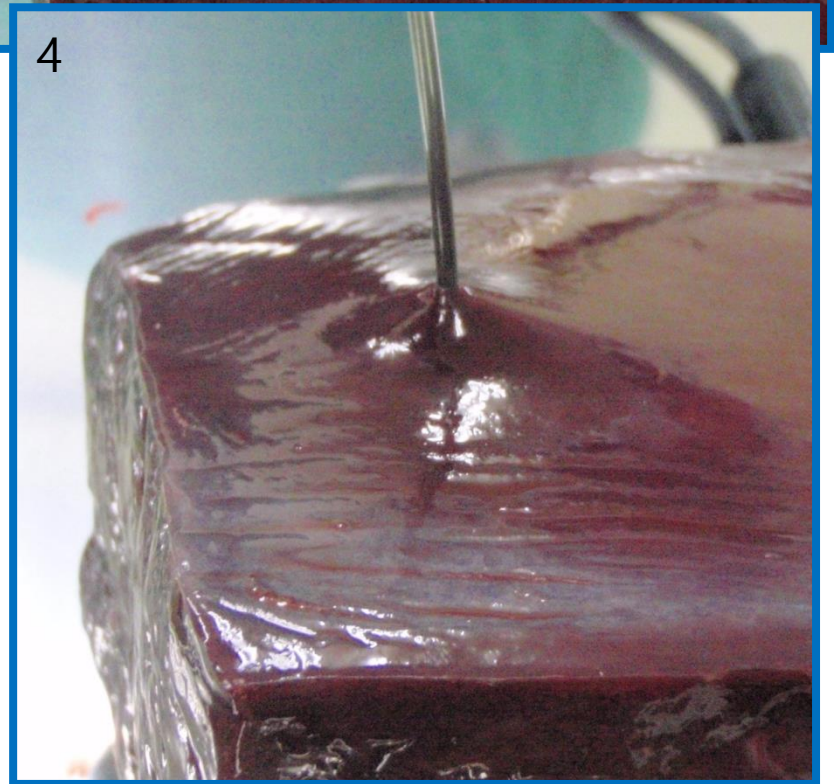
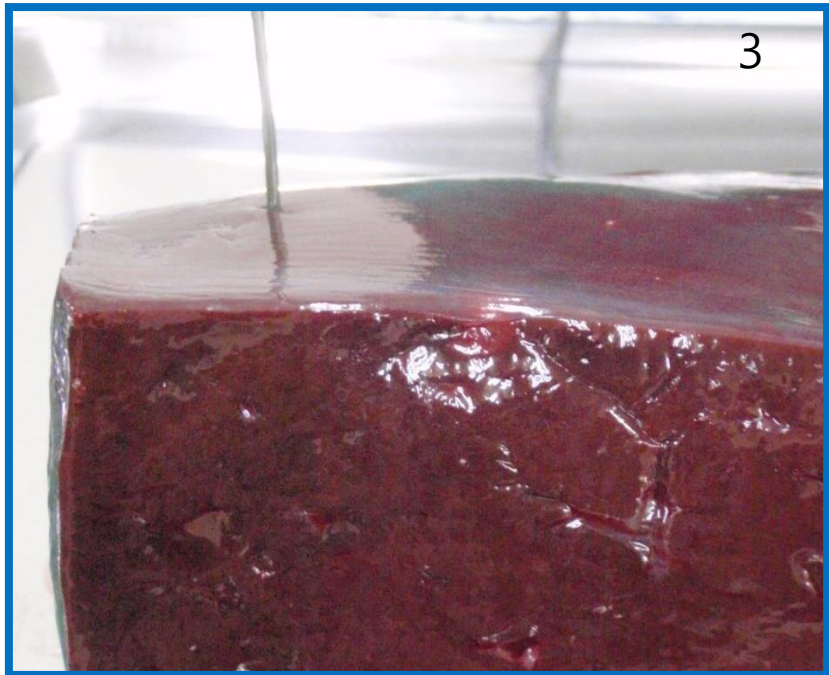
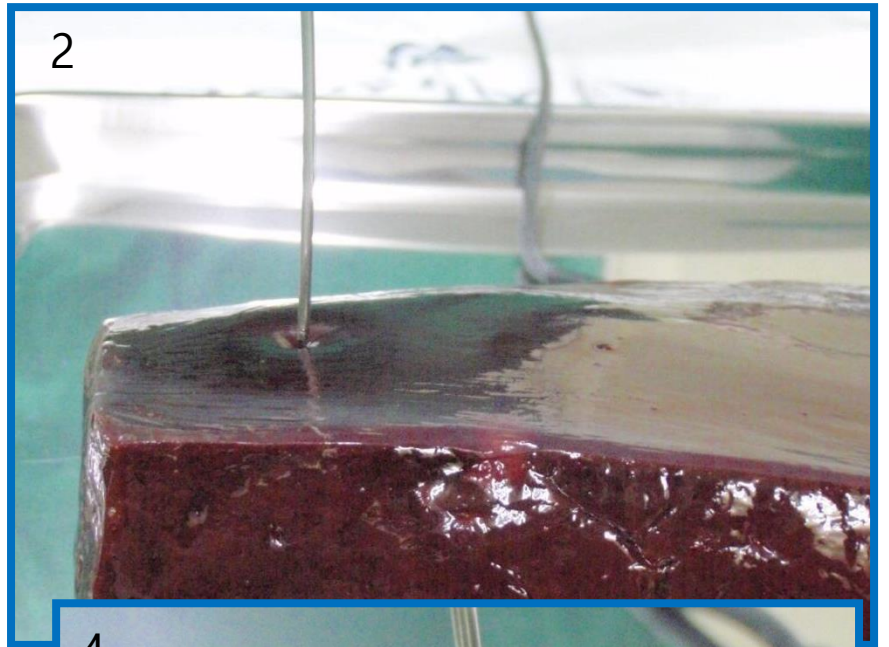
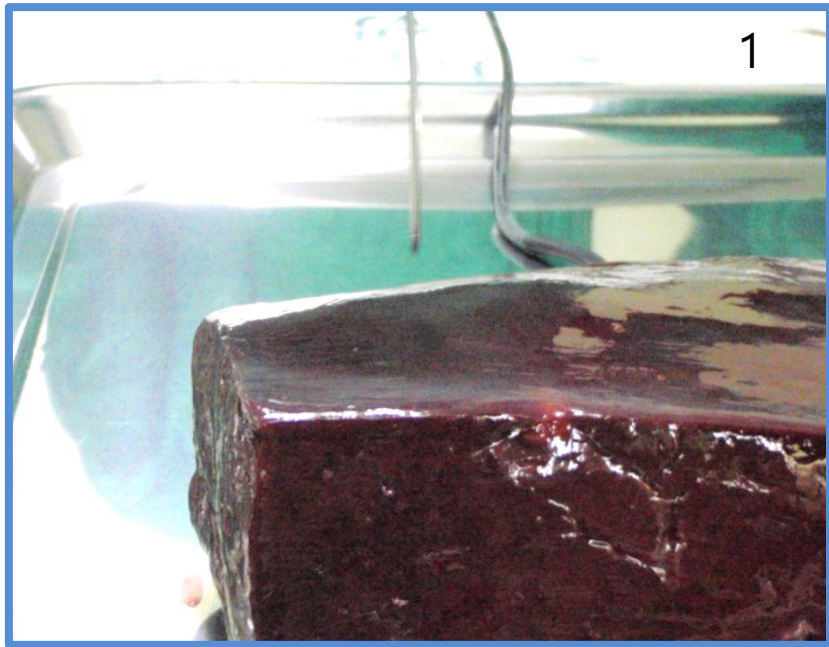
Needle : 17,18 G

Work time : 6min

RF power : 80W, 50W

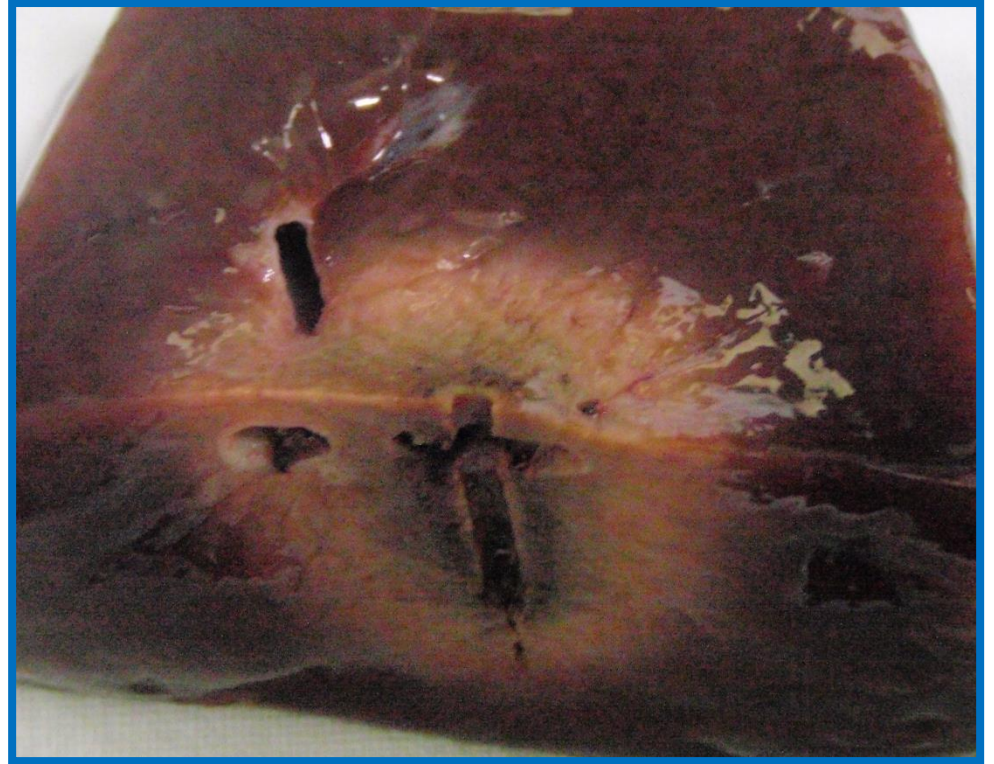
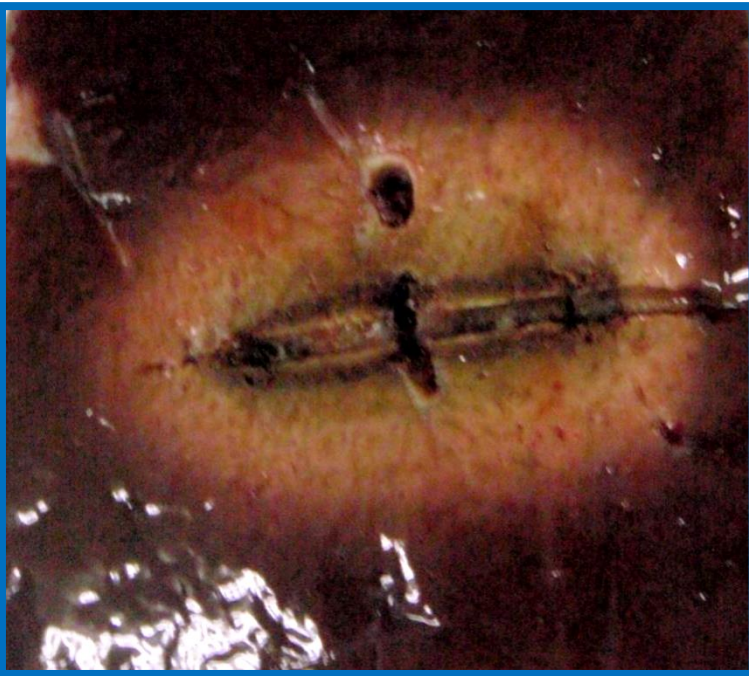
*1) 17G, 6min, 80W*

*2) 18G, 6min, 50W*





Post Tx image

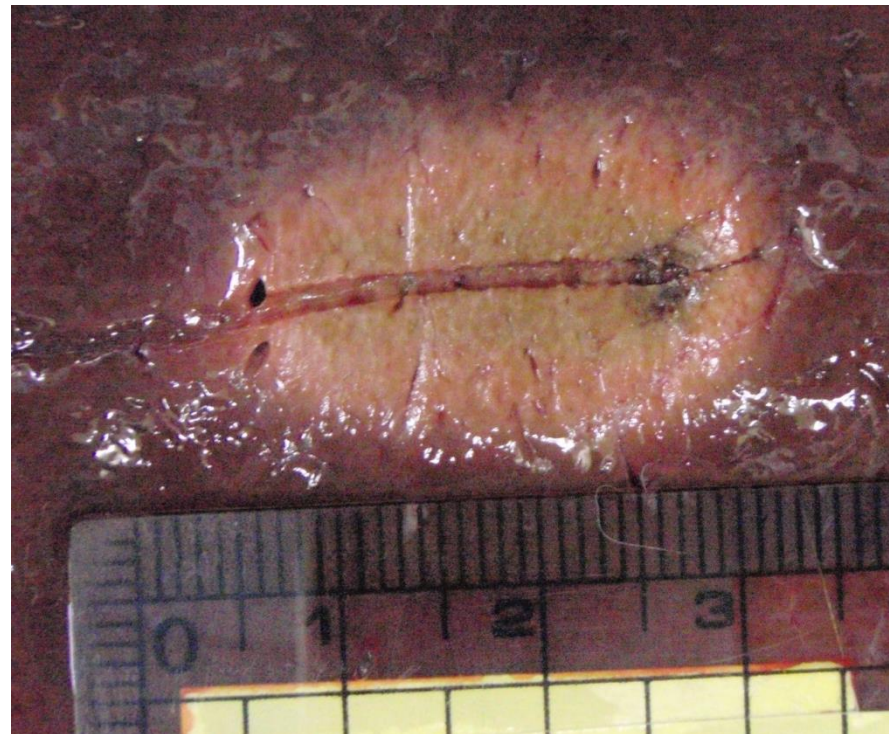
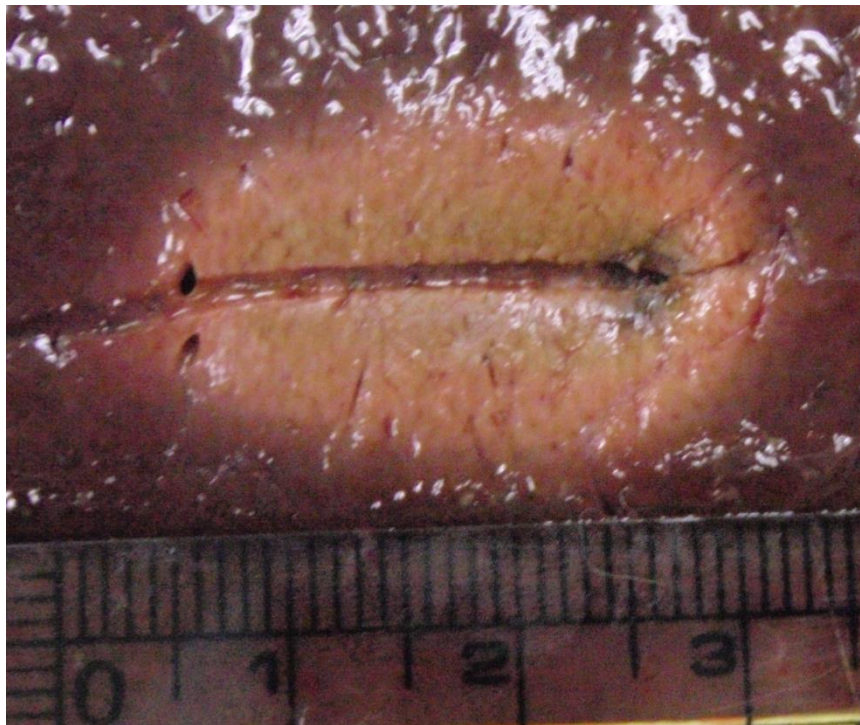


# 18G needle image



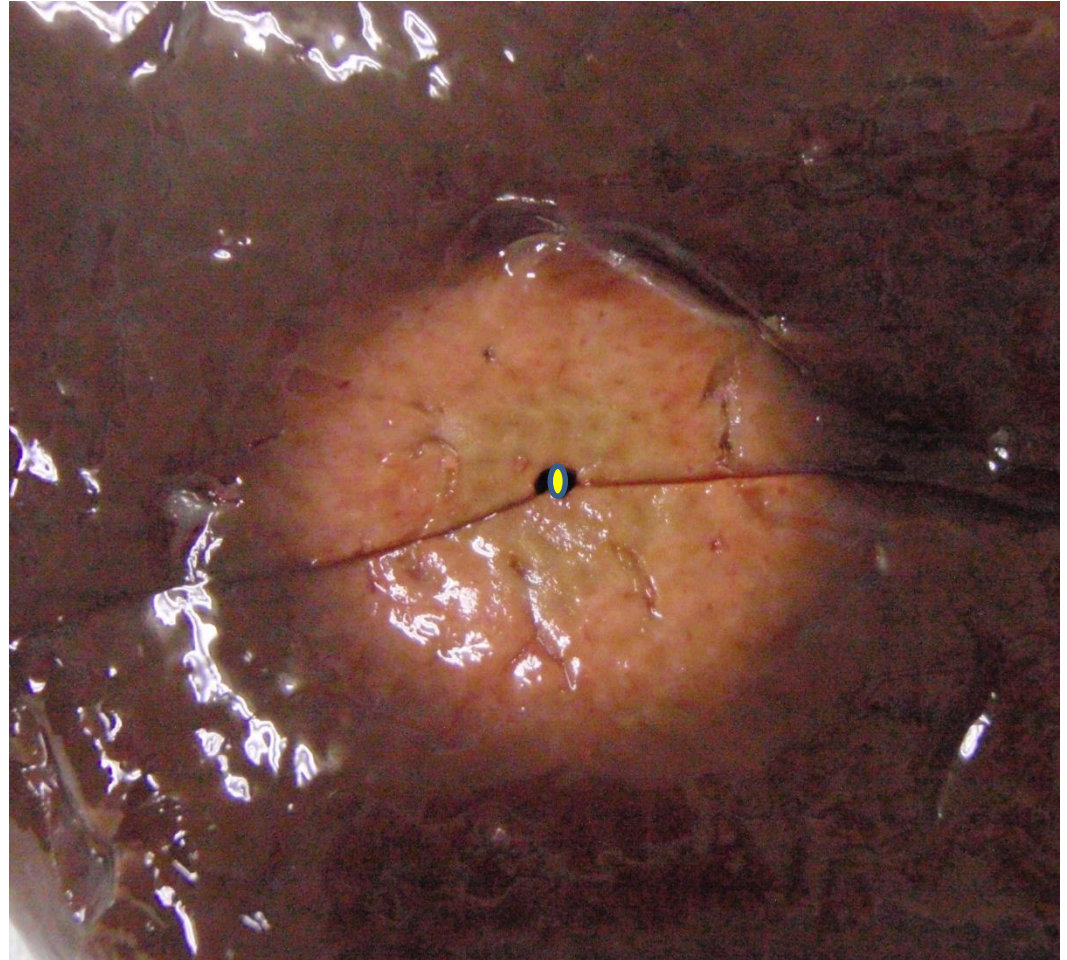
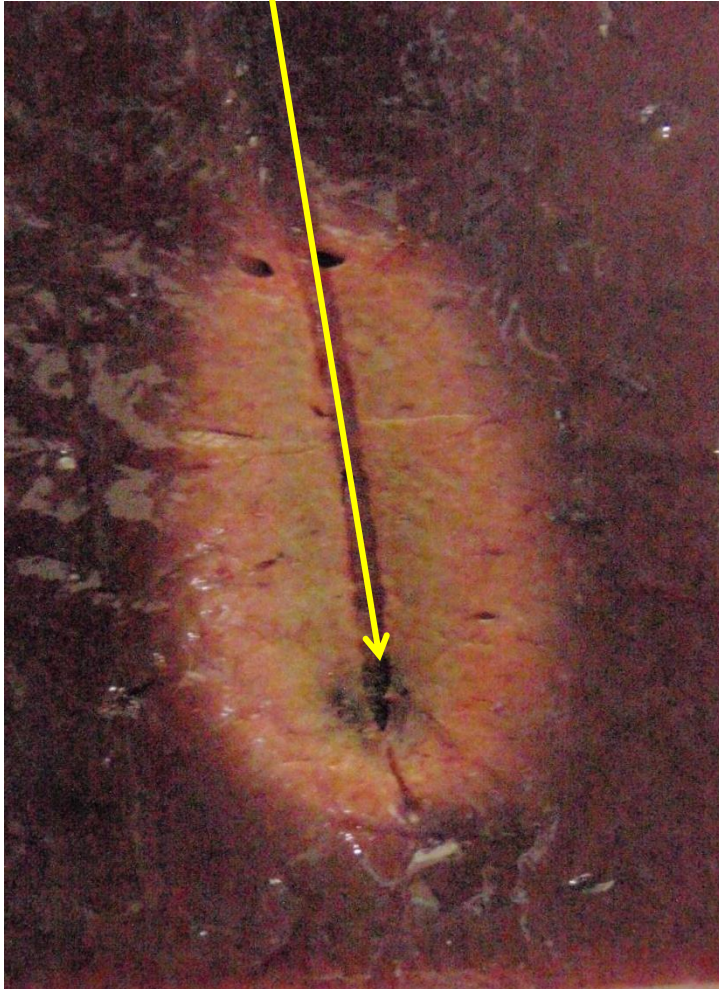


## Post Tx ablation size



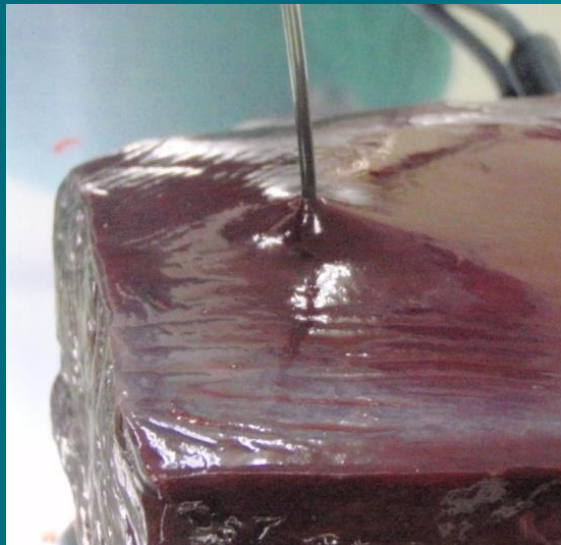


## Post Tx image



# Ex vivo test

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



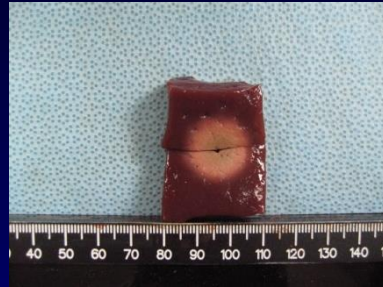
Group	Time
A	2 Min
B	4 Min
C	6 Min
D	8 Min
E	10 Min
F	12 Min



# EUSRA RFA ex vivo data



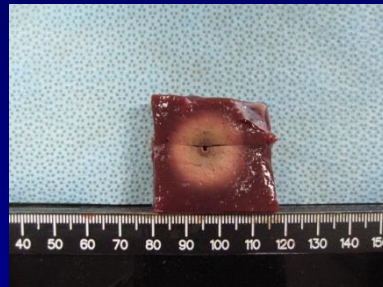
Group A : 30watt, 6min



Group B : 50watt, 6min



Group C : 80watt, 6min



Group D : 30watt, 12min



Group E : 50watt, 12min



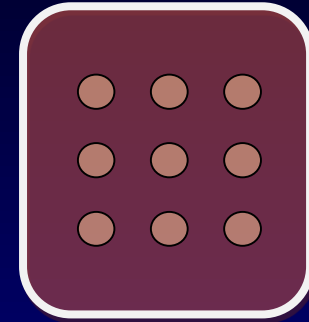
Group F : 80watt, 12min





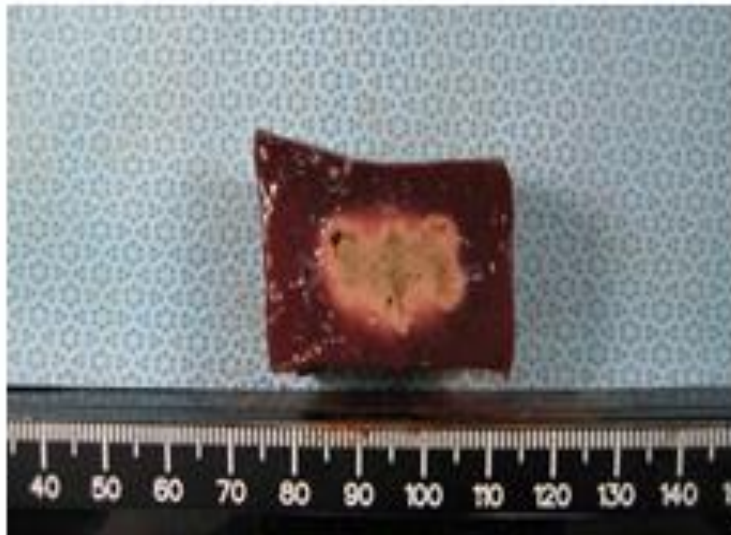
# EUSRA RFA ex vivo data

summation of ablation zone  
for large tumor ablation

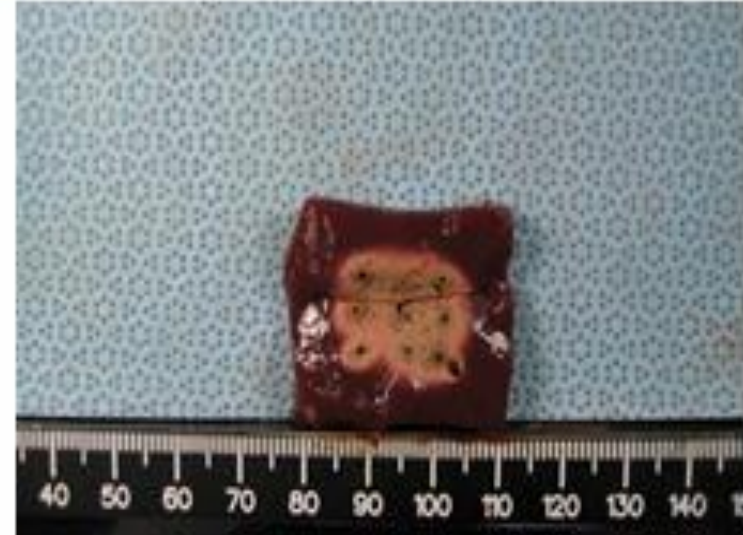


10mm, 50watt, 10sec\*9

종단면



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

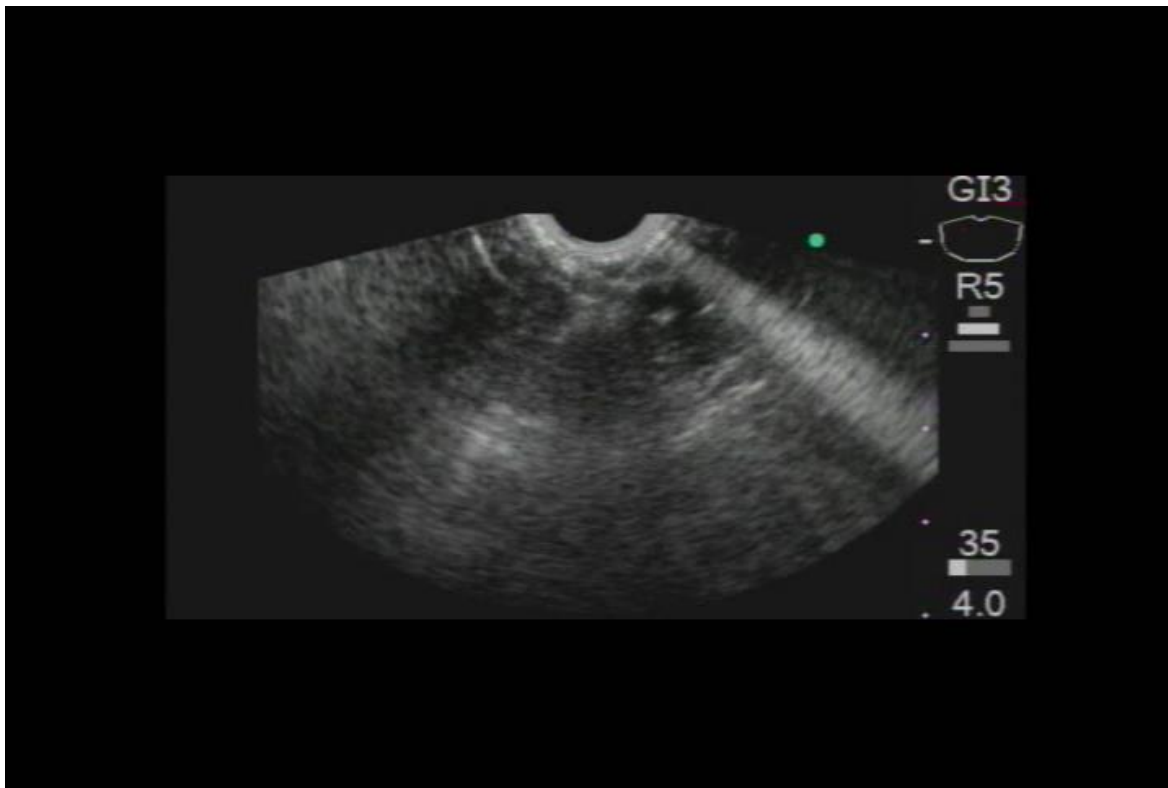
# Ultrasound image

Liver, 18G, 6min, 50W



# Ultrasound image

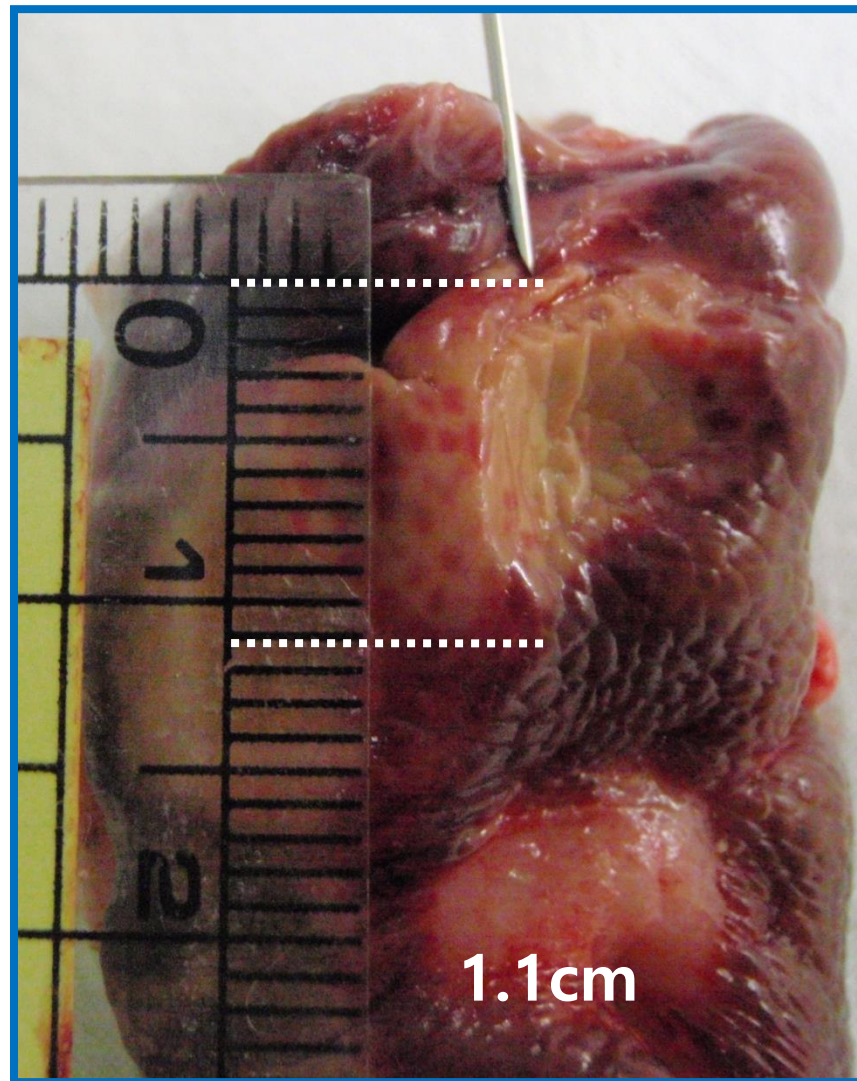
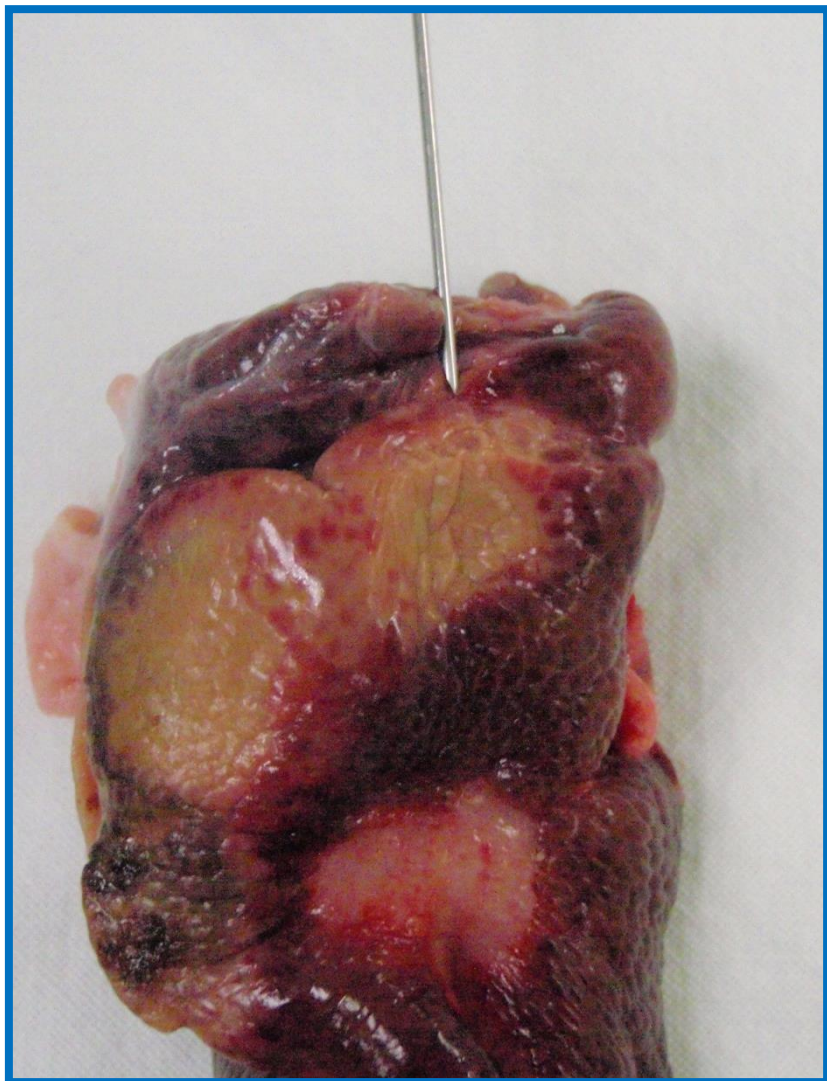
## Pancrease, 18G, 6min, 50W





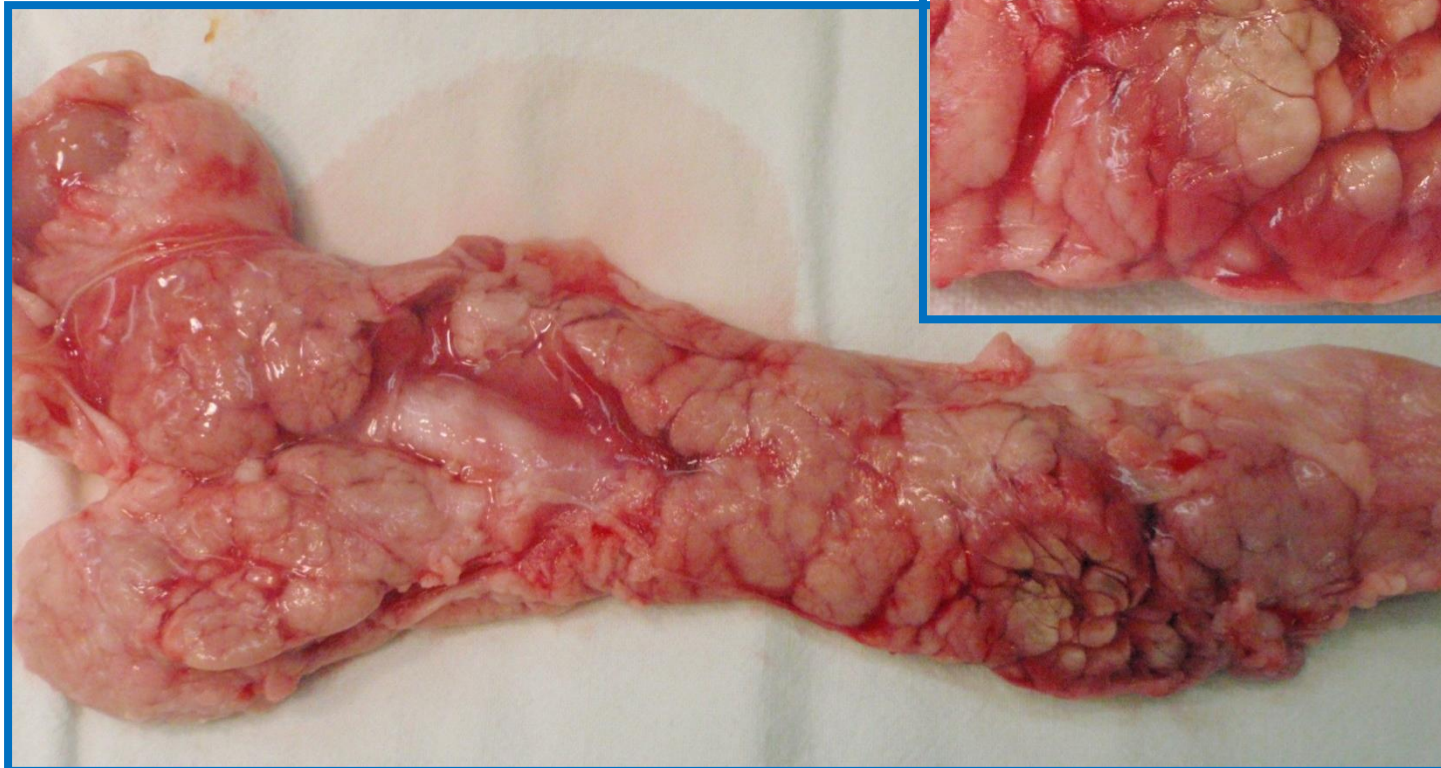
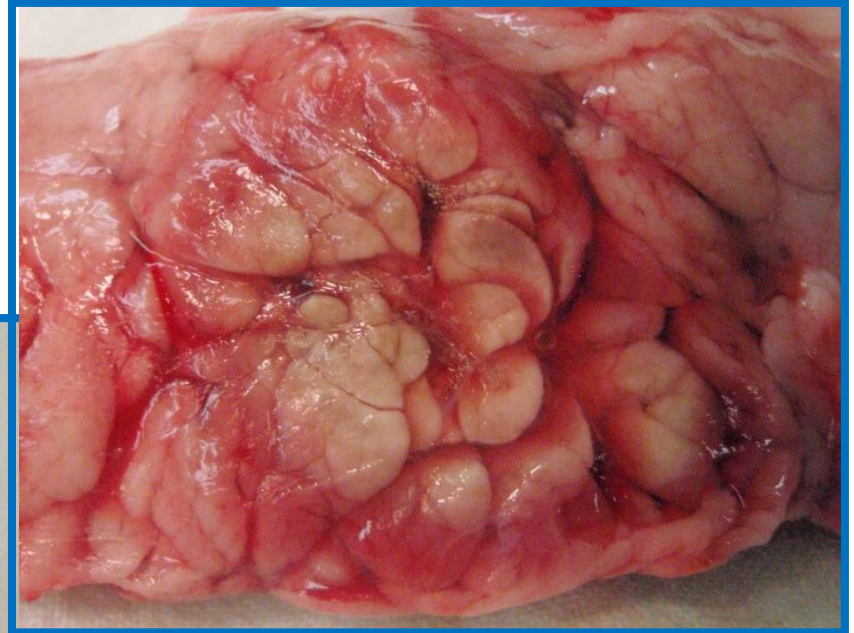
## Post Tx ablation image & size

18G, 6min, 50W



# Post Tx ablation image

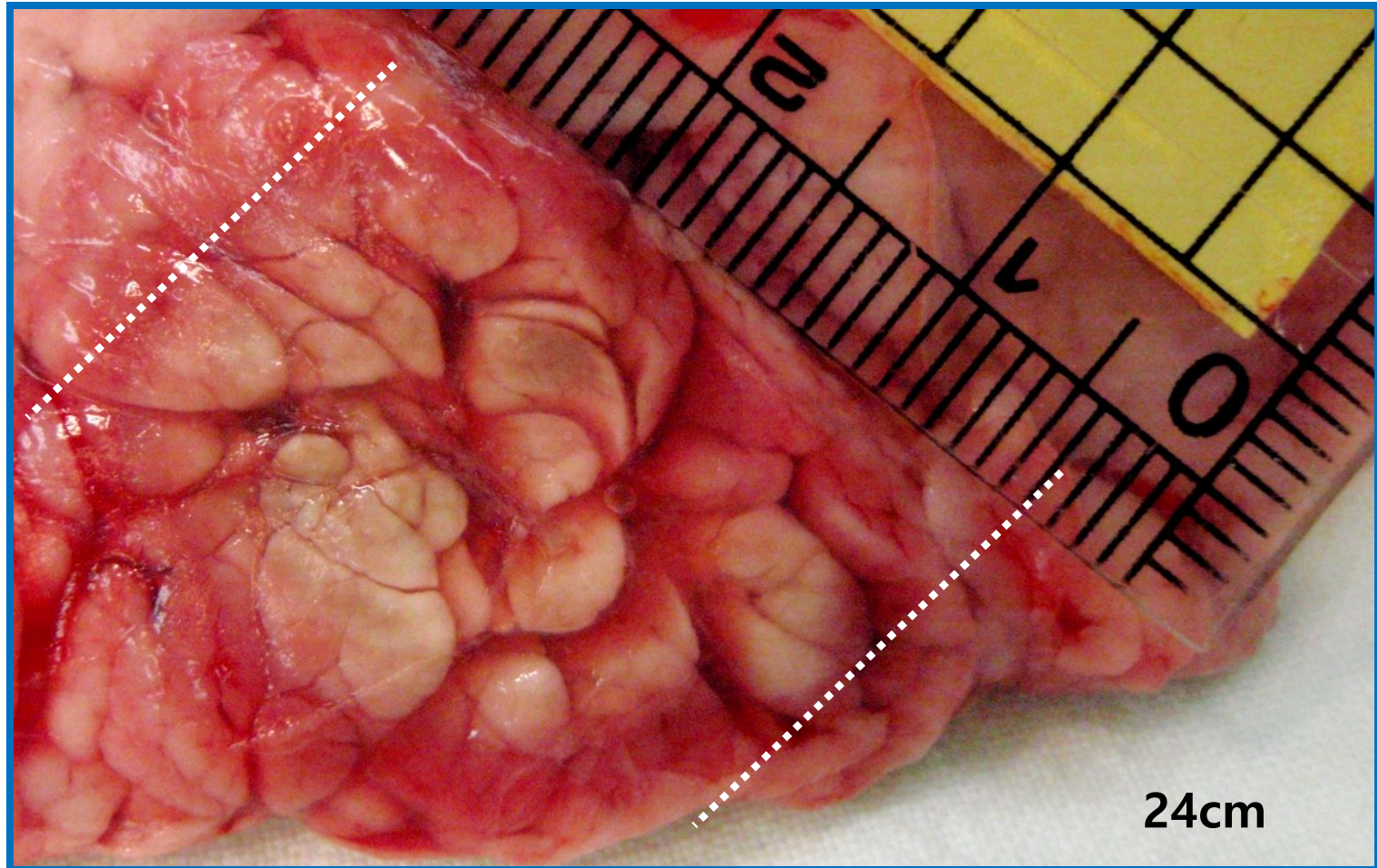
18G, 6min, 50W





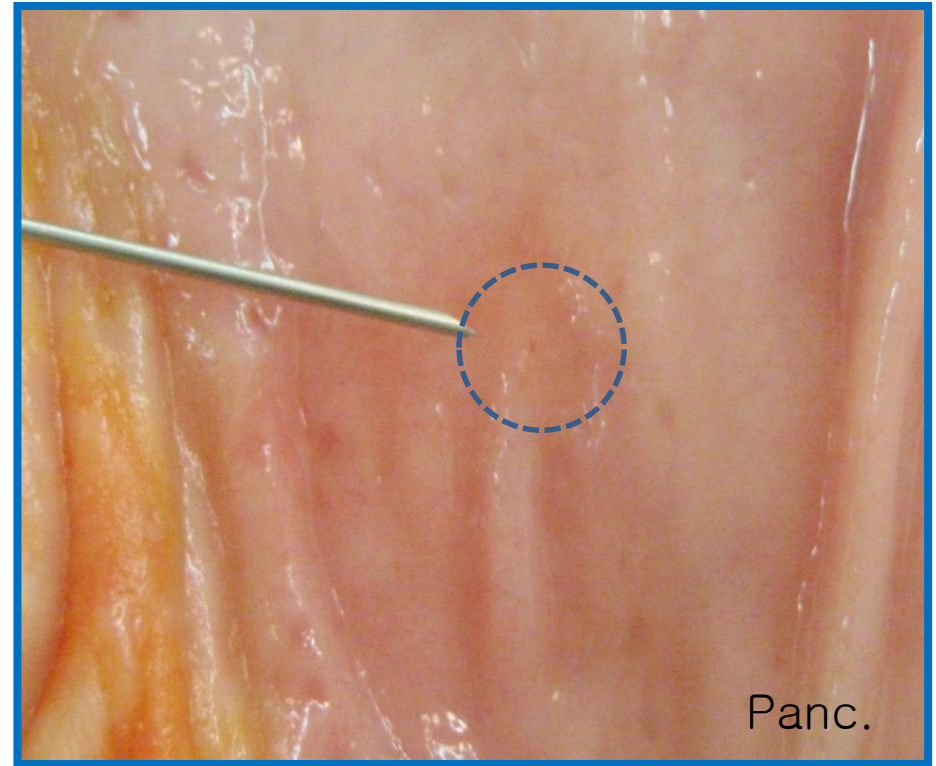
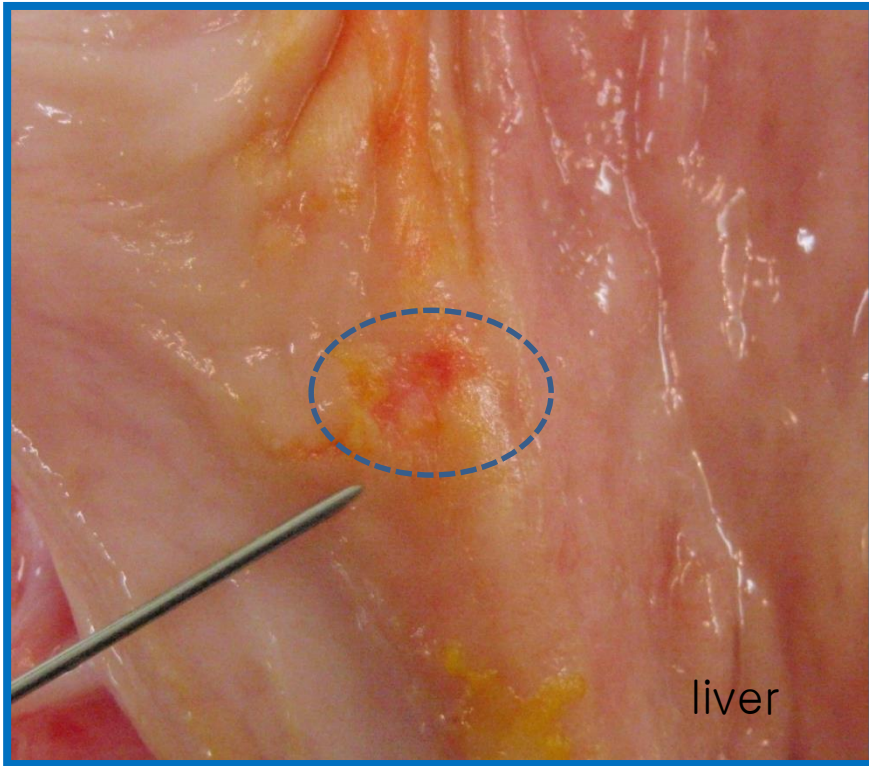
## Post Tx ablation size

18G, 6min, 50W





## Scope이 지나간 stomach wall image





서울아산병원

# EUS-guided radiofrequency ablation of porcine pancreas

Hong Jun Kim, Dong Wan Seo, Su Hui Kim<sup>1</sup>, Choong Heon Ryu, Sang Soo Lee, Sung-Koo Lee, Myung-Hwan Kim

Department of Internal Medicine, Asan Medical Center,  
<sup>1</sup>Asan 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 : 1cm

Echogenic

Needle-shaped

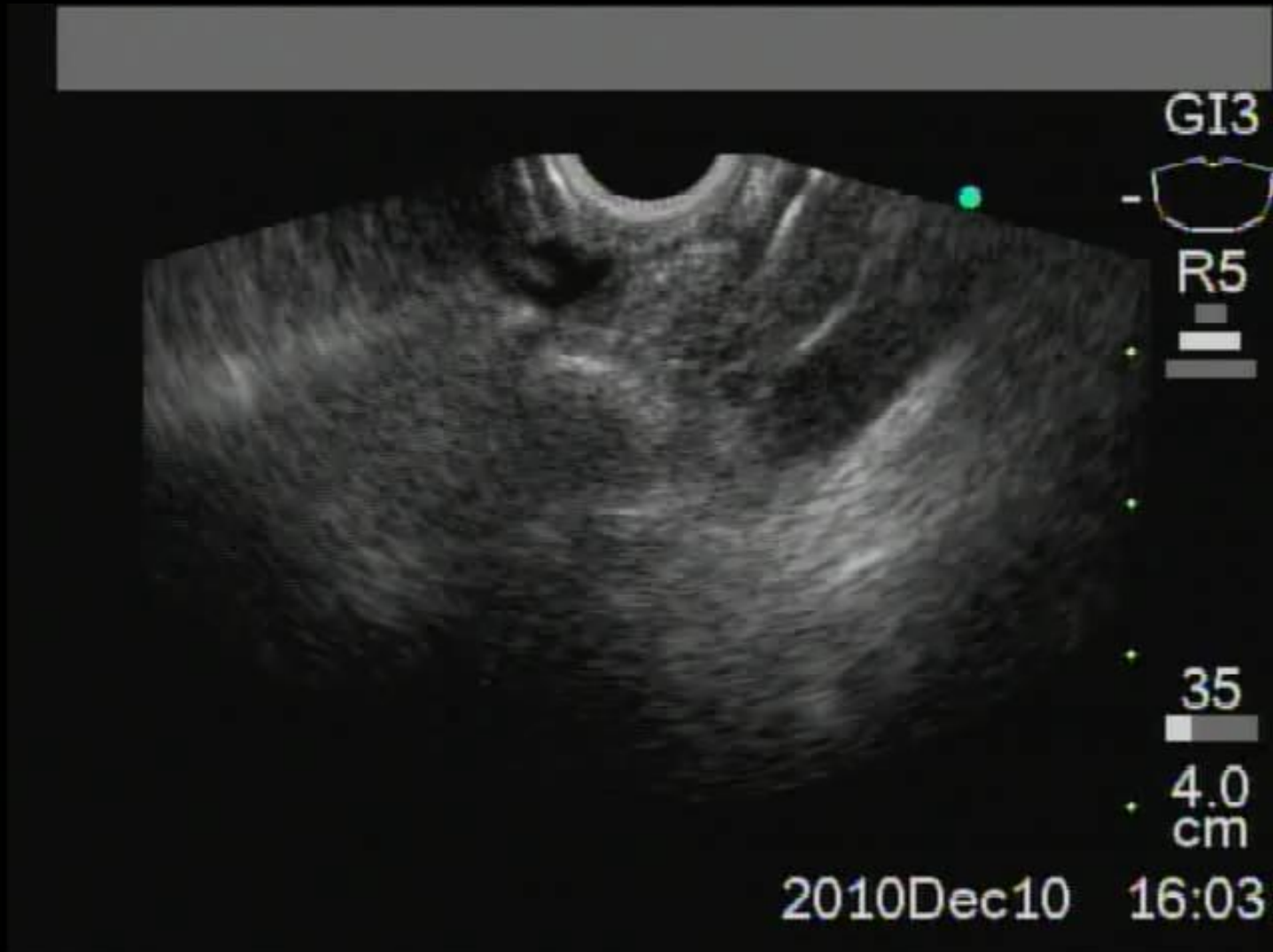
Cooling system : 30ml/min



- **VIVA RF system** (STARmed, Korea)

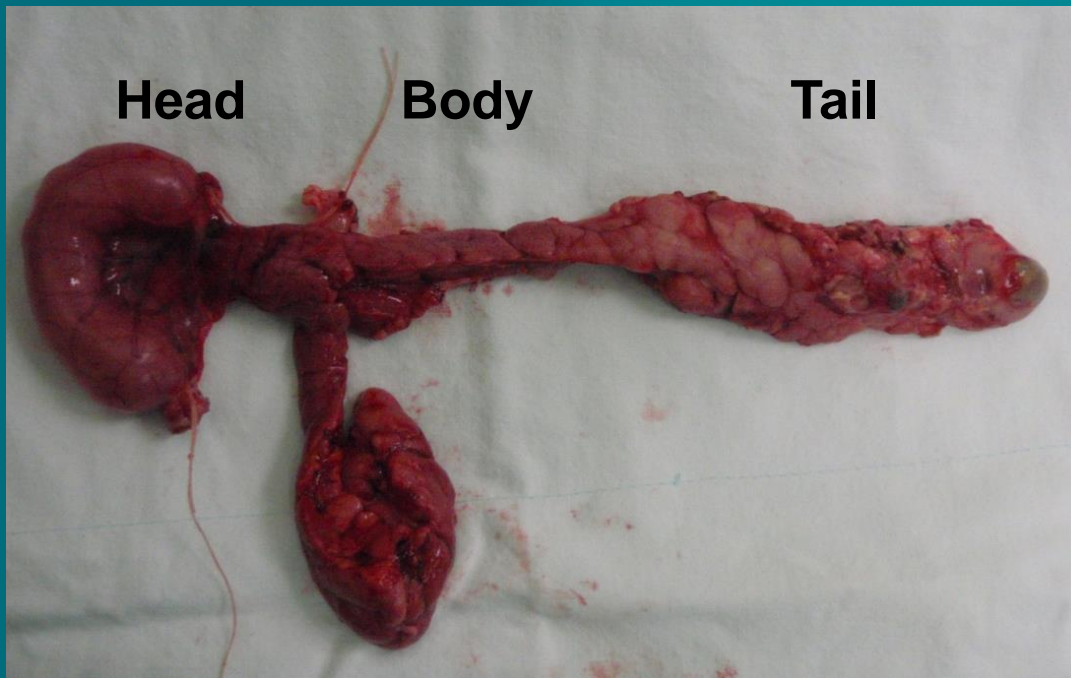


# EUS-guided RFA in animal model



# On day 7 after EUS-RFA

## 1. Laparotomy



2. Body weight and performance

3. Laboratory tests



# RESULTS

## Baseline characteristics

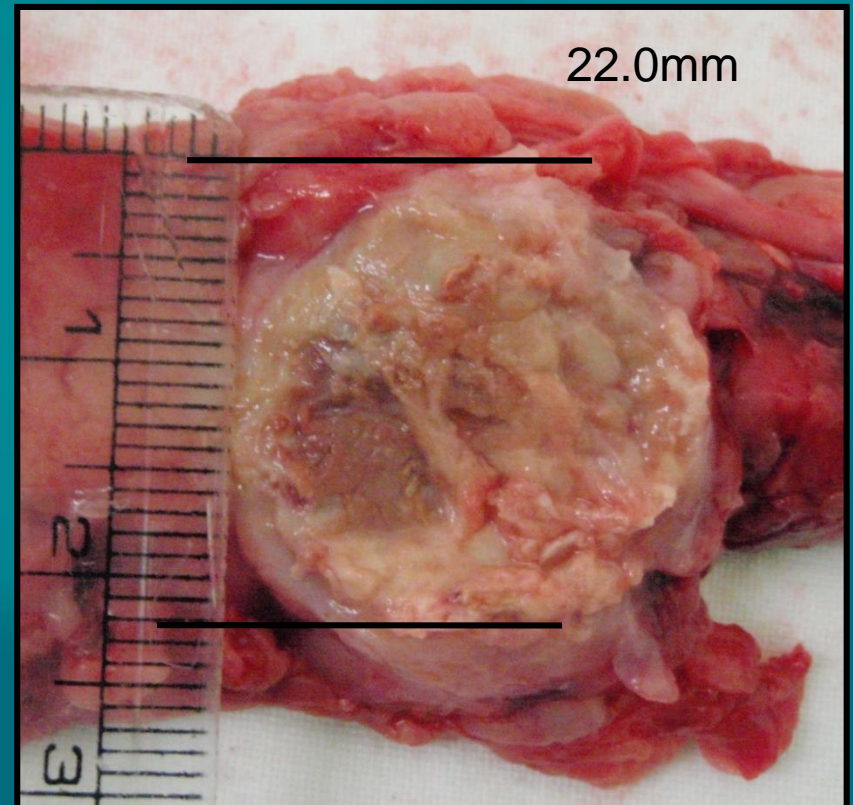
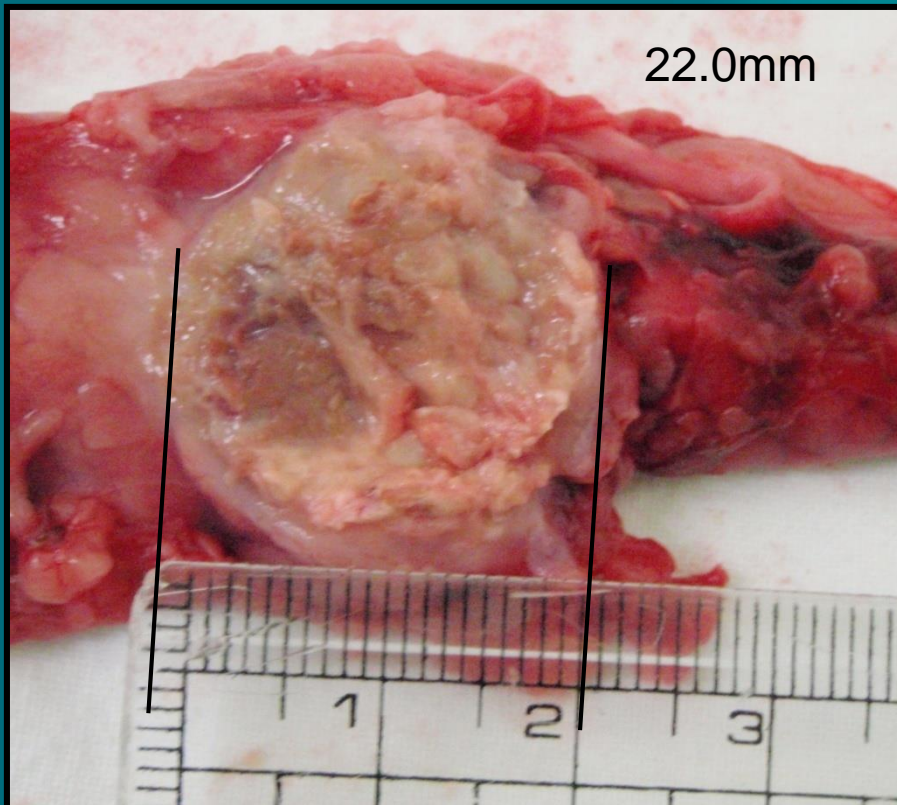
	Mean±S.D
Body weight (kg)	34.6±1.6
Serum AST (U/L)	86.3±50.0
Serum ALT (U/L)	23.3±4.9
Serum amylase (U/L)	3005.0±367.7
Serum lipase (U/L)	15.5±2.1

# Size of ablated lesions

	Mean±S.D
<b>Diameter of RFA lesion(mm) - EUS</b>	14.5±1.5
<b>Diameter of RFA lesion(mm) - laparotomy</b>	23.0±6.9

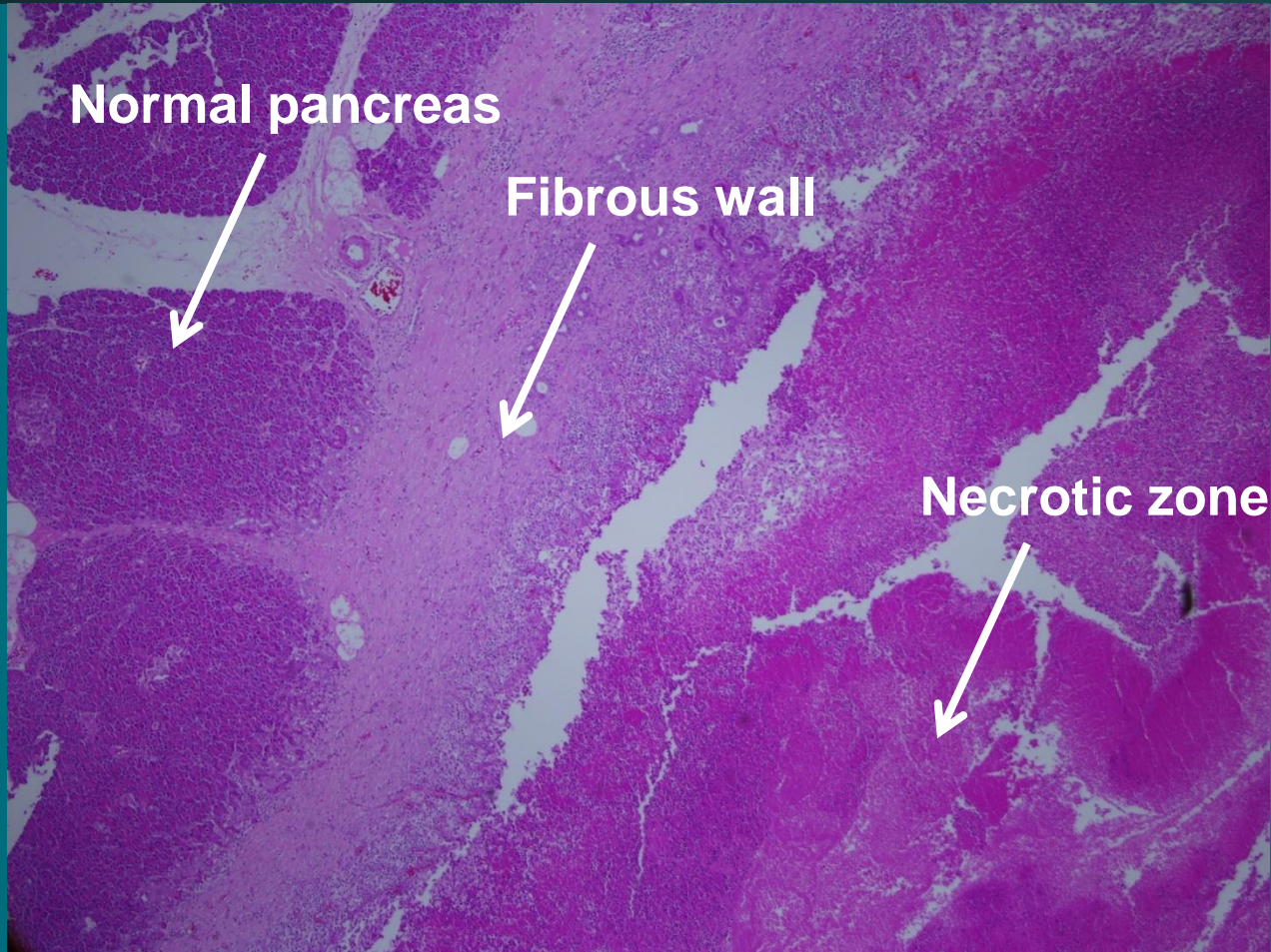
# Gross pathology

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



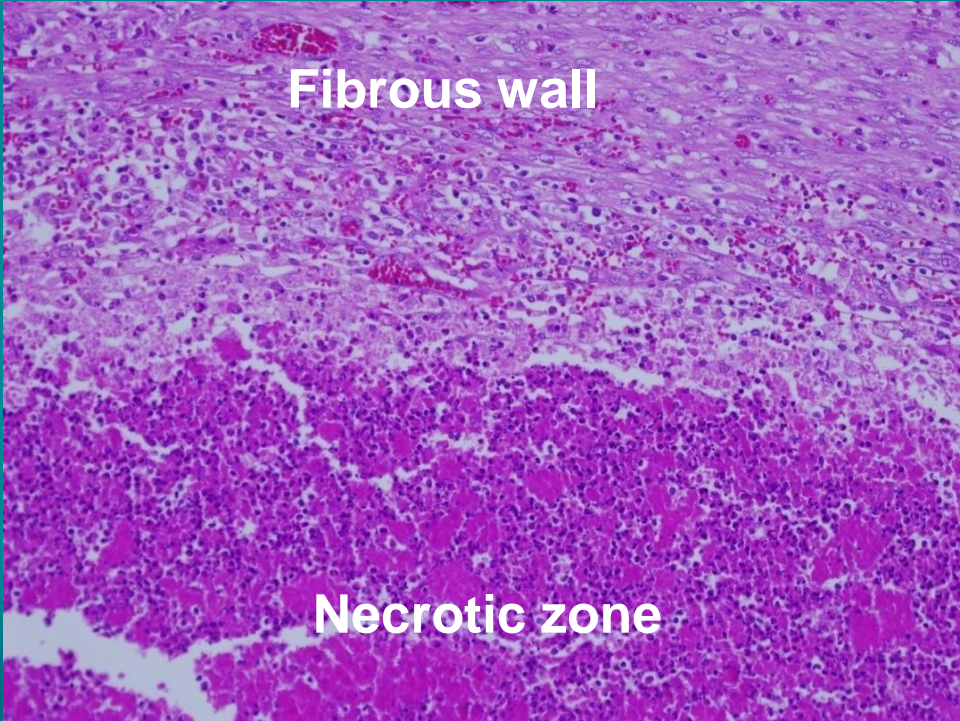
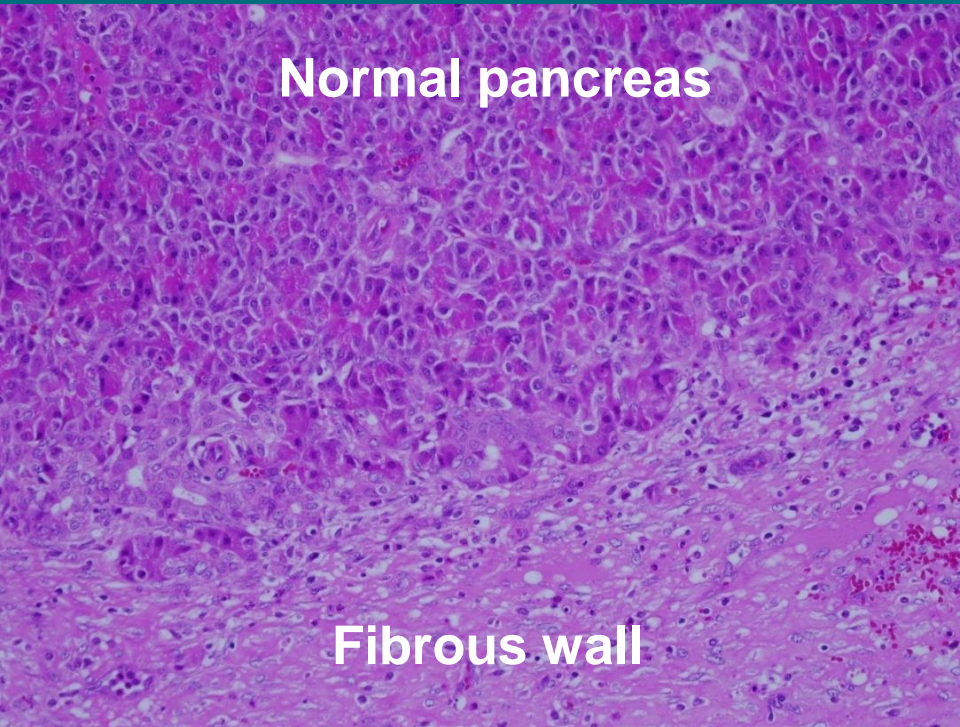


# Histopathological examination



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





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

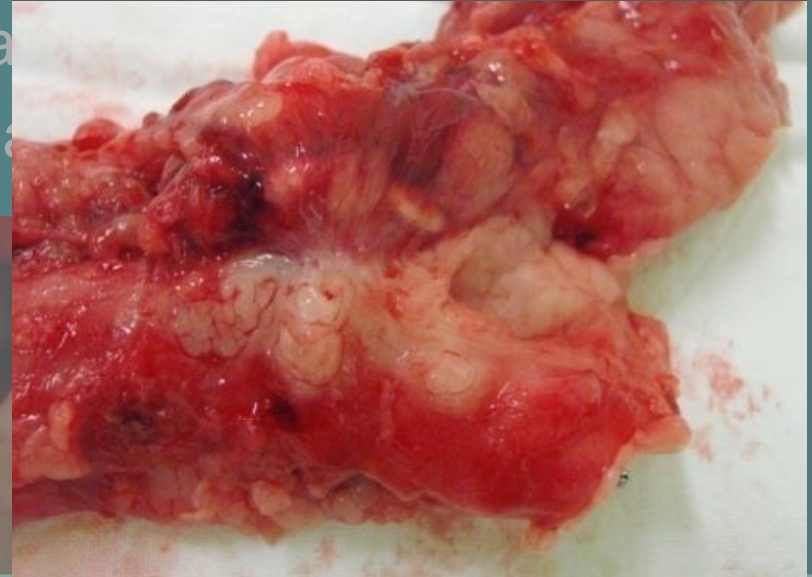
# Complications

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

**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

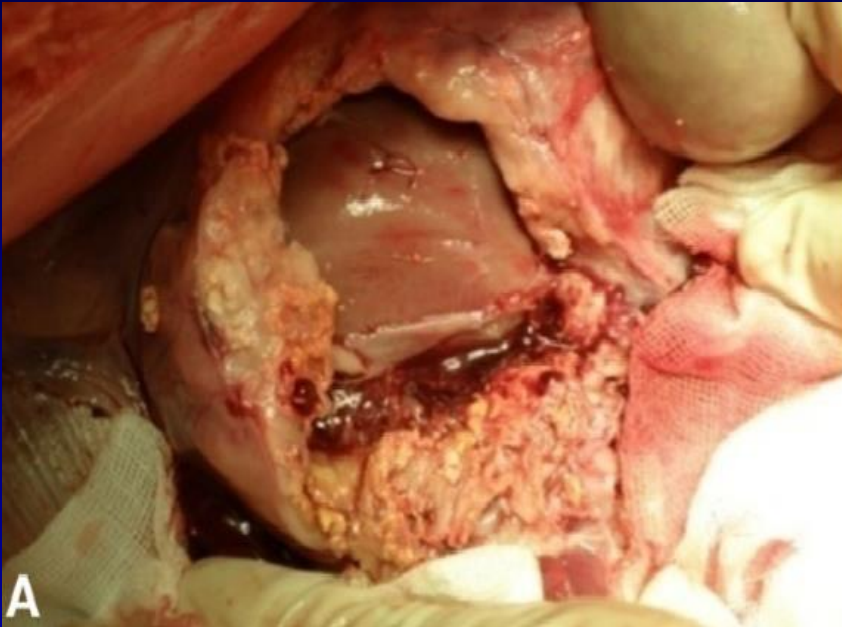
**Hong Jun Kim, MD,<sup>1</sup> Dong-Wan Seo, MD, PhD,<sup>1</sup> Aizan Hassanuddin, MMed, MRCP,<sup>1</sup> Su-Hui Kim,<sup>2</sup>  
Hee Jung Chae,<sup>3</sup> Ji Woong Jang, MD,<sup>1</sup> Do Hyun Park, MD, PhD,<sup>1</sup> Sang Soo Lee, MD, PhD,<sup>1</sup>  
Sung-Koo Lee, MD, PhD,<sup>1</sup>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

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)

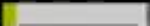
GT chemotherapy #4

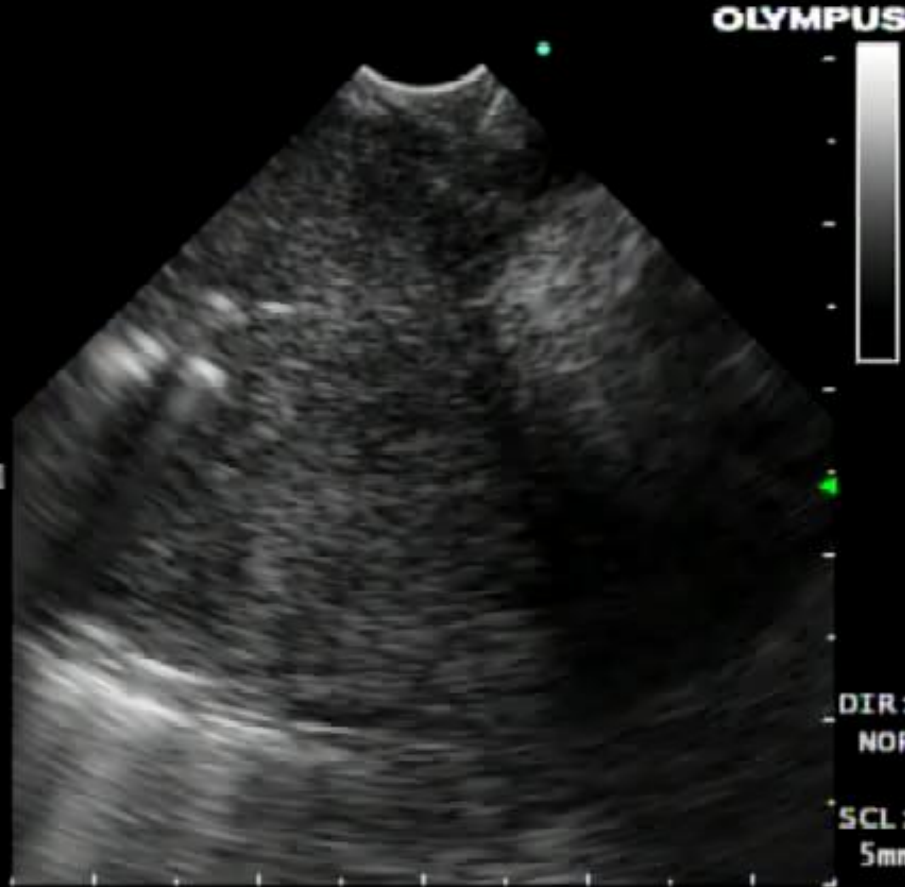
Op tried but failed d/t omental seeding

-> 2<sup>nd</sup> line CTx #3 (Folfox)-> disease progression



# EUS-RFA of Pca: Human case 3

ID:  
NAME:  
AGE:  
DOB: SEX:  
03/12/2013  
02:03:56  
7.5MHz 5cm  
G:15/19 I:5  
C:4/8 FC:3  
L.DEN:x4.0  
TX: 99%  
MEDIA   
T/B:NONE

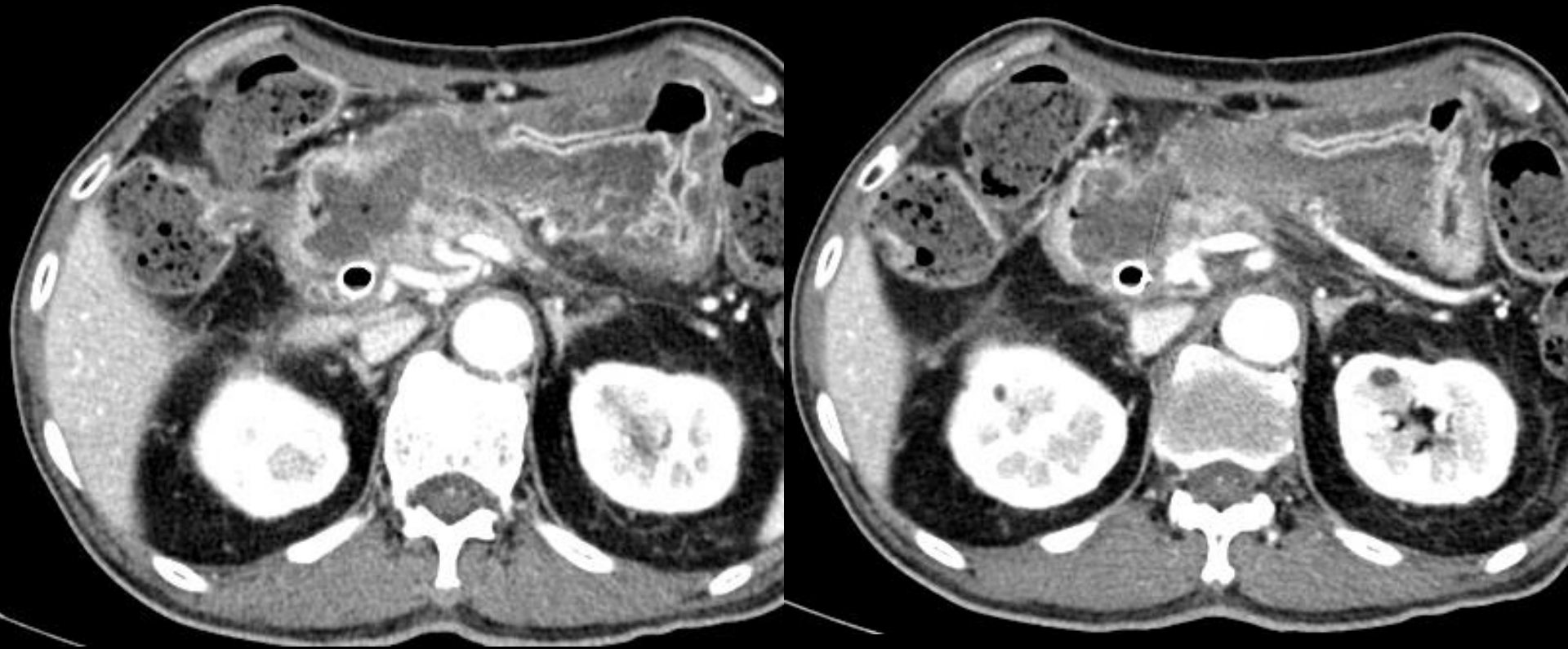


50W, 10 sec  
continuous mode  
x 8 times

CNCT:L 



# 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,<sup>1</sup> Dong Wan Seo, MD, PhD,<sup>1</sup> Sundeep Lakhtakia, MD, PhD,<sup>2</sup>  
Nageshwar Reddy, MD, PhD,<sup>2</sup> Dong Wook Oh, MD,<sup>1</sup> Do Hyun Park, MD, PhD,<sup>1</sup> Sang Soo Lee, MD, PhD,<sup>1</sup>  
Sung Koo Lee, MD, PhD,<sup>1</sup> Myung-Hwan Kim, MD, PhD<sup>1</sup>

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)



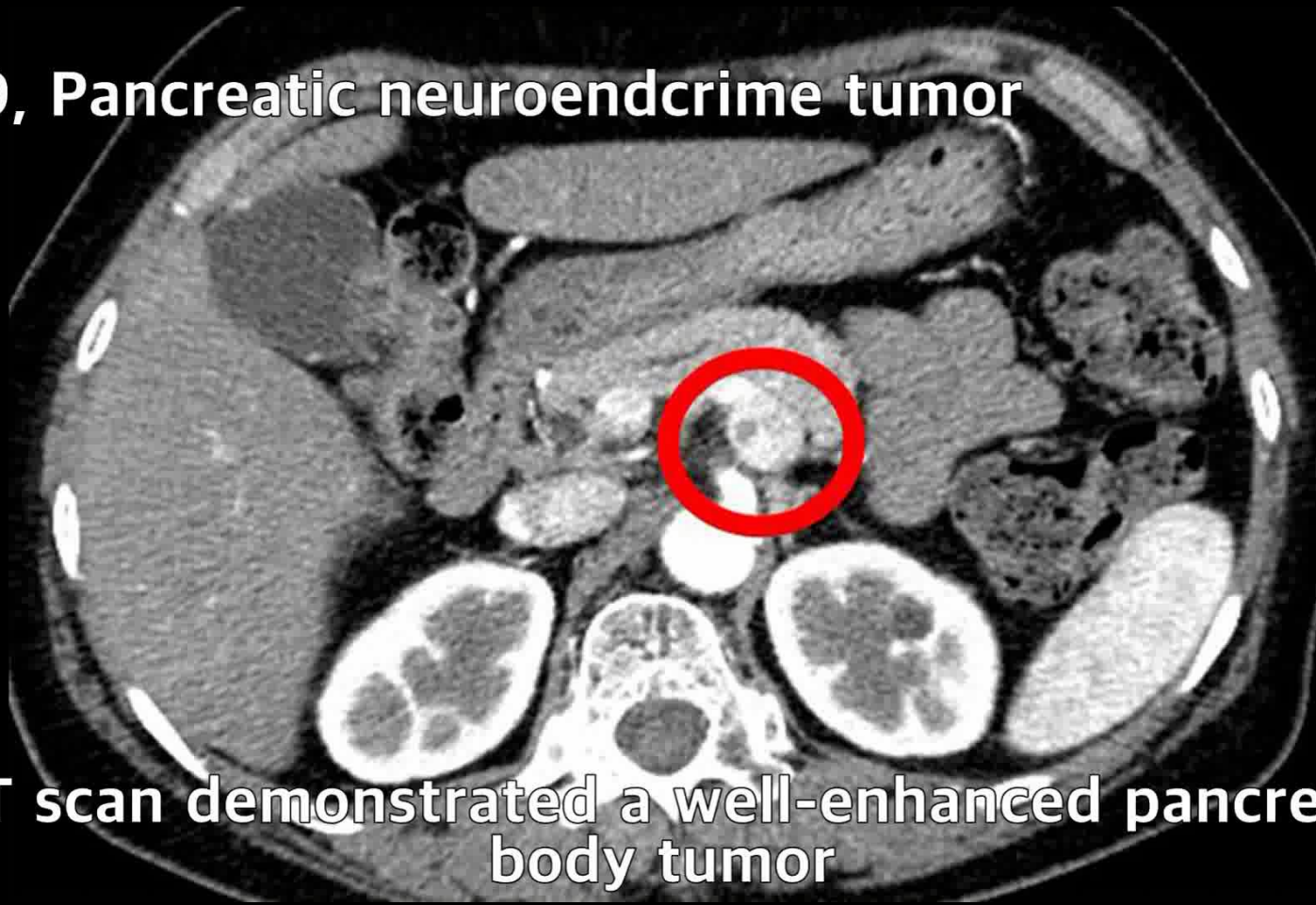
# Thickness of needle design



# EUS-RFA for Benign Pancreatic Tumor

# Case

F/69, Pancreatic neuroendocrine tumor



A CT scan demonstrated a well-enhanced pancreatic body tumor



# Baseline characteristics and outcomes (n=10)

No.	Age	Sex	Symptom	Dx	site	Size ( mm)	Post-ablation size	Response	Sessions	Adverse event
1	34	M	Hypoglycemia	Insulinoma	Head	12	0	Complete	1	-
2	21	F	Incidental	SPN	Head	23	19	Incomplete	1	-
3	53	F	Incidental	SPN	Tail	20	0	Complete	1	-
4	53	F	Incidental	NET	Body	8	0	Complete	1	-
5	43	M	Incidental	NET	Body	28	7	Incomplete	2	-
6	69	F	Incidental	NET	Body	19	9	Complete	2	-
7	70	M	Incidental	NET	Body	20	16	Incomplete	1	-
8	40	M	Incidental	NET	Body	16	0	Complete	1	-
9	69	F	Incidental	NET	Head	28	5	Complete	3	Abdominal pain
10	62	F	Incidental	NET	Head	23	10	Complete	3	Pancreatitis

## 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