VI Corso Nazionale di Ecografia Clinica SIEMC Napoli

Applicazioni I.O. dell'ecografia

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Why intraoperative ultrasound?

IOUS is considered to be the one of the MOST SENSITIVE imaging modalities for assessing **small focal lesions** of the liver and can affect the choice of **surgical strategy** and lead to **greater oncological radically**

For PRIMARY AND SECONDARY malignancy:

- Facilitates to improve detection and characterization of tumor
- Localize the target lesion
- Guide intraoperative procedures (ethanol ablation, RFA, MWA, resection)

Ultrasonography 2015

Why intraoperative ultrasound?

- **To detect new lesions/vanishing lesions**
- To guide liver surgery (ablation, resection)
- To check ablation efficacy

Intraoperative ultrasonography and surgical strategy in hepatic resection: What difference does it make?

121 liver resection

Table 3. Changes in surgical plan in the IOUS group (*n* = 88)

Reason for change	No. (%) of changes owing to IOUS, *n* = 15	No. (%) of changes not owing to IOUS, *n* = 7
Additional tumour(s) found via IOUS	10 (11.4)	0 (0)
Additional tumour(s) found via inspection	0 (0)	4 (4.5)
Liver conditions	0 (0)	3 (3.4)
Tumour location	3 (3.4)	0 (0)
Tumour size	2 (2.3)	0 (0)

IOUS = intraoperative ultrasonography.

Table 4. Diagnoses in operative plans changed due to IOUS

Diagnosis	No. (%) of changes owing to IOUS, *n* = 15
Gallbladder adenoma	1 (6.7)
Gallbladder cancer	1 (6.7)
Hepatocellular carcinoma	1 (6.7)
Cholangiocarcinoma	1 (6.7)
Metastatic colorectal cancer	10 (66.7)
Focal nodular hyperplasia	1 (6.7)

Table 5. Secondary outcome analysis

Factor	IOUS	Non-IOUS	*p* value
Margin length, mean ± SD, cm	1.09 ± 1.18	1.18 ± 1.05	0.74
R1 resection rate, no. (%)	3 (3.4)	2 (6.0)	0.61

IOUS was used in 88
Change in surgical plan 17% cases
Additional tumor detection in 10 pts
R0 > IOUS (NS)

J Can Surgery 2015

Why intraoperative ultrasound?

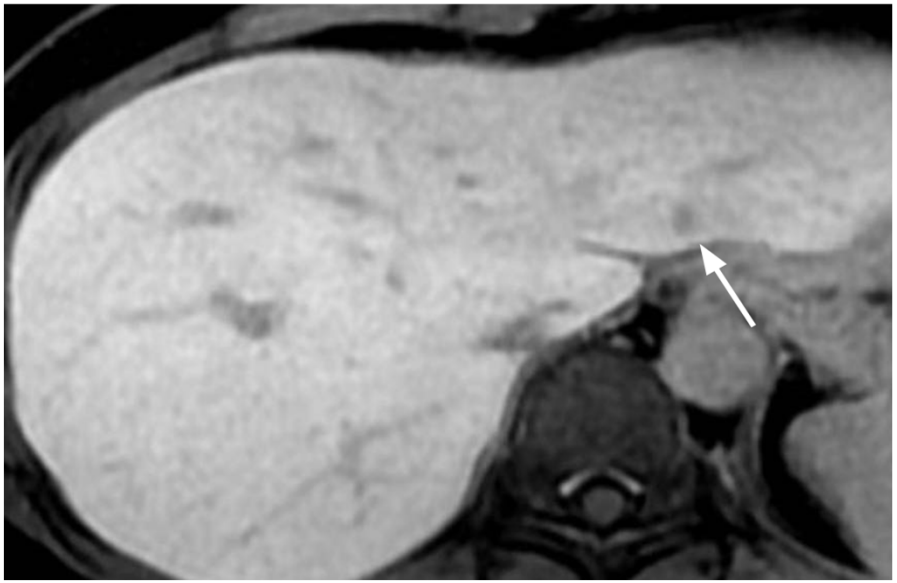
CRLM: intraoperative detection and/or localization of CRLM using IOUS can play a crucial role during hepatic surgery

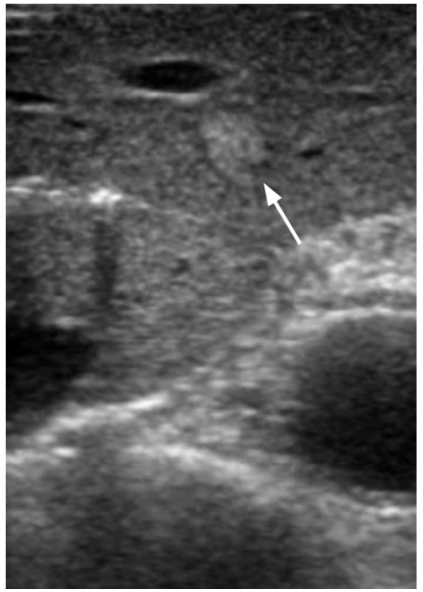
In the treatment of CRLM, the surgical resection of all macroscopically visible disease remains the gold standard and has been shown to result in improved long- term survival. In addition, local tumor ablation alone or ablation combined with surgical resection has been demonstrated to achieve local tumor control even in patients with unresectable disease

An important issue of note is the **DISAPPERANCE** of CRLM after chemotherapy, as shown by a complete response on preoperative imaging.

Why intraoperative ultrasound?

CRLM



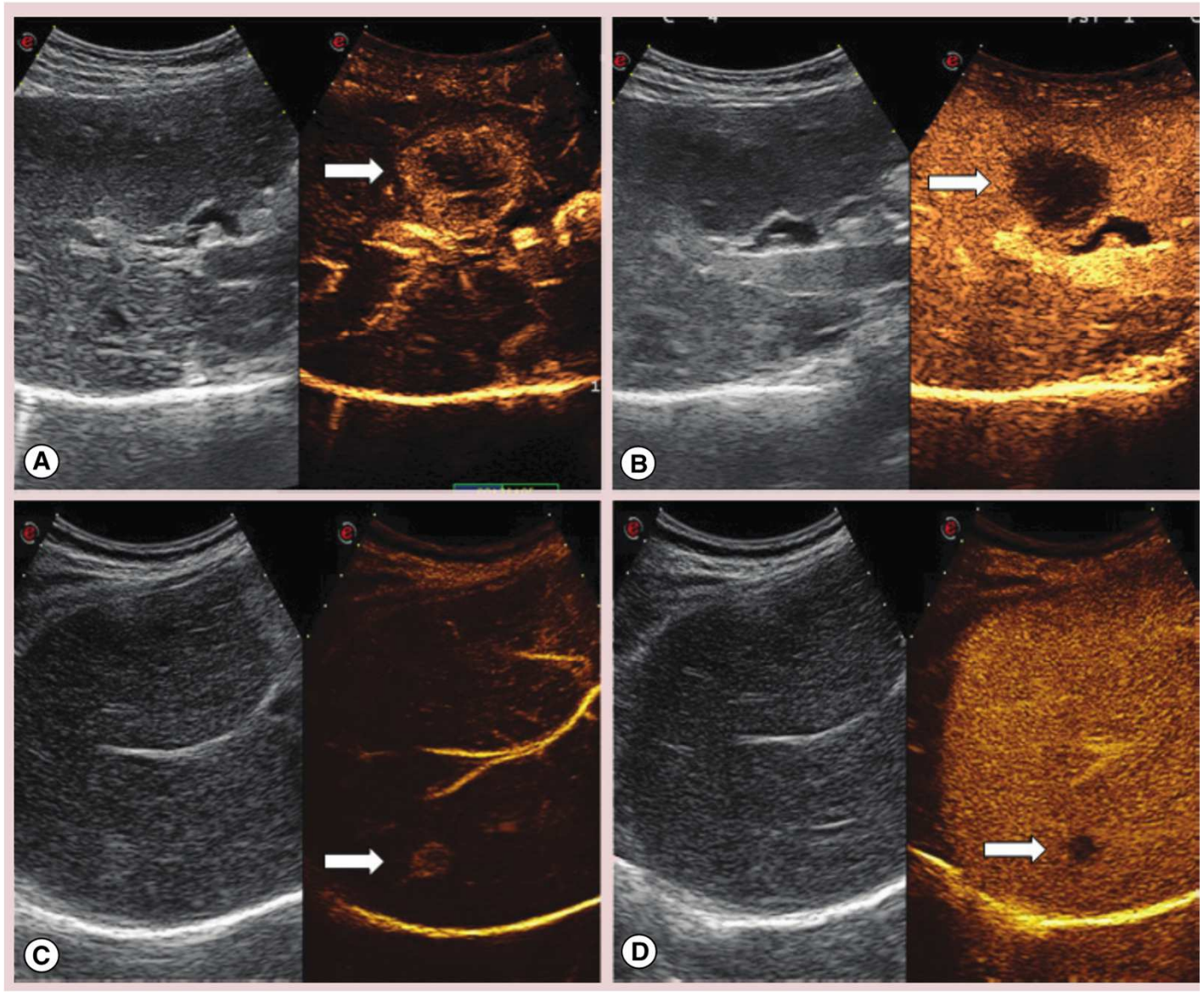


CRLM

Ultrasonography 2015

Arterial phase

Late phase



Typical vascular pattern of CRLM

Hepat Oncology 2015

Impact of contrast-enhanced intraoperative ultrasound on operation strategy in case of colorectal liver metastasis

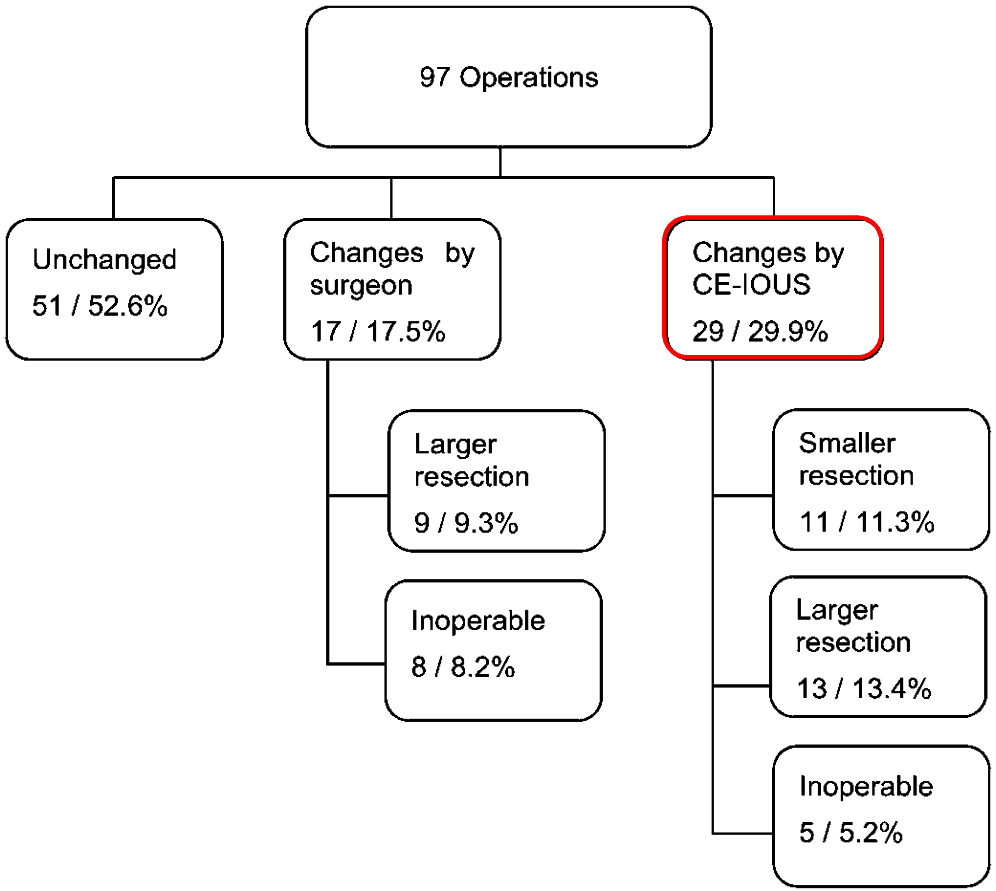
Anselm Schulz[1], Johann Baptist Dormagen[1], Anders Drolsum[1], Bjørn Atle Bjørnbeth[2], Knut Jørgen Labori[2] and Nils-Einar Kløw[1]

86 pts **CRLM**

Pre-op CT/MRI ➔ 328 CRLM

I.O additional lesions ➔ 72 lesions

- 41 by palpation and CE-IOUS
- 31 by CE-IOUS



Planned surgical procedure was modified in 29 cases

Acta Radiologica 2012

Impact of contrast-enhanced intraoperative ultrasound on operation strategy in case of colorectal liver metastasis

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31 additionally detected CRLM by CE-IOUS

Sex	Age (years)	Segmental location (S)	Size (mm)	Consequences
Female	74	S3; S5	5; 8	Larger resection
Male	49	S8	5	Larger resection
Male	61	S8	5	Larger resection
Male	77	S5	11	Larger resection
Male	53	S2; S2	3; 5	Larger resection
Male	65	S7; S7	5; 8	Larger resection
Female	56	S4	5	Larger resection
Male	69	S7; S8	3; 12	Larger resection
Male	74	S8	8	Larger resection
Female	65	S6	2	Larger resection
Male	40	S4; S4	3; 7	Larger resection
Male	61	S3; S4	3; 3	No changes*
Male	78	S3; S8; S8; S8	3; 9; 9; 12	Inoperable
Female	49	S3	2	Inoperable
Male	66	S3; S4; S7	10; 8; 20	Inoperable
Male	54	S1; S3; S6	14; 10; 8	Inoperable
Male	69	S1; S4	10; 10	Inoperable
Size (mean/ median/ range)	7.3/ 8.0/ 2–20			

CE-IOUS increases resection results in 5.8% of cases

Acta radiologica 2012

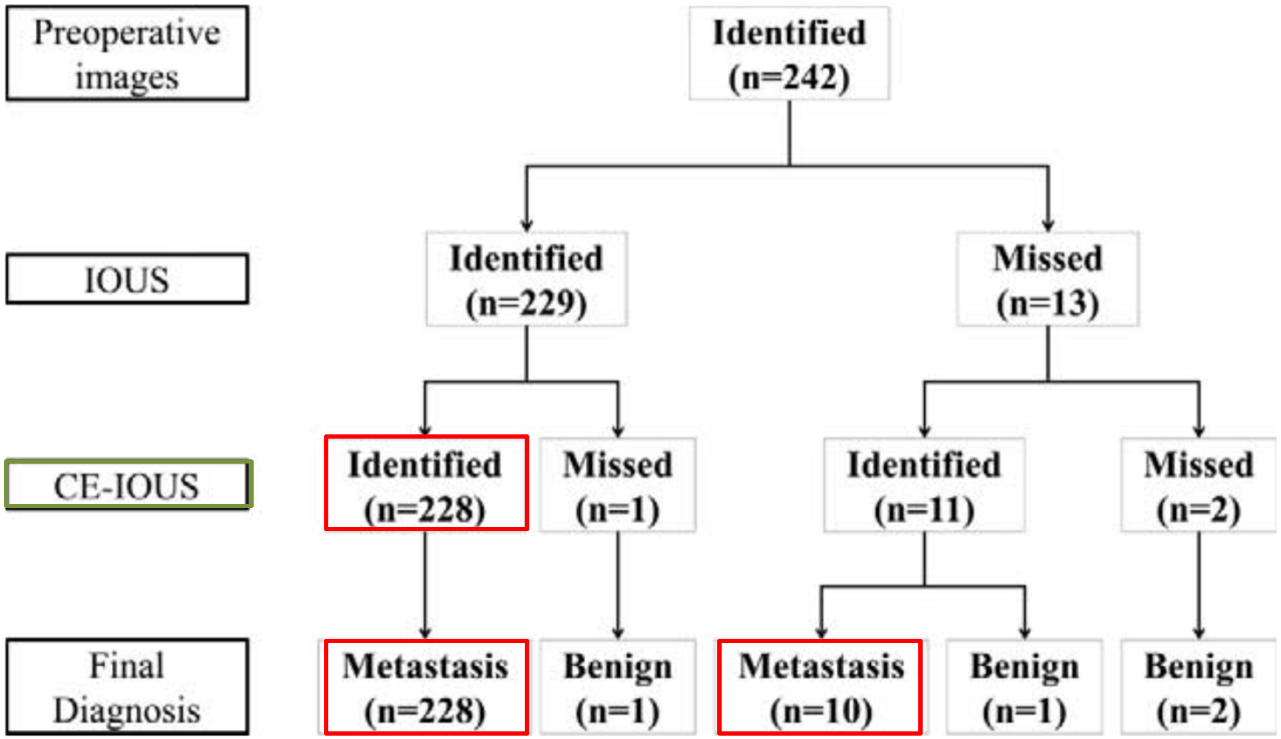
Routine Preoperative Liver-specific Magnetic Resonance Imaging Does Not Exclude the Necessity of Contrast-enhanced Intraoperative Ultrasound in Hepatic Resection for Colorectal Liver Metastasis

Junichi Arita, MD, PhD, Yoshihiro Ono, MD, PhD, Michiro Takahashi, MD, Yosuke Inoue, MD, PhD, Yu Takahashi, MD, PhD, Kiyoshi Matsueda, MD, PhD, and Akio Saiura, MD, PhD

2011-2012

100 pts **CRLM**

IOUS/ CE IOUS Intraoperative (OPEN)



Ann Surgery 2015

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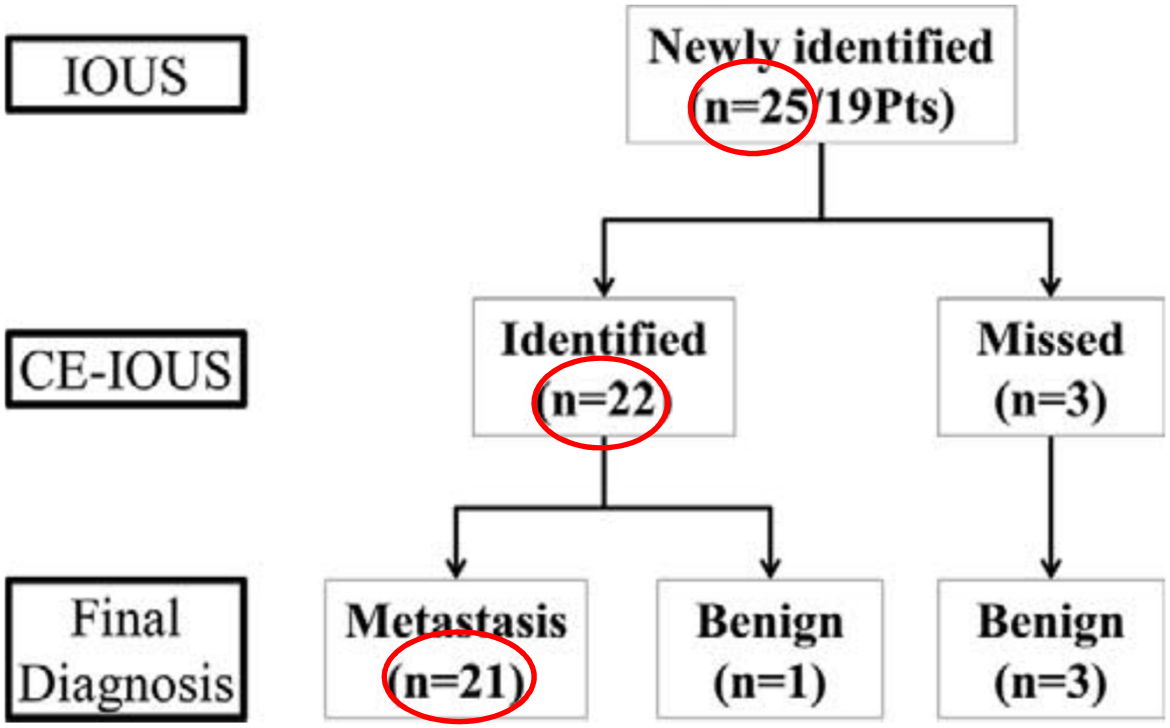
100 pts CRLM

IOUS/ CE IOUS Intraoperative (OPEN)



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100 pts CRLM

TABLE 2. Diagnostic Scores of the Imaging Modalities for Liver Metastases

Imaging Modality	Sensitivity	Positive Predictive Value	Accuracy
EOB-MRI	82% (232/280)	99% (232/235)	83% (242/293)
CE-CT	81% (227/280)	99% (227/230)	81% (237/293)
CEUS	75% (210/280)	98% (210/214)	75% (219/293)
IOUS	89% (249/280)	98% (249/254)	88% (257/293)
CE-IOUS	99% (276/280)	98% (276/283)	97% (283/293)

Planned surgical procedure was modified in 14 pts

Ann Surgery 2015

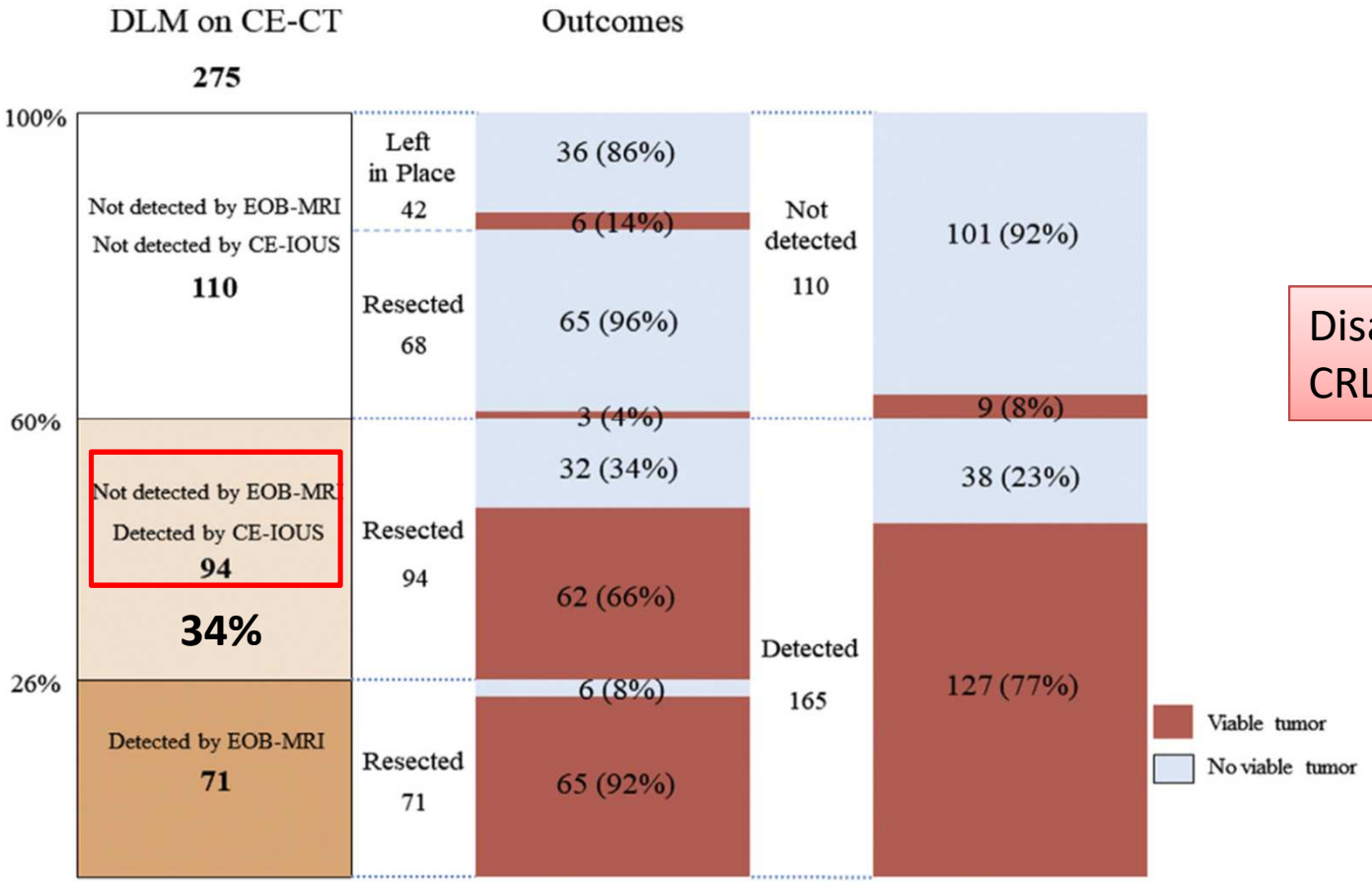
ORIGINAL ARTICLE

Clinical implications of disappearing colorectal liver metastases have changed in the era of hepatocyte-specific MRI and contrast-enhanced intraoperative ultrasonography

Atsushi Oba[1], Yoshihiro Mise[1], Hiromichi Ito[1], Makiko Hiratsuka[2], Yosuke Inoue[1], Takeaki Ishizawa[1], Junichi Arita[1], Kiyoshi Matsueda[2], Yu Takahashi[1] & Akio Saiura[1]

2010-2015

184 pts CRLM underwent hepatic resection



Disappearing CRLM after CT

HPB 2018

ORIGINAL ARTICLE

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Atsushi Oba[1], Yoshihiro Mise[1], Hiromichi Ito[1], Makiko Hiratsuka[2], Yosuke Inoue[1], Takeaki Ishizawa[1], Junichi Arita[1], Kiyoshi Matsueda[2], Yu Takahashi[1] & Akio Saiura[1]

2010-2015

184 pts CRLM underwent hepatic resection

	Preoperative EOB-MRI	Additional CE-IOUS
Sensitivity	0.48 (65/136)	0.93 (127/136)
Specificity	0.96 (133/139)	0.73 (101/139)
PPV	0.92 (65/71)	0.77 (127/165)
NPV	0.65 (133/204)	0.92 (101/110)
Accuracy	0.72 (198/275)	0.83 (225/275)

Only 4% of DLMs invisible on CE-IOUS contained viable disease when resected, and 14% recurred in situ when left during surgery

DLMs should be resected when detected by sequential inspection using EOB-MRI and CE-IOUS that visualize DLMs containing residual tumors.

HPB 2018

ORIGINAL ARTICLE

Contrast-enhanced intraoperative ultrasound improves detection of liver metastases during surgery for primary colorectal cancer

Ankur J. Shah[1], Mark Callaway[2], Michael G. Thomas[3] & Meg D. Finch-Jones[1]

21 pts CRLM

IOUS / CE-IOS during CRC resection (OPEN)

Detection of new lesion in 7 pts

Patient details	CT findings	Laparotomy	IOUS	CE-IOUS	Contrast made a difference?	Change in management	Histology of CRC
Age, years/sex							
73/M	1 cyst	0	2 cysts	2 cysts	No	No	Sigmoid colectomy T3N0
77/F	1 cyst (segment II)	2 cysts (segments II, VI)	1 equivocal (segment II)	1 metastasis (segment II)	Yes	Yes Oxaliplatin-based chemotherapy	Anterior resection T4N0
			2 cysts (segments VI, VII)	2 cysts (segments VI, VII)			
82/F	0	0	2 lesions (segment V); 1 equivocal	Both benign	Yes	Probably	Right hemicolectomy T3N0
61/M	2 metastases (segments II, IV)	2 metastases	4 metastases (1 in segment II, 2 in segment IV, 1 in segment V)	All confirmed as metastases	No	No R2 resection	Abdomino-perineal resection T4N1
30/F	0	1 lesion (segments II) (felt benign)	2 (segment II, metastasis; segment VI, benign)	3 (segment II, metastasis; segment VI, benign; segment VII, metastasis)	Yes	Yes Had neoadjuvant chemotherapy and liver resection	Anterior resection T3N2
77/F	0	1 equivocal lesion (segment II) (soft on palpation)	3 metastases (1 in each of segments II, VI, VII)	Same as IOUS	No	Locally perforated, aided decision not to resect	Palliative bypass
65/M	0	0	1 equivocal	1 benign	Yes	No	Left hemiolectomy. T0N0

C O S C O S C C f

HPB 2010

Intraoperative Ultrasound as a Screening Modality for the Detection of Liver Metastases during Resection of Primary Colorectal Cancer - A Systematic Review

Systematic review **CRLM**: 6 studies

IOUS vs Pre-Op Radiology

Study	Modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)	Number of detected metastases	Additional metastases detected only by IOUS (%)
Studies before 2005 (period 1)								
Machi [19] *n = 84*	IOUS US CE-CT	97.8 p < 0.01[a] 41.3 47.8	94.0 95.5 92.5	91.8 86.4 81.5	98.4 p < 0.01[a] 70.3 72.1	95.4 p < 0.01[a] 73.5 74.3	45 19 22	51
Olsen A.K. [20] *n = 213*	IOUS US	98.3 66.1					354 238	33
Machi [21] *n = 189*	IOUS US CT	93.3 p < 0.001[a] 41.3 47.1	94.7 96.7 94.1	92.4 p < 0.001[a] 89.6 84.5	95.4 p < 0.05[a] 70.9 72.2	94.1 p < 0.001[a] 74.2 75.0	97 43 49	50
Stadler [22] *n = 85*	IOUS US/CE-CT	89.9 p < 0.001[a] 48.5	98.3 93.3				62 27	57
Rafaelsen [25] *n = 295*	IOUS US	94.1 p < 0.0001[a] 63.7	97.8 92.0				192 130	32
Study after 2005 (period 2)								
Mazzoni [34] *n = 167*	IOUS US CE-CT	– 56 49	– 94 92				84 47 41	44

Additional lesions 32% -57%

Ultrasound international 2017

Intraoperative Ultrasound as a Screening Modality for the Detection of Liver Metastases during Resection of Primary Colorectal Cancer - A Systematic Review

ic Review **CRLM**: 7 studies

pic US vs Pre-Op Radiology

Study	Imaging modality	Number of detected metastases	Number of metastases detected only by LUS (%)
Studies before 2005 (Period 1)			
Foley [30] *n = 13*	LUS IOUS	4 5	0
Marchesa [26] *n = 22*	LUS CE-CT	8 7	13
Milsom et al. [32] *n = 77*	LUS CE-CT	51 50	2
Per patient analysis			
Study	Imaging modality	Number of patients with detected metastases	Number of patients with metastases only detected by LUS (%)
Studies before 2005 (period 1)			
Goletti [29] *n = 33*	LUS CE-CT	8 5	9
Hartley [31] *n = 76*	LUS US MRI	5 0 2	4
Studies after 2005 (period 2)			
Skrovina [35] *n = 70*	LUS CE-CT	14 6	11
Itabashi [37] [a] *n = 148*	LUS + CE-LUS CE-CT MRI	4 0 0	3

Laparoscopic US

Sensitivity 80%
Specificity 91%

Additional lesions 2% -13%

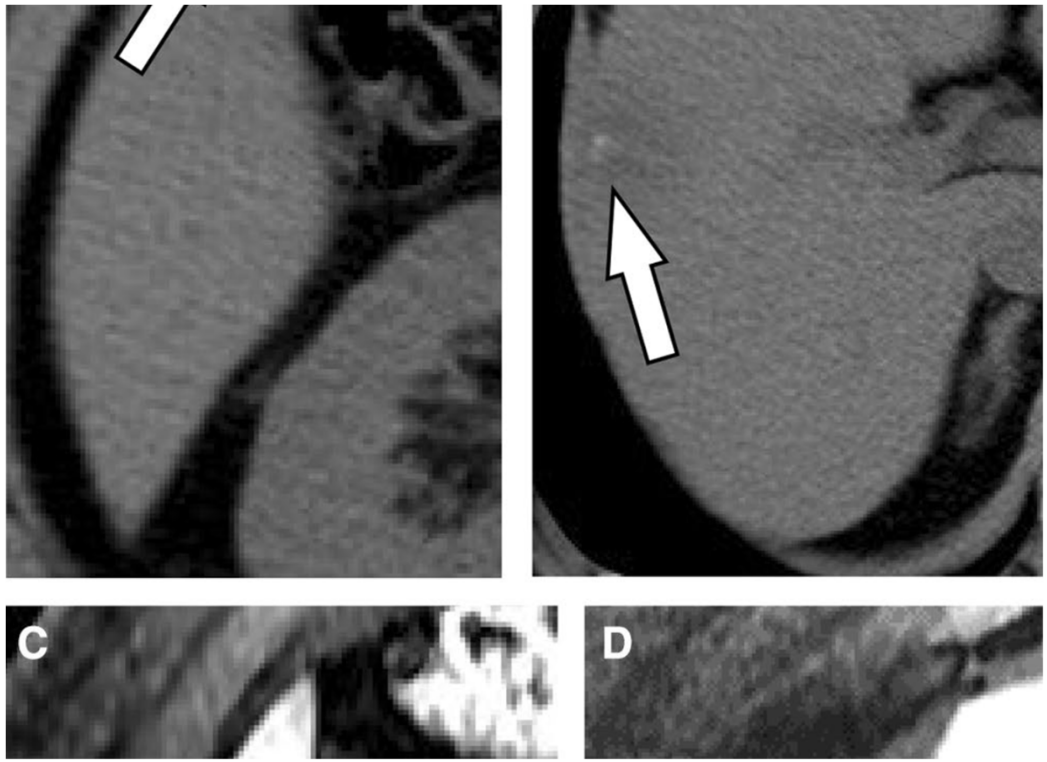
Ultrasound international 2017

Contrast-enhanced intraoperative ultrasound in the resection of colorectal liver metastases with intrabiliary growth

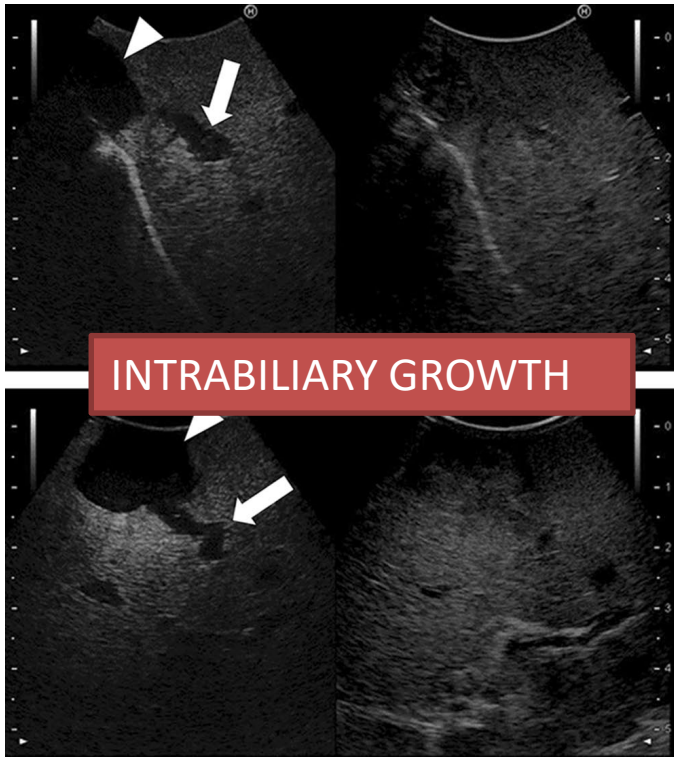
Junko Hiroyoshi[1] · Suguru Yamashita[1] · Mariko Tanaka[2] · Akimasa Hayashi[2] · Tetsuo Ushiku[2] · Junichi Kaneko[1] · Nobuhisa Akamatsu[1] · Junichi Arita[1] · Yoshihiro Sakamoto[1] · Kiyoshi Hasegawa[1]

68 yrs ; M
LMs from rectal cancer

Pre-op MRI Sg V-Sg VII



CE-IOUS (Kupffer phase)



Clin J of gastroenterology 2018

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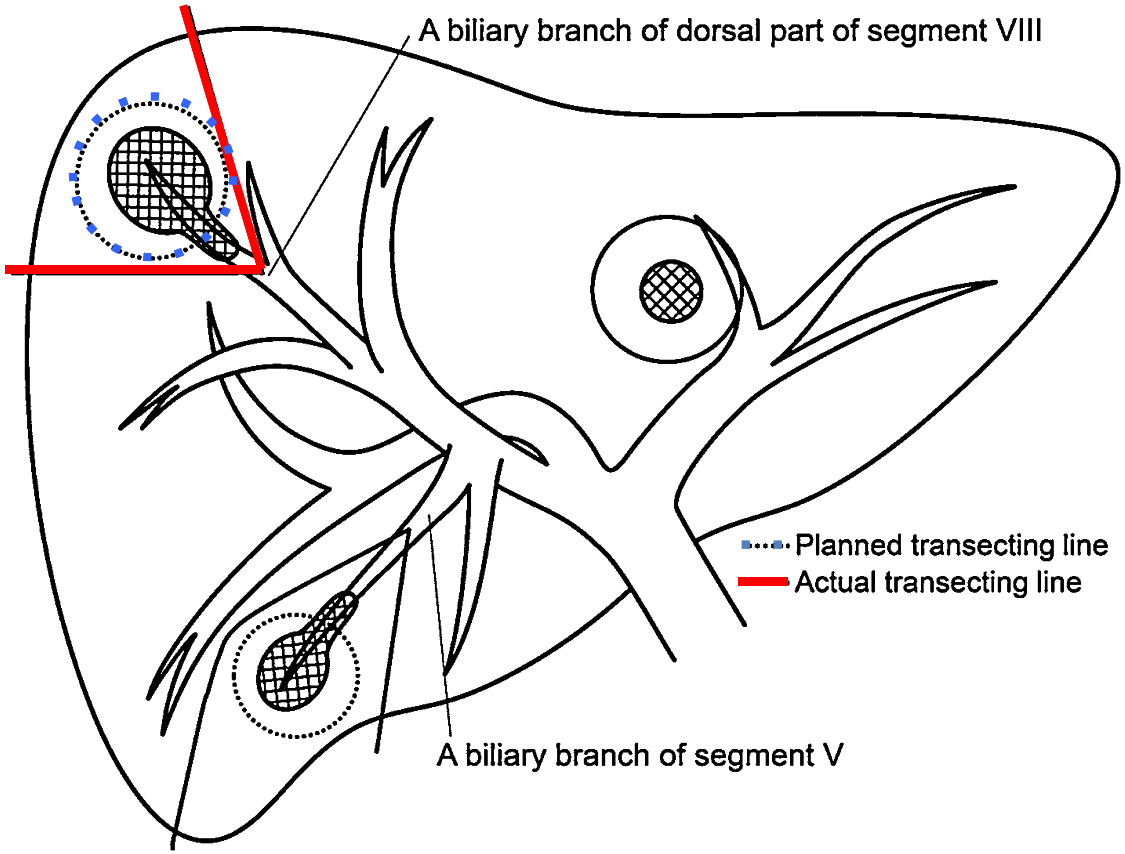


Clear visualization of extent of intrabiliary growth using CE-IOUS guide
CURATIVE RESECTION and **CHANGE PLANNED SURGERY**

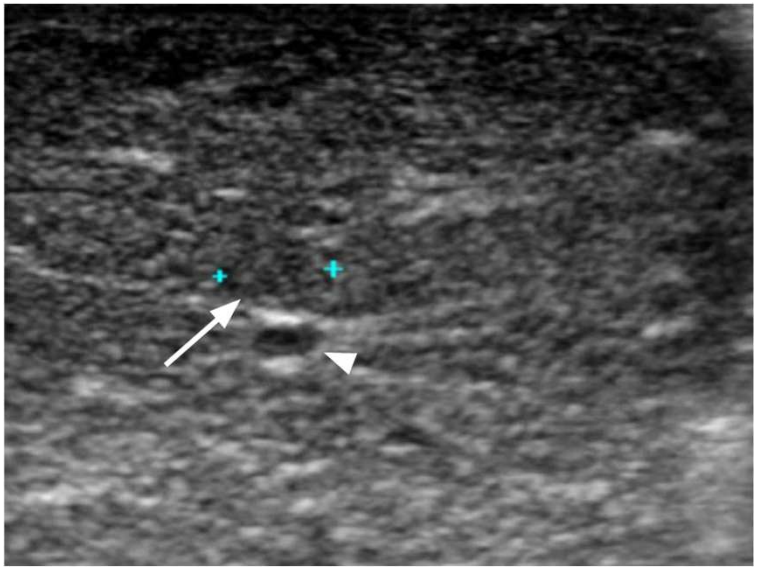
Clin J of gastroenterology 2018

Why intraoperative ultrasound?

HCC is usually associated with cirrhosis

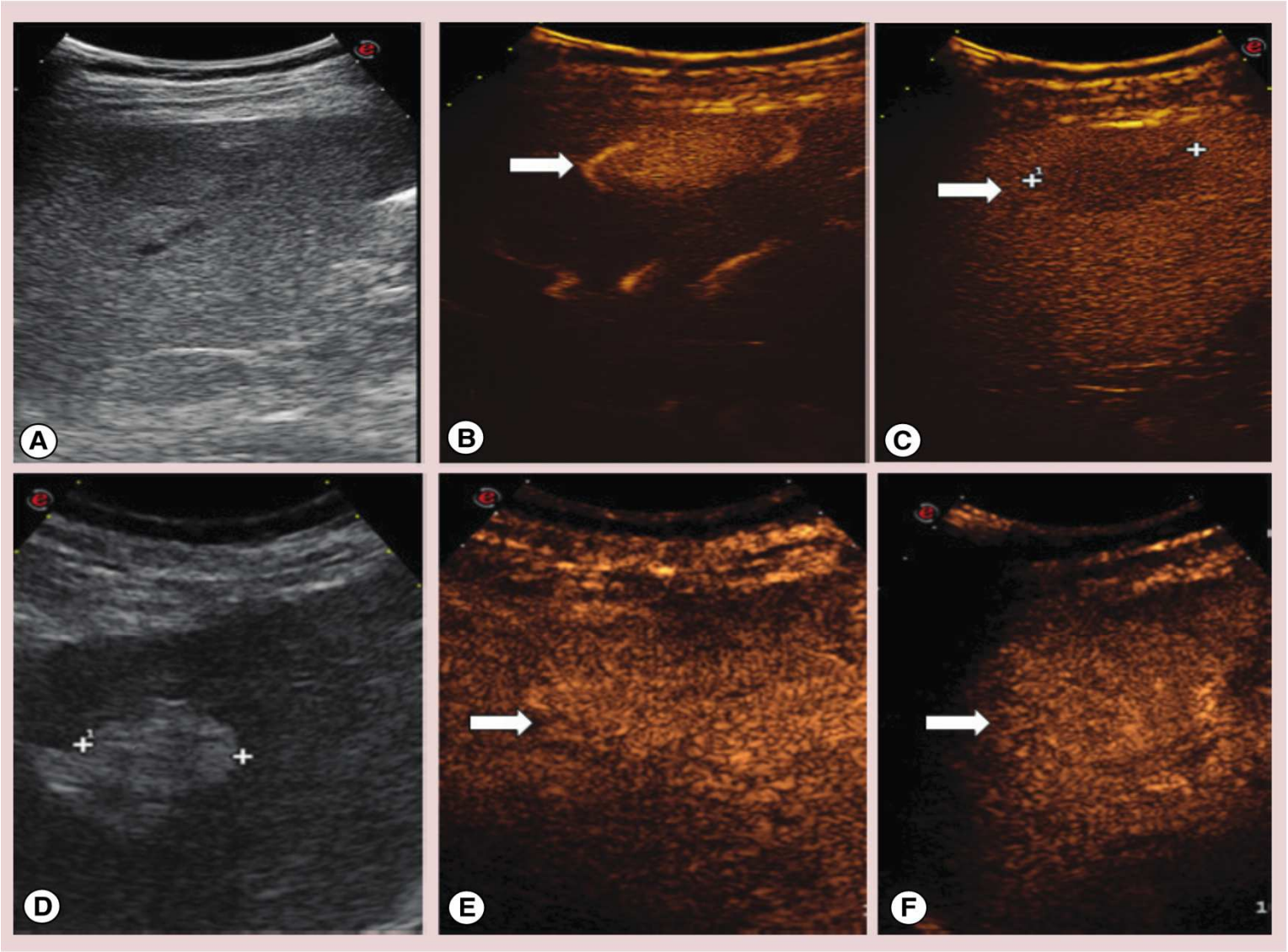
Hepatic tumorectomy or local tumor ablation under **IOUS** localization and guidance can be performed in order to minimize the volume of the liver parenchyma removed, while still achieving oncological radicality

Contrast-enhanced IOUS (CE-IOUS) can be of use in the differential diagnosis of indeterminate nodules of this type and may help improve the detection rate of small HCCs



Ultrasonography 2015

Arterial phase *Late phase*



Typical vascular pattern of HCC

Atypical vascular pattern of HCC

Hepat Oncology 2015

Intraoperative US and contrast-enhancement intraoperative US during hepatic for HCC patients with cirrhosis resection

2014-2016
21 HCC pts underwent hepatic resection
27 lesions

Characteristic	Pre-US	Intra-US	P value
N of tumor			
- Mean	21	**27**	0.031
- Median	1(1)	1.19 (1-2)	
Tumor size			
- Mean	19.8	21.9	<0.001
- Median	21.5	23.5	

6 additional lesions

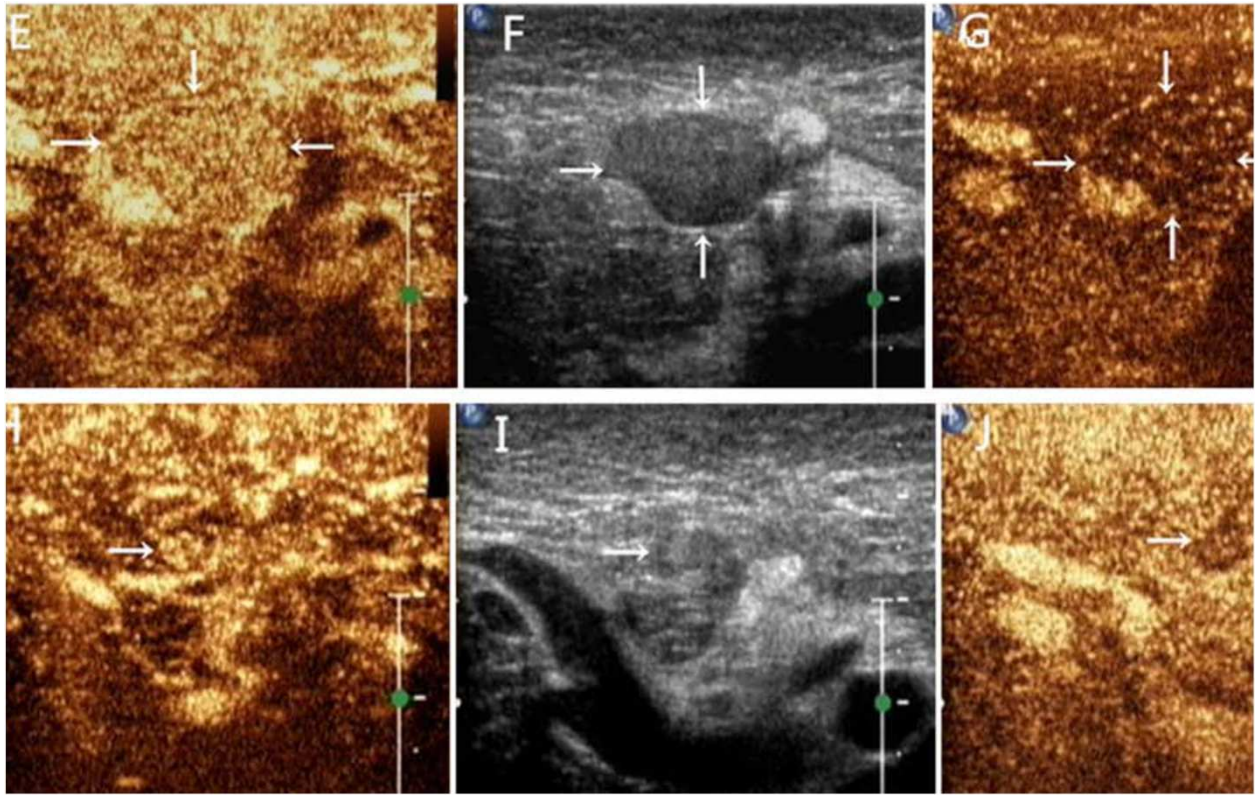
- 3 moderately differentiated HCC
- 1 CCA
- 2 high grade dysplastic nodule

Additional lesions change plan treatment in 28.6%

Clinical Hemor and Micro 2018

Intraoperative US and contrast-enhancement intraoperative US during hepatic for HCC patients with cirrhosis resection

2014-2016
21 HCC pts underwent hepatic resection
27 lesions



IOUS- CE IOUS confirm pre-TC

IOUS- CE IOUS detect additional 0.6 cm nodule not identified at pre-TC

Clinical Hemor and Micro 2018

Ultrasound-Guided Intraoperative Radiofrequency Ablation and Surgical Resection for Liver Metastasis from Malignant Gastrointestinal Stromal Tumors

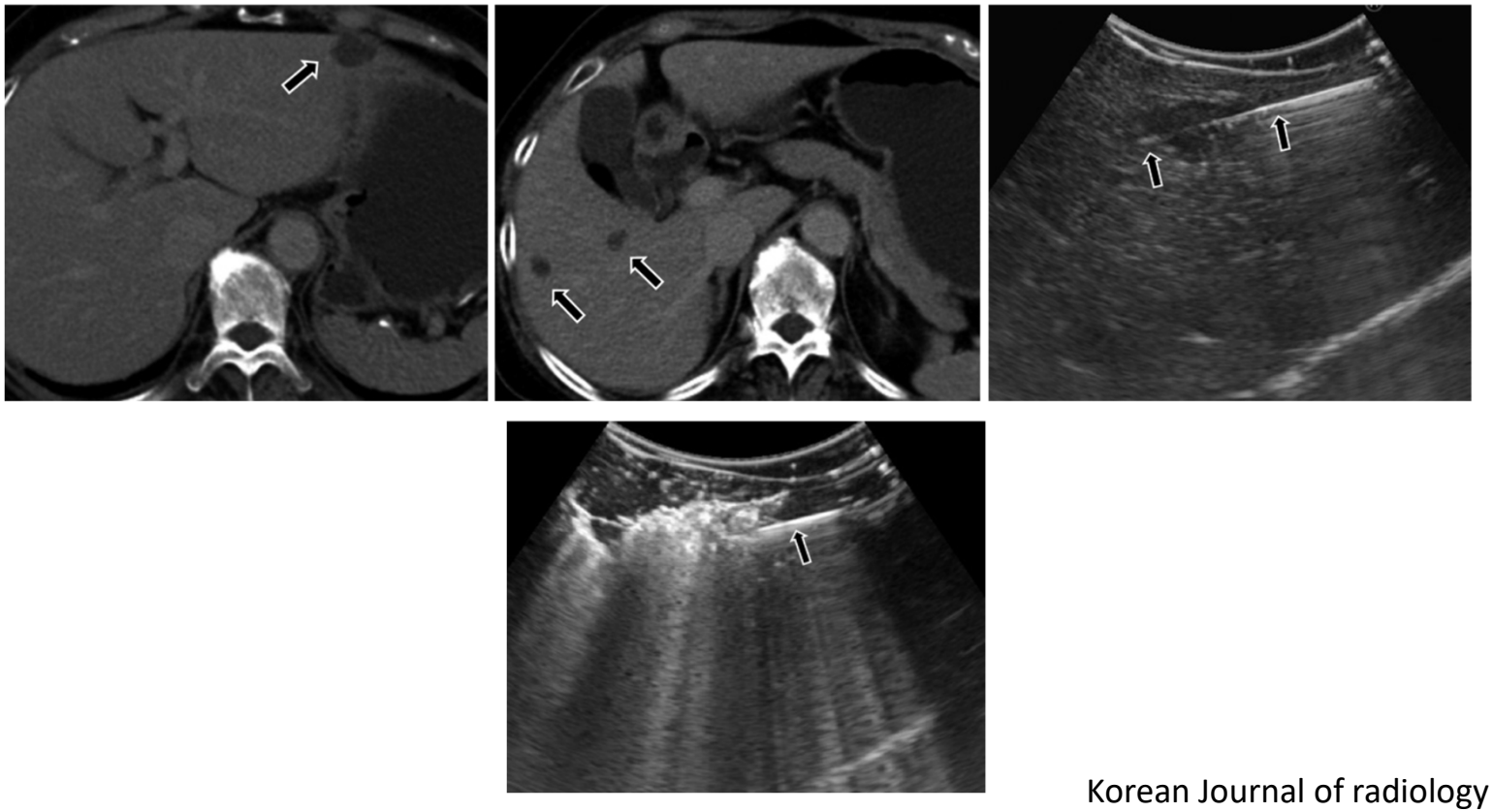
In Sun Yoon, BSE, MD[1], Ji Hoon Shin, MD, PhD[1], Kichang Han, MD, PhD[1], Pyo Nyun Kim, MD, PhD[1], Ki Hun Kim, MD, PhD[2], Yoon-Koo Kang, MD, PhD[3], Heung Kyu Ko, MD, PhD[1]

Departments of [1]Radiology, [2]Surgery, and [3]Oncology, Asan Medical Center, Ulsan University College of Medicine, Seoul 05505, Korea

2009-2019, 24 pts with liver metastasis from GIST

Open laparotomy

RFA ± resection



Korean Journal of radiology 2018

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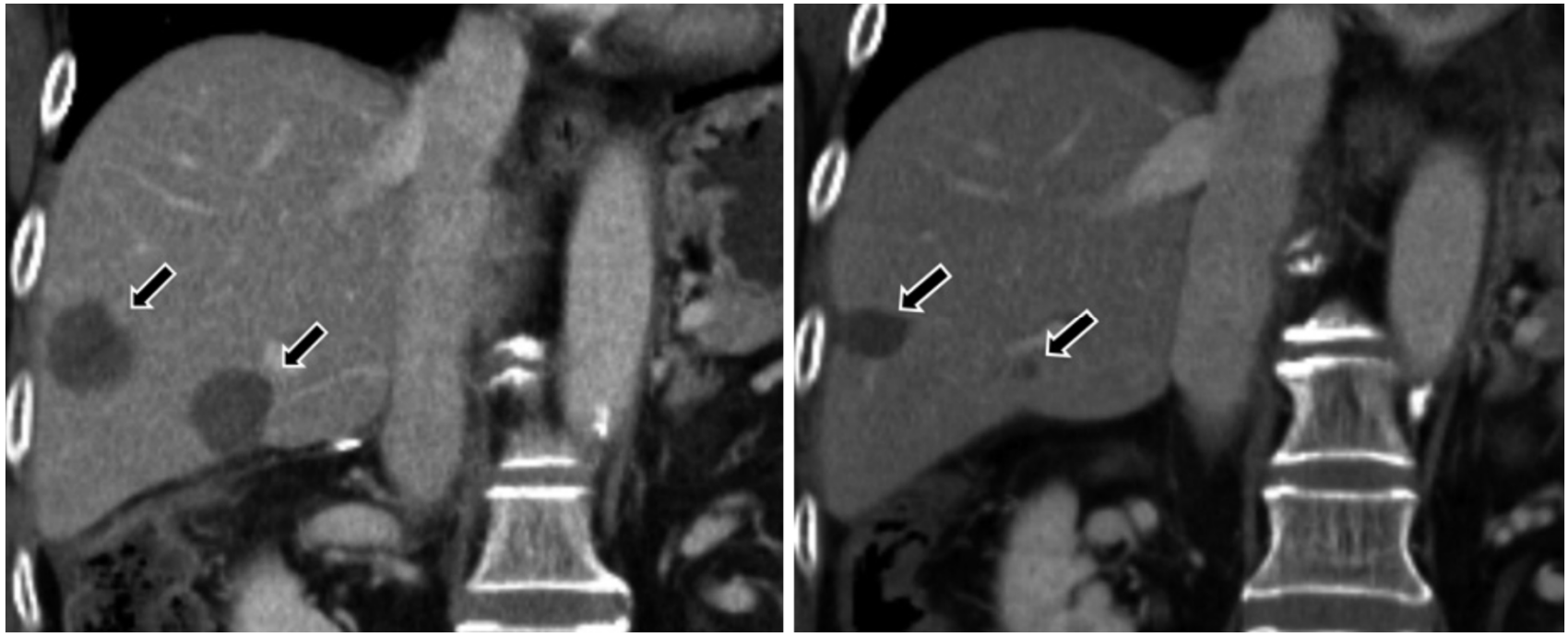
7 days after RFA

13 months after RFA: no tumor progression



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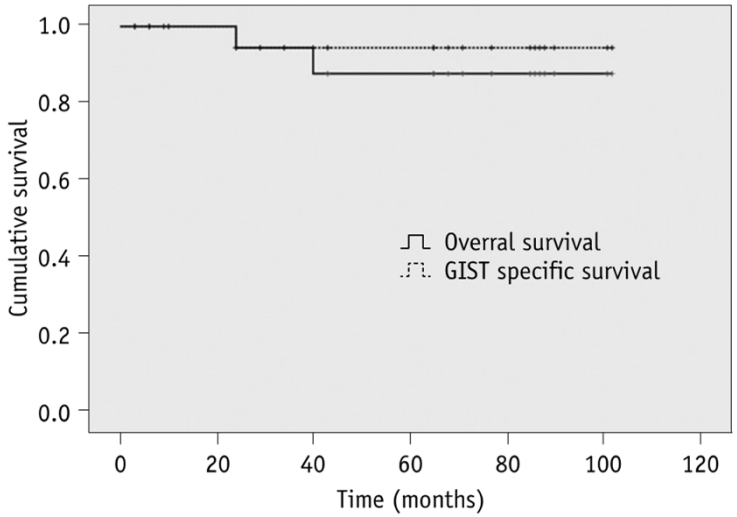
Departments of [1]Radiology, [2]Surgery, and [3]Oncology, Asan Medical Center, Ulsan University College of Medicine, Seoul 05505, Korea

No.	Response of IORFA	Major Complication	Recurrence	Imatinib after IORFA	Follow-Up Period (Months)	Alive/Death	Cause of Death
1	Complete	-	-	+	40	Death	Pulmonary emphysema
2	Complete	-	-	+	85	Alive	
3	Complete	-	-	+	77	Alive	
4	Complete	-	+*	+	102	Alive	
5	Complete	-	-	+	88	Alive	
6	Complete	-	-	+	101	Alive	
7	Complete	-	+†	+	24	Death	Tumor progression
8	Complete	-	+‡	+	87	Alive	
9	Complete	-	-	+	86	Alive	
10	Complete	-	-	+	68	Alive	
11	Complete	-	-	+	90	Alive	
12	Complete	-	-	+	71	Alive	
13	Complete	-	-	+	65	Alive	
14	Complete	-	-	+	65	Alive	
15	Complete	-	-	+	43	Alive	
16	Complete	-	-	+	34	Alive	
17	Complete	Biliary stricture	-	+	24	Alive	
18	Complete	-	-	+	10	Alive	
19	Complete	Abscess	-	+	9	Alive	
20	Complete	-	-	+	6	Alive	
21	Complete	-	-	+	3	Alive	
22	Complete	-	-	+	29	Alive	
23	Complete	-	-	+	6	Alive	
24	Complete	-	-	+	3	Alive	
					50.7 ± 34.7		



US guide RFA and resection may be complementary, helping to obtain complete response in unresecable liver mestastasis to GIST

Korean Journal of radiology 2018

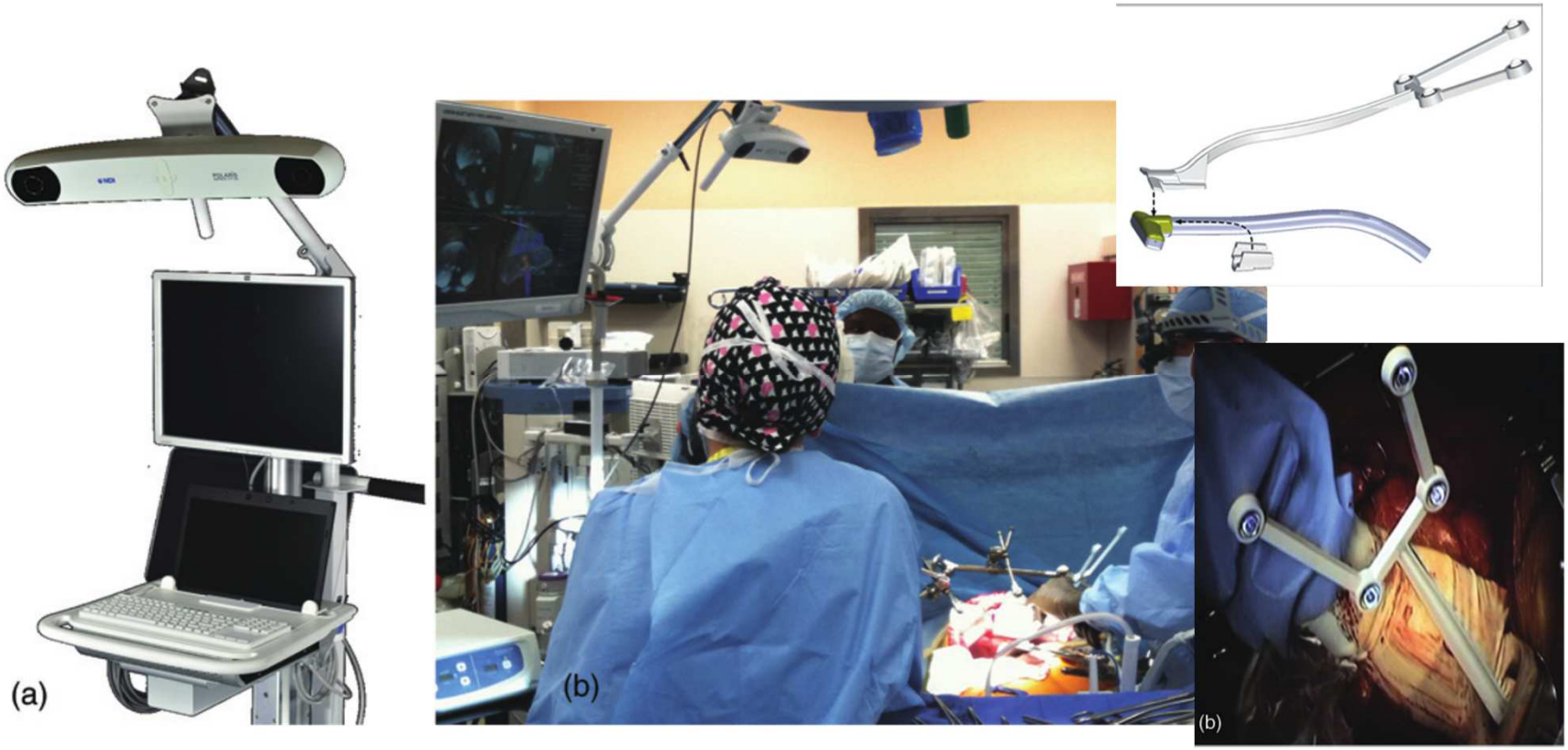
Why intraoperative ultrasound?

- To detect new lesions/vanishing lesions
- **To guide liver surgery (ablation, resection)**
- To check ablation efficacy

ORIGINAL ARTICLE

Image-guided liver surgery: intraoperative projection of computed tomography images utilizing tracked ultrasound

T. Peter Kingham[1], Michael A. Scherer[2], Benjamin W. Neese[2], Logan W. Clements[2], James D. Stefansic[2] & William R. Jarnagin[1]

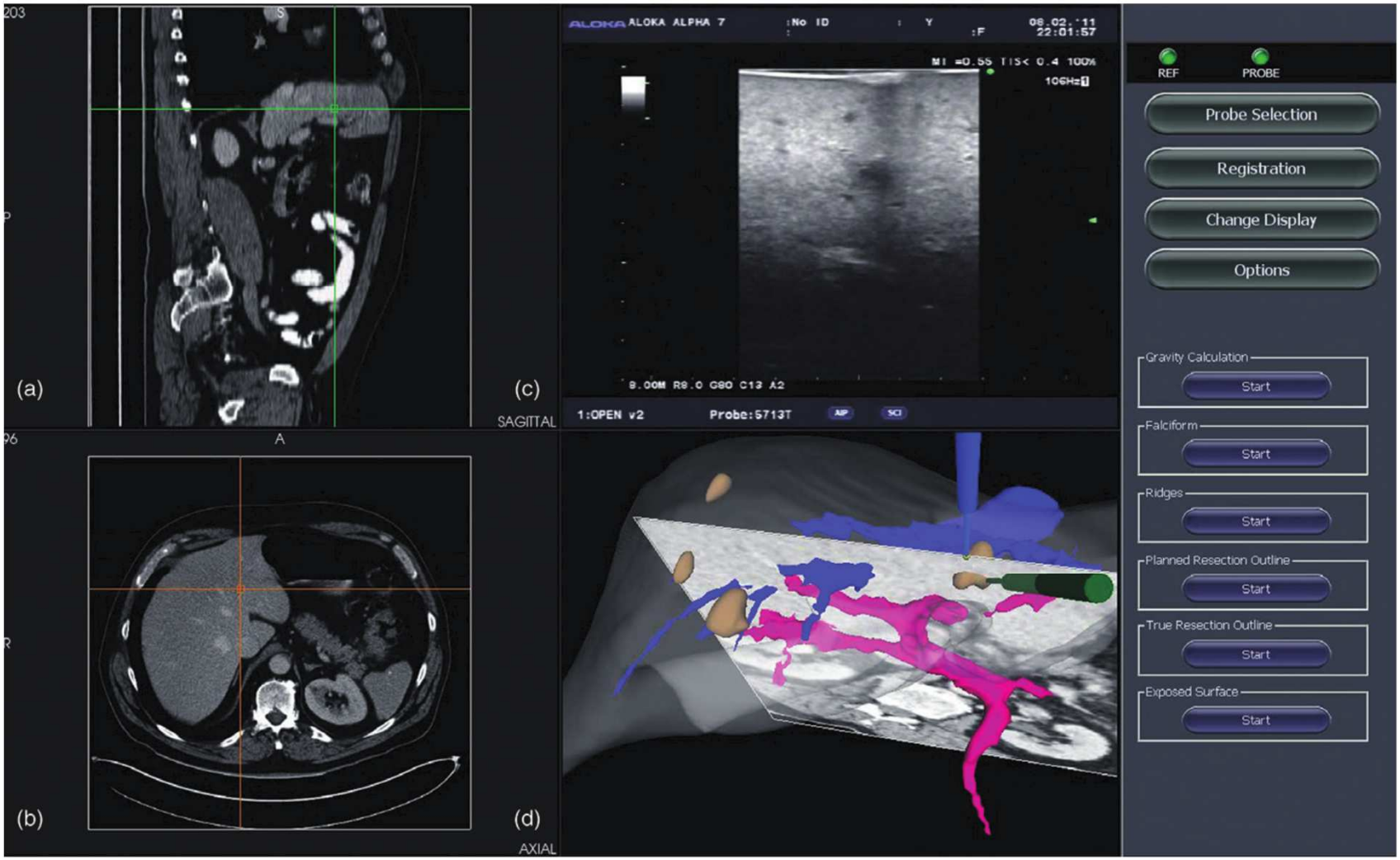


The system combines pre-operative imaging, IOUS and real time instrument tracking to guide liver surgery

HPB 2012

Explorer Liver Imagine Guide

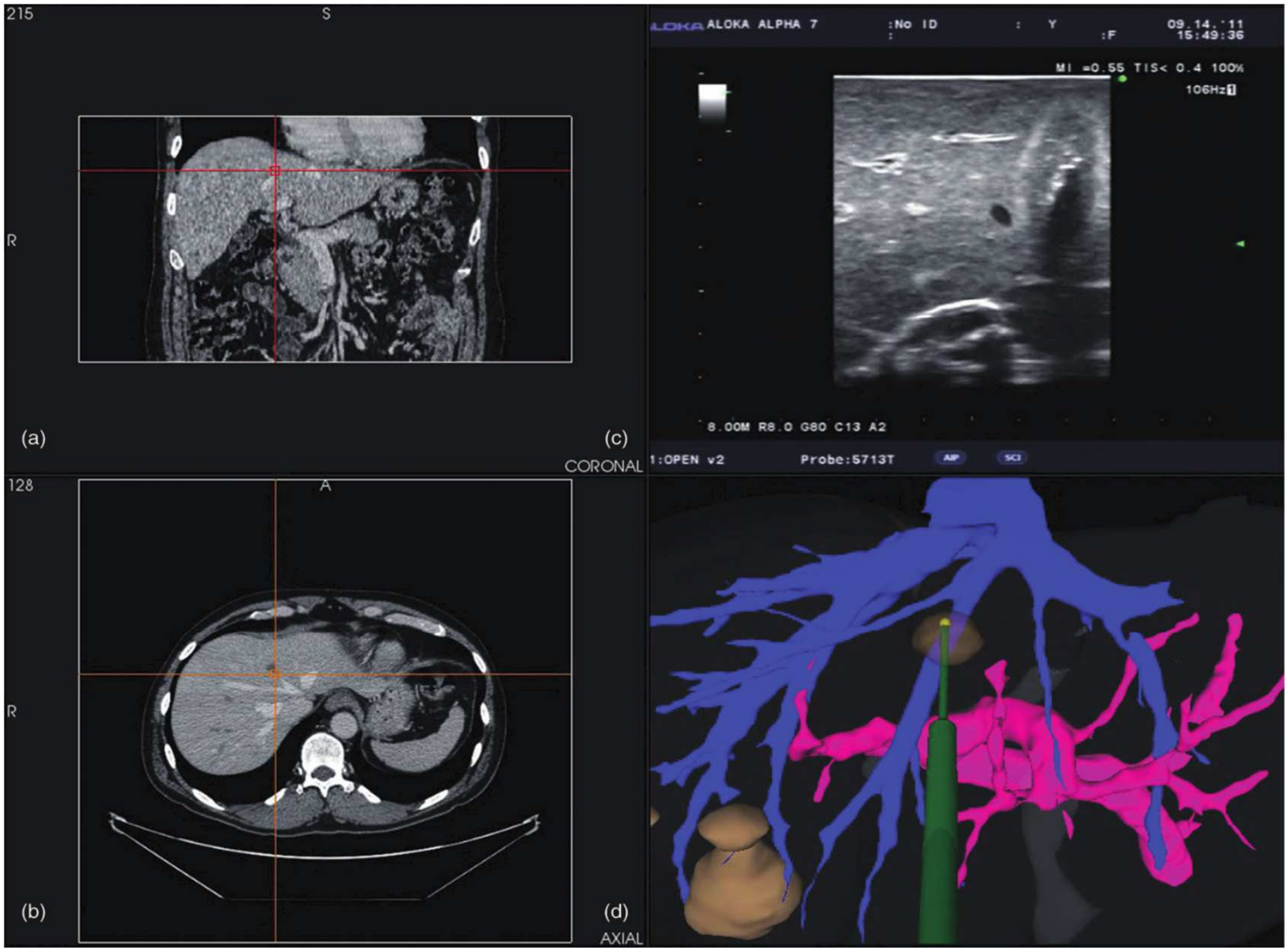
65 yrs, M. Multiple bilobar CRLM
Planning: right hepatectomy + ablation left lobe



HPB 2012

Explorer Liver Imagine Guide

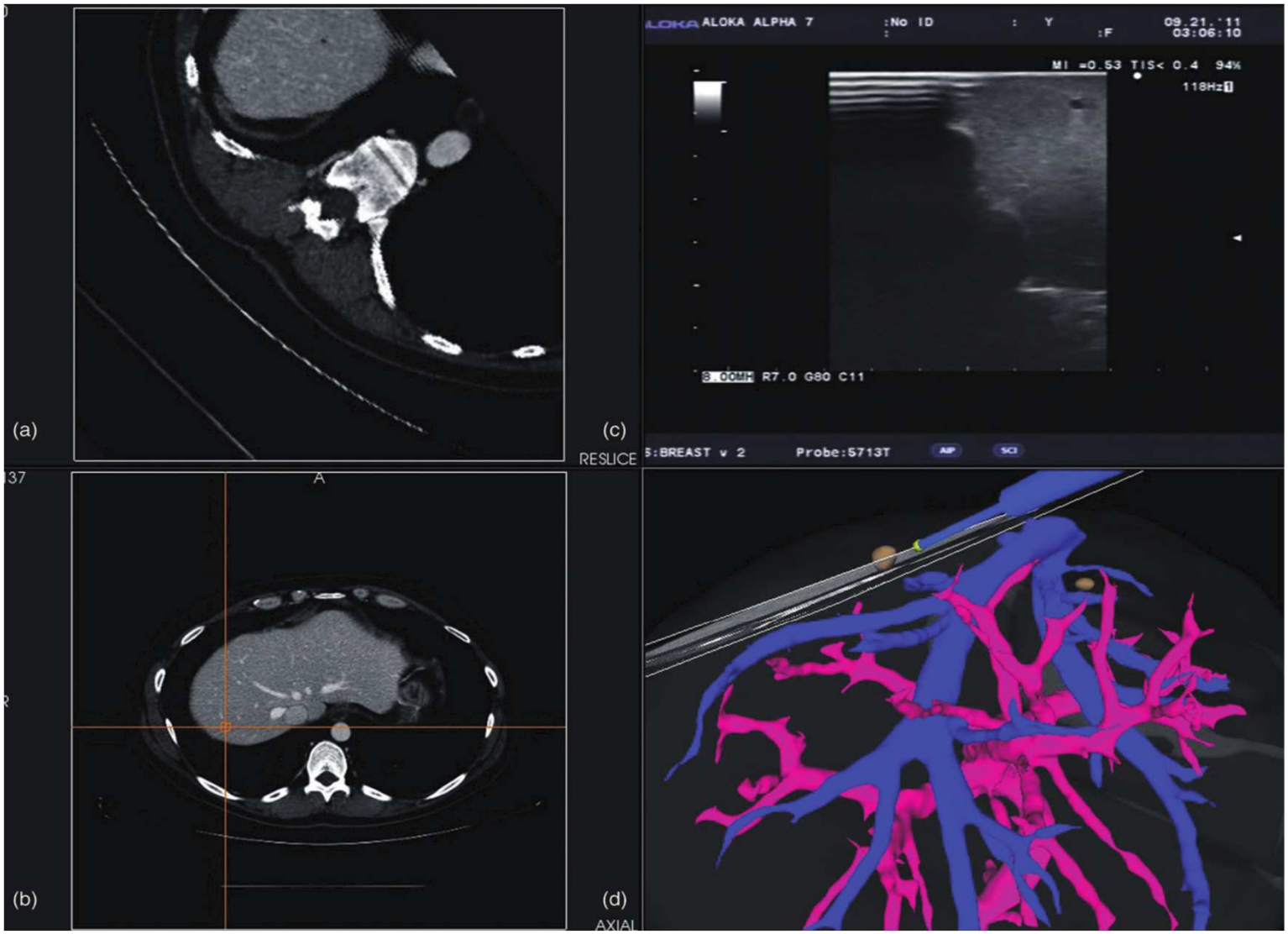
54 yrs, M. Multiple bilobar CRLM
Planning: wedge resection + ablation



HPB 2012

Explorer Liver Imagine Guide

46 yrs, M, CRLM Sg VI + Sg II and VII (cysts)
Planning: wedge resection + ablation



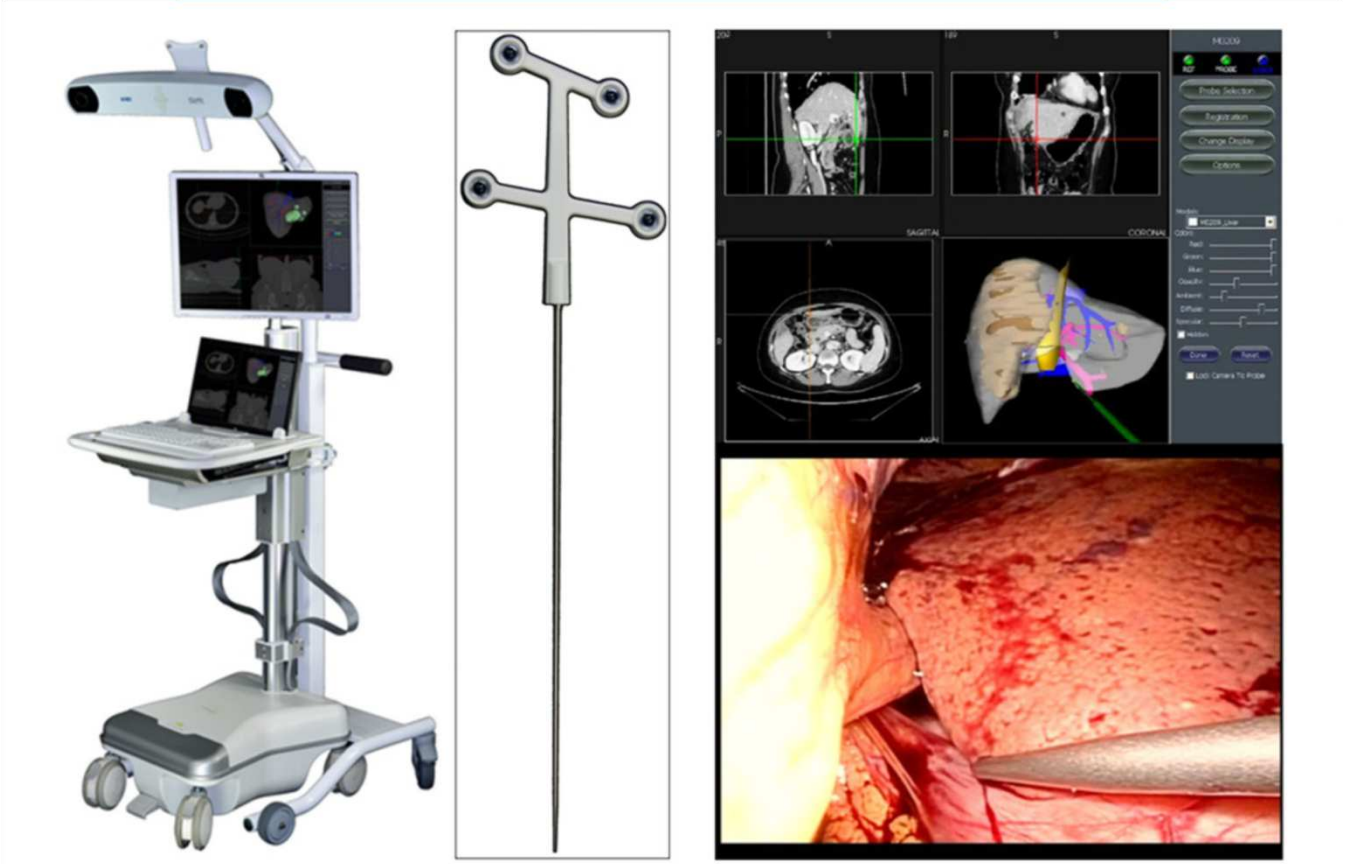
HPB 2012

Surg Innov 2014

Evaluation of a Minimally Invasive Image-Guided Surgery System for Hepatic Ablation Procedures

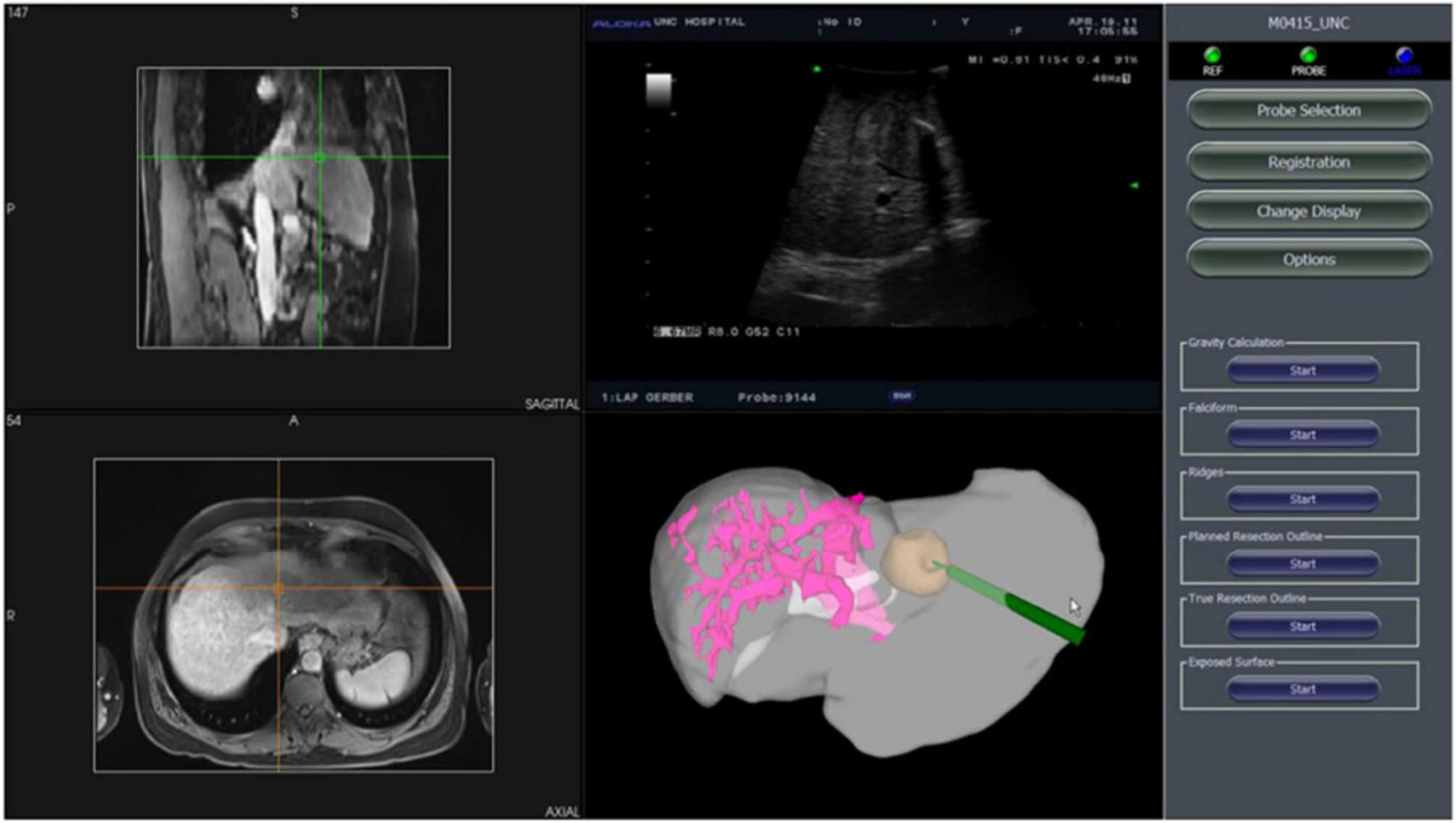
Chet W. Hammill, MD[1,5], **Logan W. Clements, PhD**[2], **James D. Stefansic, PhD**[3], **Ronald F. Wolf, MD**[1,5], **Paul D. Hansen, MD**[1,5], and **David A. Gerber, MD**[4]

Explorer Minimally Invasive Liver (MIL) system



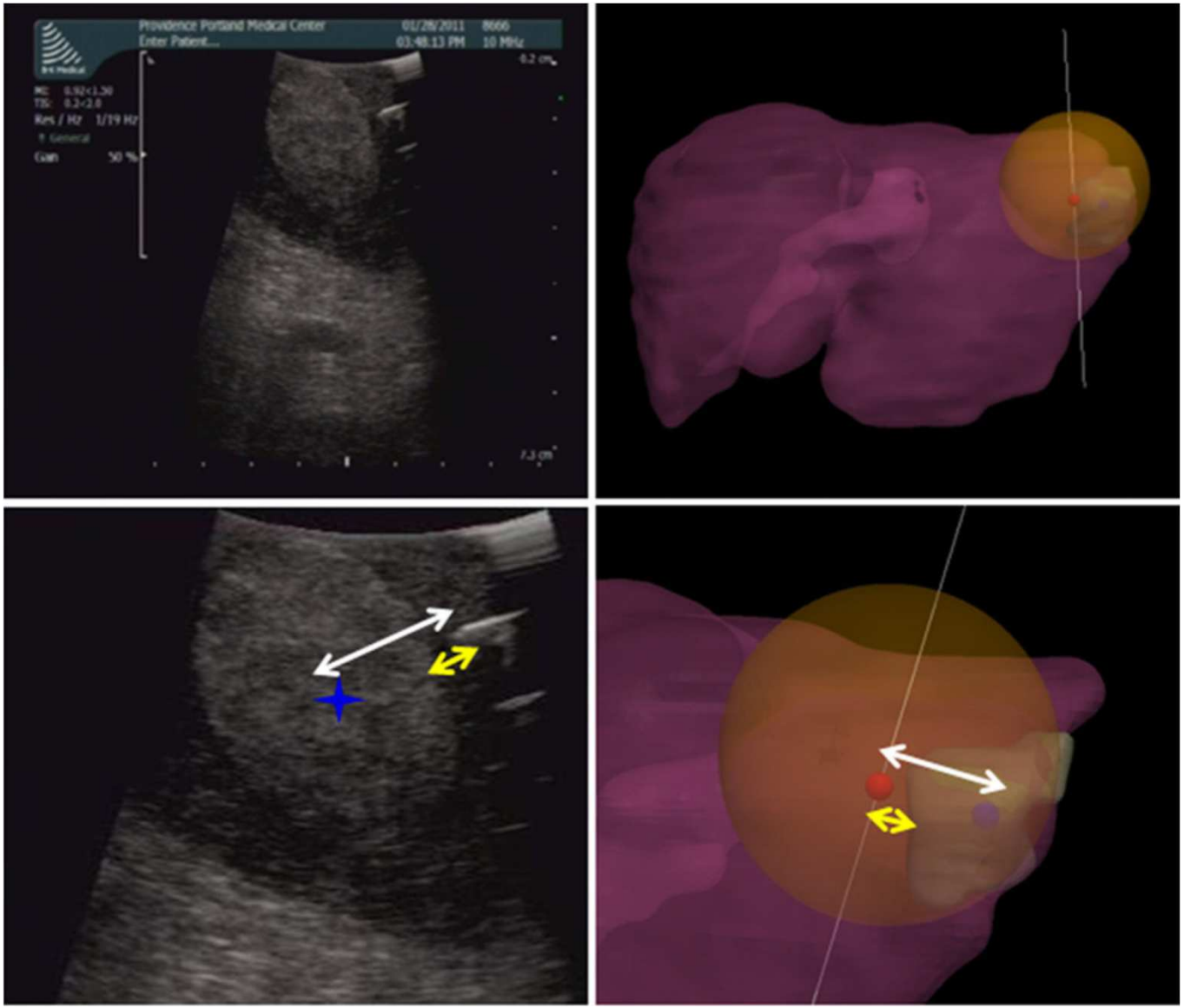
Experimental 3D image-guidance system intended to be use in conjunction with iUS during LAPAROSCOPIC liver ablation

Explorer Minimally Invasive Liver (MIL) system



Surg Innov 2014

Explorer Minimally Invasive Liver (MIL) system



Projected ablation zone

Tumor center

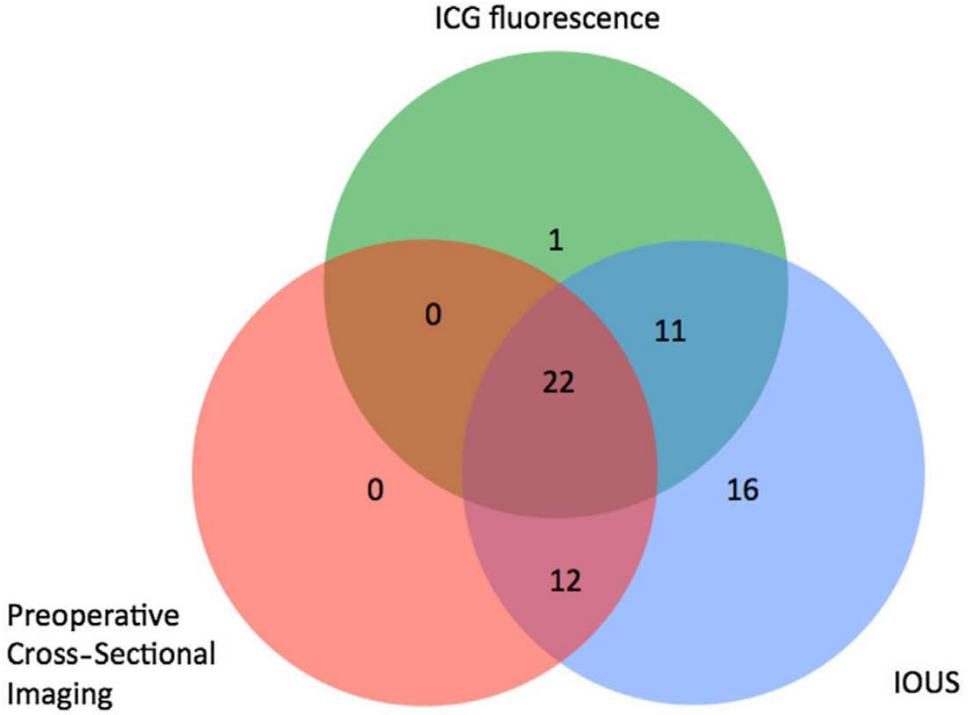
Probe tip

Surg Innov 2014

An Initial Report on the Intraoperative Use of Indocyanine Green Fluorescence Imaging in the Surgical Management of Liver Tumors

HIDEO TAKAHASHI, MD,[1] NISAR ZAIDI, MD,[2] AND EREN BERBER, MD[1,2]*
[1]Department of General Surgery, Cleveland Clinic, Ohio
[2]Department of Endocrine Surgery, Cleveland Clinic, Ohio

ICG administrated 24-48 hours before surgery



Patient	Preoperative study	Number of lesions detected IOUS	ICG
1	1	1	0
2	1	1	1
3	3	14	14
4	1	1	1
5	2	2	2
6	6	8	5
7	1	1	1
8	5	7	0
9	2	2	0
10	4	16	4
11	1	1	1
12	1	1	0
13	4	4	2
14	2	N/A	N/A
15	2	2	3
Total	36	61	34

J Surg Oncology 2016

An Initial Report on the Intraoperative Use of Indocyanine Green Fluorescence Imaging in the Surgical Management of Liver Tumors

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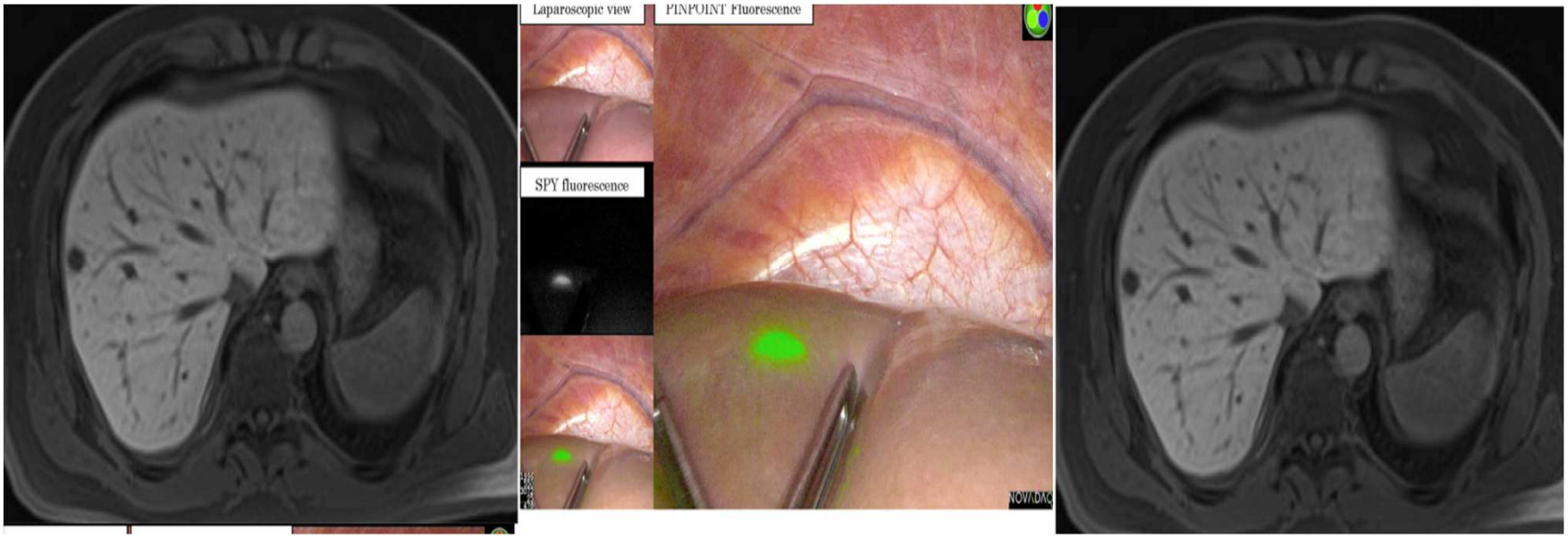
[1]Department of General Surgery, Cleveland Clinic, Ohio
[2]Department of Endocrine Surgery, Cleveland Clinic, Ohio

2014-2016
15 cases underwent liver surgery



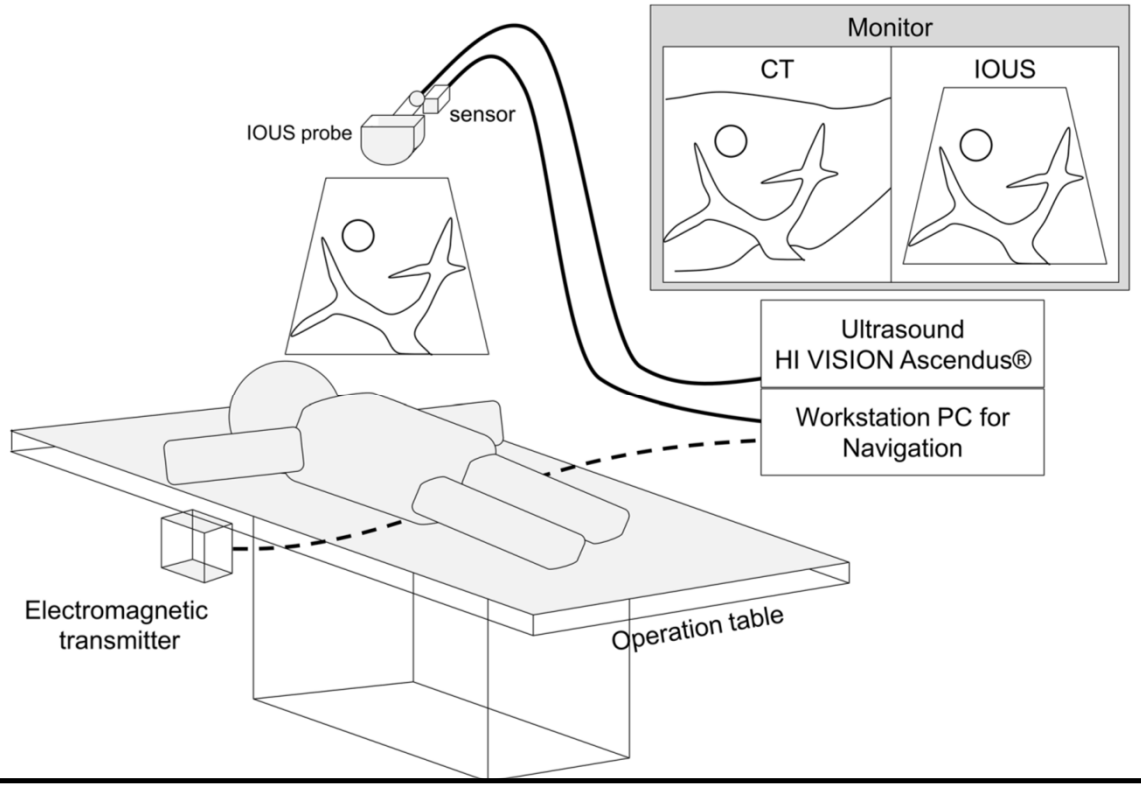
Indocyanine green is a good adjunct to I.O ultrasound in demostrating superficial lesions and guide resection

J Surg Oncology 2016

Feasibility of Intraoperative Navigation for Liver Resection Using Real-time Virtual Sonography With Novel Automatic Registration System

Takeshi Takamoto[1] · Yoshihiro Mise[2] · Shouichi Satou[3] · Yuta Kobayashi[4] · Koui Miura[5] · Akio Saiura[2] · Kiyoshi Hasegawa[4] · Norihiro Kokudo[4] · Masatoshi Makuuchi[1]

RVS real time navigation system

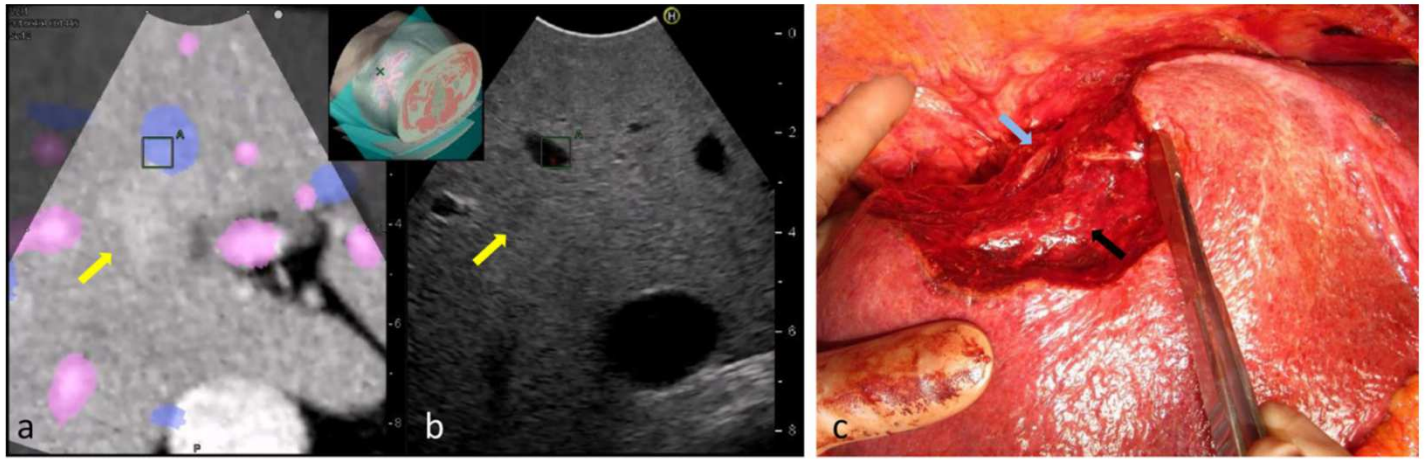


A combination of I.O ultrasonography and electromagnetic tracking technology
Ultrasound scanner + convex type US probe + electromagnetic device + workstation

WJ of Surgery 2017

Feasibility of Intraoperative Navigation for Liver Resection Using Real-time Virtual Sonography With Novel Automatic Registration System

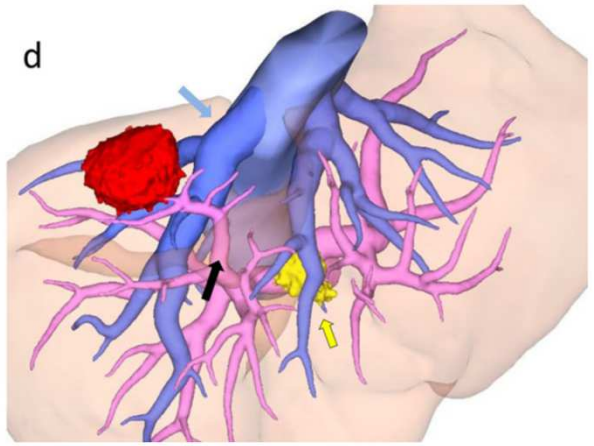
Takeshi Takamoto[1] · Yoshihiro Mise[2] · Shouichi Satou[3] · Yuta Kobayashi[4] · Koui Miura[5] · Akio Saiura[2] · Kiyoshi Hasegawa[4] · Norihiro Kokudo[4] · Masatoshi Makuuchi[1]



72 yrs, M

HCC Sg VIII + suspected lesion Sg IV-V

<u>Anatomical resection Sg VIII</u>



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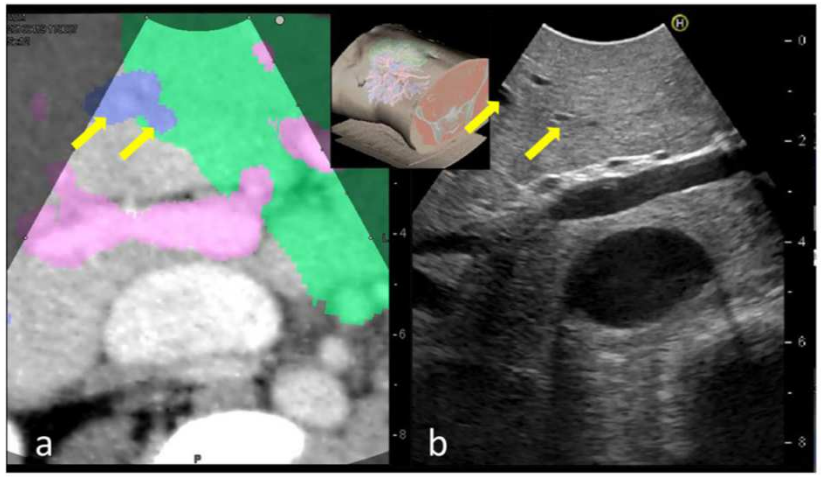
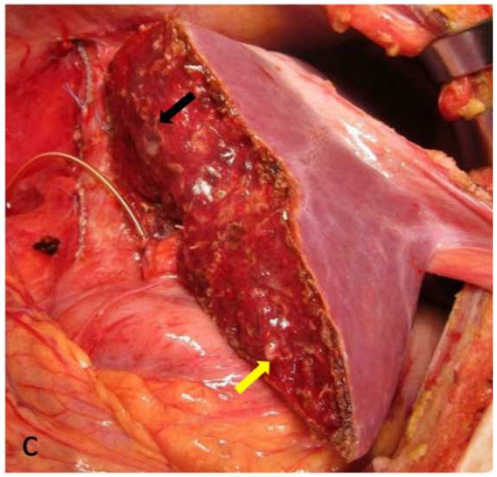
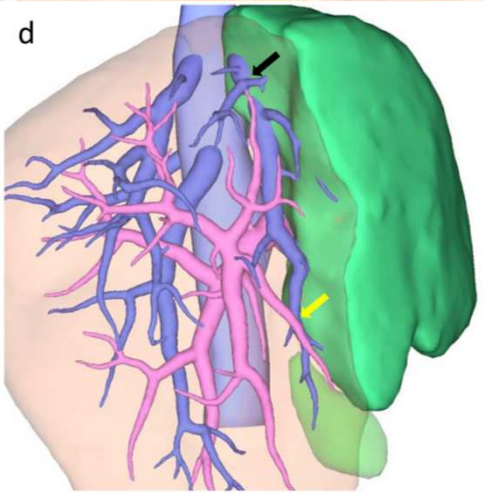






29 yrs, F

Living donor

Right hepatectomy

WJ of Surgery 2017

Intraoperative ultrasonography of robot-assisted laparoscopic hepatectomy: initial experiences from 110 consecutive cases

Peng Zhu[1] · Wei Liao[1] · Ze-yang Ding[1] · Hong-chang Luo[2] · Bin-hao Zhang[1] · Wan-guang Zhang[1] · Wei Zhang[1] · Zhan-guo Zhang[1] · Bi-xiang Zhang[1] · Xiao-ping Chen[1]

2014-2015

110 robotic liver resection

Pathological diagnoses	
Hepatocellular carcinoma	63
Cholangiocarcinoma	6
Metastatic carcinoma	6
Hemangioma	20
Focal nodular hyperplasia	6
Others	9
Types of hepatectomy performed	
Segment 1/2/3/4/5/6/7/8/	1/1/1/6/9/8/1/6
Segment 2,3/2,3,4/5,6,7,8 resection	30/8/3
Segment 5,8/6,7/4b, 5/5,6 resection	6/23/4/5
Operation time (min)	216.7 ± 91.7
Total blood loss (mL)	50–2000 (375)
Numbers of transfused patients	23
Units of blood transfused#(units)	2.35 ± 1.17
Overall complications	
Grade 1/2	1/25
Grade 3/4/5	9/0/0

11 additional lesion detected I.O

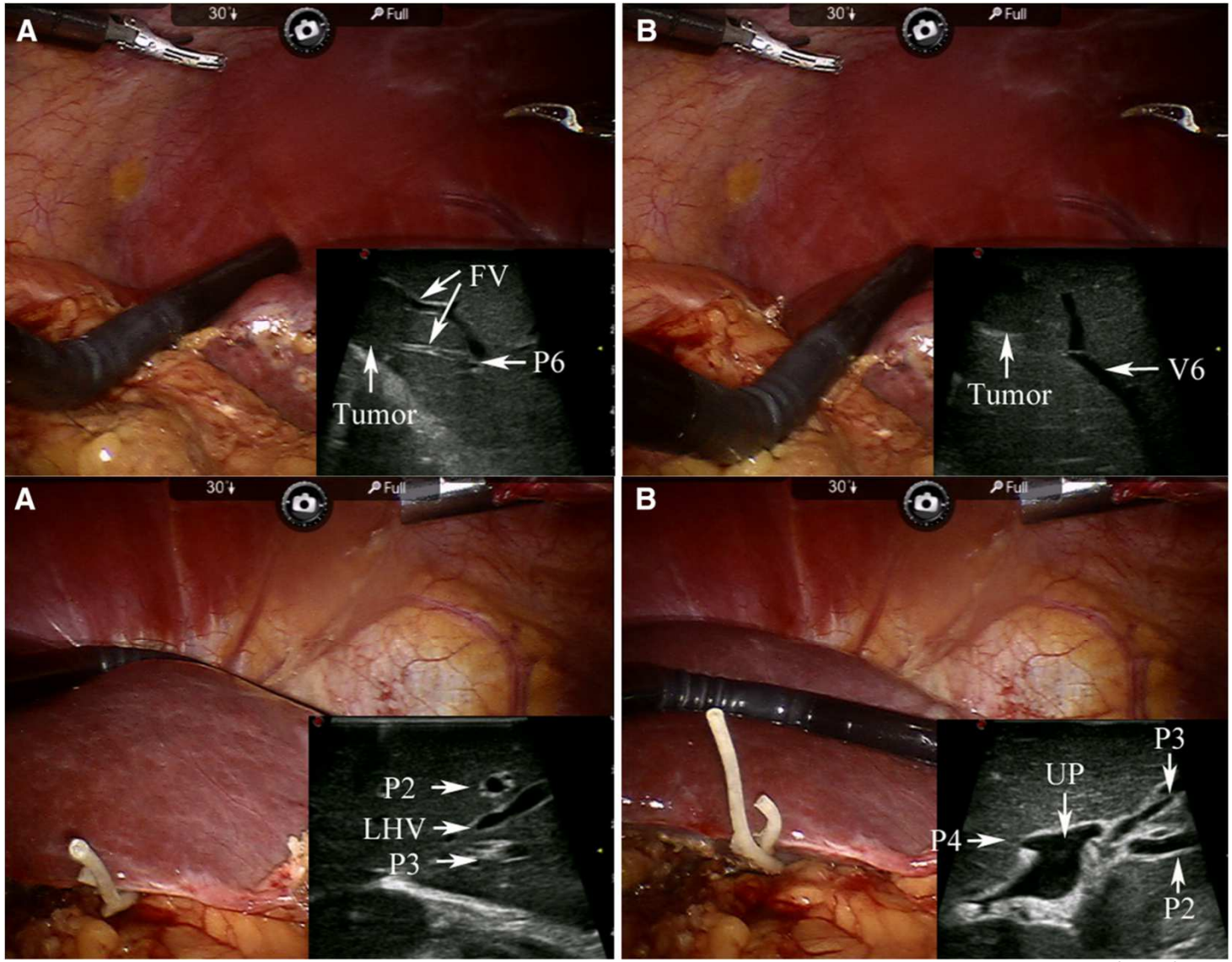
7 cases of modification of planned surgery

	Previous lesion		New lesion		Surgical strategy	
	Location	Number	Location	Number	Previous plan	Additional plan
MLC(rectal)	S6	1	S4	1	S6 resection	S4 resection
Hemangioma	S6, 7	4	S5	1	S6, 7 resection	S5 ablation
HCC	S6, 7	2	S8	1	S6, 7 resection	S8 resection
HCC	S2, 3	1	S4	1	S2, 3 resection	S4 resection
HCC	S2	1	S8	1	S2, 3 resection	S8 resection
MLC(Yolk sac tumor)	S6, 7	1	S7	1	S6, 7 resection	No change
HCC	S6	1	S6	1	S6 resection	No change
Hemangioma	S5, 8	1	S8	1	S5, 8 resection	No change
HCC	S4, 5	1	S6	1	S4, 5 resection	S6 resection
HCC	S5, 8	2	S6	1	S5, 8 resection	S6 resection
FNH	S2, 3	1	S2	1	S2, 3 resection	No change

Surgical Endoscopy 2018

Intraoperative ultrasonography of robot-assisted laparoscopic hepatectomy: initial experiences from 110 consecutive cases

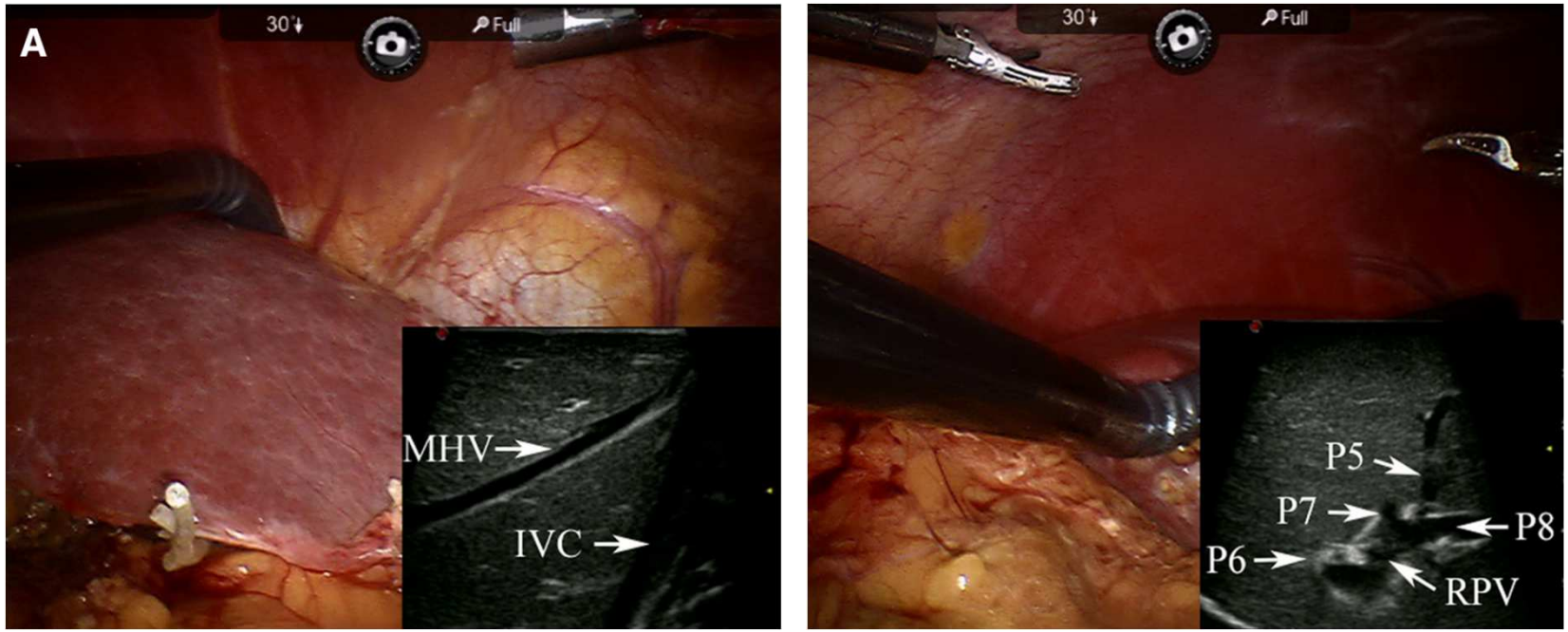
Peng Zhu[1] · Wei Liao[1] · Ze-yang Ding[1] · Hong-chang Luo[2] · Bin-hao Zhang[1] · Wan-guang Zhang[1] · Wei Zhang[1] · Zhan-guo Zhang[1] · Bi-xiang Zhang[1] · Xiao-ping Chen[1]



Surgical Endoscopy 2018

Intraoperative ultrasonography of robot-assisted laparoscopic hepatectomy: initial experiences from 110 consecutive cases

Peng Zhu[1] · Wei Liao[1] · Ze-yang Ding[1] · Hong-chang Luo[2] · Bin-hao Zhang[1] · Wan-guang Zhang[1] · Wei Zhang[1] · Zhan-guo Zhang[1] · Bi-xiang Zhang[1] · Xiao-ping Chen[1]



IOUS is indispensable to understand lesions and vessels in the liver, prevent accidental bleeding during transection, ensure no vascular damage, and residual tumor in the remnant liver

Surgical Endoscopy 2018

Why intraoperative ultrasound?

- To detect new lesions/vanishing lesions
- To guide liver surgery (ablation, resection)
- **To check ablation efficacy**

RESEARCH ARTICLE Open Access

Improvement of ablative margins by the intraoperative use of CEUS-CT/MR image fusion in hepatocellular carcinoma

Kai Li[1], Zhong-Zhen Su[1], Er-Jiao Xu[1], Jin-Xiu Ju[1], Xiao-Chun Meng[2] and Rong-Qin Zheng[1*]

2009-2012
RF ablation

I.O determination of ablation margin
(10-15 minutes after ablation)

Guide supplementary ablation

Reduce the rate of LTP

Success rate of CEUS CT/MR fusion was 99.2%

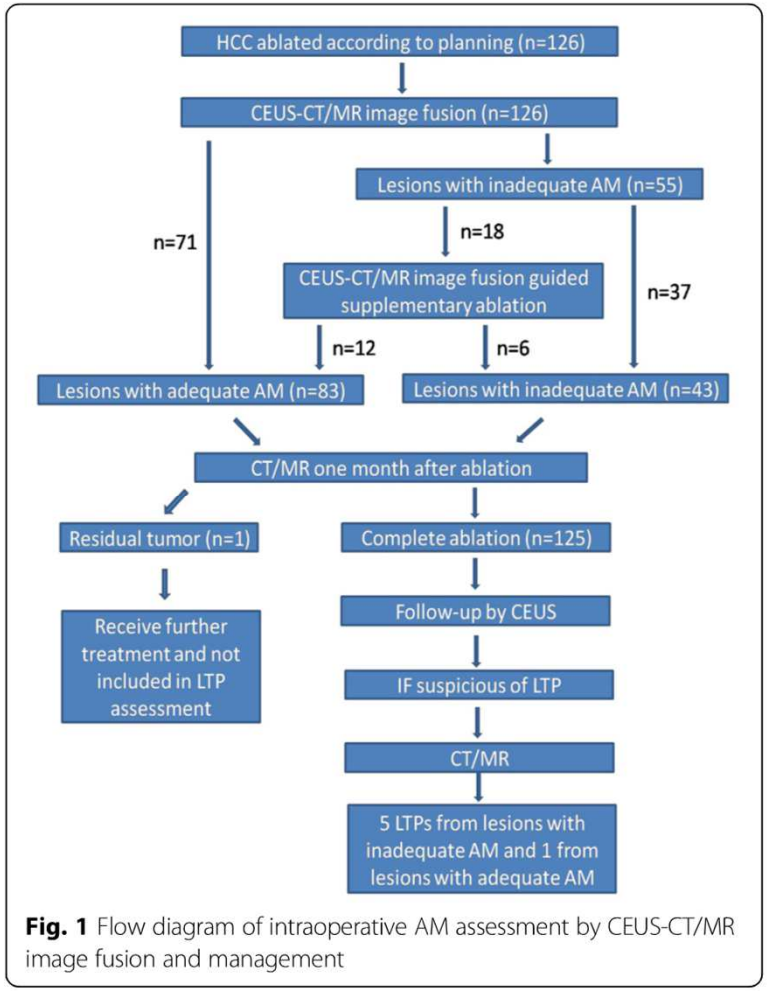


Fig. 1 Flow diagram of intraoperative AM assessment by CEUS-CT/MR image fusion and management

BMC 2016

RESEARCH ARTICLE Open Access

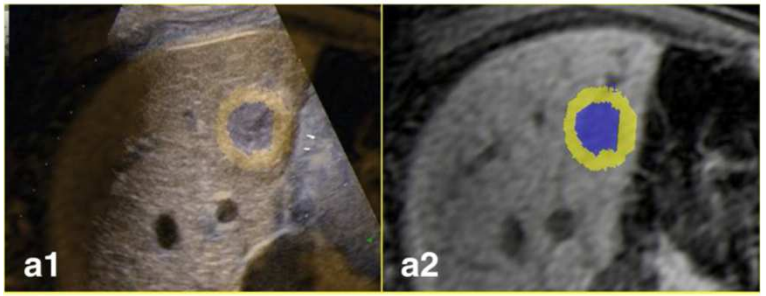
Improvement of ablative margins by the intraoperative use of CEUS-CT/MR image fusion in hepatocellular carcinoma

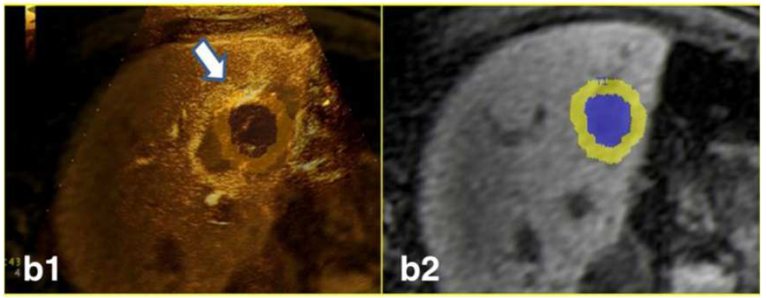
Kai Li[1], Zhong-Zhen Su[1], Er-Jiao Xu[1], Jin-Xiu Ju[1], Xiao-Chun Meng[2] and Rong-Qin Zheng[1*]

21.8% of lesions with inadeguate AM became AM

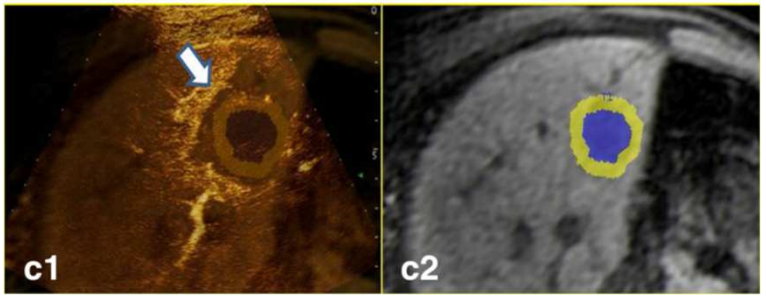
US MRI

After ablation: **inadeguate AM**





After supplementary ablation: **adeguate AM**



BMC 2016

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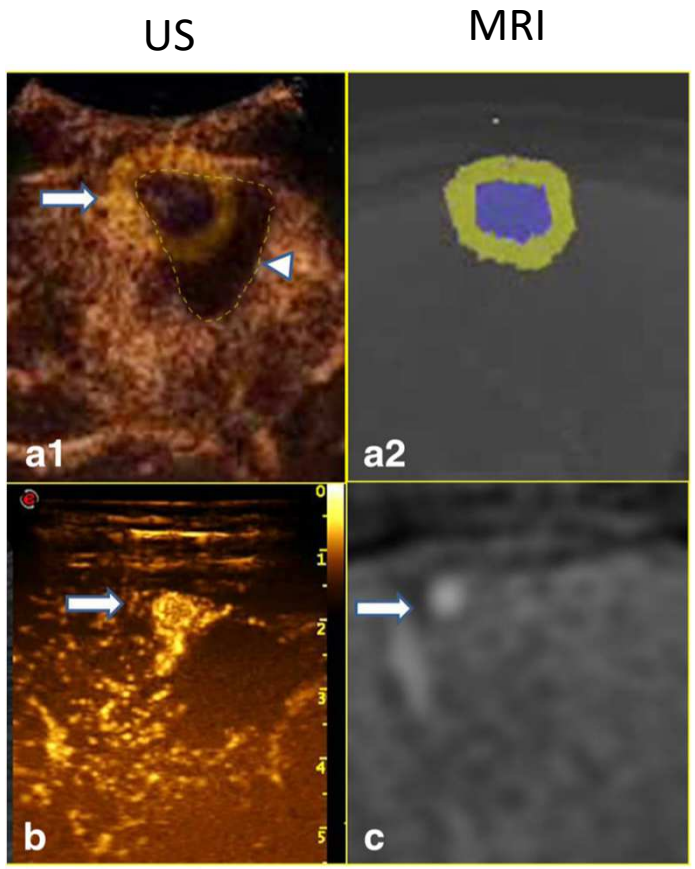
Success rate of CEUS CT/MR fusion was 99.2%

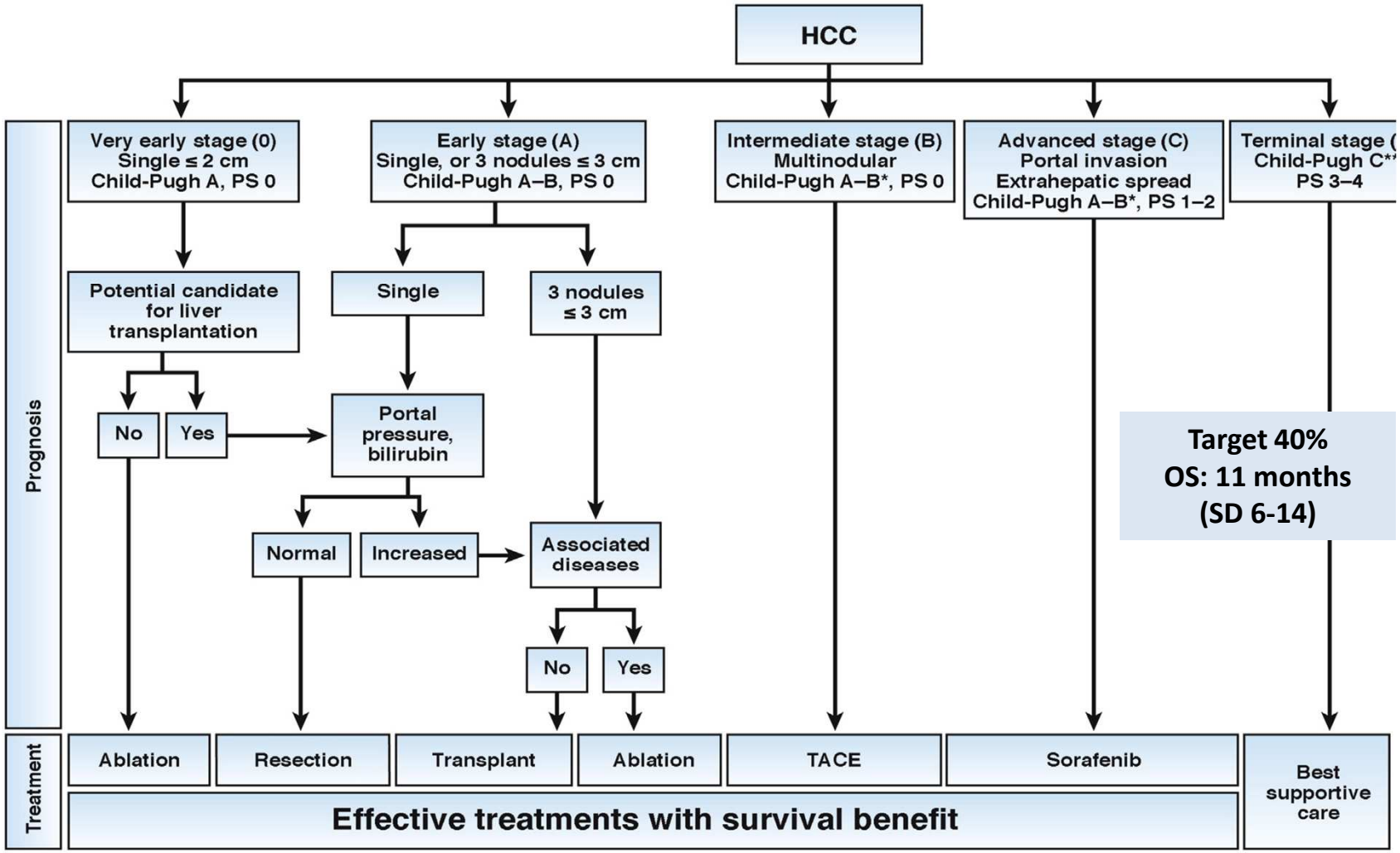
Table 2 Main reasons for inadequate AMs in quadrants

Reasons for inadequate AM	Number of quadrants
Blood vessel-related	142 (86.6 %)
Non-vessel-related	
Close to critical structures, supplementary ablation was not applied	14 (8.5 %)
Insufficient liver function, supplementary ablation was not applied	4 (2.4 %)
Tough puncture pathway, supplementary ablation was not applied	4 (2.4 %)
Total	164



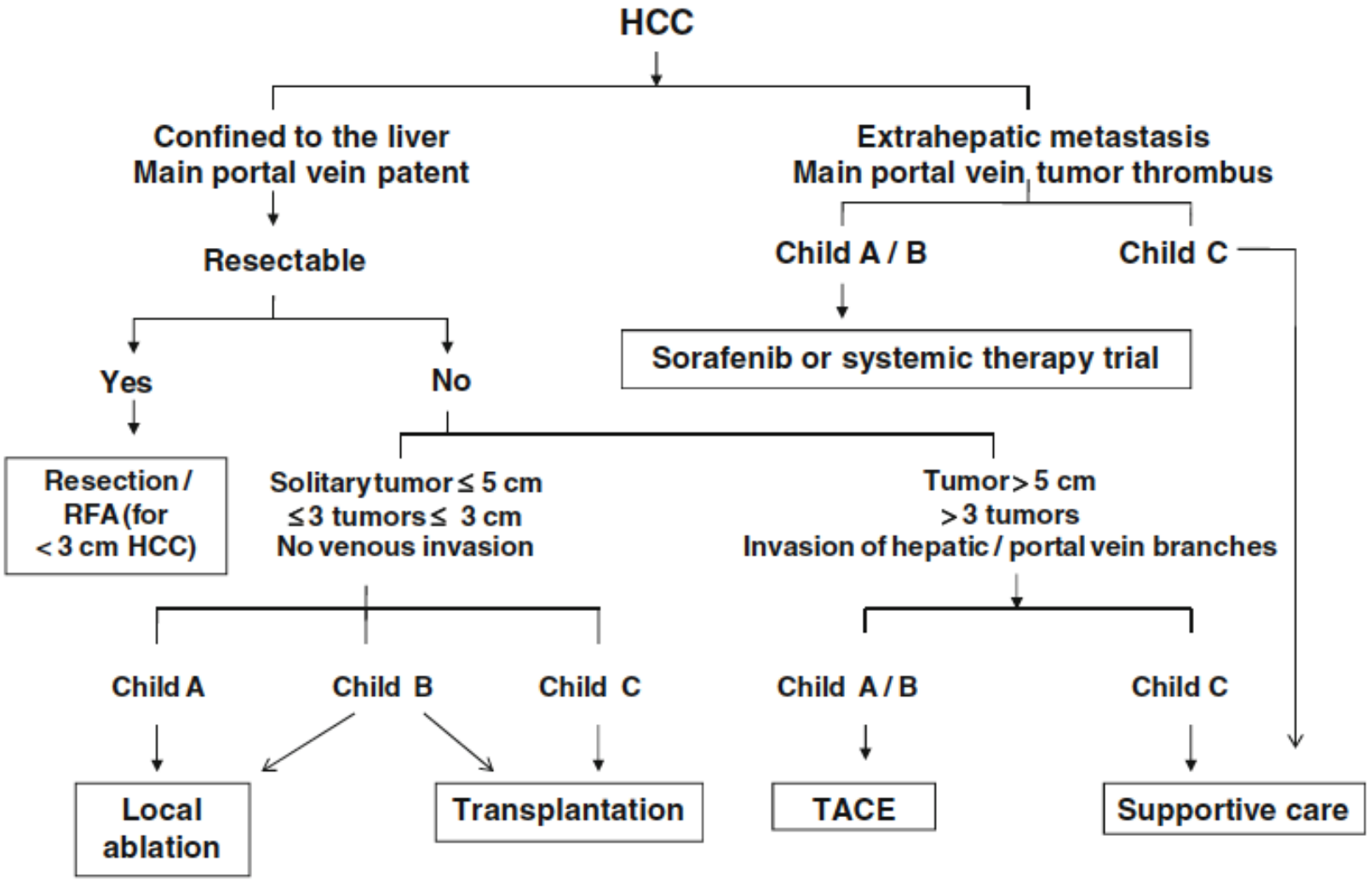
BMC 2016

The BCLC algorithm: Any role for LA?



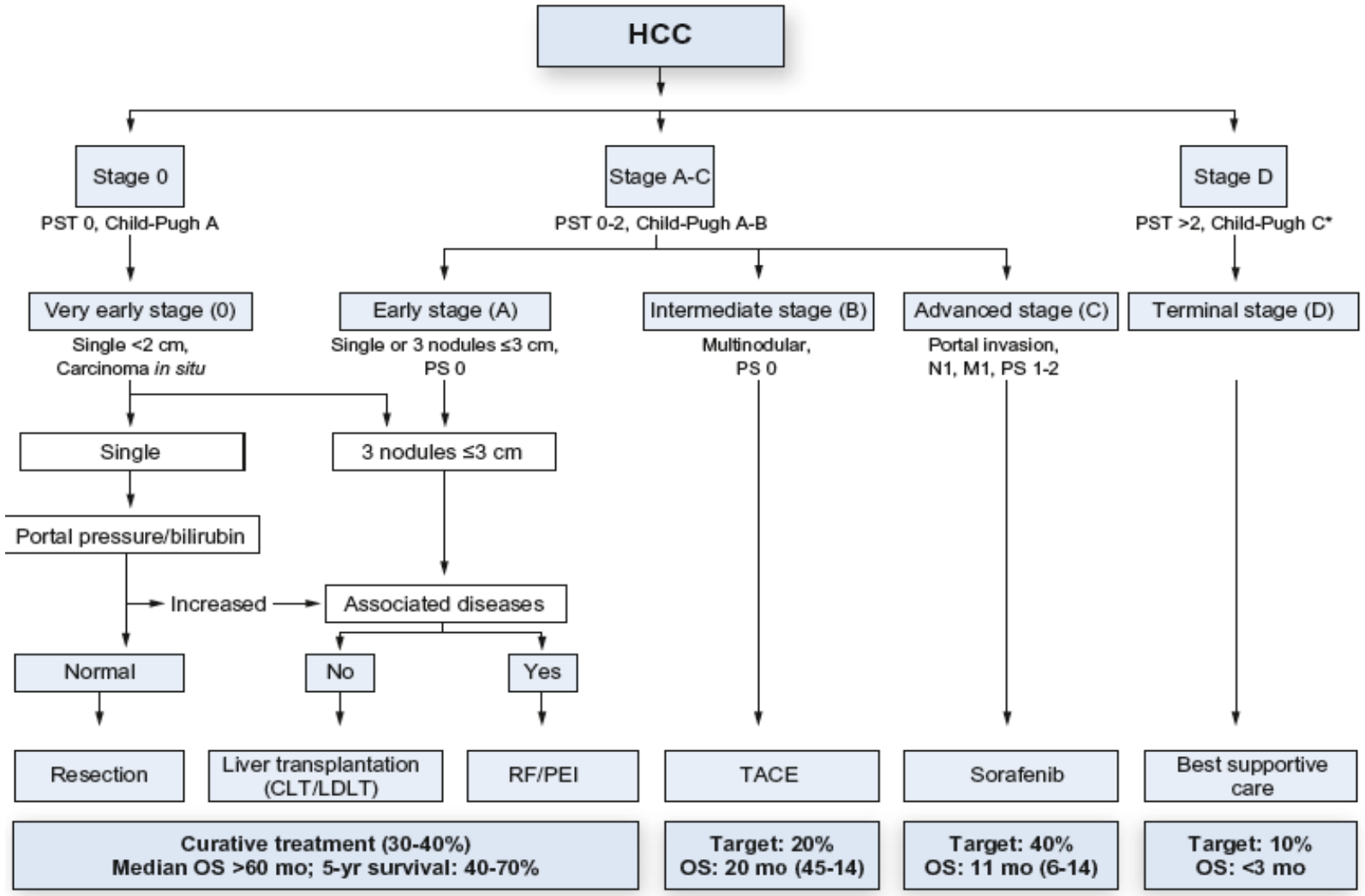
Bruix J et al, Gastroenterology 2016;150:835–853

APASL Guidelines: Any role for LA?



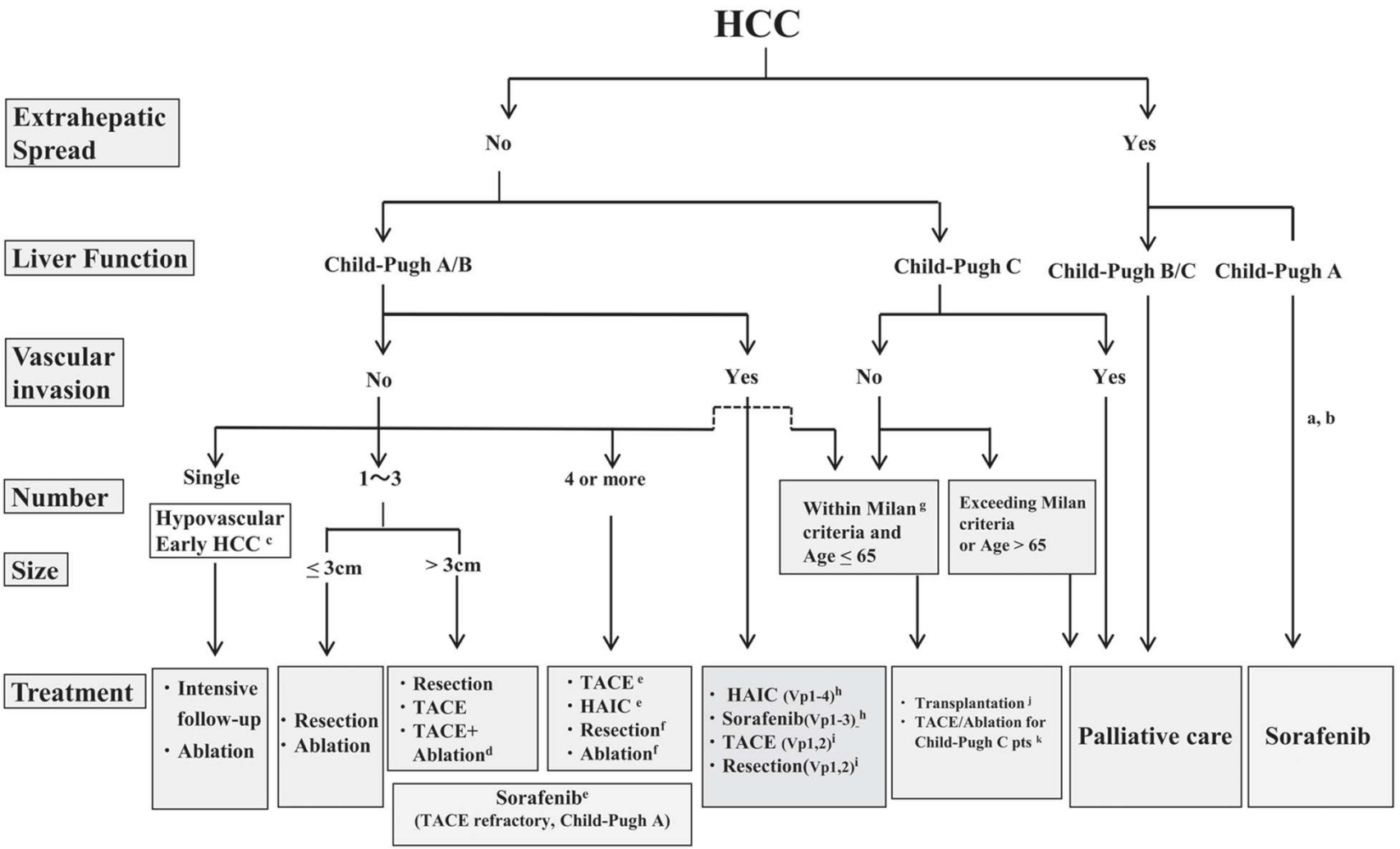
Omata M et al, Hepatol Int (2010) 4:439–474

EASL-EORTC Guidelines: Any role for LA?



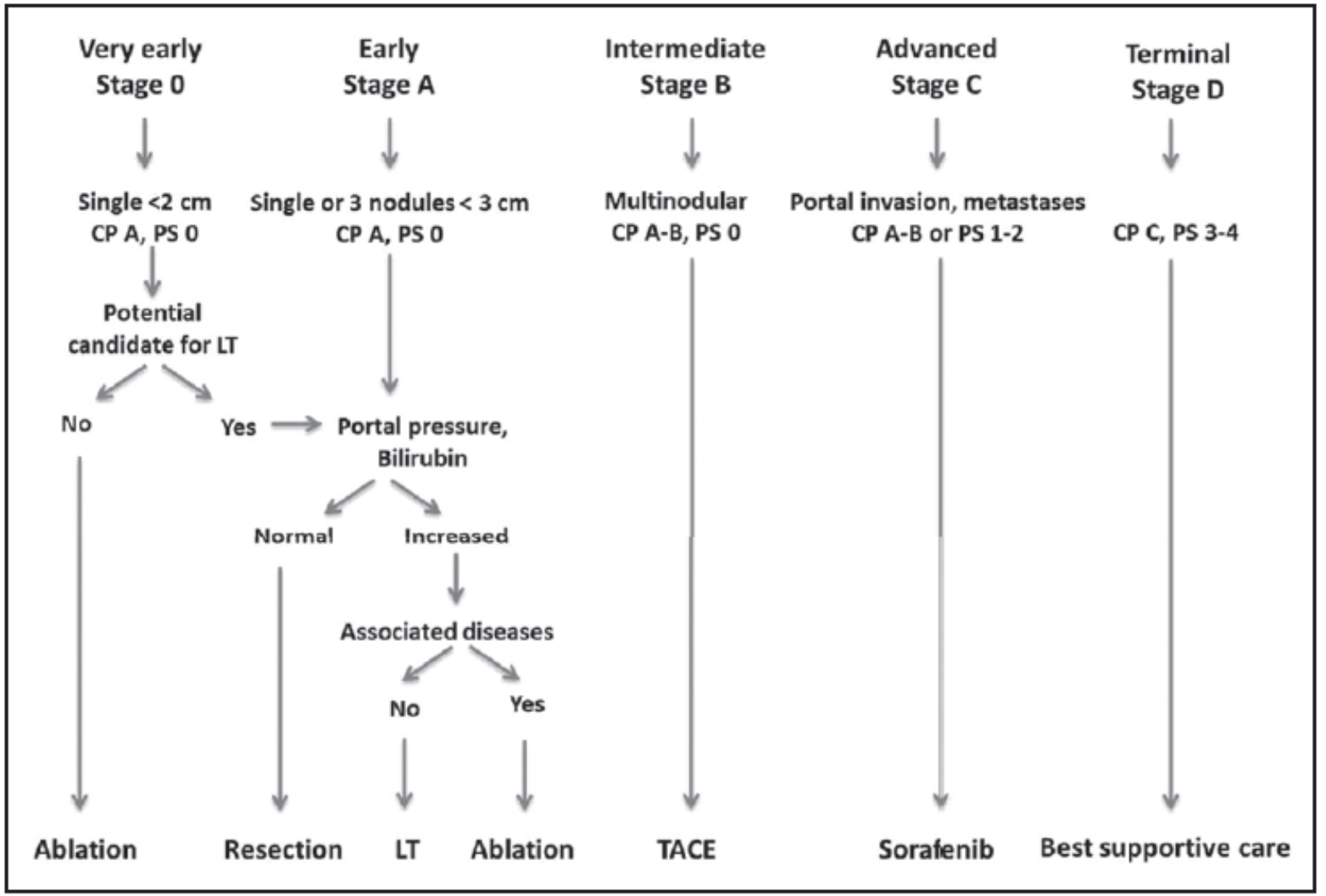
Llovet et al, Journal of Hepatology 2012 vol. 56 j 908–943

JSH Guidelines:
Any role for LA?



Kudo et al, Liver Cancer 2014;3:458–468

Canadian Guidelines: Any role for LA?



Burak et al, Can J Gastroenterol Hepatol Vol 29 No 4 May 2015

KLCSG-NCC Guidelines: Any role for LA?

Table 2. Summary of the Recommendations of the 2014 KLCSG-NCC Korea Practice Guidelines for the Management of Hepatocellular Carcinoma

Topic	Recommendation
Staging	1. This guideline adopts the modified Union for International Cancer Control stages as a primary staging system, with the Barcelona Clinic Liver Cancer staging system serving as a complementary system (B1).
Local ablation	1. RFA provides survival comparable to that of resection in patients with single-nodular HCCs ≤3 cm in diameter (A2). 2. RFA is superior to PEIT in terms of anticancer effect and survival (A1). For HCCs ≤2 cm in diameter, PEIT can be considered if RFA is unfeasible, because the outcomes of both modalities are similar (A2). 3. Survival outcome can be improved by combining TACE and RFA compared to RFA alone in patients with tumors 3–5 cm in diameter if resection is unfeasible (A2).

Gut and Liver, Vol. 9, No. 3, May 2015, pp. 267-317

AASLD Guidelines:
Any role for LA?

AASLD GUIDELINES FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMA

Any good news for laparoscopic ablations?

The word “Laparoscopy”
is never cited
in the 2017 Edition
of AASLD Guidelines

Heimbach J et al, Hepatology. 2017 Jan 28

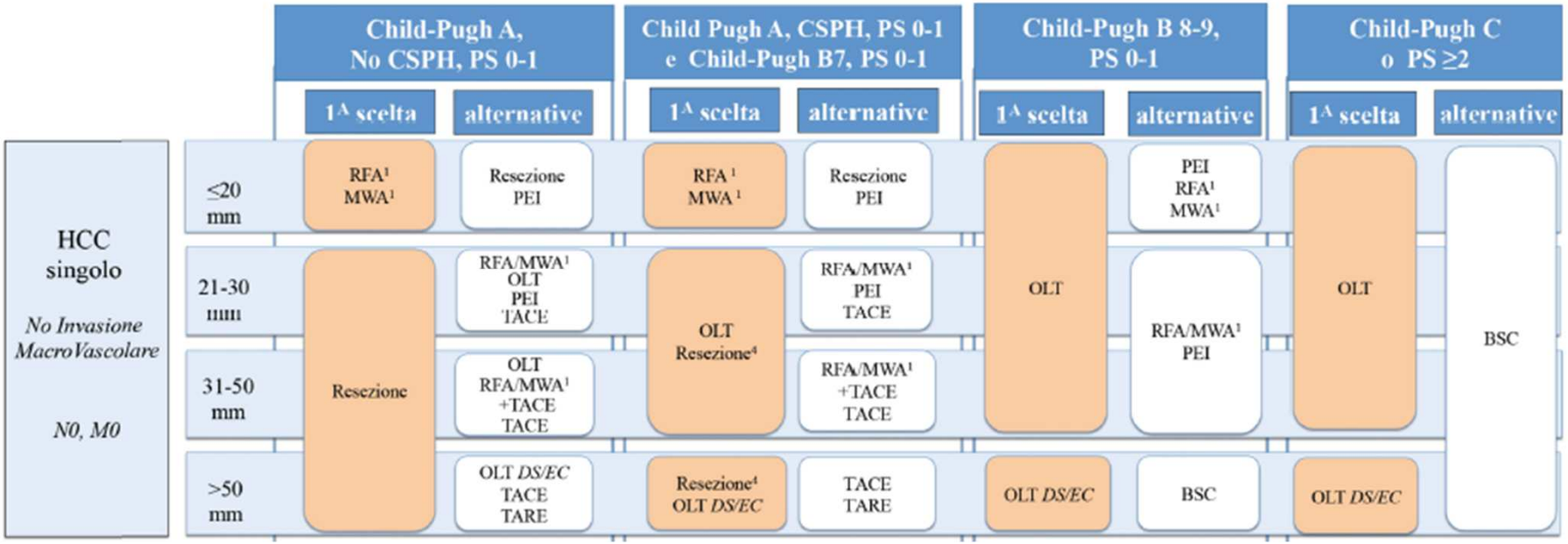
AISF Position Paper 2013: Any role for LA?

6.3.3. AISF expert panel recommendations

- **For HCC ≤2 cm, in the setting of a multi-disciplinary evaluation, RFTA can be considered the first-line treatment when performed in expert centres (*3b-B*).**
- **For HCC of 2.1–3 cm, the choice between surgery and RFTA should be made on a case-by-case after a multi-disciplinary evaluation (*5-D*)**
- **Patients with nodules >3 cm should be treated with surgery, when feasible (*5-D*).**
- **In case of failure of percutaneous ablation, patients should be reassessed by a multidisciplinary team for the most appropriate treatment modality, at first considering surgery if feasible.**
- **When technically feasible, RFTA should be preferred to PEI due to better efficacy and predictability of treatment result (*2a-B*).**
- **In non-resectable cases where RFTA is not feasible (due to insufficient ultrasound visibility or proximity to hollow organs or coagulopathy), video-laparoscopic RFTA, performed in expert centres, should be considered (*5-D*).**
- **Response to ablation can be assessed with CEUS, MRI, or CT approximately 1 month after treatment, and every 3–4 months thereafter up to 2 years of follow-up. In this setting, CT or MRI should be performed every 6 months. After 2 years of follow-up without recurrence, the usual semiannual ultrasound surveillance programme can be re-started (*5-D*).**

Digestive and Liver Disease 45 (2013) 712– 723

RACCOMANDAZIONI MULTISOCIETARIE ITALIANE (AISF, AIOM, IT-HPBA, SIC, SIRM, SITO) PER LA GESTIONE CLINICA INTEGRATA DEL PAZIENTE CON EPATOCARCINOMA


Child-Pugh A, No CSPH, PS 0-1
Child Pugh A, CSPH, PS 0-1 e Child-Pugh B7, PS 0-1
Child-Pugh B 8-9, PS 0-1
Child-Pugh C o PS ≥2
1A scelta
alternative
HCC singolo
No Invasione MacroVascolare
N0, M0
≤20 mm
21-30 mm
31-50 mm
>50 mm
RFA1 MWA1
Resezione PEI
Resezione
RFA/MWA1 OLT PEI TACE
OLT RFA/MWA1 +TACE TACE
OLT DS/EC TACE TARE
OLT Resezione4
TACE TARE
OLT
PEI RFA1 MWA1
RFA/MWA1 PEI
BSC

Nei pazienti non resecabili e non trattabili con ablazione percutanea (per scarsa visibilità ecografica, contiguità con visceri cavi) va considerato l'impiego di un approccio video-laparoscopico o l'uso di ascite artificiale, da effettuarsi presso Centri esperti.

TERAPIA TERMOABLATIVA – AFFERMAZIONI CONCLUSIVE MULTISOCIETARIE 2016

- → **La RFA, quando decisa in un contesto multidisciplinare, può essere considerata il trattamento di prima linea per il nodulo singolo fino a 2 cm, in quanto rispetto alla resezione chirurgica è gravata da minori morbilità e mortalità e comporta una durata del ricovero e spese sanitarie inferiori, a fronte di sopravvivenze sovrapponibili.** Non sembrano esservi differenze in termini di efficacia e sicurezza tra i diversi dispositivi di RFA più largamente utilizzati.

- → **Per il nodulo di dimensioni fra 2.1 e 3 cm, la scelta fra resezione e RFA va valutata sempre in modo interdisciplinare e caso per caso, in relazione alle caratteristiche del paziente e dell'ubicazione della lesione.** Nel caso di nodulo >3 cm, la scelta, ovunque possibile, va indirizzata verso la resezione.

- → **Pazienti non resecabili e non trattabili con ablazione percutanea (per scarsa visibilità ecografica, contiguità con visceri cavi) va considerato l'impiego di un approccio video-laparoscopico o l'uso di ascite artificiale, da effettuarsi presso Centri esperti.**

- → **Oltre i 3 cm, nel paziente non resecabile, è ragionevole considerare l'impiego di trattamenti combinati/sequenziali (chemioembolizzazione + ablazione) in alternativa, a termoablazione con plurime inserzioni.**

Survival Advantage of Radiofrequency Ablation Over Transarterial Chemoembolization for Patients with Hepatocellular Carcinoma and Good Performance Status Within the Milan Criteria

706 HCC Milan-IN patients

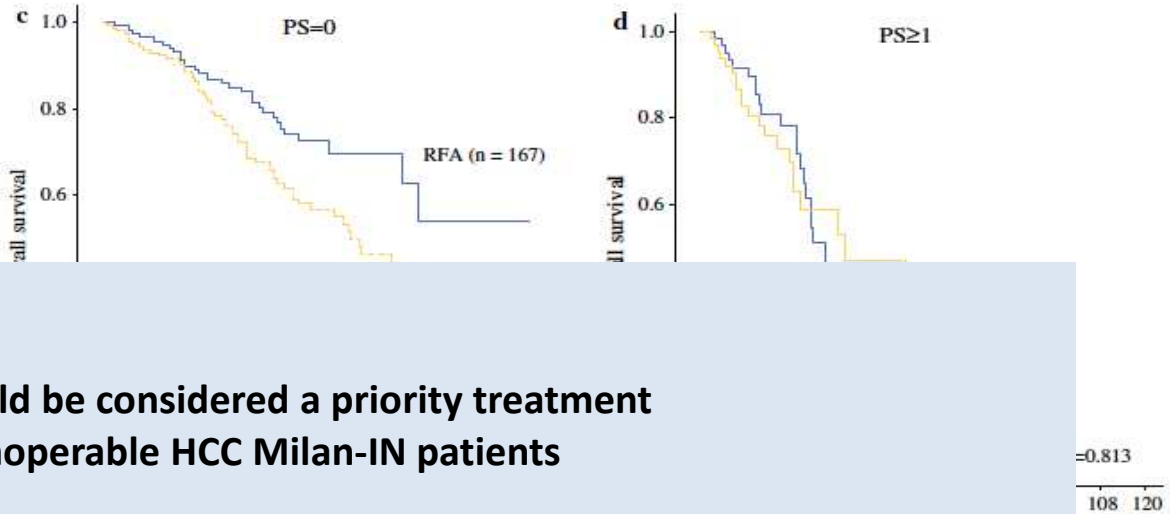
- 424 RFA
- 282 TACE

Performance status:

-
-

→

-
-



RFA should be considered a priority treatment in inoperable HCC Milan-IN patients

Performance status is a feasible surrogate marker to enhance treatment allocation

RFA provided better long-term OS than TACE ($p<0.05$)

TACE is associated with 1.784x increased risk of mortality (95 % CI 1.075–2.506)

Liu HP et al, Ann Surg Oncol 2014, 21: 3835-3843

LRFA vs TACE in BCLC-B

Comparison of transcatheter arterial chemoembolization, laparoscopic radiofrequency ablation, and conservative treatment for decompensated cirrhotic patients with hepatocellular carcinoma

100 HCC, CPT B-C patients
Between October 2000 and July 2003

- 40 L_RFA (LRFA group)
- 20 TACE (TACE group)
- 40 Conservative treatment (control group)

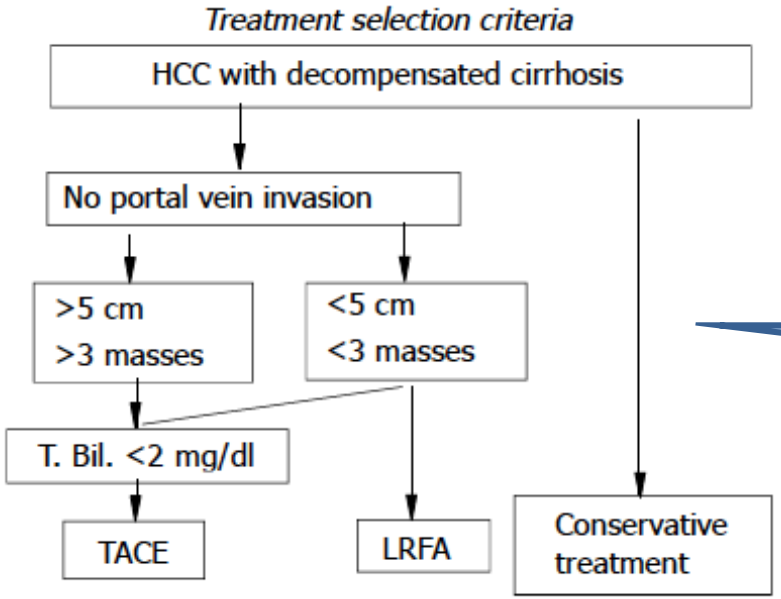


Table 2 Comparison between LRFA and TACE treatment groups in mortality, complication, and recurrence rates

	LRFA (n=40)	TACE (n=20)	P value
One-month mortality[a]	1 (2.5%)	1 (5%)	
Major complications: total	7 (17.5%)	9 (45%)	<0.05
Hepatic failure[b]	3	3	
Pulmonary embolism	0	1	
Stroke	0	1	
UGI[c] bleeding	2	2	
Pneumonia	1	0	
Refractory ascites	1	2	
Minor complications: total	7 (17.5%)	7 (35%)	
Pneumothorax	3	0	
W[illegible]l infection	2	0	
Burns	2	0	
Post embolization syndrome[d]	0	7	
Local recurrence rate			
One year	12	7	
Two years	19	11	

Hsieh CB et al, World J Gastroenterol 2004;10(4):505-508

Laparoscopic approach

The goal of a local ablative treatment is complete tumor destruction with minimal side effects

Miniaturization of the access

Advantages of laparoscopy:

Direct visualization of the abdominal cavity

Better tumor staging using IOUS
→ Higher frequency
→ More accurate and precise needle placement

Opportunity to detect extrahepatic spread

Therapeutic implications in preventing thermal injury

Pneumoperitoneum:
•Decreases tissue perfusion
•Reduces convective heat sink phenomena → larger ablation areas
•Less local treatment failures

Eisele RM, World J Gastroenterol 2016 April 21; 22(15): 3885-3891

HCC:
Criteria for Laparoscopic Approach

Patients meeting at least one of the following criteria:

1. Patients not eligible for HR:
   - Major HR in BCLC A2-A3-A4 patients
   - Technical contraindications

2. Patients not suitable for percutaneous ablation:
   - Critical location (proximity to GI tract or bladder or major hepatic vessels; superficial exophytic nodules)
   - Tumor extension (size ≥ 3 cm or ≥3 nodules)
   - Untreatable ascites
   - Severe coagulopathy (PT<40% and/or PTLS <30.000)

Exclusion criteria:
Severe liver disease (CPT-C, MELD > 20)
Large multinodular HCC (size > 7 cm, Number >5)

Cillo U et al, PLoS one 2013, Vol 8, 2, e57249

Patients meeting at least one of the following criteria:

1. Patients with a single nodule or up to three nodules <3 cm not suitable for OLT

1. Patients not eligible for HR:
   - Severe PH
   - Impaired liver function
   - Coexistent comorbidities

2. Patients not suitable for percutaneous RFA because of:
   - PLTS < 40.000 and/or INR >1.20
   - Superficial lesions adjacent to abdominal viscera
   - Deep-sited lesions with very difficult or impossible percutaneous approach (HCCs undetectable at US, or contiguous to primary biliary or portal tributaries);
   - Short-term recurrence of HCC (<3 months) following PEI; RFA or TACE

Exclusion criteria:
- Complete portal thrombosis and/or
- Coexisting severe liver disease (CPT-C)

Santambrogio R et al, Surg Endosc (2016) 30:2103–2113

ABLAZIONI ESTREME

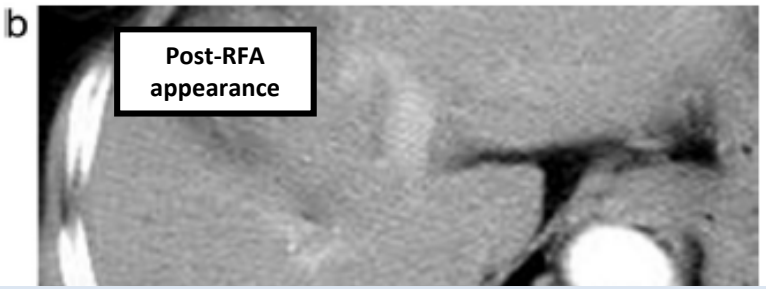
RFA vs MWA in HCC: is it the same?

Comparison of two different thermal techniques for the treatment of hepatocellular carcinoma

198 Milan-in HCC patients
RFA: 85 patients (98 lesions)
MWA: 113 patients (131 lesions)

No patient deaths due to treatment

	RFA	MWA	p
Complete ablation rate	99%	98.5%	1.0
Local recurrence rates	5.2%	10.9%	0.127
Major complications	2.4%	2.7%	1.0
DFS • 1yr • 3 ys • 4 ys	 80.3% 39.5% 19.0%	 75.0% 32.1% 16.1%	0.376
OS • 1yr • 3 ys • 4 ys	 98.7% 82.7% 77.8%	 98.0% 77.6% 77.6%	0.729

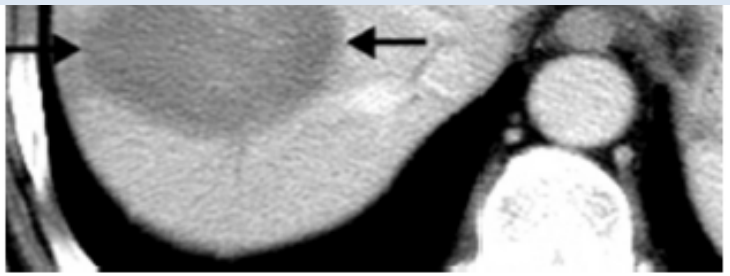


RFA and MWA

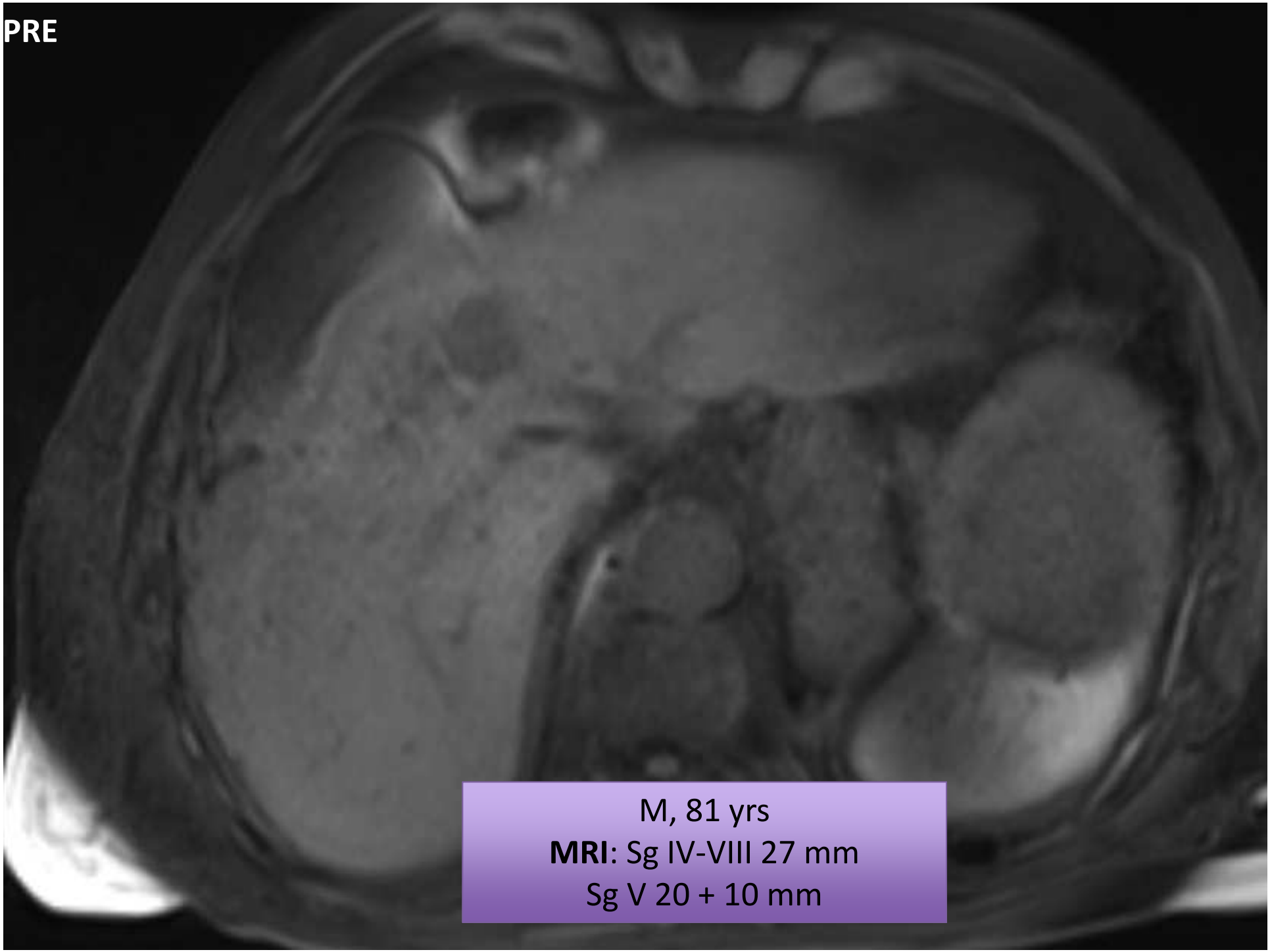
same clinical value in treating Milan-in HCC

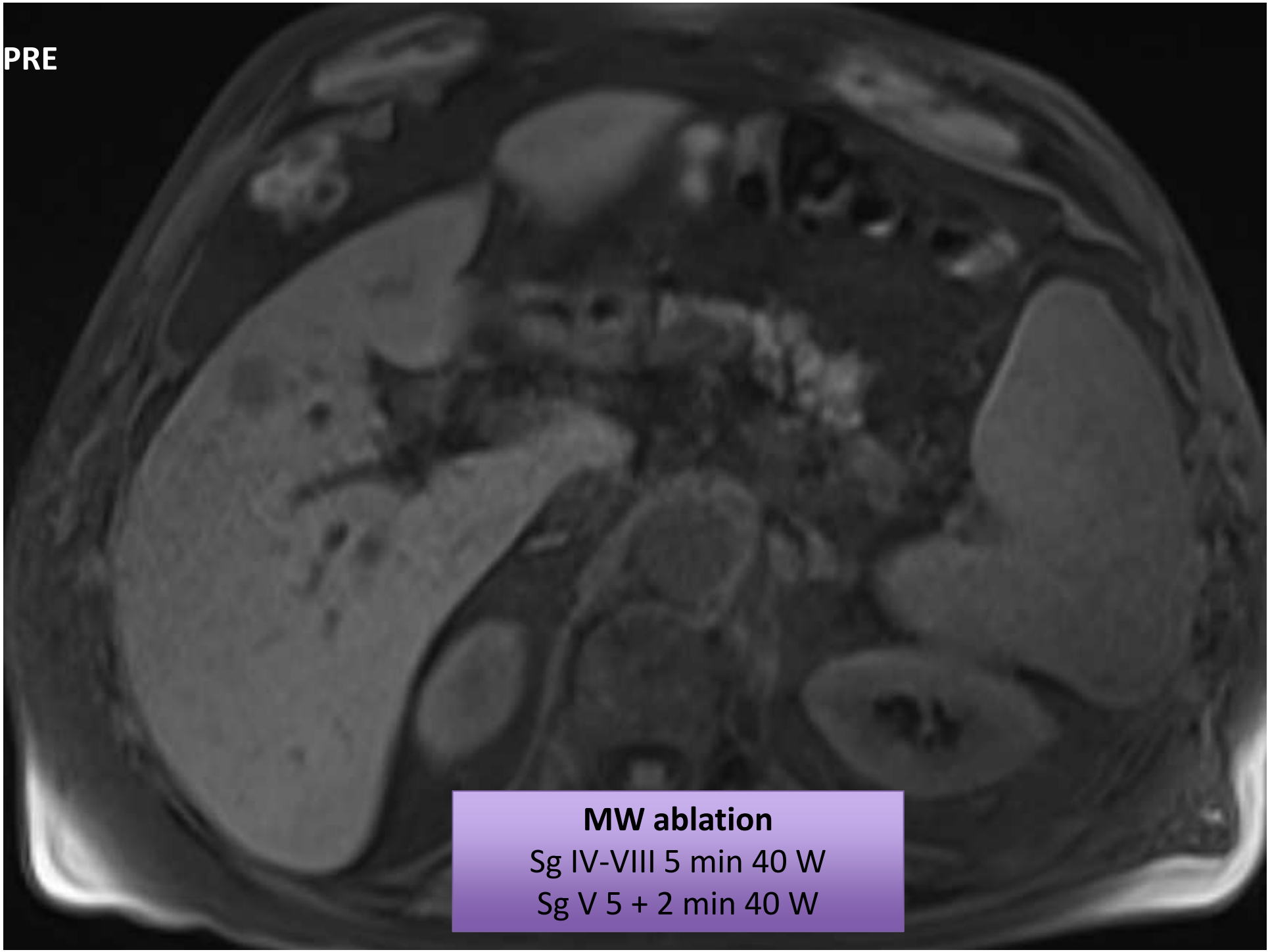
Both safe and effective techniques for HCC

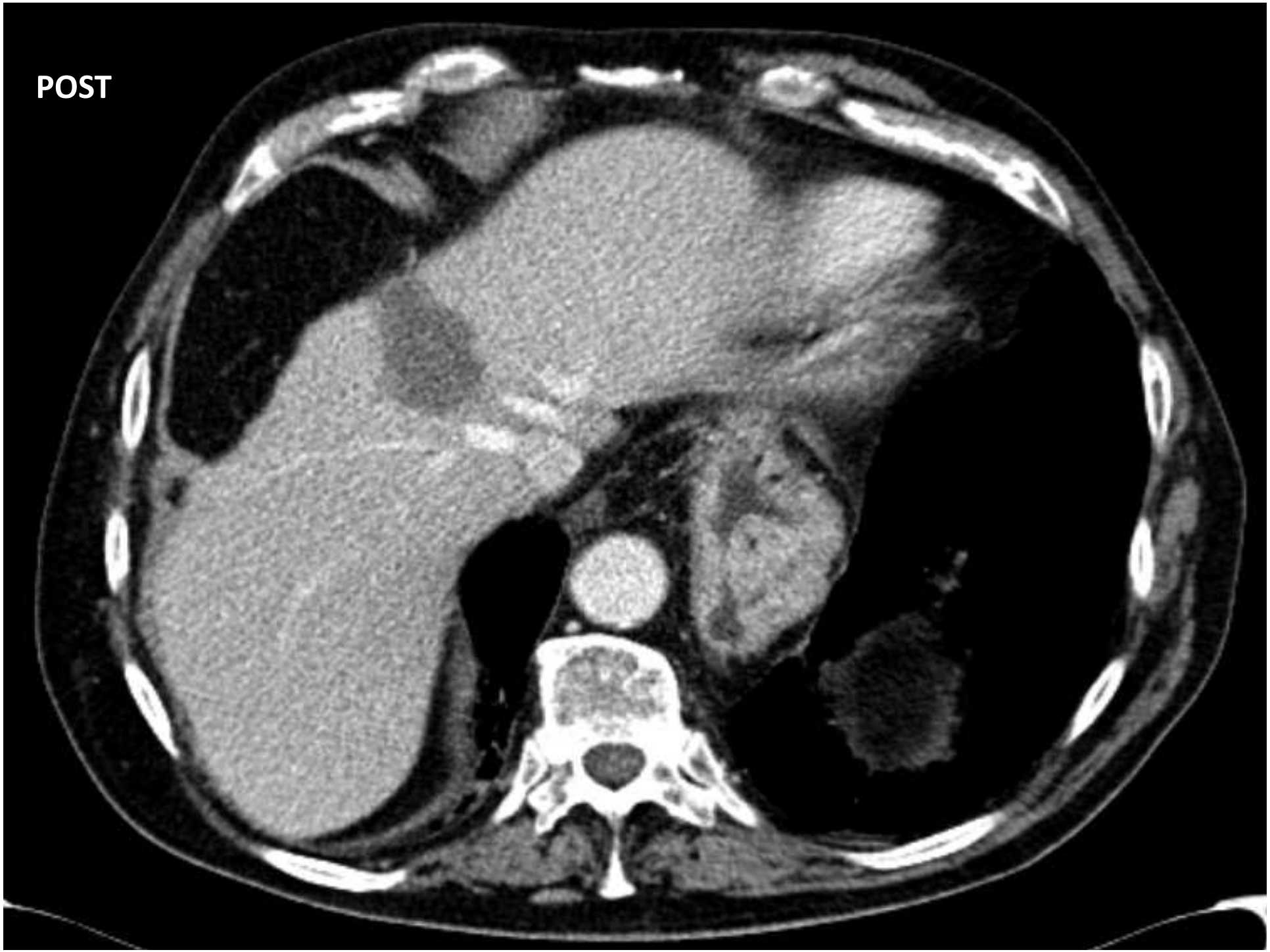
as clinical application



Ding J et al European Journal of Radiology 82 (2013) 1379– 1384


PRE
M, 81 yrs
MRI: Sg IV-VIII 27 mm
Sg V 20 + 10 mm


PRE
MW ablation
Sg IV-VIII 5 min 40 W
Sg V 5 + 2 min 40 W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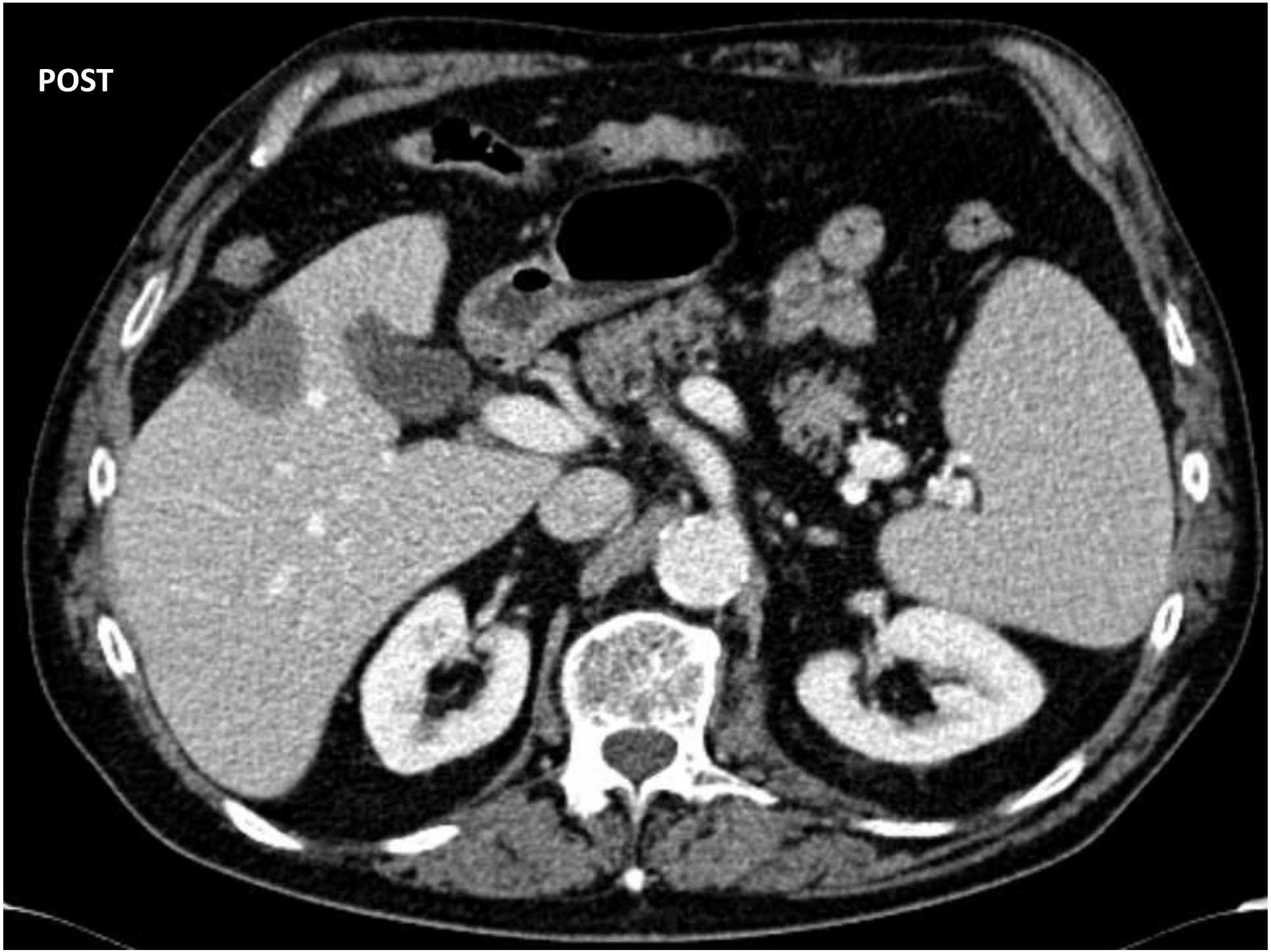
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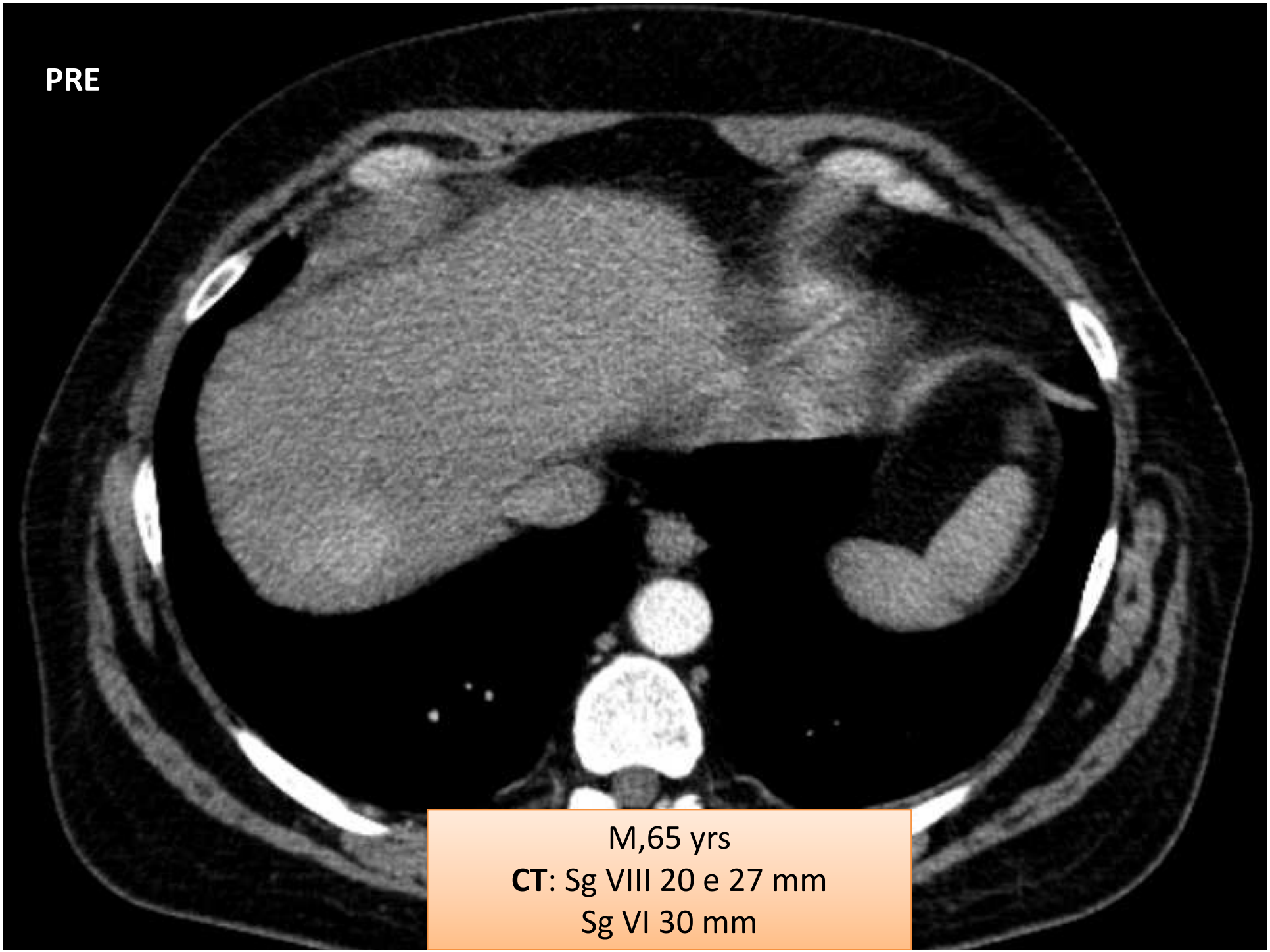
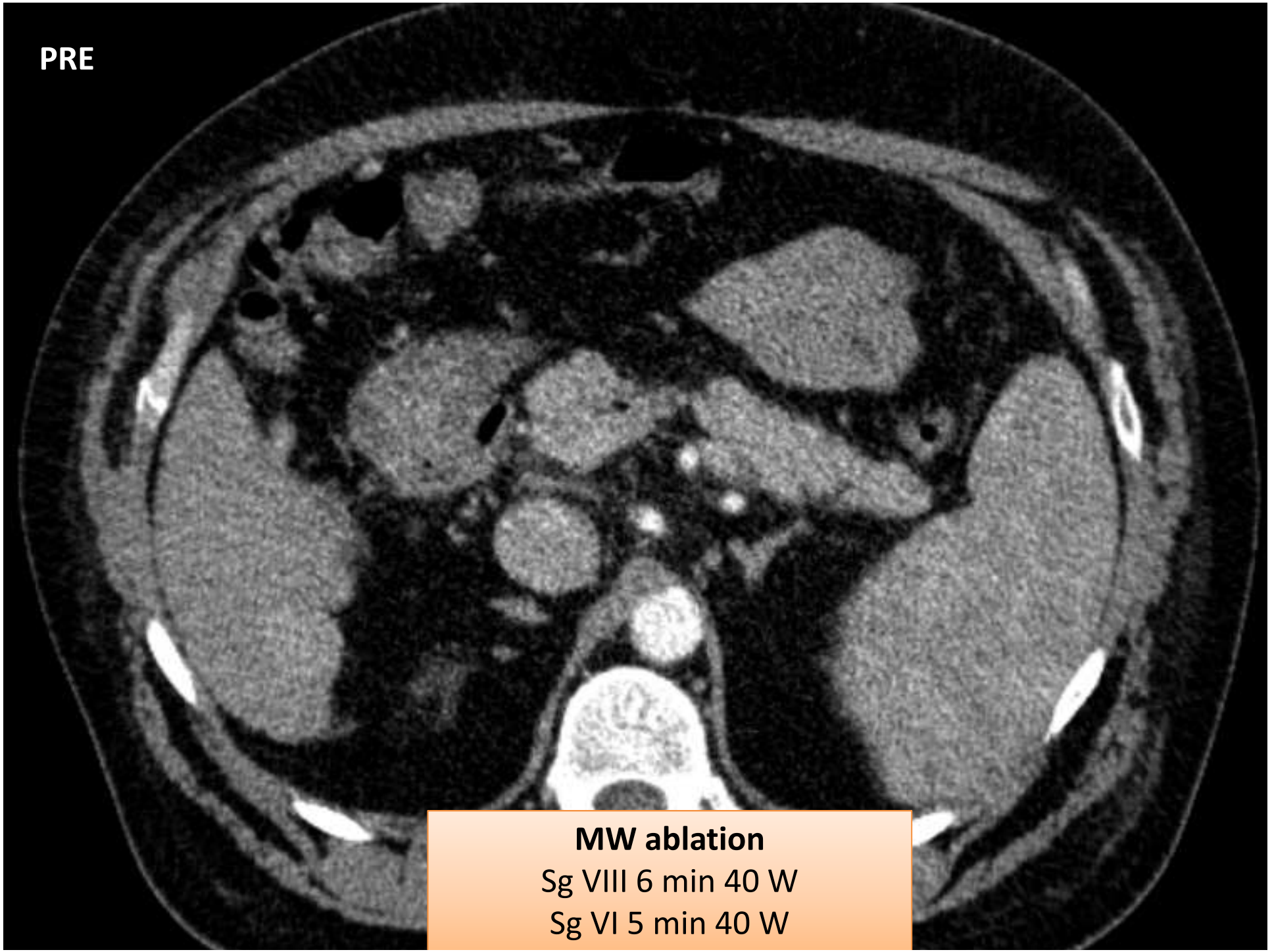
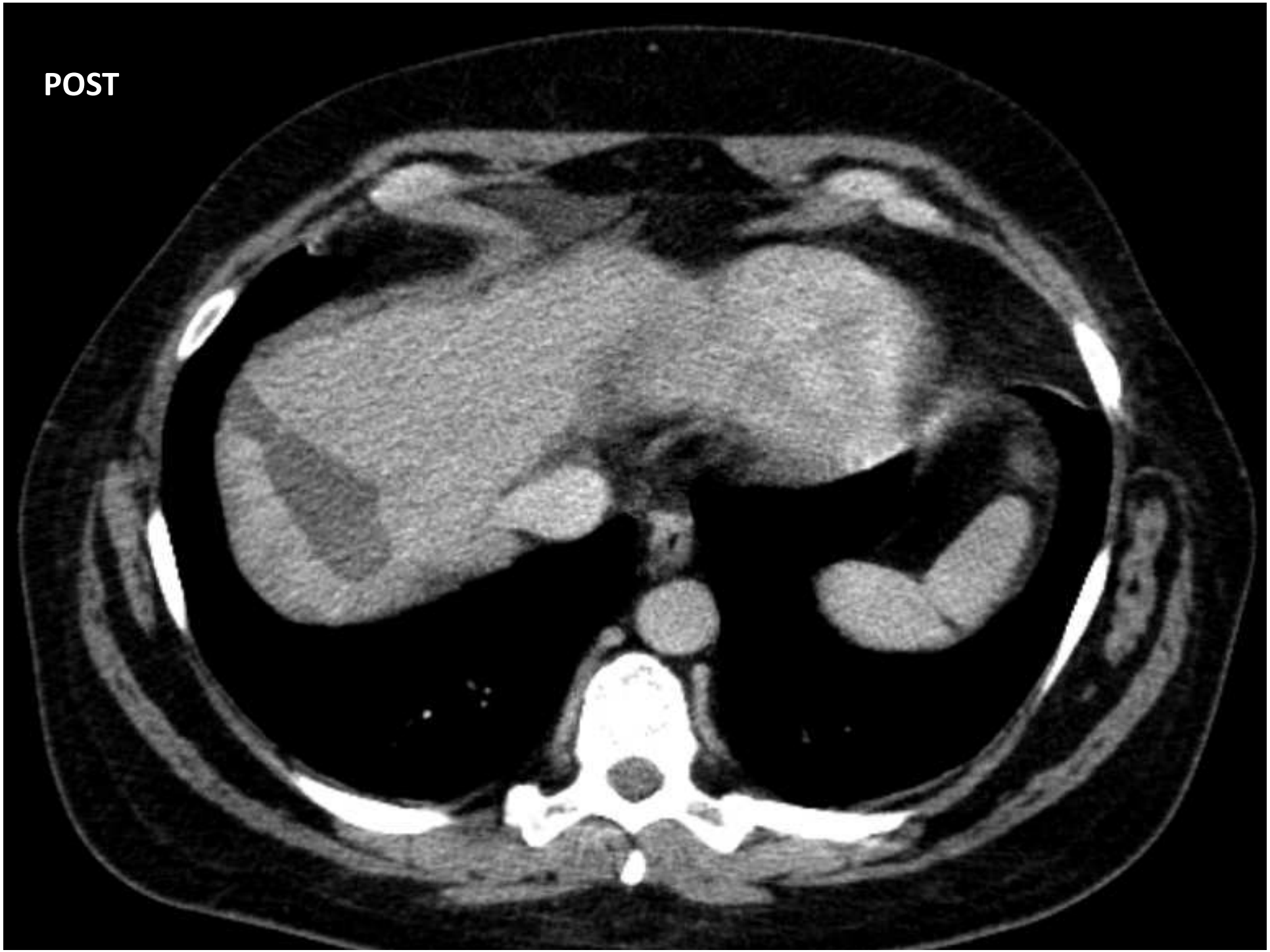

PRE
M,65 yrs
CT: Sg VIII 20 e 27 mm
Sg VI 30 mm


PRE
MW ablation
Sg VIII 6 min 40 W
Sg VI 5 min 40 W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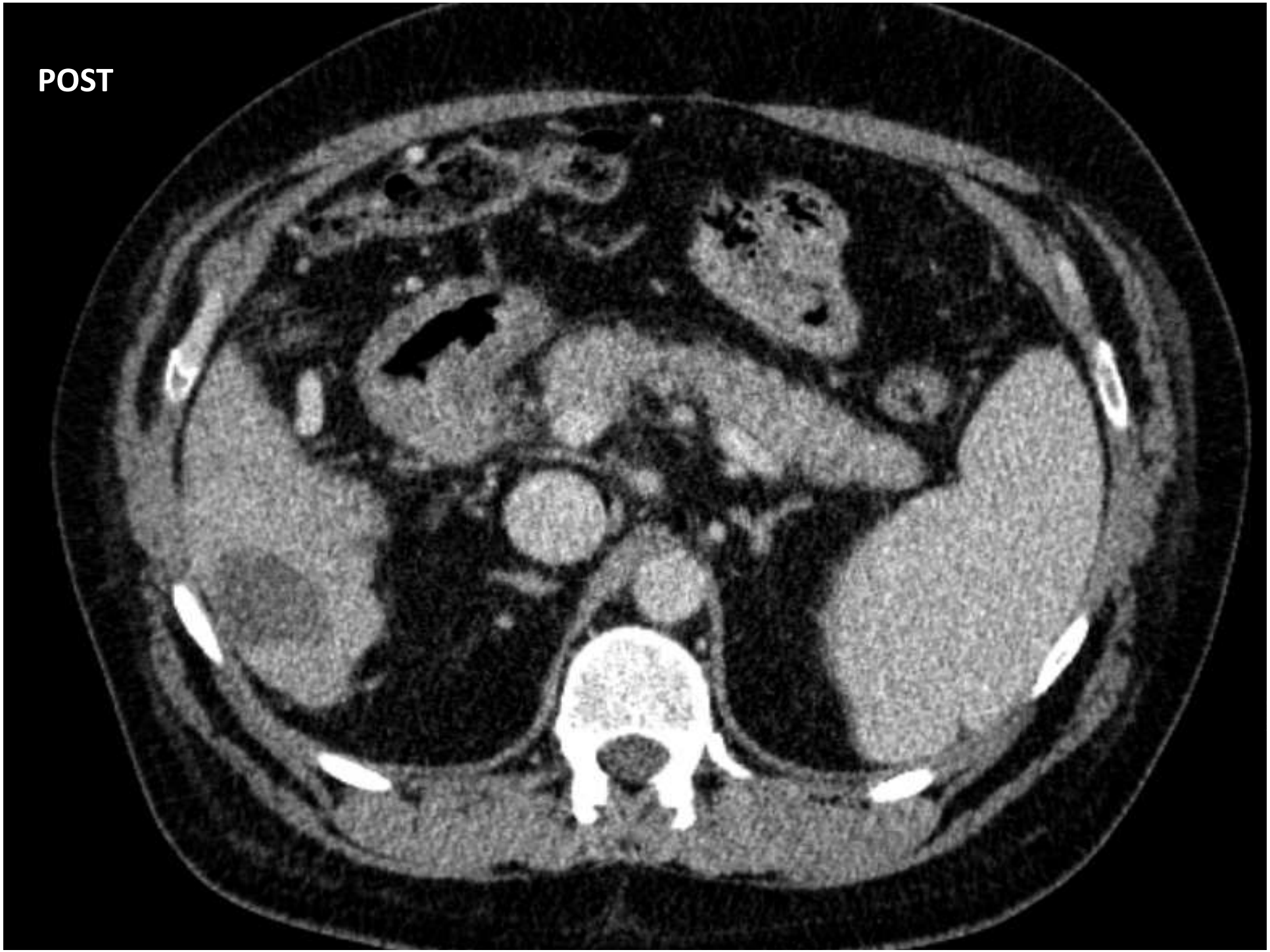
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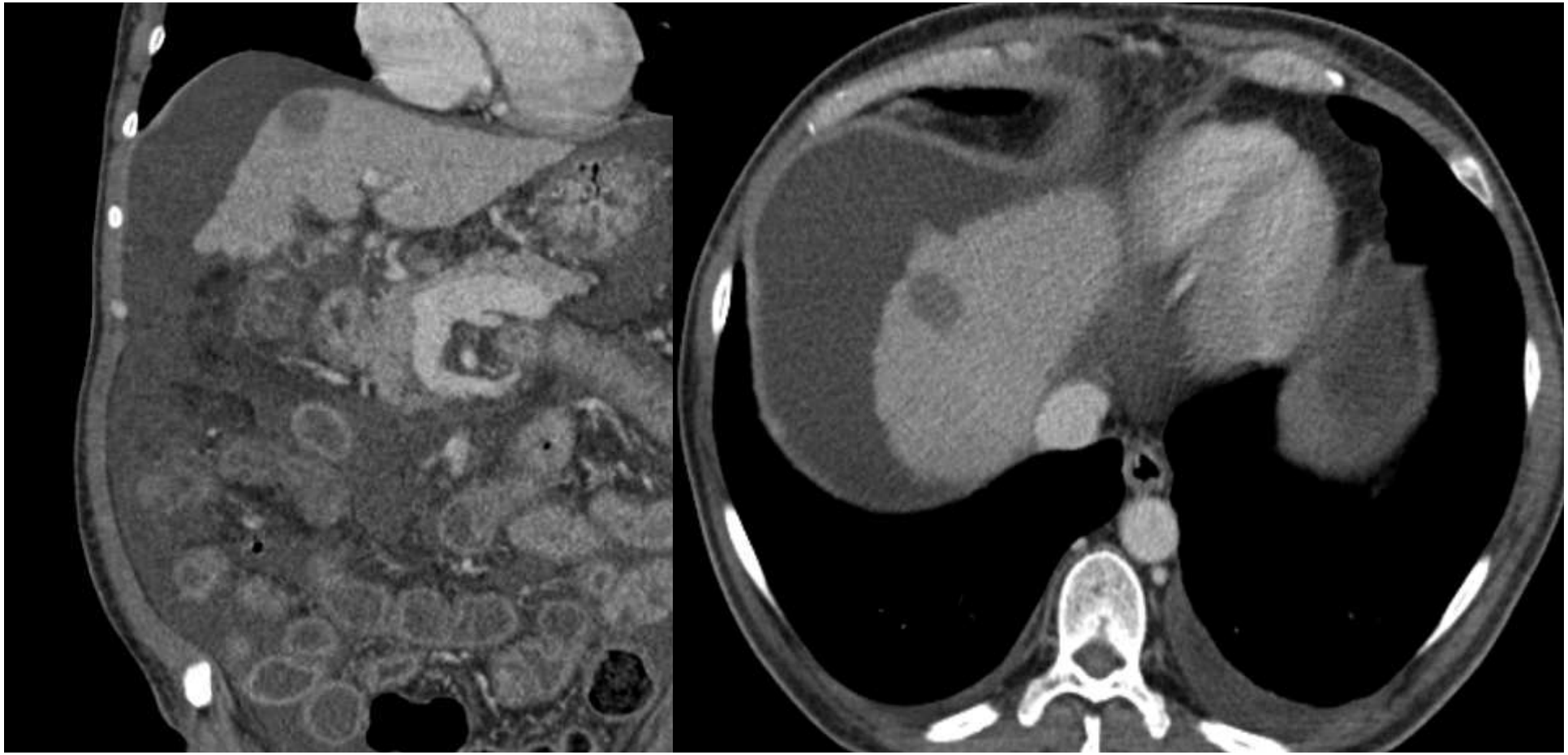
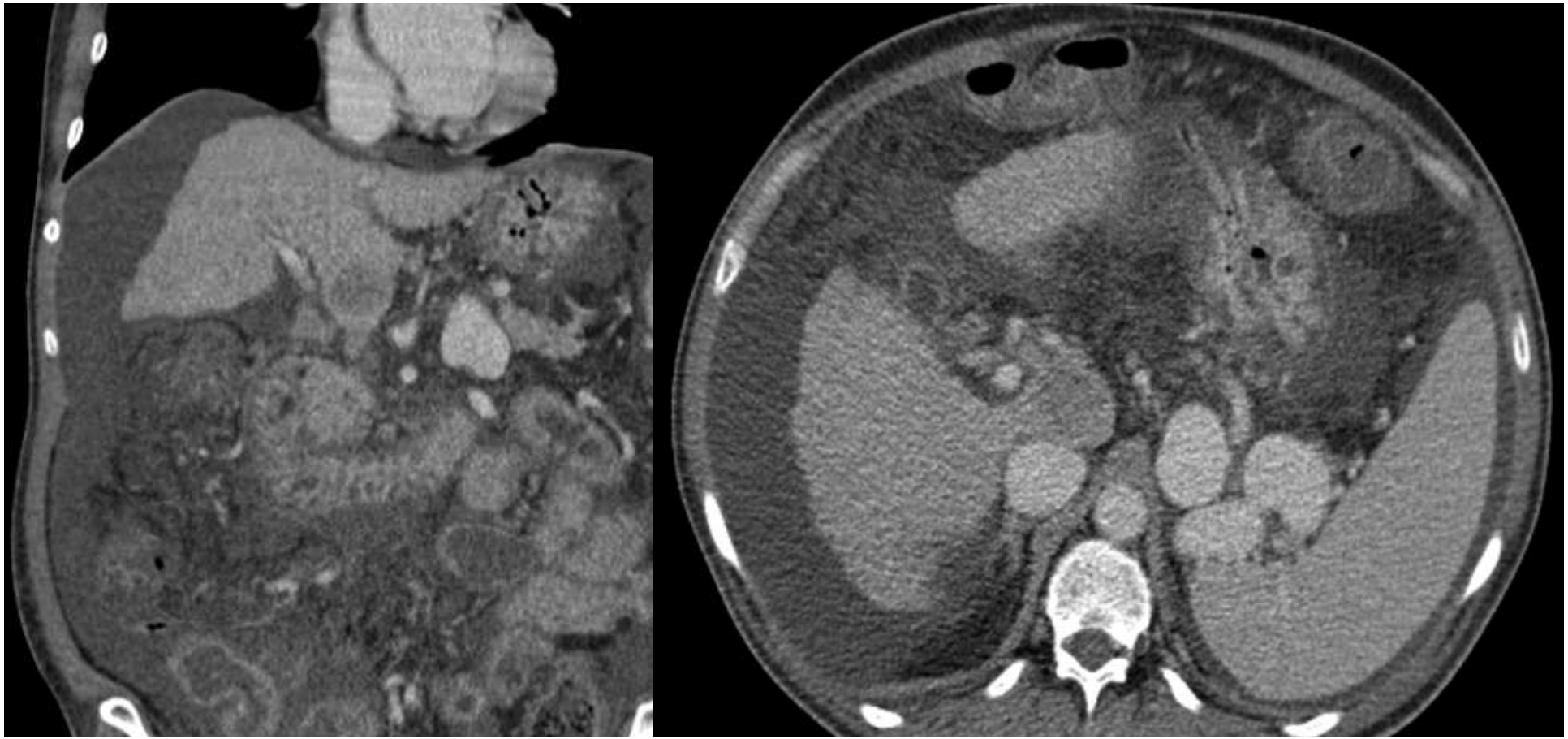
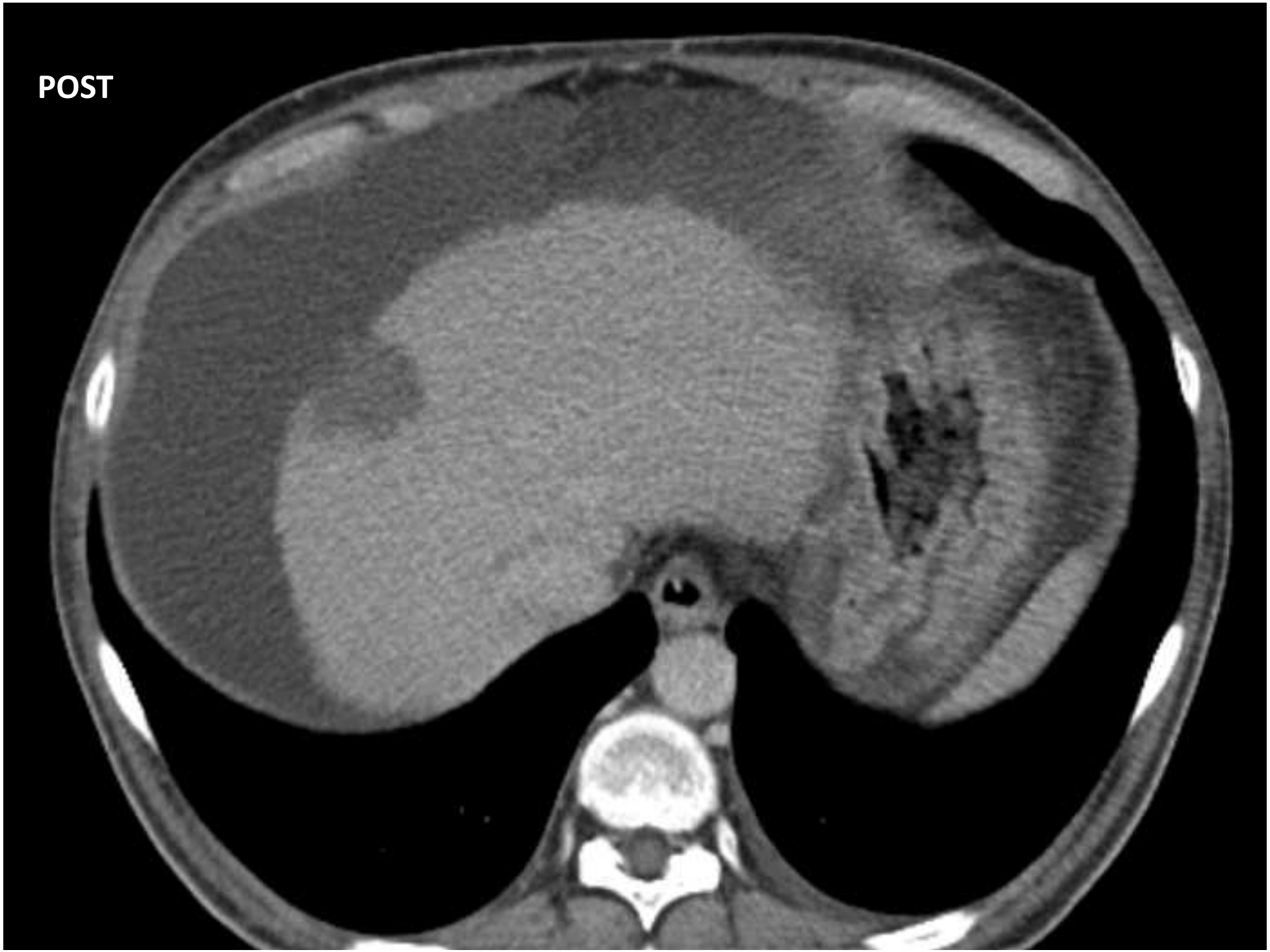


M,62 yrs
CT: Sg VIII 25 mm



M,62 yrs
CT: Sg I 30 mm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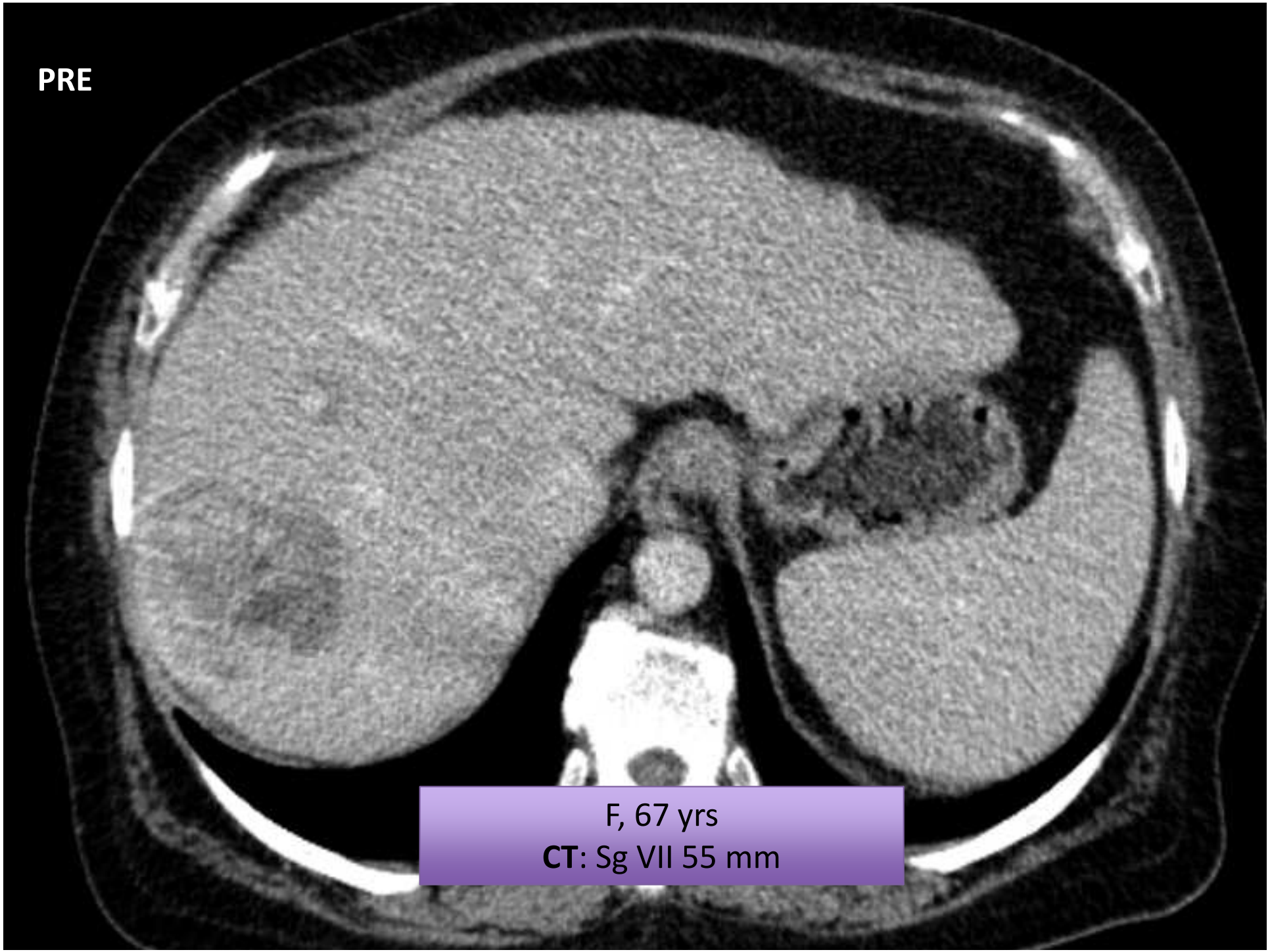
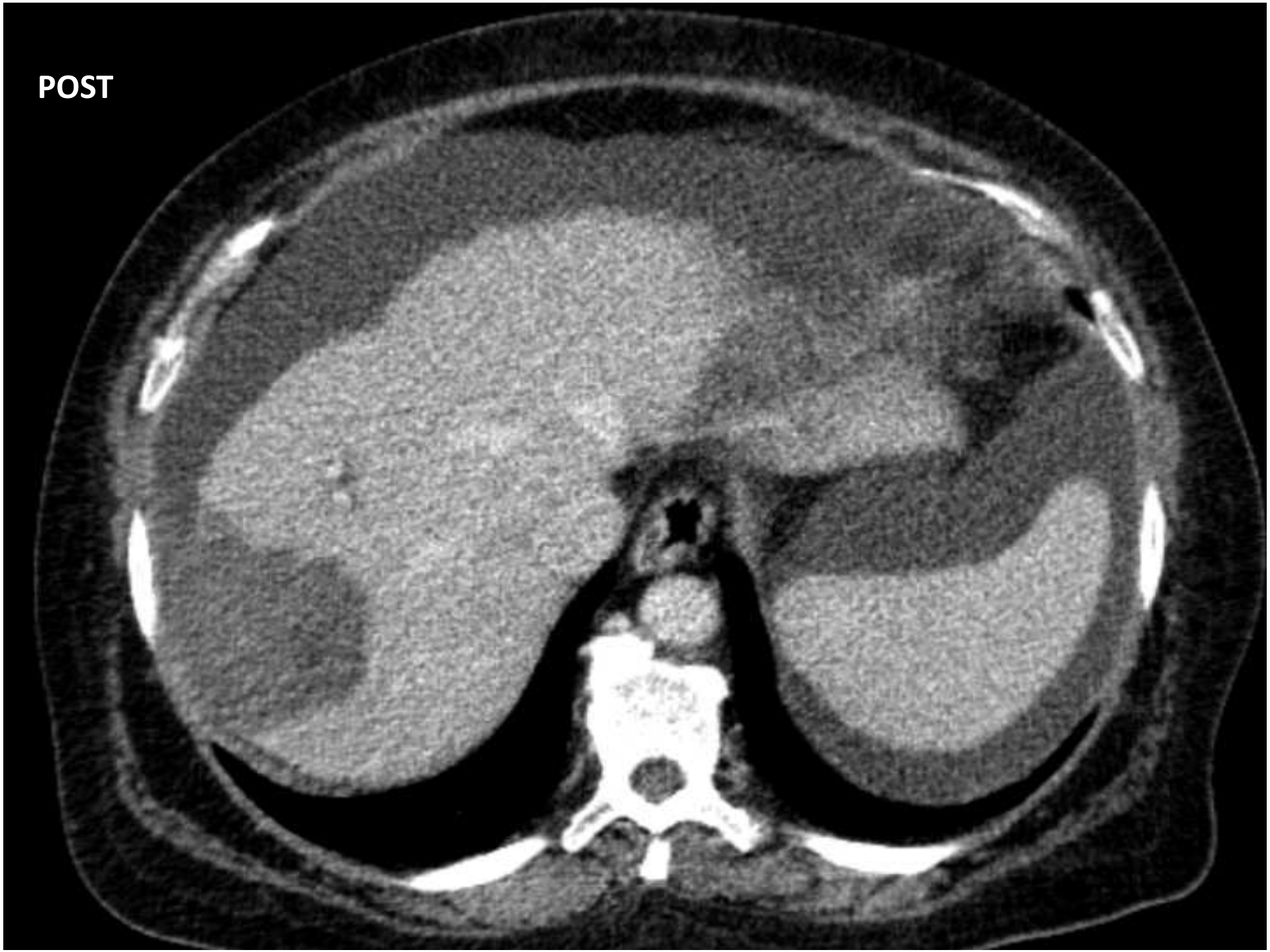

PRE
F, 67 yrs
CT: Sg VII 55 mm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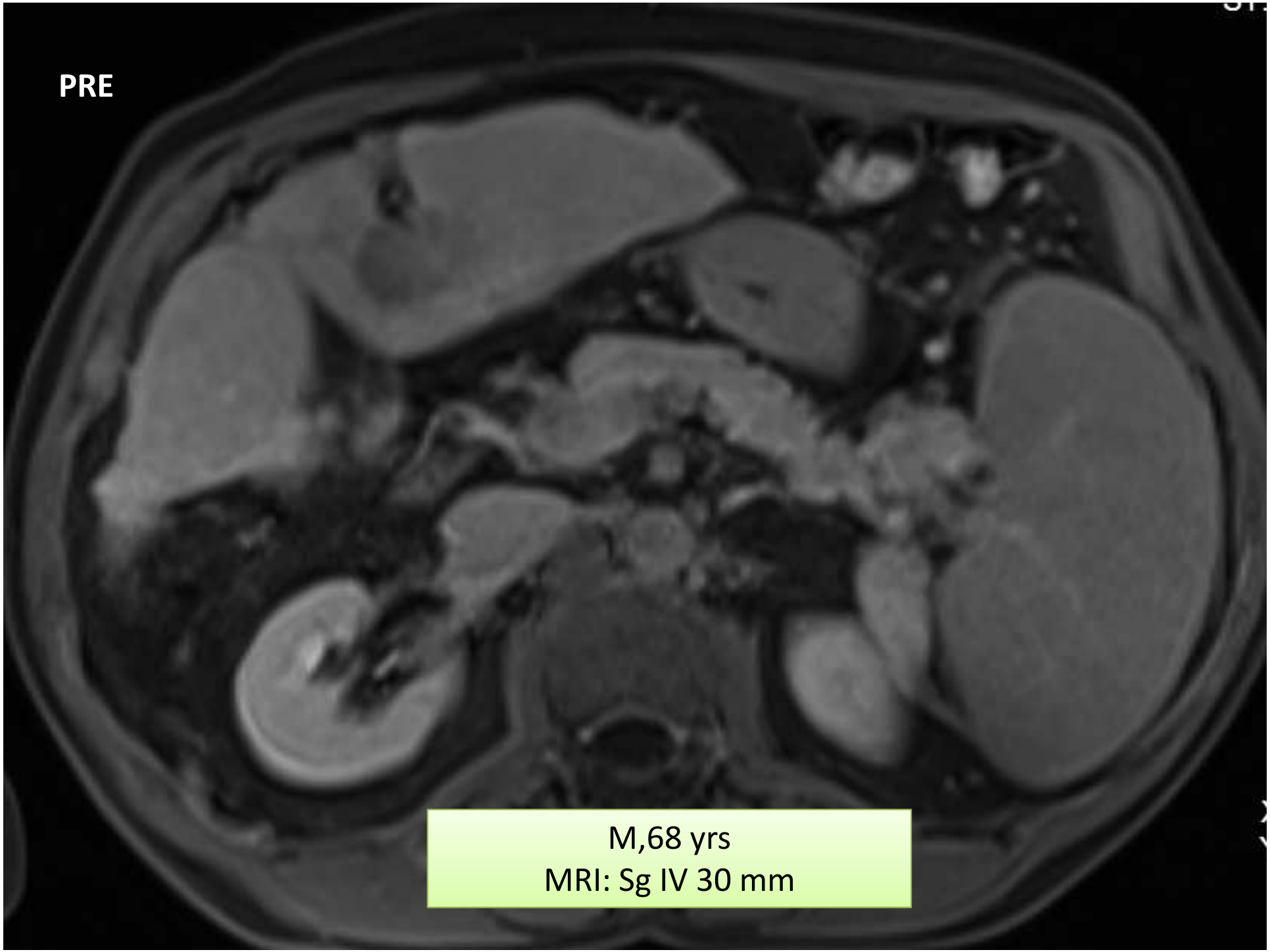
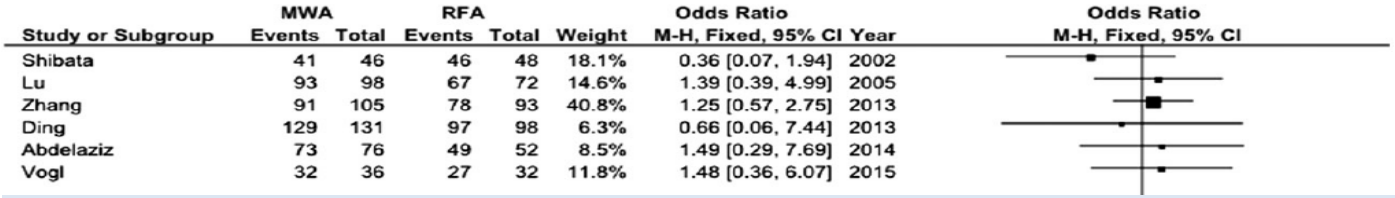

PRE
M,68 yrs
MRI: Sg IV 30 mm


POST
MW ablation
16 min 40 W

Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: A systematic review and meta-analysis

Systematic review

- 1 RCT
- 6 retrospective studies → 774 patients were included



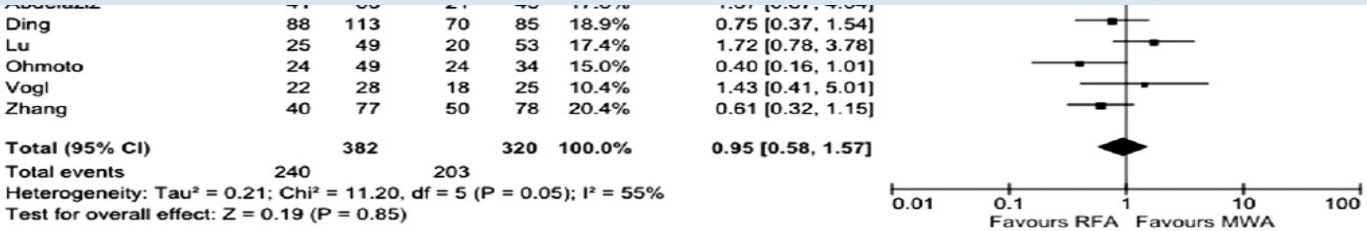
Study or Subgroup	MWA Events	MWA Total	RFA Events	RFA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Shibata	41	46	46	48	18.1%	0.36 [0.07, 1.94]	2002
Lu	93	98	67	72	14.6%	1.39 [0.39, 4.99]	2005
Zhang	91	105	78	93	40.8%	1.25 [0.57, 2.75]	2013
Ding	129	131	97	98	6.3%	0.66 [0.06, 7.44]	2013
Abdelaziz	73	76	49	52	8.5%	1.49 [0.29, 7.69]	2014
Vogl	32	36	27	32	11.8%	1.48 [0.36, 6.07]	2015

Complete Response Rate

Major complications → more frequent in MWA (OR 1.63, p=0.12)

Similar efficacy between the two percutaneous techniques

with an apparent superiority of MWA in larger neoplasms



Ding	88	113	70	85	18.9%	0.75 [0.37, 1.54]
Lu	25	49	20	53	17.4%	1.72 [0.78, 3.78]
Ohmoto	24	49	24	34	15.0%	0.40 [0.16, 1.01]
Vogl	22	28	18	25	10.4%	1.43 [0.41, 5.01]
Zhang	40	77	50	78	20.4%	0.61 [0.32, 1.15]
Total (95% CI)		**382**		**320**	**100.0%**	**0.95 [0.58, 1.57]**
Total events	240		203			

Heterogeneity: Tau² = 0.21; Chi² = 11.20, df = 5 (P = 0.05); I² = 55%
Test for overall effect: Z = 0.19 (P = 0.85)

3-ys OS

Facciorusso A et al, Int J Hyperthermia, 2016; 32(3): 339–344

Comparison of Laparoscopic Microwave to Radiofrequency Ablation of Small Hepatocellular Carcinoma (≤3 cm)

Retrospective, Single center
From February 2009 to May 2015

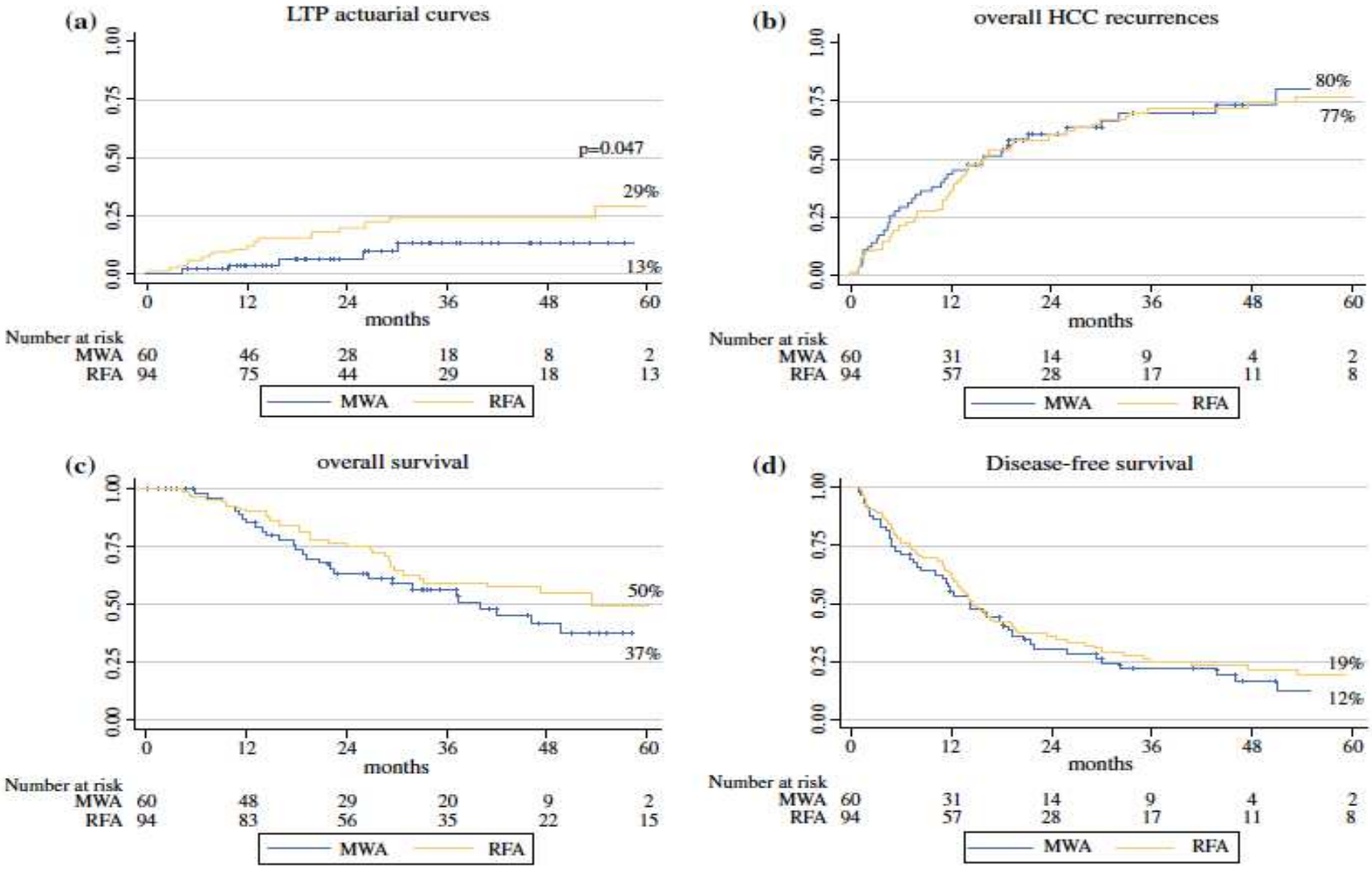
154 patients with HCC treated laparoscopically:

- 94 RFA
- 60 MWA

	RFA N = 94	MWA N = 60	p
Major complications	1%	2%	0.747
Complete ablation rate	95%	95%	0.931
LTP rates	21.1%	8.3%	0.034
5ys DFS	19%	12%	0.434
5 ys OS	50%	37%	0.185

Santambrogio R et al, Ann Surg Oncol (2017) 24:257–263

Comparison of Laparoscopic Microwave to Radiofrequency Ablation of Small Hepatocellular Carcinoma (≤3 cm)



Santambrogio R et al, Ann Surg Oncol (2017) 24:257–263

*all indications

L-RFA:
Summary of published series

Paper	Pts N°	RFA/MWA	Mean Tumor Size (cm)	Morbidity	Mortality	Local recurrence	DFS	OS
Santambrogio, 2003	88	RFA	1.0 ± 0.4	29%	0%	11%	-	4-ys: 50%
Hsieh, 2004	40	RFA	3.4 ± 0.8	17.5%	30d: 2.5%	1-yr: 30%	-	-
Kawamoto, 2004	69	MWA	2.3 ± 0.7	4.34%	0%	17.4%	5-ys: 17.8%	5-ys: 63.9%
Seki, 2005	68	MWA	2.0	-	-	12%	-	1-yr: 97% 5-ys: 43%
Berber 2007	109*	RFA	2.7 ± 1.6*	30d 3.8%*	30d 0.4%*	-	-	-
Casaccia, 2008	24	RFA	-	16.6%	4.16%	-	-	-
Ballem, 2008	104	RFA	3.5	-	-	-	Median 14 months	Median 26 months
Berber, 2008	335*	RFA	2.6 ± 1	-	-	1yr: 18%	-	-
Tanaka, 2009	26	RFA	-	19.2%	-	3.8%	-	-
Santambrogio, 2009	74	RFA	2.9 ± 1.2	65%	50%	24%	5-ys: 38%	5-ys: 54%
Tesche, 2010	49	RFA	2.8 ± 1.3	10%	2.0%	1y: 37%	-	1y: 81%
Cassera, 2011	18	RFA	3.9 ± 1.1	20%	0%	-	-	-
CIllo, 2013	103	RFA	2.5	25%	0%	28%	.	5-YS: 40%
Cillo, 2014	42	MWA	2.5	24%	0%	2-yr: 55%	-	2-yr: 79%
Santambrogio, 2016	426	RFA/MWA	80% ≤3.0	25%	0.23%	15%	-	5-ys: 34%
Cillo, 2019	853	MWA	3.5	30.8%	0.4%	20%		5 yr:40%

Long-term outcome of laparoscopic ablation therapies for unresectable hepatocellular carcinoma: a single European center experience of 426 patients

426 HCC patients who underwent LATs

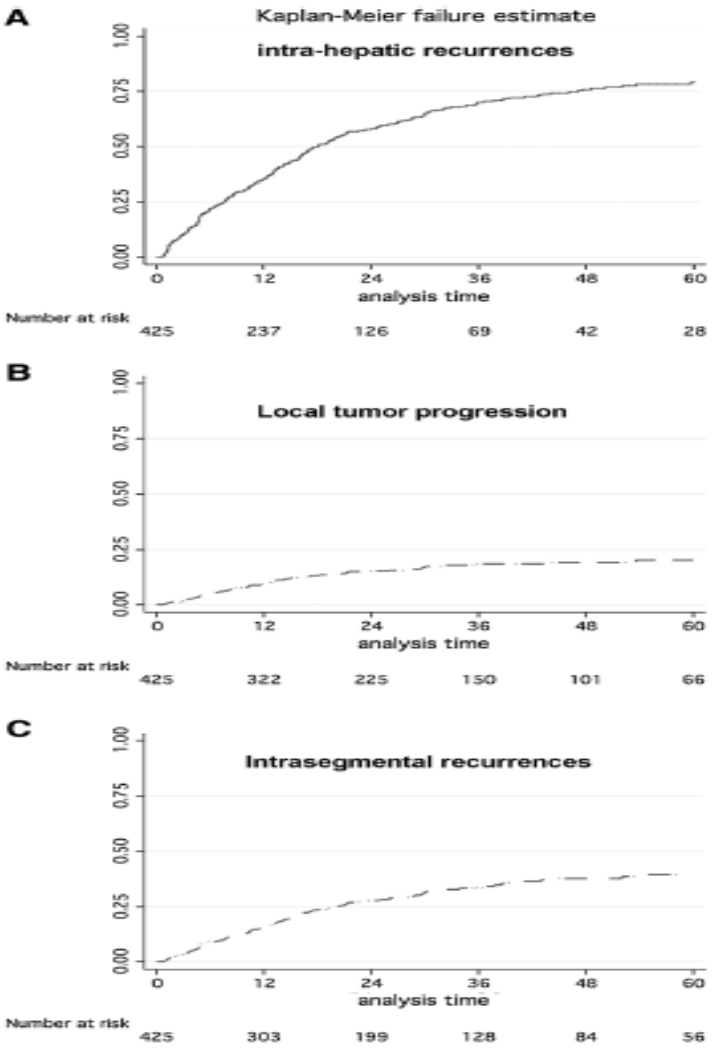
- TT-HCC not suitable for LT or HR
- HCC not suitable for percutaneous RFA (Location)
- Early HCC recurrence (< 3 months)

Successful RFA-rate (one session): 93%

30 days mortality: 0.23%
30 days morbidity: 25%

During a median follow-up of 37.2 (2-193) months:

	LATs
Intrahepatic recurrence	65% (15% LTP)
Median OS	39 months (34.8-47.2)
1-yr OS	88%
3-ys OS	55%
5-ys OS	34%



Santambrogio R et al, Surg Endosc (2016) 30:2103–2113

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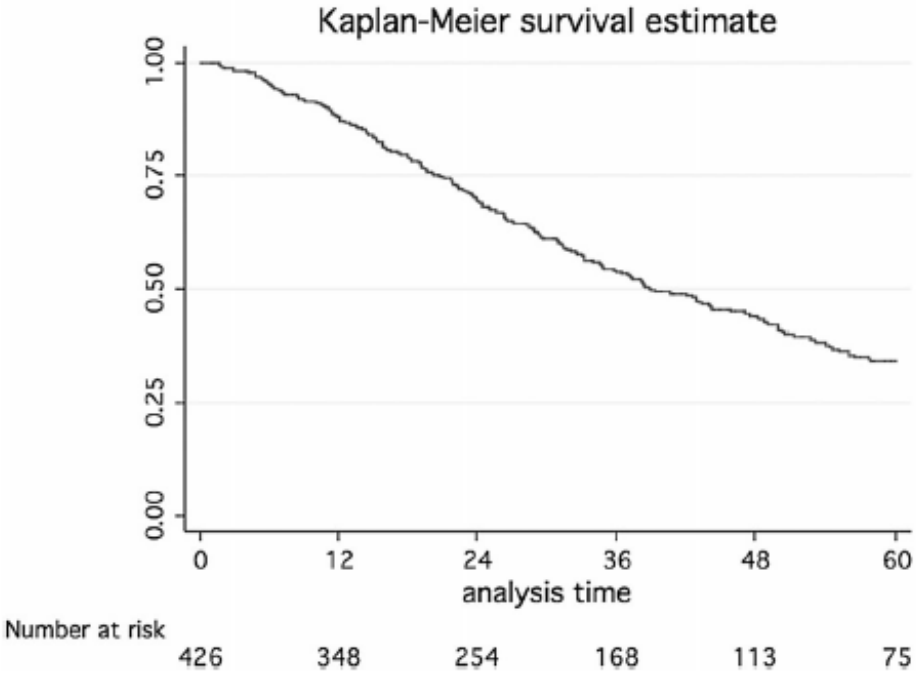


Santambrogio R et al, Surg Endosc (2016) 30:2103–2113

Personalized treatment of patients with very early hepatocellular carcinoma

According to extent of liver resection, and liver function, percutaneous ablation or liver resection are the recommended first line therapies in these patients.

Very early stage (0),
Single <2 cm

Laparoscopic surgery (resection or ablation)
is the preferable strategy
when the tumor is in the surface of the liver
or close to extra-hepatic organs

Due to scarce donor resources
and competition with patients at high transplant benefit
LT is recommended only as 2° line therapy
in patients with very early stage HCC
in case of tumor recurrence or liver failure after ablation or liver resection

Vitale A et al, Journal of Hepatology 2017 vol. 66 j 412–423

Padova Experience in Laparoscopic Ablation Therapies For HCC

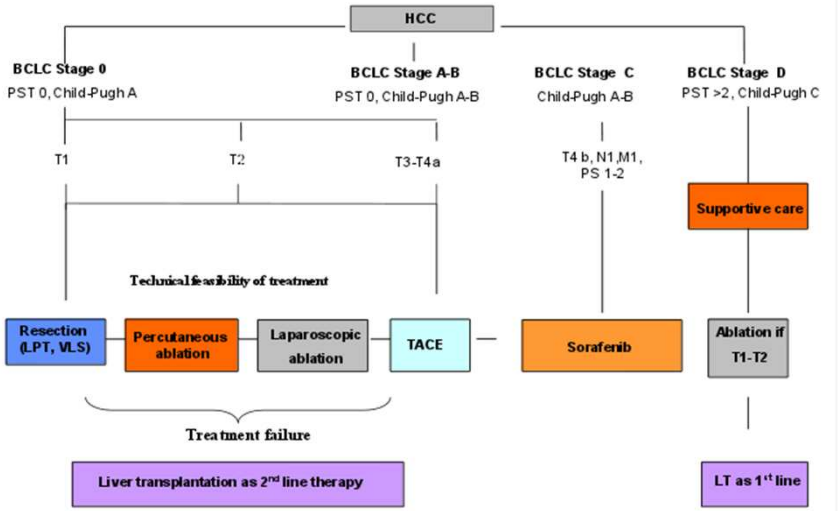
University of Padova Experience:
What we have already done

LAPAROSCOPIC ABLATION OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS UNSUITABLE FOR LIVER RESECTION OR PERCUTANEOUS TREATMENT: A COHORT STUDY

Prospective study (January 2004 → December 2009)
169 laparoscopic ablation for HCC

72% Clinically relevant portal hypertension
50% Multinodular tumors or nodules > 25 mm

Ablation techniques:
- 103/169 (61%): RFA
  - 8/169 (5%): MWA
  - 58/169 (34%): EIA



Padua's treatment algorithm

Table 4. Multivariate survival analyses.

	Hazard ratio (95% confidence interval)	*p* value
Model including only pre-operative covariates		
Age >62 years	1.47 (1.14-1.91)	0.0028
ASA >2	1.21 (0.93-1.58)	0.1455
Diabetes	1.28 (0.99-1.65)	0.0614
Albumin ≤ 37 g/l	2.99 (1.70-5.32)	0.0001
Child Pugh B	0.81 (0.47-1.40)	0.4474
Alpha fetoprotein >400 µg/l	2.17 (1.56-2.96)	<0.0001
Model including pre and post-operative covariates		
Age >62 years	1.28 (0.89-1.57)	0.2581
ASA >2	1.30 (0.99-1.69)	0.0584
Diabetes	1.37 (1.03-1.82)	0.0308
Albumin ≤ 37 g/l	2.80 (1.58-5.01)	0.0004
Child Pugh B	0.75 (0.43-1.31)	0.3131
Alpha fetoprotein >400 µg/l	2.10 (1.50-2.89)	<0.0001
Postoperative ascites[1]	1.60 (1.12-2.26)	0.0109
Postoperative complications	0.73 (0.36-1.44)	0.3646
No liver transplantation	2.07 (1.36-3.44)	0.0004

[1]leakage from abdominal drains >1000ml/day

ASA, American Society of Anesthesiologists physical status score; BCLC, Barcelona Clinic liver cancer stage

Pre-op predictors of survival

Post-op predictors of survival

Cillo et al, PlosOne 2013, February 2013 | Volume 8 | Issue 2 | e57249

University of Padova Experience:
What we have already done

LAPAROSCOPIC ABLATION OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS UNSUITABLE FOR LIVER RESECTION OR PERCUTANEOUS TREATMENT: A COHORT STUDY

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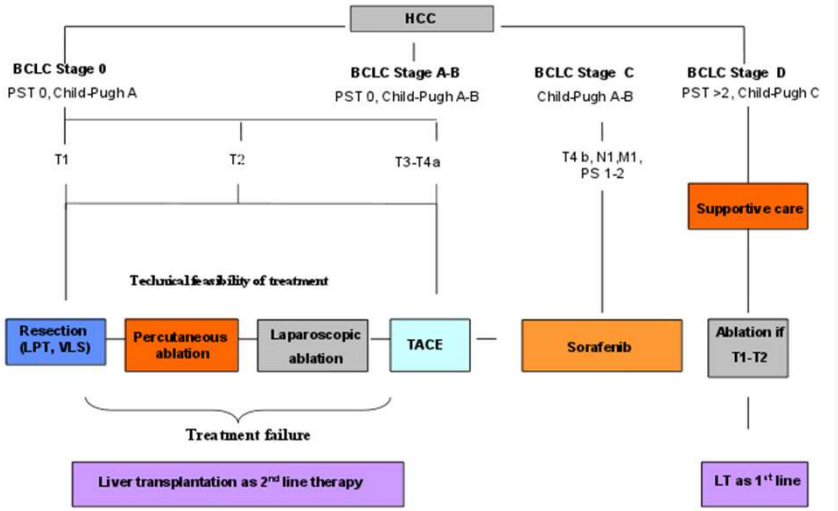
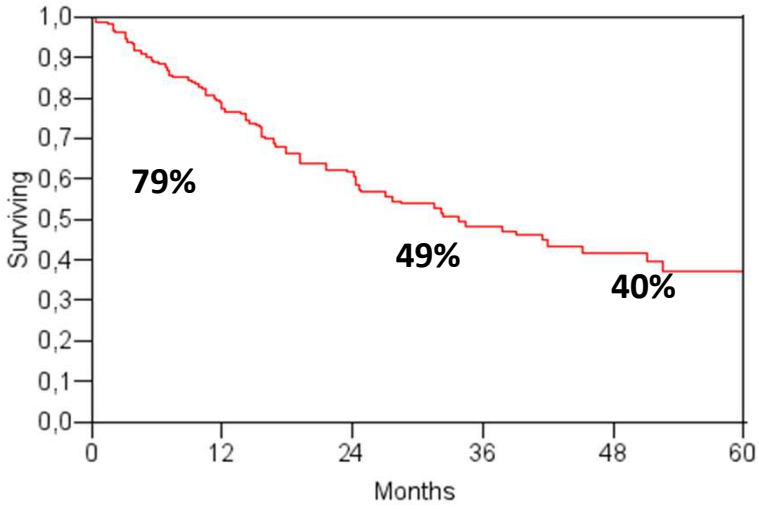


Padua's treatment algorithm



Median Survival: 33 months

Overall survival:
1-year: 79%
3-years: 49%
5-years: 40%

Cillo et al, PlosOne 2013, February 2013 | Volume 8 | Issue 2 | e57249

University of Padova Experience:
What we have already done

LAPAROSCOPIC ABLATION OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS UNSUITABLE FOR LIVER RESECTION OR PERCUTANEOUS TREATMENT: A COHORT STUDY

Prospective study (January 2004 → December 2009)
169 laparoscopic ablation for HCC

7
5

A
●

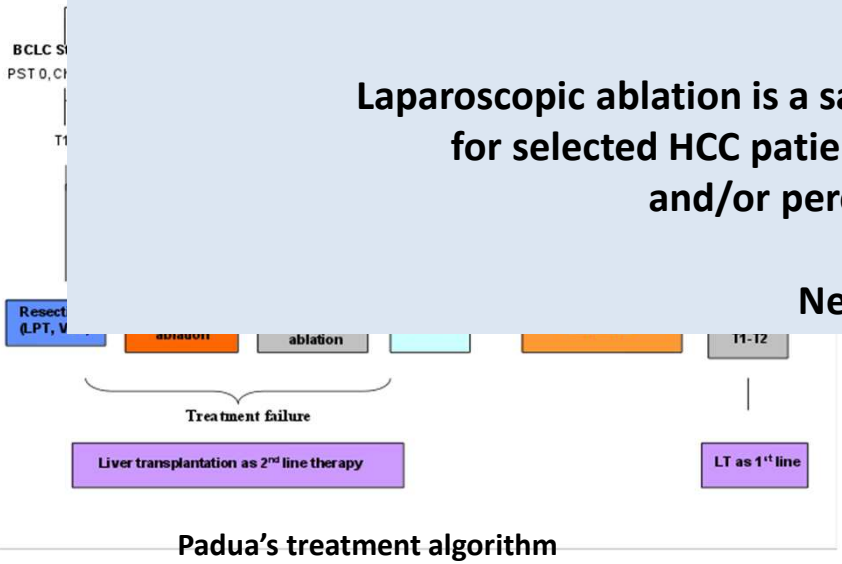
15% Incomplete LA at first imaging study

28% Incidence of early local recurrence

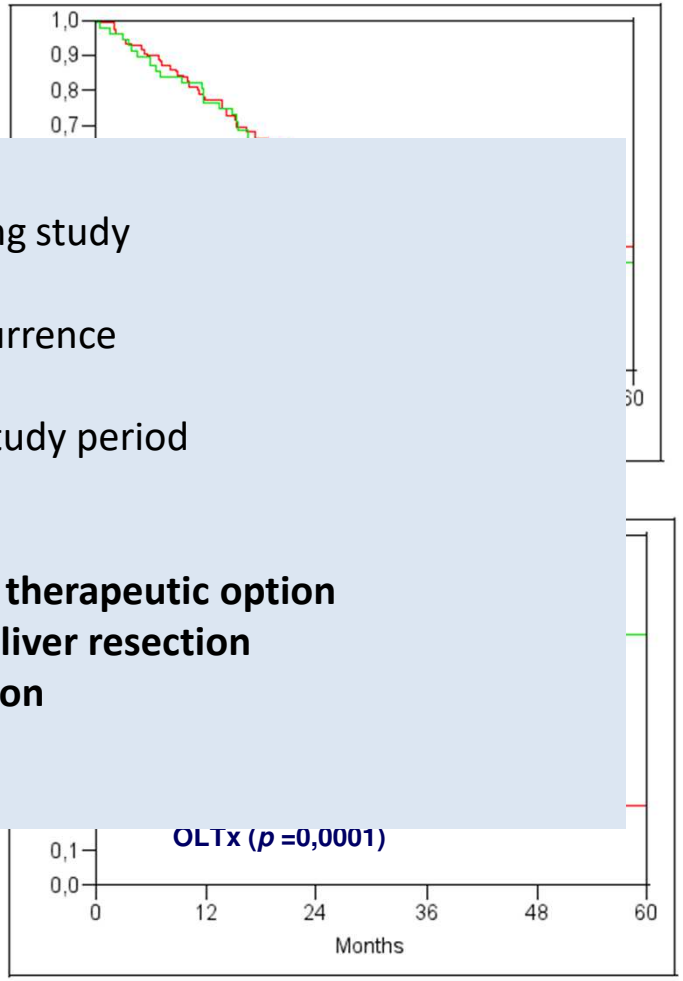
24% Distant recurrence during the study period

Laparoscopic ablation is a safe and effective therapeutic option for selected HCC patients ineligible for liver resection and/or percutaneous ablation

Need for RCT



Padua's treatment algorithm



Cillo et al, PlosOne 2013, February 2013 | Volume 8 | Issue 2 | e57249

University of Padova Experience:
What we have already done

ORIGINAL ARTICLE

Laparoscopic microwave ablation in patients with hepatocellular carcinoma: a prospective cohort study

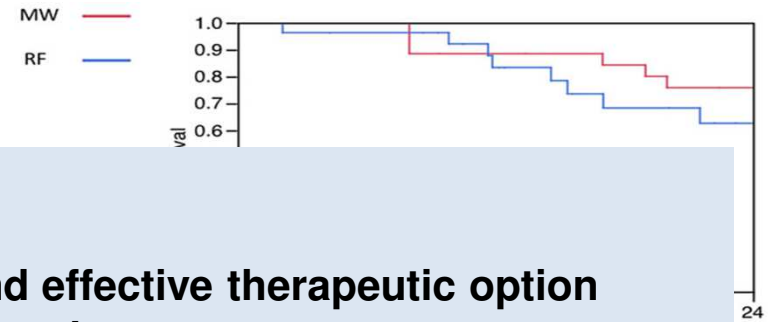
Prospective study (December 2009 → December 2010)
42 HCC patients ineligible
for liver resection and/or percutaneous ablation

RE

94

Nc
Ov

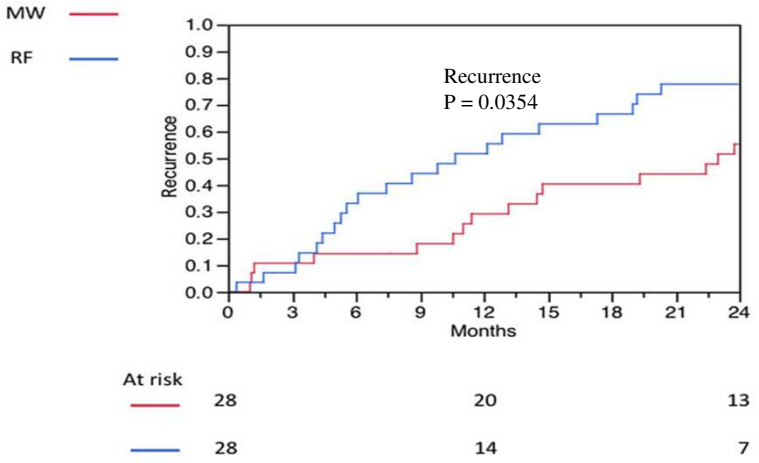
Laparoscopic MW ablation is a safe and effective therapeutic option for selected HCC patients who are ineligible for liver resection and/or percutaneous ablation



2-year survival rate: 79%
2-year recurrence rate: 55%

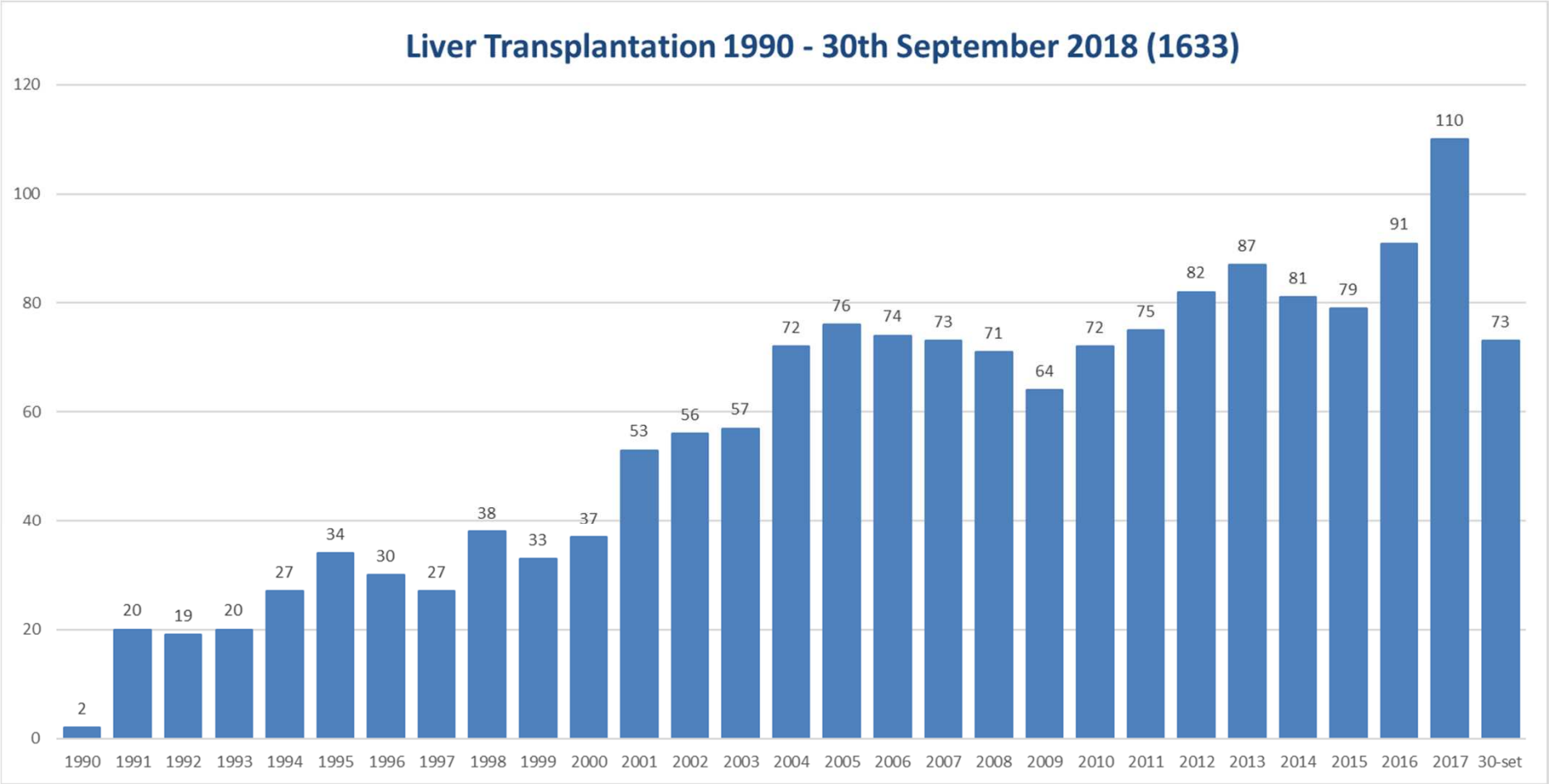
Using propensity score analysis (28 MW, 28 RF)

2-year recurrence rate:
MW: 55%
RF: 77% (P = 0.03)



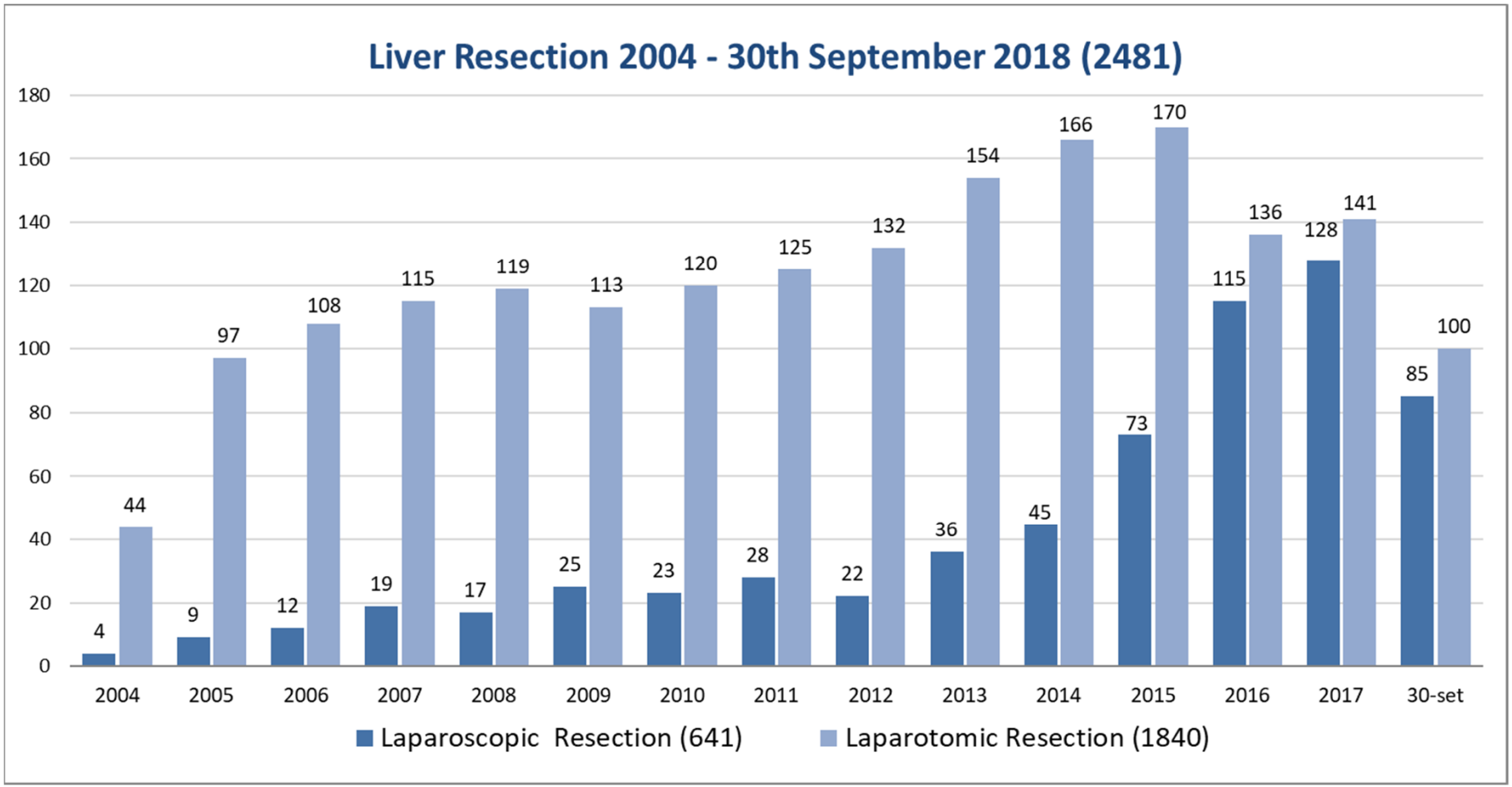
Cillo U et al, HPB 2014, 16, 979-986

Padova Experience
1633 Liver Transplantation



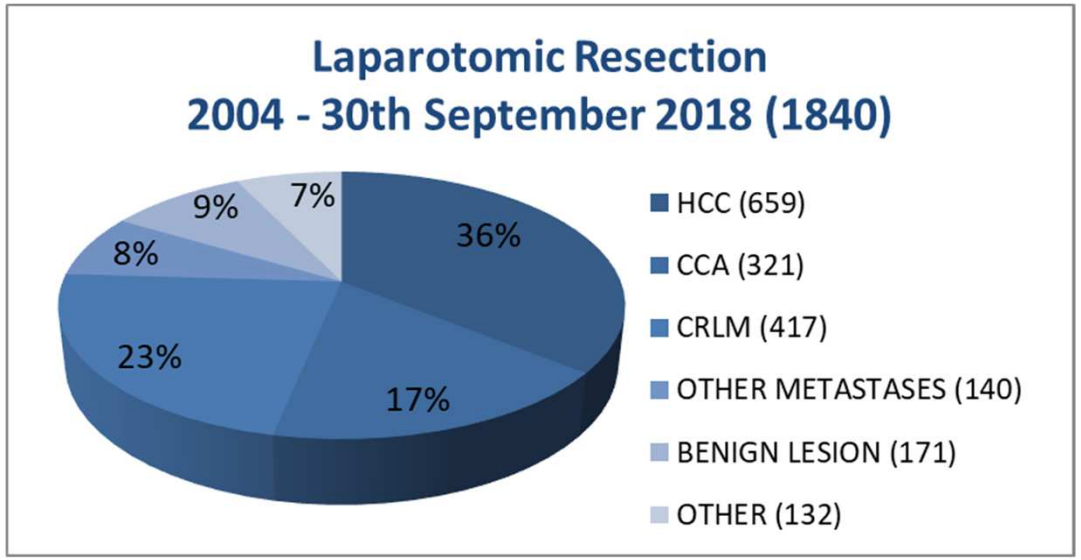
U. Cillo, Personal Experience

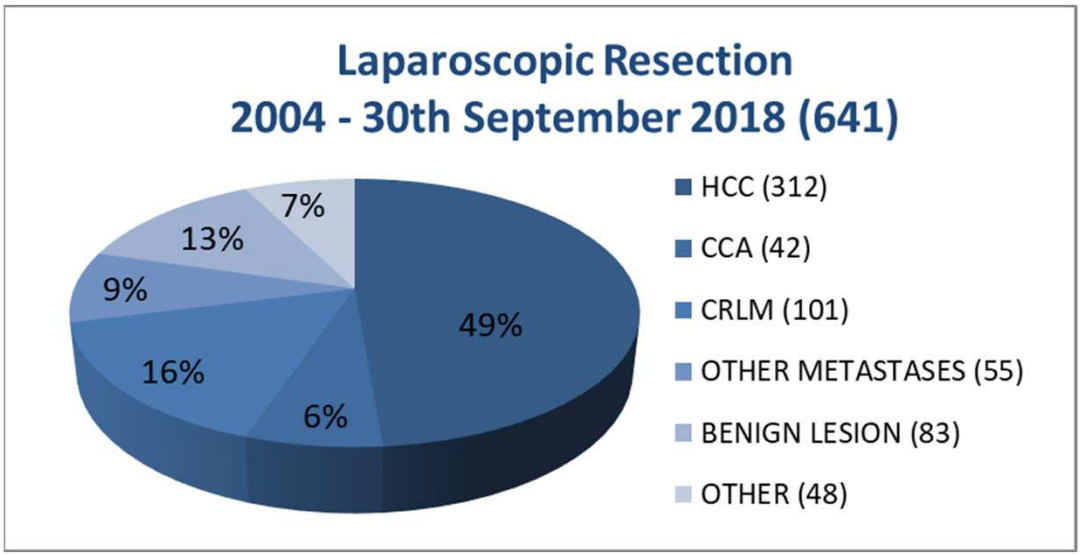
Padova Experience
2481 Liver Resection
1840 Laparotomic LR – 641 Laparoscopic LR



U. Cillo, Personal Experience

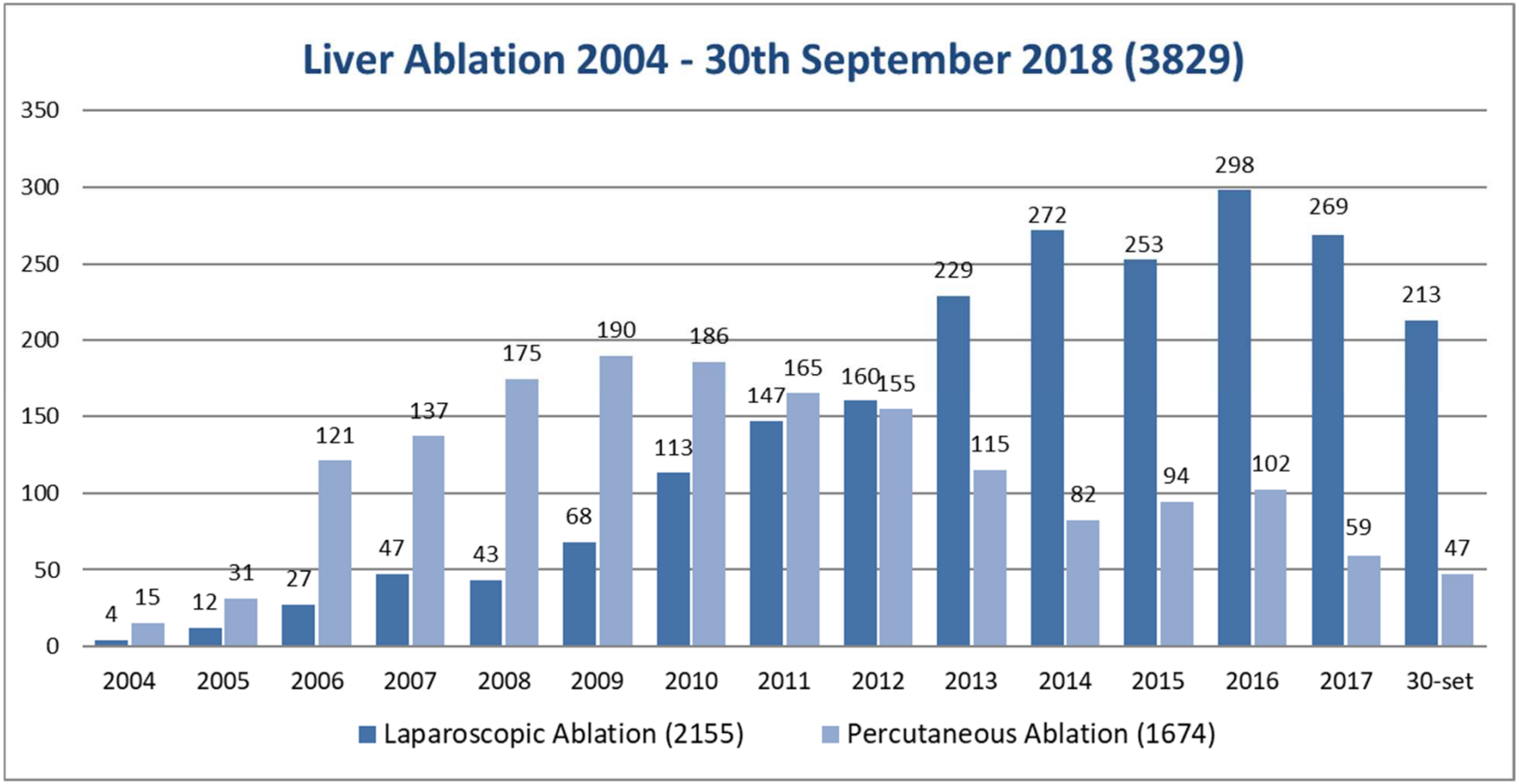
Padova Experience
2481 Liver Resection
1840 Laparotomic LR – 641 Laparoscopic LR





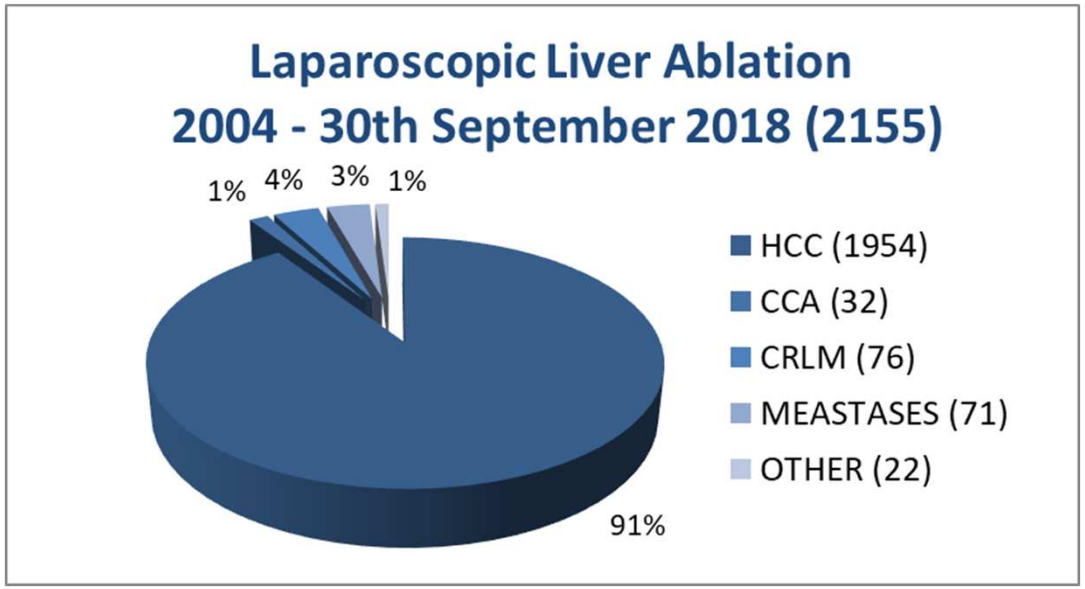
U. Cillo, Personal Experience

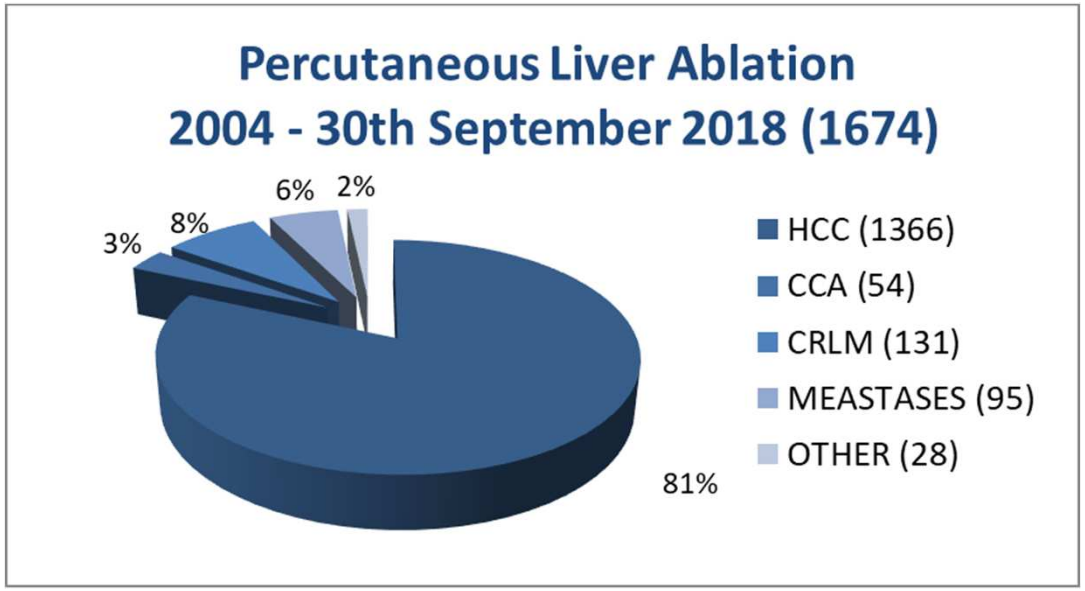
Padova Experience
3829 Liver Ablation
2155 Laparoscopic LA – 1674 Percutaneous LA



U. Cillo, Personal Experience

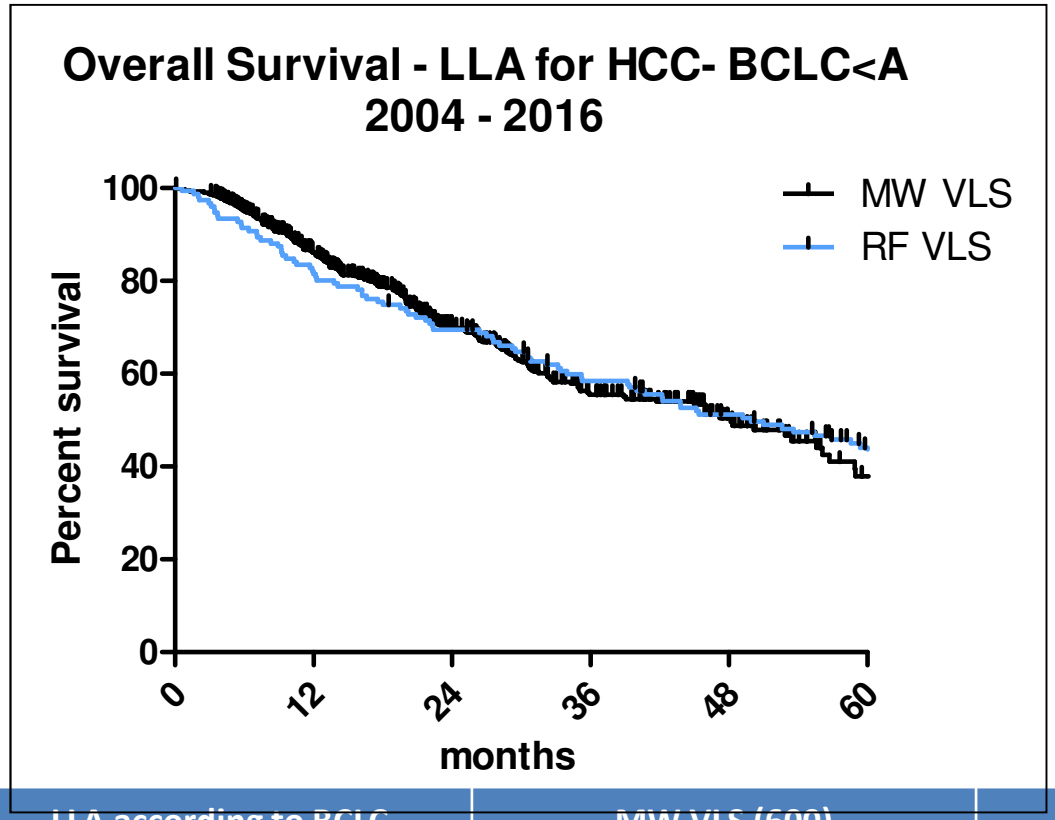
Padova Experience
3829 Liver Ablation
2155 Laparoscopic LA – 1674 Percutaneous LA





U. Cillo, Personal Experience

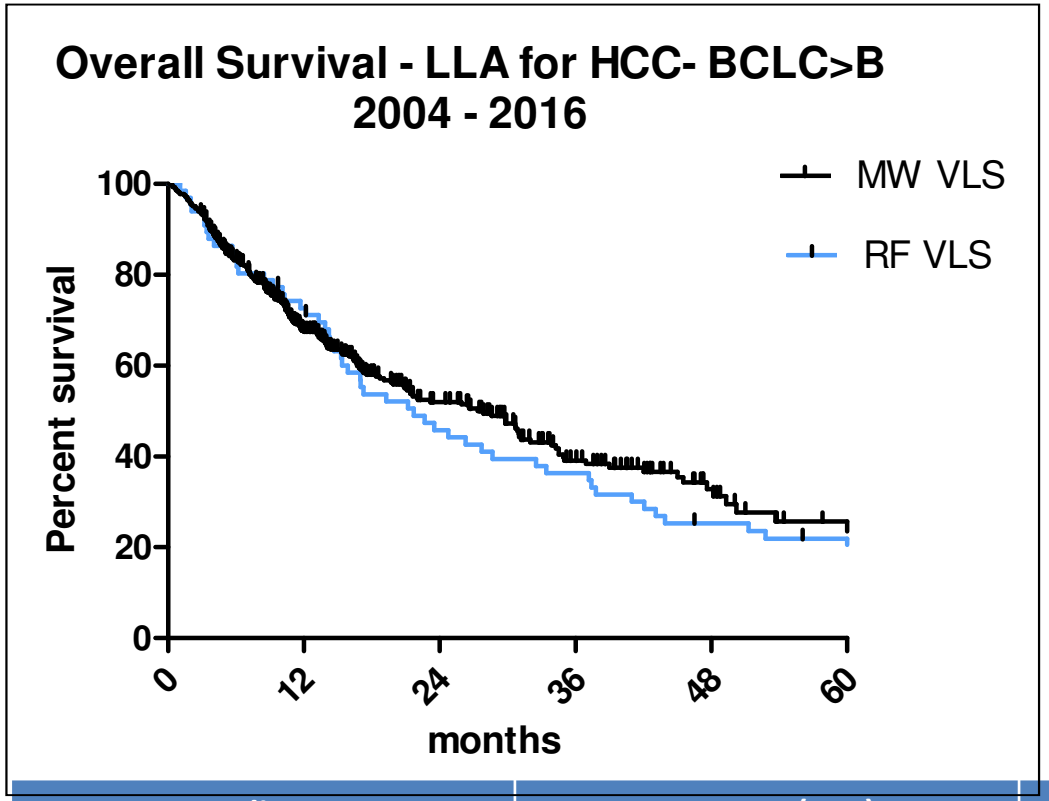
Padova Experience
600 MW VLS for HCC
151 RF VLS for HCC
2004 – 2016



P-value=ns

LLA according to BCLC	MW VLS (600)	RF VLS (151)
1 yr	86,1%	81,5%
3 yr	55,5%	58,4%
5 yr	37,9%	44,0%
Median OS	48,17 months	49,9 months

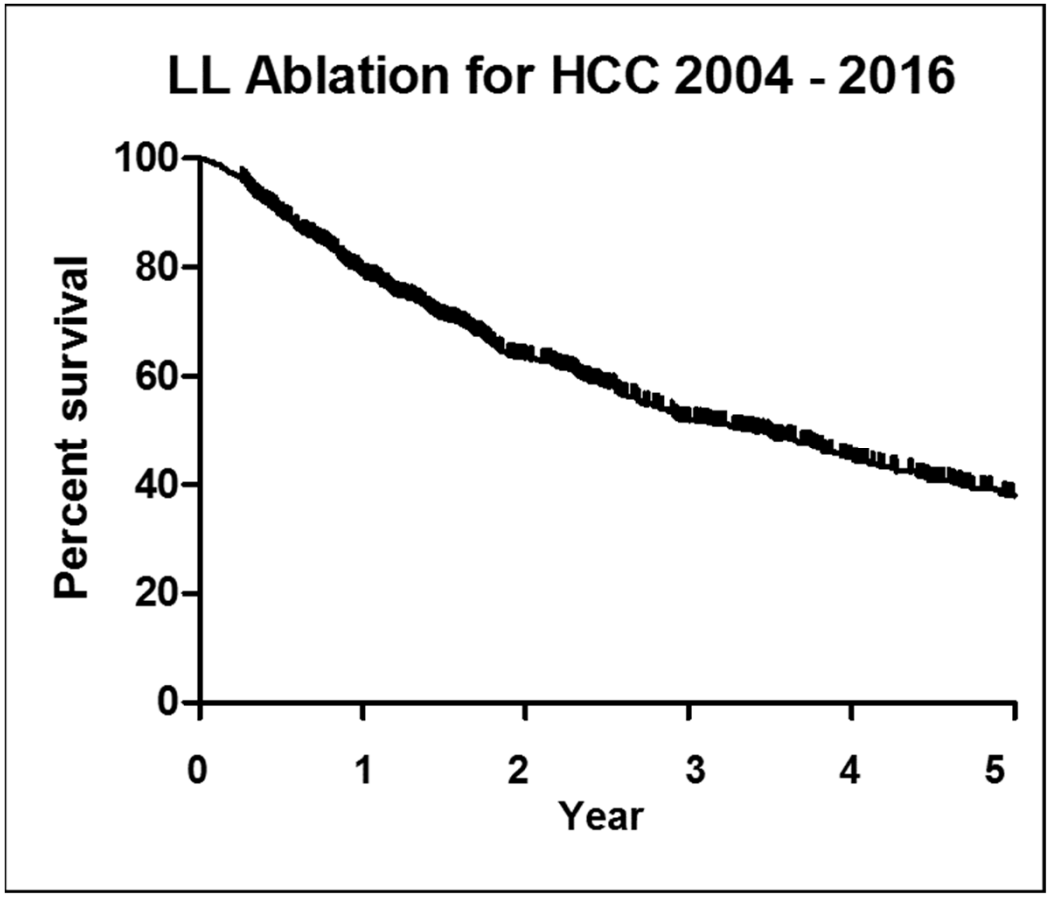
Padova Experience
448 MW VLS for HCC
66 RF VLS for HCC
2004 – 2016



P-value=ns

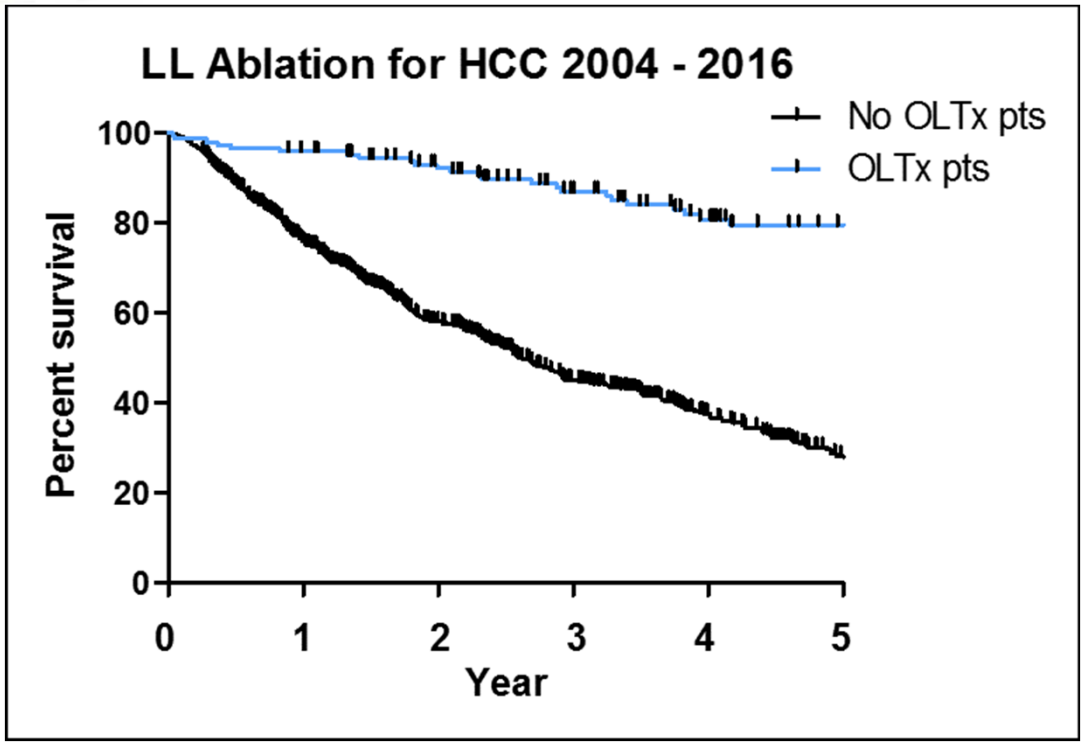
LLR according to BCLC	MW VLS (448)	RF VLS (66)
1 yr	67,5%	72,6%
3 yr	39,1%	36,3%
5 yr	25,7%	21,9%
Median OS	27,9 months	21,73 months

Padova Experience
1211 Laparoscopic Liver Ablation
2004 – 2016



N=1211	LLA 2004-2016
1 yr	78,7%
3 yr	51,9%
5 yr	38,0%
10 yr	23,1%
Median OS	40,9 months

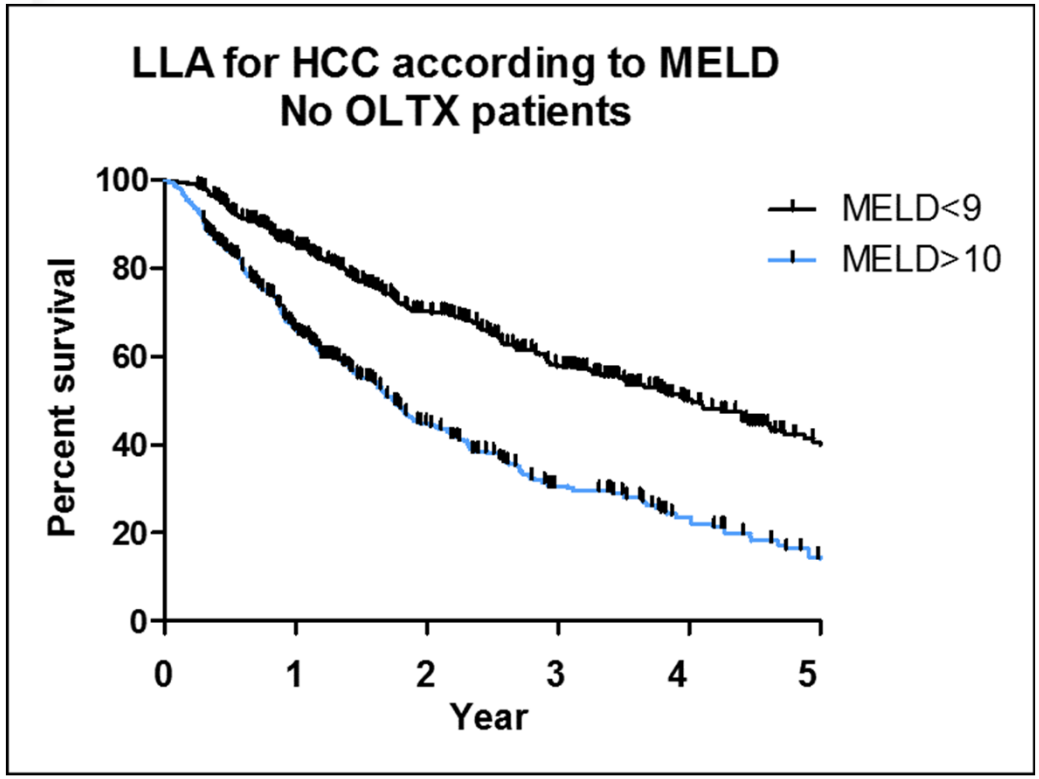
Padova Experience
1211 Laparoscopic Liver Resection
2004 – 2016



P-value=<0,0001

LLA	No OLTx pts (1067)	OLTx pts (144)
1 yr	75,9%	95,8%
3 yr	44,9%	87,0%
5 yr	28,3%	79,5%
10 yr	15,3%	53,9%
Median OS	31,5 months	120,5 months

Padova Experience
1207 Laparoscopic Liver Ablation
No OLTx patients 2004 – 2016

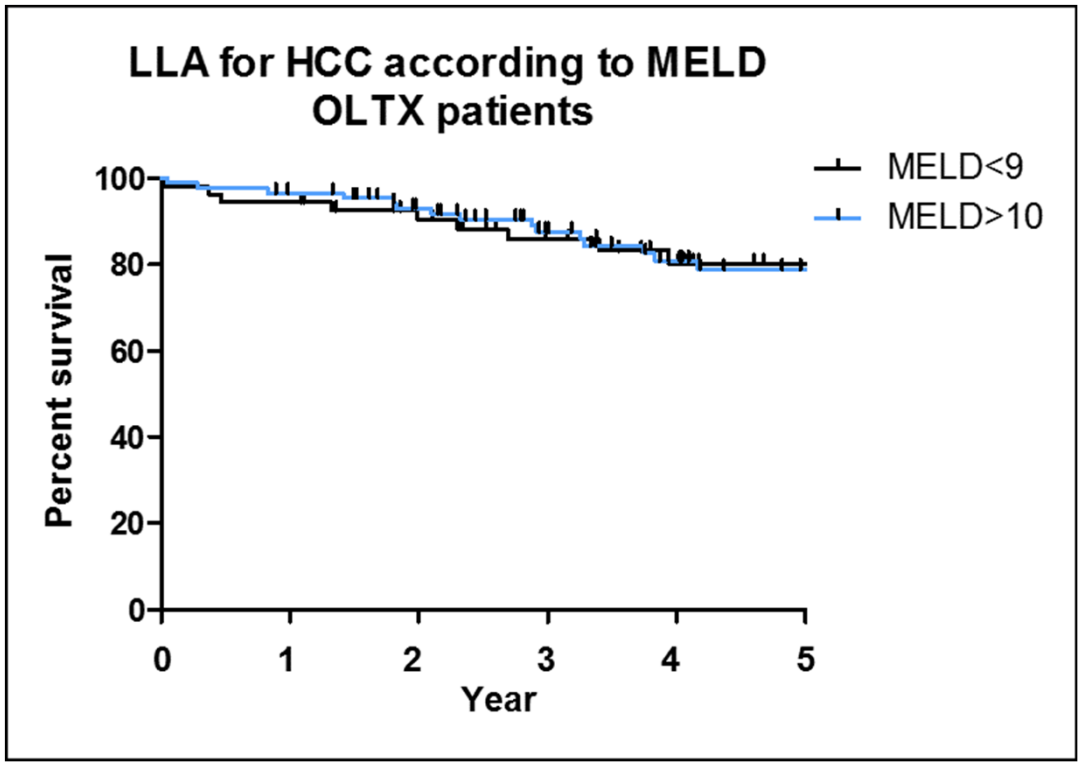


No OLTX patients

P-value<0,0001

LLA according to MELD	MELD<10 (618)	MELD≥10 (589)
1 yr	85,1%	66,0%
3 yr	57,7%	30,6%
5 yr	40,5%	14,5%
10 yr	22,9%	7,1%
Median OS	48,3 months	20,9 months

Padova Experience
144 Laparoscopic Liver Ablation
OLTx patients 2004 – 2016

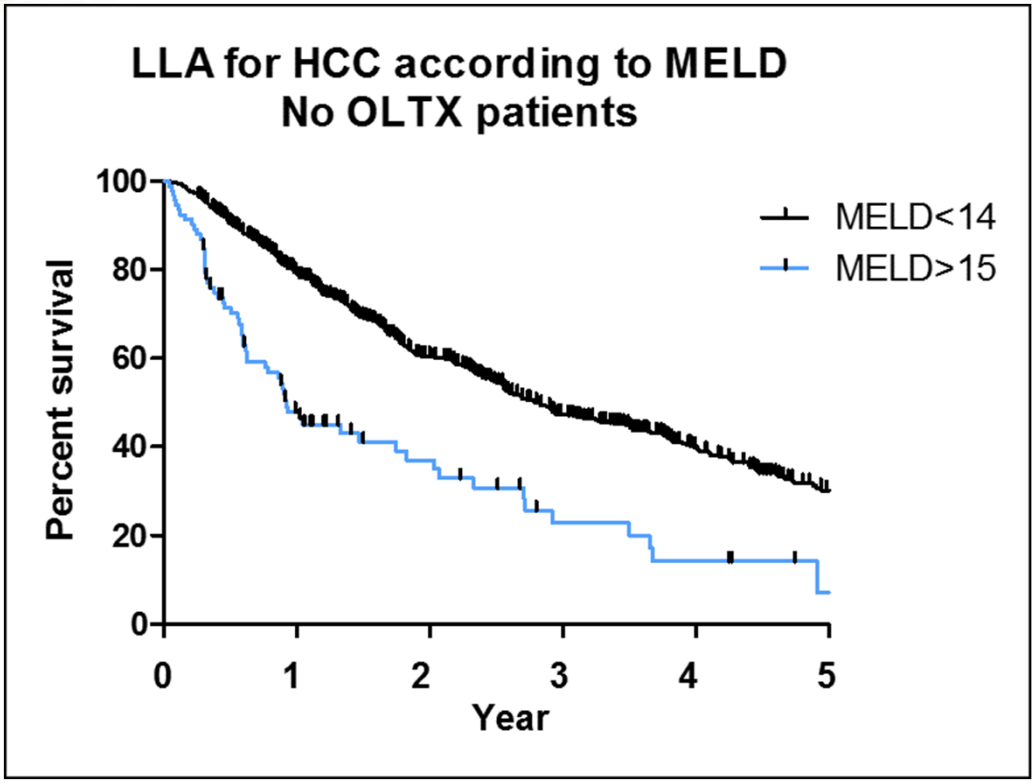


OLTX patients

P-value= ns (0,117)

LLA according to MELD	MELD<10 (54)	MELD≥10 (90)
1 yr	94,4%	96,7%
3 yr	85,9%	87,6%
5 yr	80,3%	79,1%
10 yr	35,6%	62,9%
Median OS	90,4 months	-

Padova Experience
1207 Laparoscopic Liver Ablation
No OLTx patients 2004 – 2016

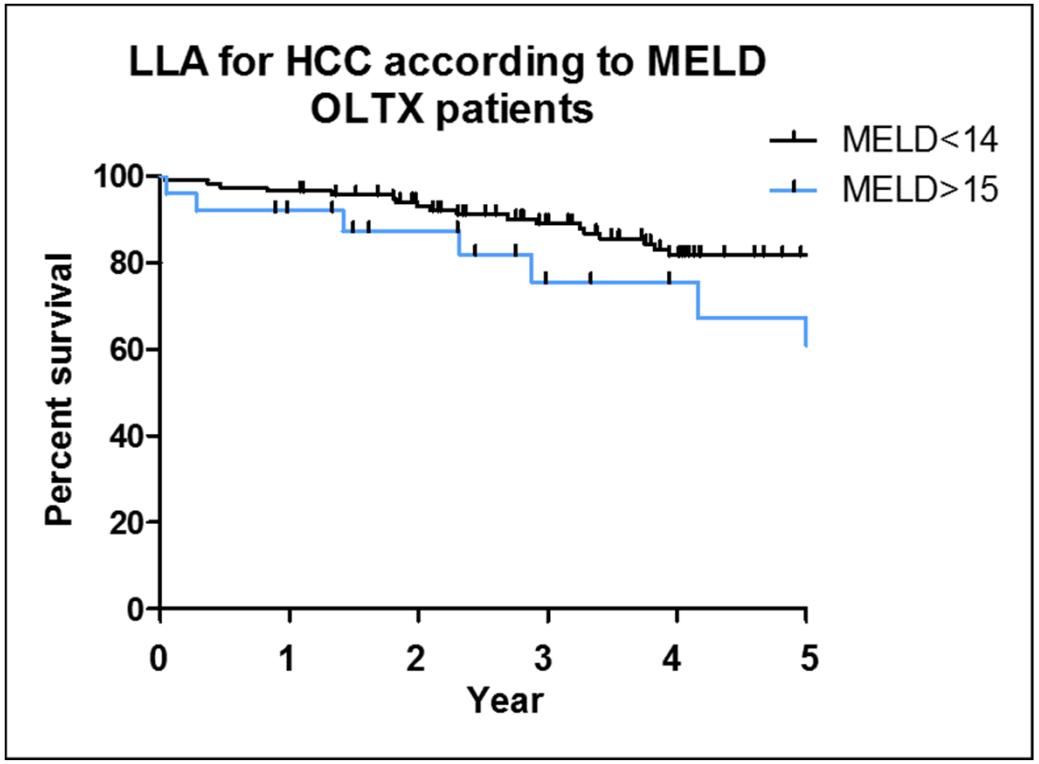


No OLTX patients

P-value<0,0001

LLR according to MELD	MELD<15 (1086)	MELD≥15 (121)
1 yr	78,9%	47,9%
3 yr	47,2%	27,8%
5 yr	30,2%	7,2%
10 yr	16,2%	-
Median OS	33,9 months	11 months

Padova Experience
144 Laparoscopic Liver Ablation
OLTx patients 2004 – 2016

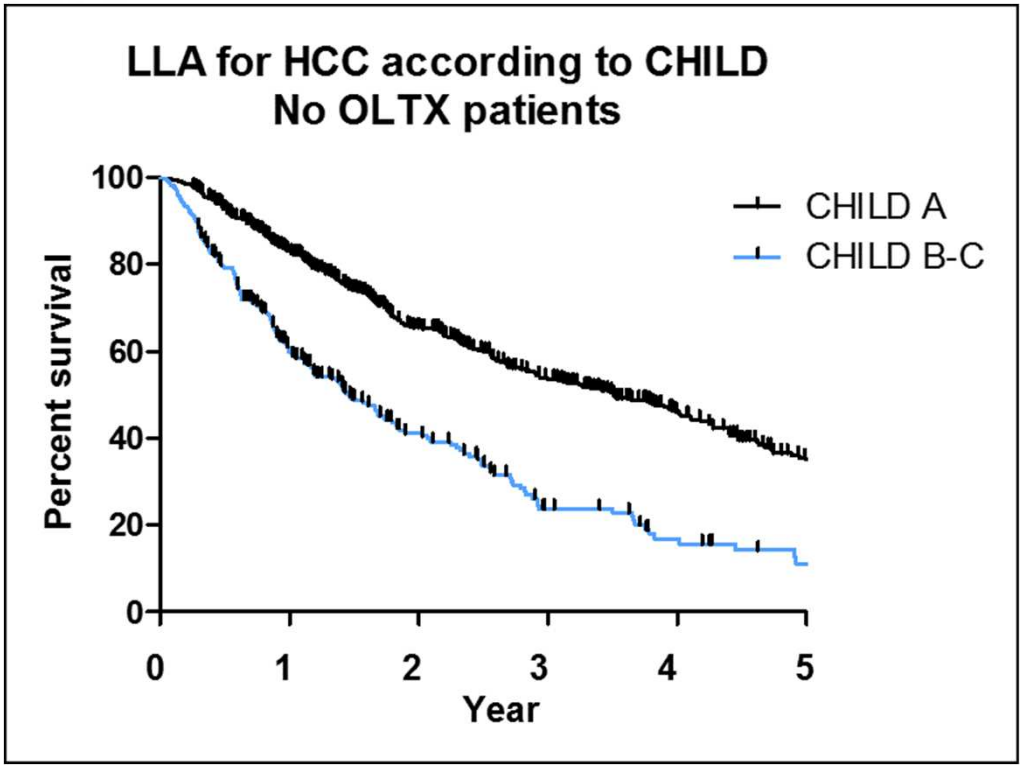


OLTX patients

P-value= ns (0,746)

LLA according to MELD	MELD<15 (119)	MELD≥15 (25)
1 yr	96,6%	92,0%
3 yr	89,1%	75,6%
5 yr	81,8%	67,2%
10 yr	53,1%	58,8%
Median OS	120,5 months	-

Padova Experience
1208 Laparoscopic Liver Ablation
No OLTx patients 2004 – 2016

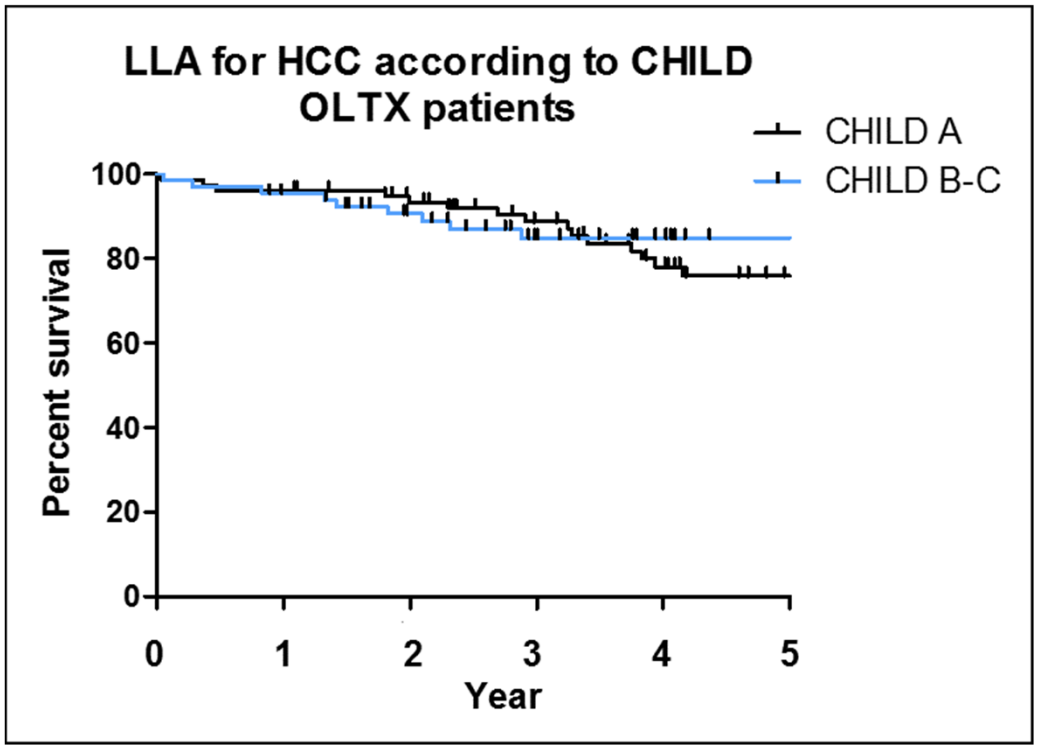


No OLTX patients

P-value=<0,001

LLA according to CHILD	CHILD A (845)	CHILD B (363)
1 yr	83,0%	59,8%
3 yr	53,6%	23,8%
5 yr	35,3%	11,1%
10 yr	18,7%	-
Median OS	42,2 months	17,6 months

Padova Experience
144 Laparoscopic Liver Ablation
OLTx patients 2004 – 2016

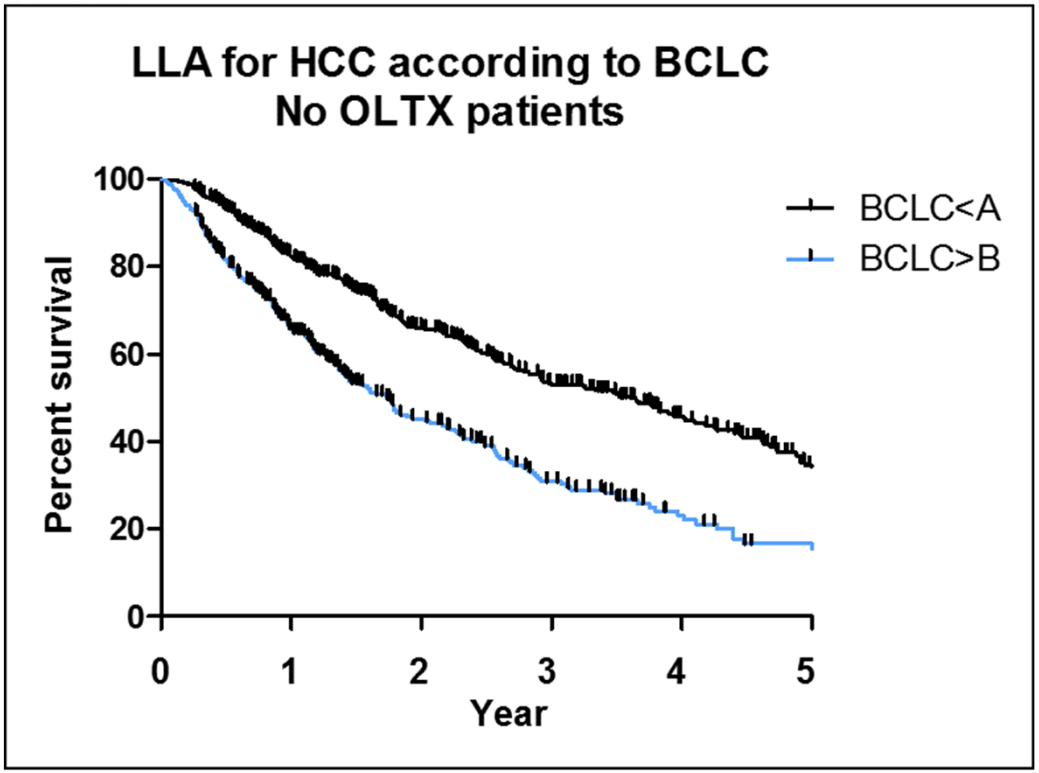


OLTX patients

P-value=ns (0,163)

LLA according to CHILD	CHILD A (78)	CHILD B (66)
1 yr	96,1%	95,5%
3 yr	88,7%	84,9%
5 yr	75,9%	84,9%
10 yr	42,8%	75,6%
Median OS	106,7 months	-

Padova Experience
1203 Laparoscopic Liver Ablation
No OLTx patients 2004 – 2016

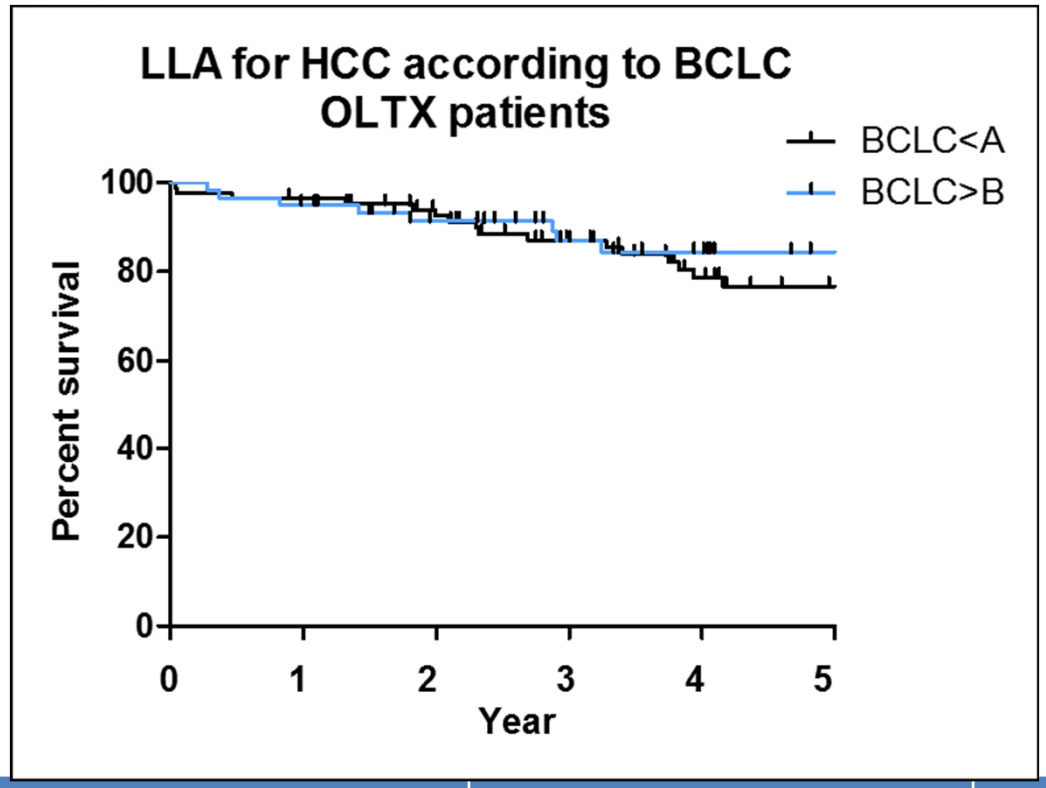


No OLTX patients

P-value=<0,001

LLR according to BCLC	BCLC≤A (720)	BCLC≥B (483)
1 yr	82,4%	65,7%
3 yr	53,1%	30,9%
5 yr	34,6%	16,7%
10 yr	19,2%	6,8%
Median OS	43,8 months	20,9 months

Padova Experience
144 Laparoscopic Liver Ablation
OLTx patients 2004 – 2016



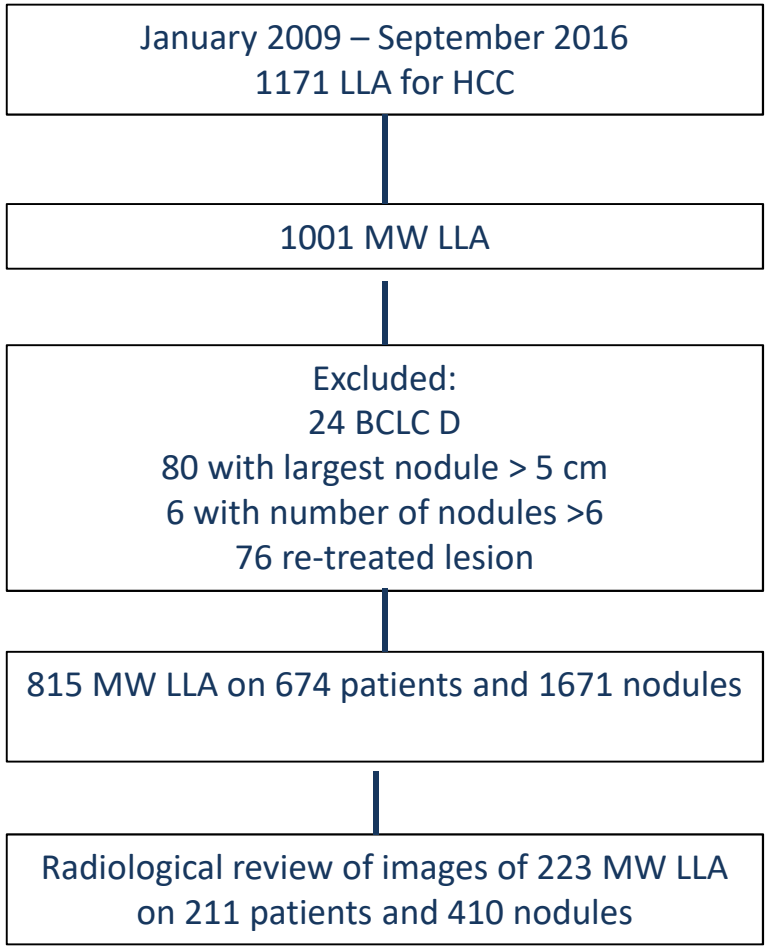
OLTX patients

P-value=ns (0,326)

LLA according to BCLC	BCLC≤A (84)	BCLC≥B (60)
1 yr	96,4%	95,0%
3 yr	87,0%	86,9%
5 yr	76,7%	84,4%
10 yr	55,1%	60,1%
Median OS	-	120,5 months

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures

Selection of population



U. Cillo, Eur J Surg Oncol 2019

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures

674 - Patients Characteristic

Variables	674 pts	%	Median (range min-max)
Age <70/≥70	466/208	69.1/30.9	64.3 (25-87)
Gender male/female	556/118	82.5/17.5	
ECOG PS 0/≥1	569/104	84.5/15.5	
Etiology: HBV. HCV. other	106/330/238	15.7/49/35.3	
Portal hypertension not/yes	223/451	33.1/66.9	
Esophageal varices not/yes	435/239	64.5/35.5	
Ascites not/yes	507/167	75.2/24.8	
Splenomegaly not/yes	356/318	52.8/47.2	
Platelets count (10^3) ≤100/>100	357/305	53.9/46.1	88 (11-334)
INR ≤1.18/>1.18	369/298	55.3/44.7	1.18 (0.9-353)
Creatinine (mg/dl) ≤1/>1	518/144	78.2/21.8	0.83 (0.12-2.56)
Bilirubin (mg/dl) ≤1/>1	252/412	38/62	1.3 (0.19-6.37)
Albumin (mg/dl) ≤3.5/>3.5	148/201	42.4/57.6	3.7 (2.4-5)
Alpha-fetoprotein (ng/ml) ≤20/>20	369/240	60.6/39.4	9.85 (0.51-8441)
Child A/B	455/215	67.9/32.1	6 (5-9)
MELD score <10/≥10	339/327	50.9/49.1	10 (6-23)
BCLC 0/A/B/C	60/321/139/154	8.9/47.6/20.6/22.8	
Diameter <3/3-4/4-5 cm	468/129/73	69.9/19.3/10.9	26 (7-50)
Single nodule not/yes	355/319	52.7/47.3	
ASA score ≤2/>2	264/270	49.4/50.6	

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VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures

Clinical characteristic of all procedures

Variables	815 procedures	%	Median (range min-max)
Total operative time (min)			70 (25-375)
Conversion not/yes	812/3	99.6/0.4	
Intra-operative blood requirement not/yes	795/20	97.6/2.4	
Long of stay (days)			2 (1-29)
Re-admission not/yes	786/29	96.5/3.5	
No post-operative complications	564	69.2	
Dindo-Clavien grade I-II	235	28.8	
Dindo-Clavien grade ≥III	16	2	
Type of complications			
Ascites	124	15.2	
Anemia	27	3.3	
Fever	35	4.3	
Pulmonary	21	2.6	
Other	44	5.4	
Intraoperative mortality (yes)	0	0	
In hospital mortality (yes)	3	0.4	
30-days mortality (yes)	66	0.7	
90-days mortality (yes)	21	2.6	
6-months mortality (yes)	60	7.4	

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures Univariate e multivariate analysis for 6-months mortality

Variables	Univariate Analysis		Multivariate Analysis	
	OR	95% CI	OR	95% CI
Age ≥70/<70	1.438	0.854-2.423		
Gender male/female	1.201	0.636-2.269		
ECOG PS ≥1/0	1.014	0.502-2.047		
Etiology: other (baseline)	-			
HBV	2.389 (p=0.021)	1.143-4.993		
HCV	1.652	0.884-3.087		
Portal hypertension yes/not	2.643 (p=0.004)	1.360-5.137		
Esophageal varices yes/not	1.31	0.784-2.188		
Ascites yes/not	2.733 (p<0.001)	1.636-4.566		
Splenomegaly yes/not	1.547	0.930-2.573		
Platelets count (10^3) ≤100/>100	1.814 (p=0.031)	1.058-3.112		
INR >1.16/≤1.16	1.891 (p=0.018)	1.115-3.208		
Creatinine (mg/dl) >1/≤1	0.722	0.369-1.414		
Bilirubin (mg/dl) ≤1/>1	3.653 (p<0.001)	1.831-7.287		
Albumin (mg/dl) ≤3.5/>3.5	2.728 (p=0.005)	1.355-5.495		
Alpha-fetoprotein (ng/ml) >20/≤20	3.114 (p<0.001)	1.778-5.455	2.485 (p=0.002)	1.383-4.464
CTP score B vs A	3.681 (p<0.001)	2.181-6.214	4.051 (p<0.001)	2.015-8.144
MELD score ≥10/<10	1.841 (p=0.023)	1.088-3.116	1.054	0.522-2.126
BCLC 0A (baseline)	(p=0.004)		(p=0.091)	
BCLC B	2.291 (p=0.010)	1.220-4.300	1.646 (p=0.174)	0.802-3.380
BCLC C	2.521 (p=0.002)	1.384-4.590	2.032 (p=0.033)	1.059-3.901
Diameter <3cm (baseline)	(p=0.002)			
3-4 cm	0.809	0.385-1.701		
4-5 cm	2.922 (p=0.001)	1.537-5.556		
Single nodule not/yes	1.996 (p=0.013)	1.158-3.440		
Number of lesions 1 (baseline)	(p=0.006)			
2-3	1.691	0.945-3.027		
4-6	3.183 (p=0.001)	1.563-6.483		
RX-Vascular invasion yes/not	3.440 (p<0.001)	1.824-6.485		
Previous therapies yes/not	1.452	0.858-2.459	1.826 (p=0.051)	0.999-3.338
Local recurrence yes/not	2.684 (p=0.002)	1.416-5.087		
Liver Transplantation yes/not	0.208 (p=0.030)	0.050-0.862	0.196 (p=0.028)	0.046-0.838

U. Cillo, Personal Experience

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures Overall survival

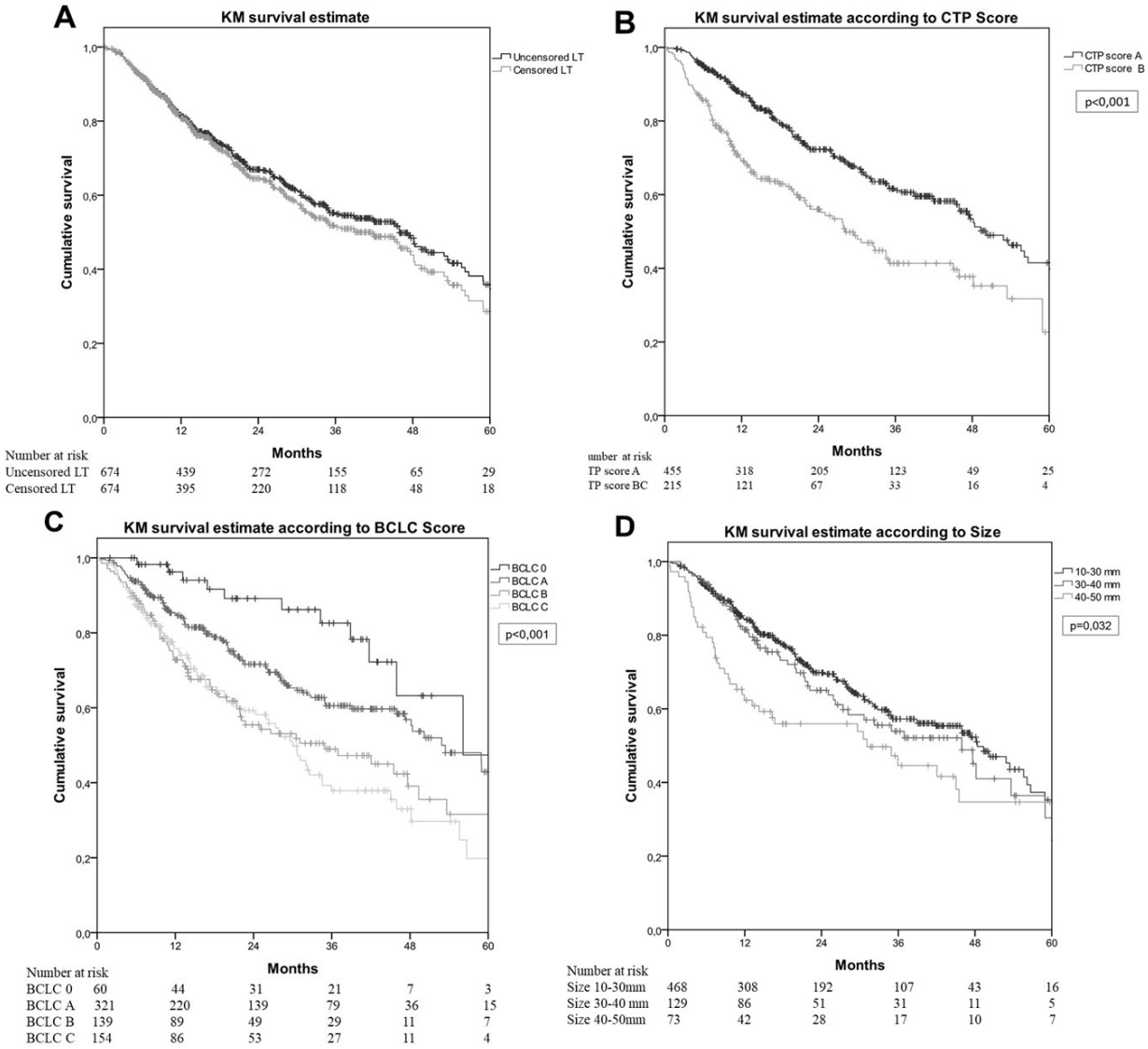


Figure 1: Kaplan–Meier survival estimation for 674 patients.

1A-Overall survival estimation.

1B-Survival estimation according to CTP score

1C-Survival estimation according to BCLC score

BCLC 0 vs BCLC A p=0.082
BCLC 0 vs BCLC B p=0.001
BCLC 0 vs BCLC C p<0.001
BCLC A vs BCLC B p<0.001
BCLC A vs BCLC C p<0.001
BCLC B vs BCLC C p=0.437

1D-Survival estimation according to size

Size 1-3cm vs 3-4 cm p=0.257
Size 1-3 cm vs 4-5 cm p=0.008 Size 3-4 cm vs 4-5 cm p=0.185

U. Cillo, Personal Experience

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures
Univariate e multivariate analysis for overall survival

Variables	Univariate Analysis		Multivariate Analysis	
	HR	95% CI	HR	95% CI
Age ≥70/<70	1.477 (p=0.001)	1.170-1.865		
Gender male/female	1.109	0.835-1.472		
ECOG PS ≥1/0	1.332	0.997-1.778		
Etiology: other (baseline)	-			
HBV	1.068	0.778-1.517		
HCV	1.086	0.834-1.368		
Portal hypertension yes/not	1.718 (p<0.001)	1.335-2.212		
Esophageal varices yes/not	1.264 (p=0.042)	1.008-1.584		
Ascites yes/not	1.762 (p<0.001)	1.389-2.236		
Splenomegaly yes/not	1.228	0.984-1.532		
Platelets count (10^3) ≤100/>100	1.352 (p=0.009)	1.079-1.694		
INR >1.16/≤1.16	1.309 (p=0.017)	1.049-1.634		
Creatinine (mg/dl) >1/≤1	1.279	0.992-1.647		
Bilirubin (mg/dl) ≤1/>1	1.841 (p<0.001)	1.446-2.343		
Albumin (mg/dl) ≤3.5/>3.5	1.816 (p<0.001)	1.350-2.443		
Alpha-fetoprotein (ng/ml) >20/≤20	1.600 (p<0.001)	1.269-2.018	1.539 (p<0.001)	1.214-1.951
CTP score B vs A	1.899 (p<0.001)	1.515-2.380	1.810 (p<0.001)	1.366-2.399
MELD score ≥10/<10	1.680 (p<0.001)	1.343-2.101	1.552 (p=0.002)	1.179-2.044
BCLC 0A (baseline)	(p<0.001)	1.524-2.381	(p<0.001)	
BCLC B	1.749 (p<0.001)		1.769 (p<0.001)	1.316-2.377
BCLC C	1.996 (p<0.001)		1.699 (p<0.001)	1.286-2.246
Diameter <3cm (baseline)	-			
3-4 cm	1.125	0.848-1.493		
4-5 cm	1.365	0.979-1.905		
Single nodule not/yes	1.748 (p<0.001)	1.388-2.201		
Number of lesions 1 (baseline)	-			
2-3	1.575 (p<0.001)	1.233-2.012		
4-6	2.530 (p<0.001)	1.824-3.509		
Rx - Vascular invasion yes/not	2.433 (p<0.001)	1.754-3.375		
Previous therapies yes/not	1.507 (p<0.001)	1.199-1.894	1.754 (p<0.001)	1.366-2.251
Local recurrence yes/not	1.261	0.958-1.660		
Intra-segmental recurrence yes/not	1.175	0.861-1.423		
Hepatic recurrence yes/not	1.107	1.056-2.222		
Liver Transplantation yes/not	0.151 (p<0.00)	0.082-0.275	0.101 (p<0.001)	0.053-0.192

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures
Recurrence estimation

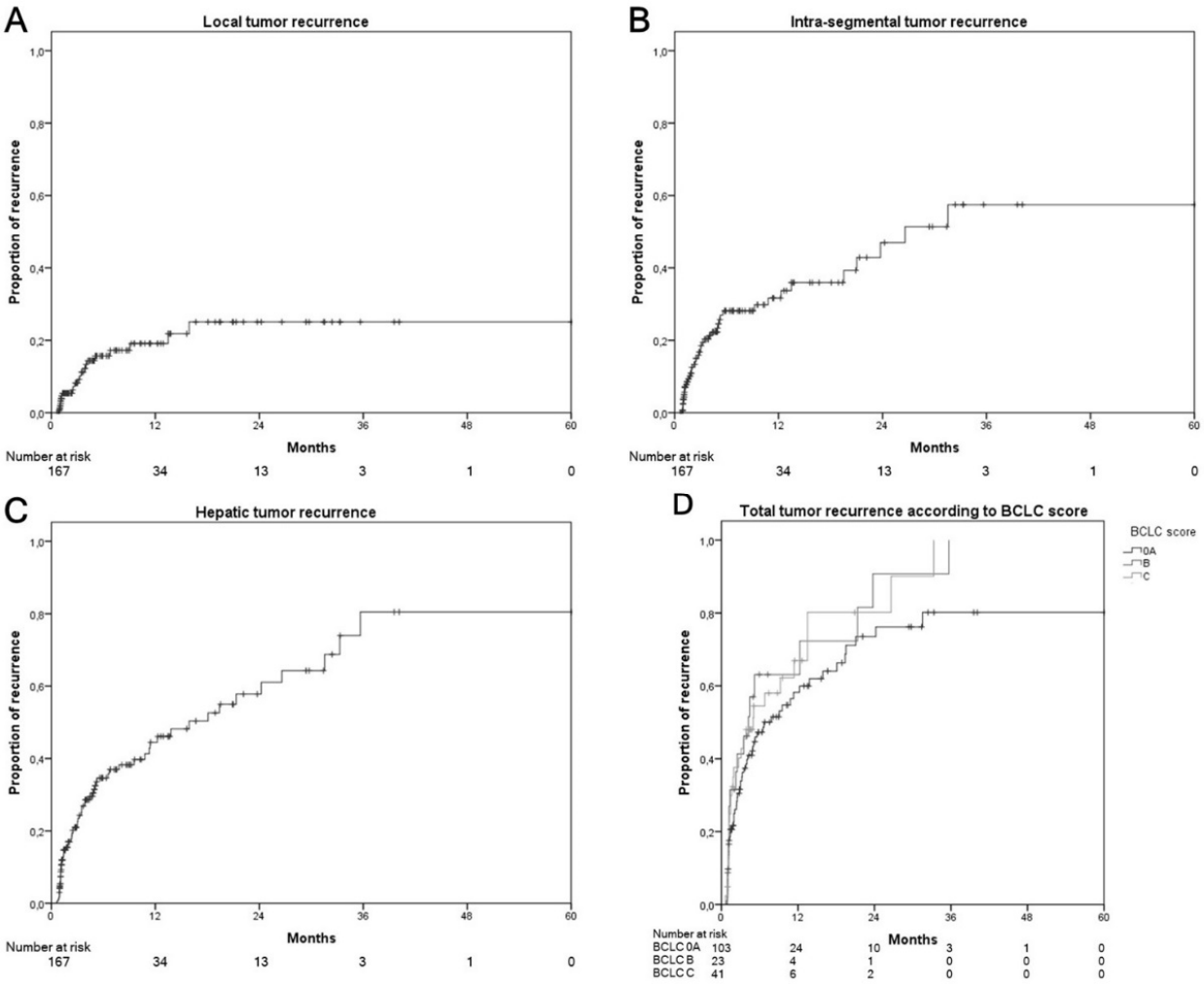


Figure 2: Kaplan–Meier recurrence estimation for 167 patients.

2A Local tumor recurrence estimation.

2B Intra-segmental tumor recurrence estimation.

2C Hepatic tumor recurrence estimation.

2D Total tumor recurrence estimation according to BCLC score (p=0.213)

BCLC 0A vs BCLC B p=0.178 BCLC 0A vs BCLC C p=0.173 BCLC B vs BCLC C p=0.972

U. Cillo, Personal Experience

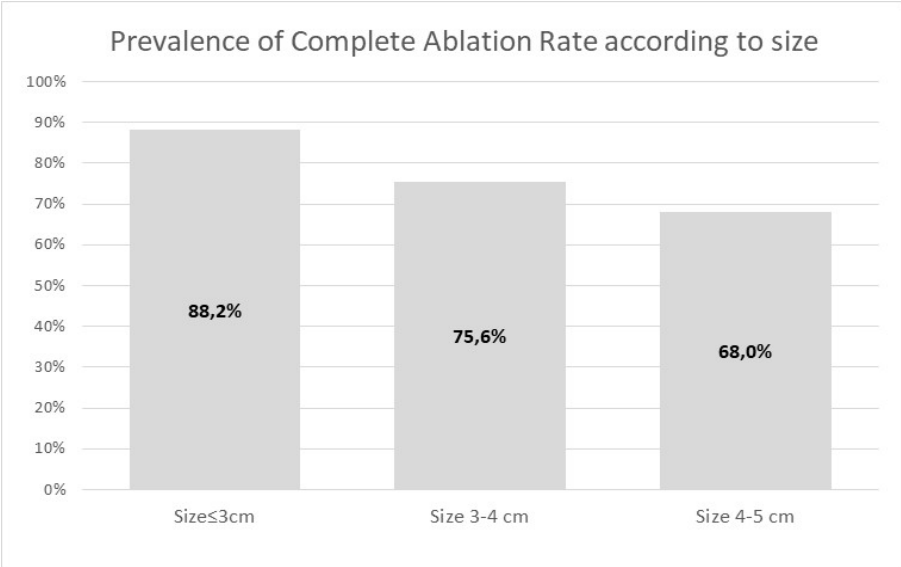
VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures Univariate e multivariate analysis for overall survival 565 Patients Recurrence

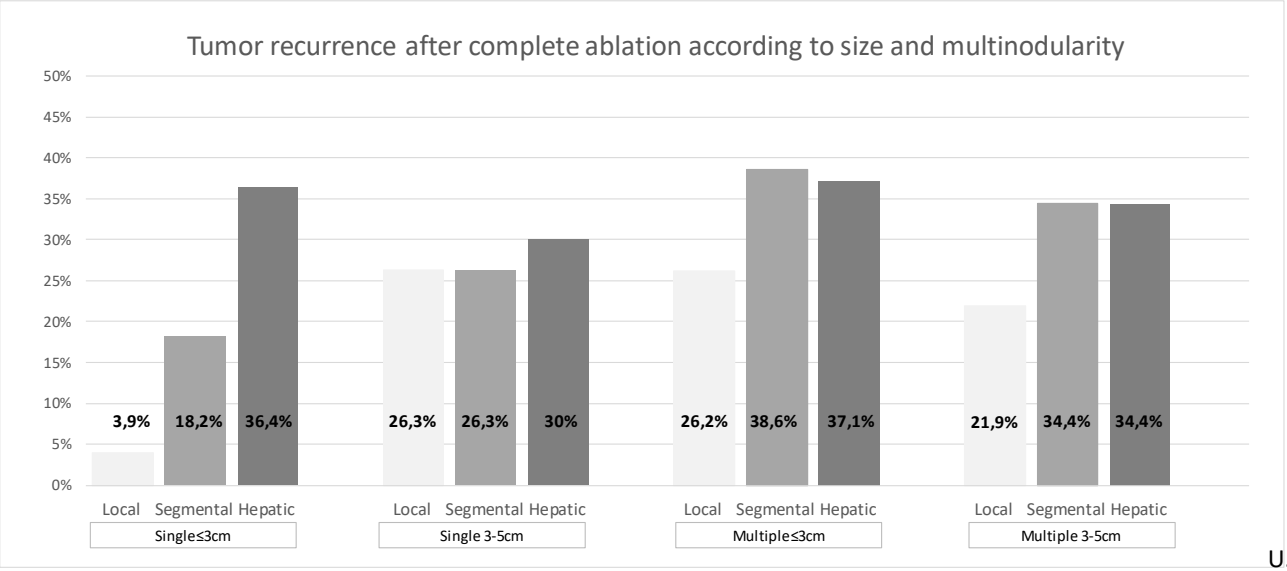
	Local Recurrence	Segmental Recurrence	Hepatic Recurrence	Recurrence
1 yr	28,6%	37,8%	44,3%	66,6%
3 yr	40,9%	61,8%	70,8%	88,1%
5 yr	40,9%	79,4%	82,8%	95,4%
Median Rec	-	19,6	17,6	5,5

U. Cillo, Personal Experience

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures
Ablation Efficacy – 223 procedures

Complete ablation according to the external revision was achieved in 86.3% of single nodule and in 85.3% of nodules in the context of multifocal disease.
Technical success rate differed according to tumor size.





U. Cillo, Personal Experience

VLS MW Ablation in a European High Volume Center: Safety, Efficacy and Recurrence Profile of 815 procedures
Total Tumor Recurrence

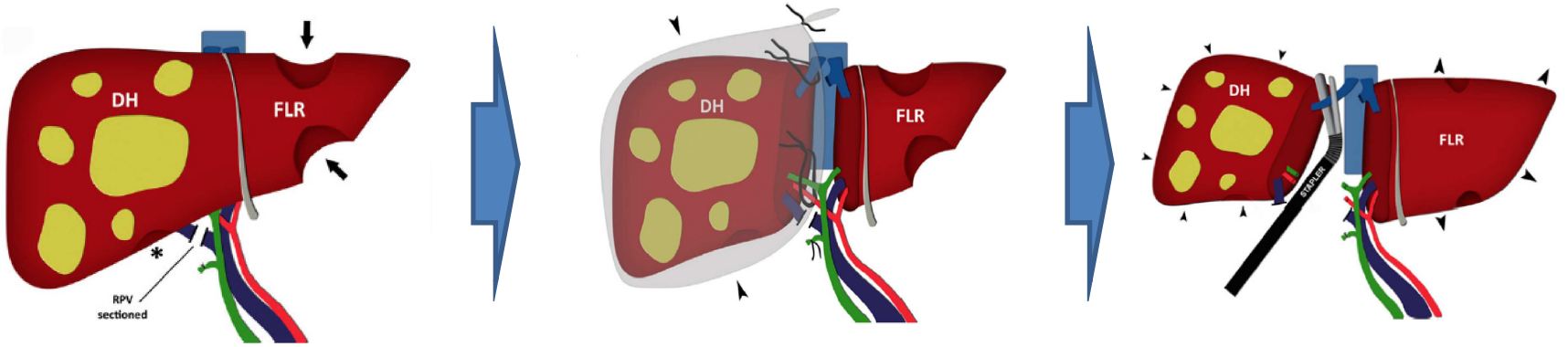
Variables	Univariate Analysis		Multivariate Analysis	
	HR	95% CI	HR	95% CI
Age ≥70/<70	0.998	0.652-1.530		
Gender male/female	1.049	0.615-1.787		
ECOG PS ≥1/0	0.755	0.421-1.352		
Etiology: other (baseline)	(p=0.002)		-	
HBV	2.632 (p<0.001)	1.531-4.525	1,888 (p=0,049)	1,003-3,554
HCV	1.611 (p<0.038)	1.027-2.527	1,303	0,778-2,182
Bilirubin (mg/dl) ≤1/>1	1.151	0.767-1.727		
Albumin (mg/dl) ≤3.5/>3.5	1.324	0.734-2.388		
Alpha-fetoprotein (ng/ml) >20/≤20	1.734 (p=0.008)	1.152-2.612	1,634 (p=0,031)	1,046-2,551
CTP score BC vs A	0.802	0.528-1.219		
MELD score ≥10/<10	0.859	0.581-1.270		
BCLC 0A (baseline)	-			
BCLC B	1.457	0.849-2.499		
BCLC C	1.382	0.880-2.169		
Diameter 3-4cm/<3cm	1.527 (p=0.051)	0.997-2.339	1,209	0,750-1,948
Single nodule not/yes	1.806 (p=0.003)	1.217-2.679	1,480 (p=0,079)	0,955-2,294
Number of lesions 1 (baseline)	(p=0.009)			
2-3	1.887 (p=0.002)	1.259-2.828		
4-5	1.293	0.515-3.250		
Vascular invasion yes/not	2.577 (p=0.002)	1.432-4.636	1,910 (p=0,048)	1,006-3,627
Previous therapies yes/not	1.424	0.892-2.274		

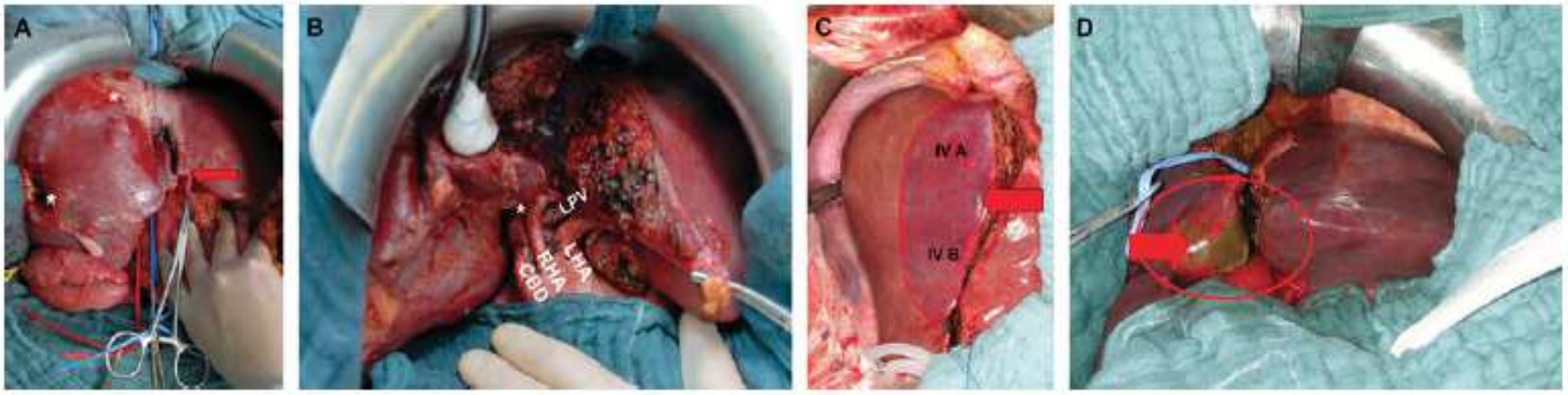
U. Cillo, Personal Experience

New perspectives...

Can we adopt laparoscopic ablations as a part of a two-stage strategy for major LR?

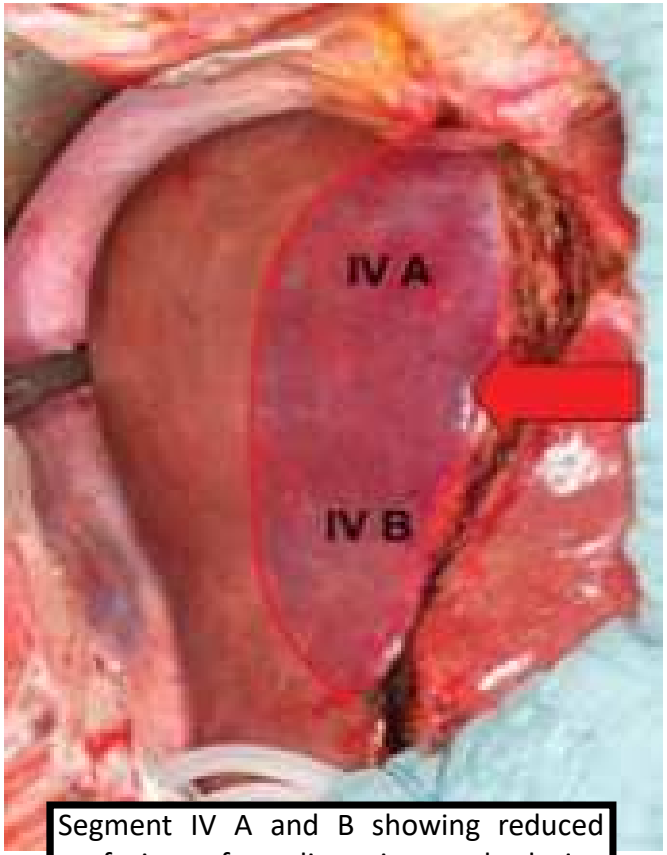
Right Portal Vein Ligation Combined With In Situ Splitting Induces Rapid Left Lateral Liver Lobe Hypertrophy Enabling 2-Staged Extended Right Hepatic Resection in Small-for-Size Settings





Schnitzbauer, Lang et al Annals of Surgery Volume 255, Number 3, March 2012

Right Portal Vein Ligation Combined With In Situ Splitting Induces Rapid Left Lateral Liver Lobe Hypertrophy Enabling 2-Staged Extended Right Hepatic Resection in Small-for-Size Settings

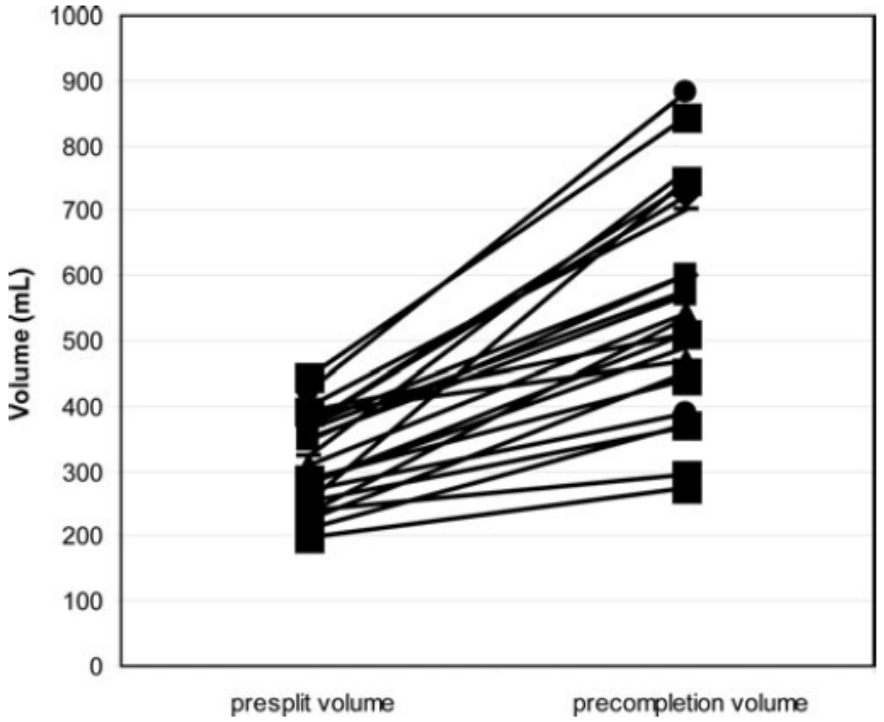


Segment IV A and B showing reduced perfusion after dissecting and closing supplying portal venous and arterial structures (red arrow) at the end of ISS procedure

Median Interval

9 days

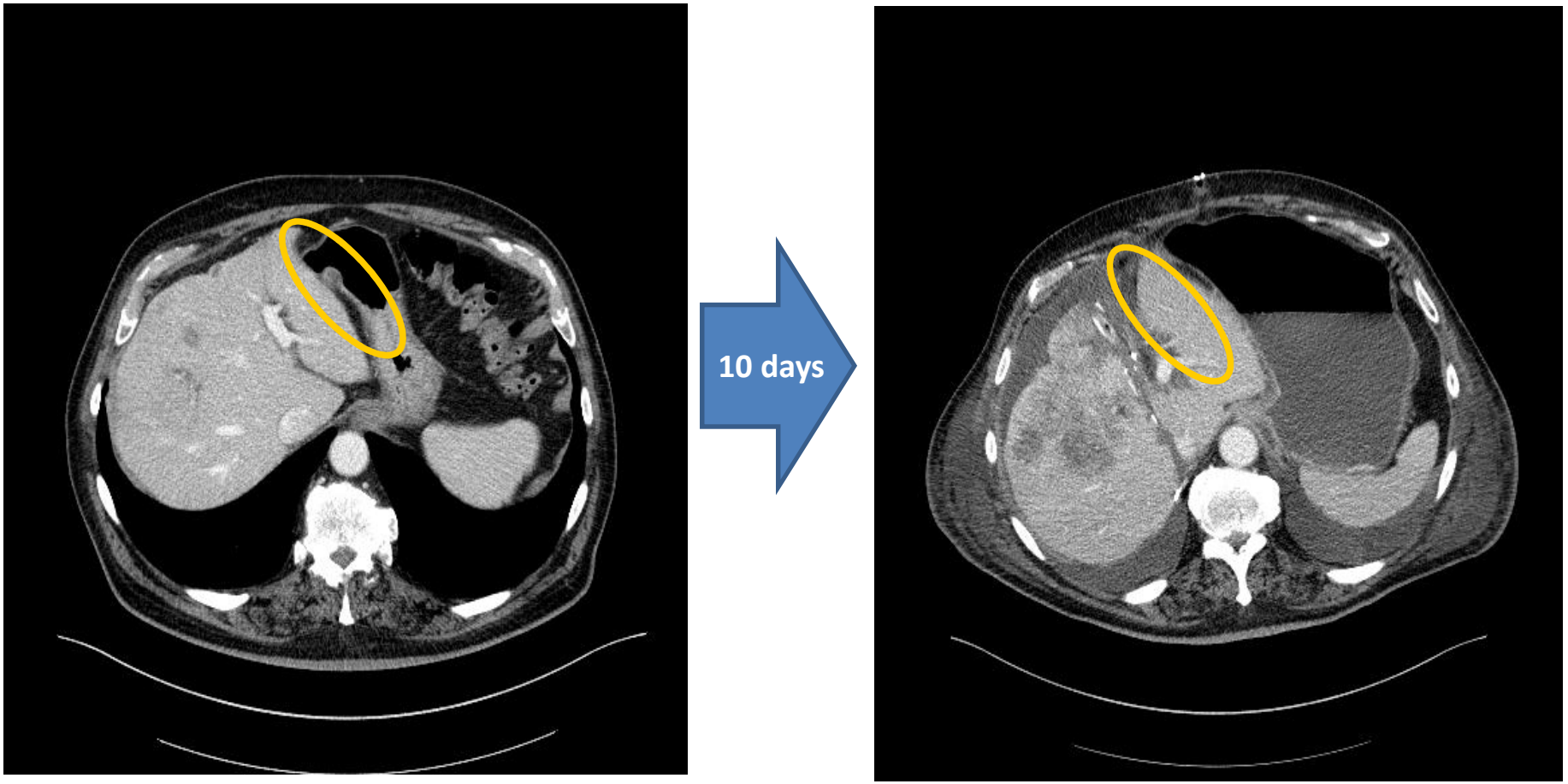
The median Δ-volume was 225 mL
Median increase in volume of 74%
(P < 0.001)



CTvolumetry results of left lateral liver lobe before ISS and before completion surgery

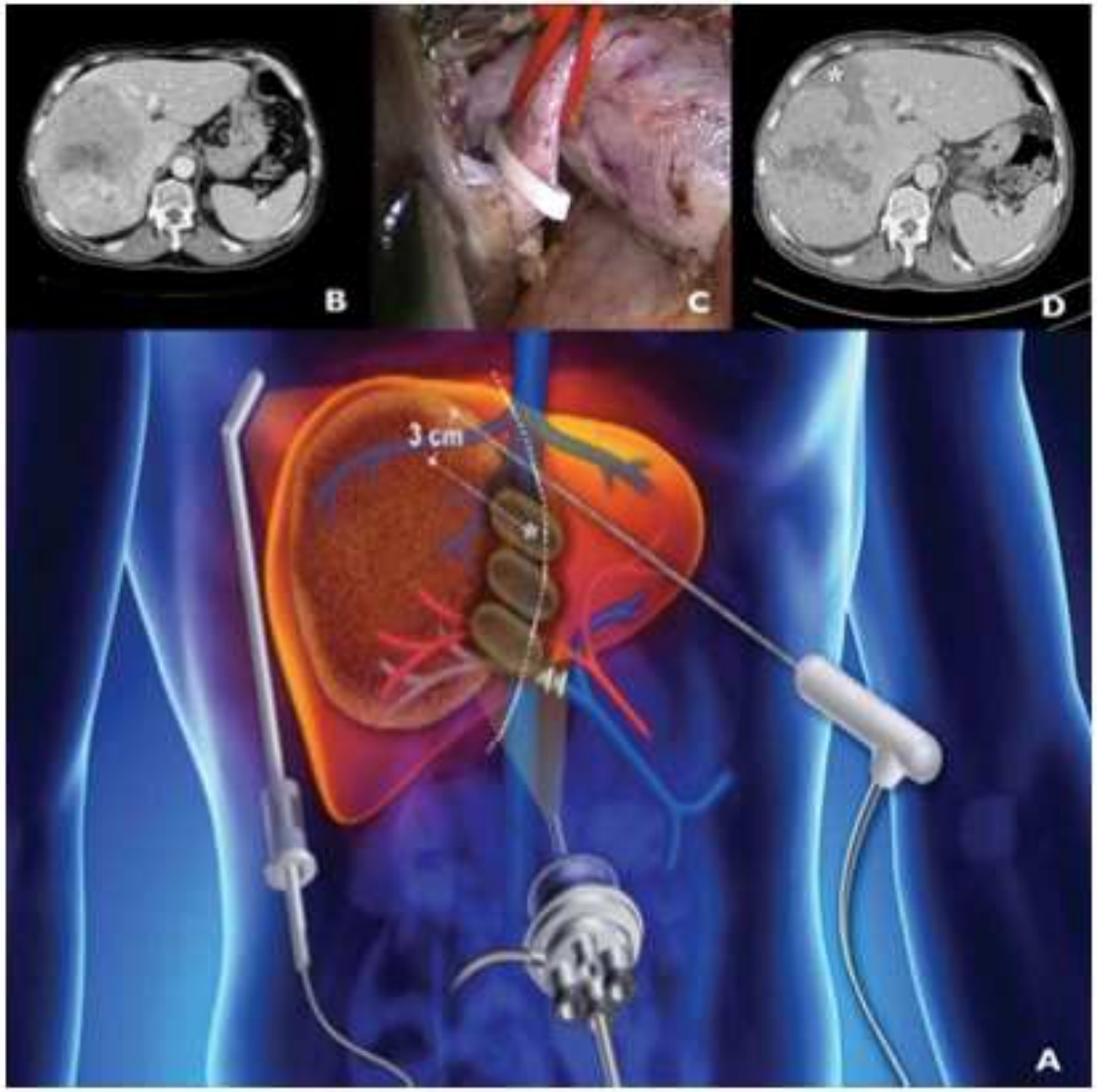
Schnitzbauer, Lang et al Annals of Surgery Volume 255, Number 3, March 2012

ALPPS:
rapid increase of FRL



U. Cillo, personal experience 2012

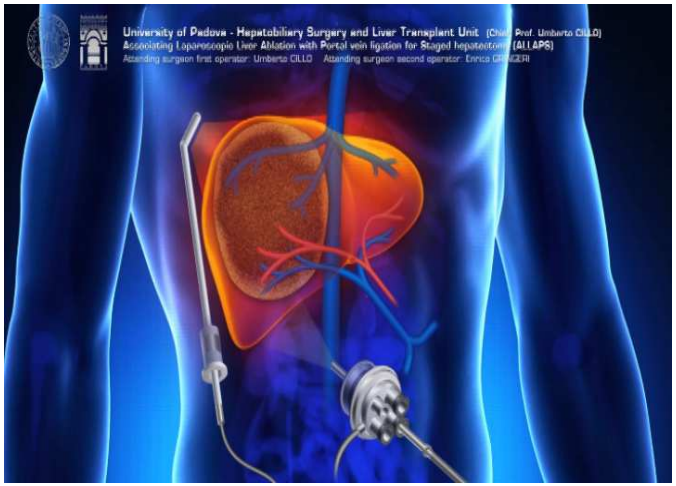
University of Padova Experience: From ALPPS to LAPS

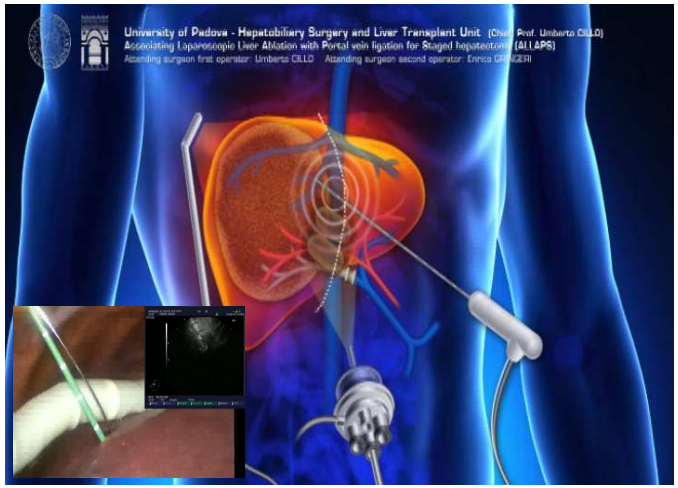


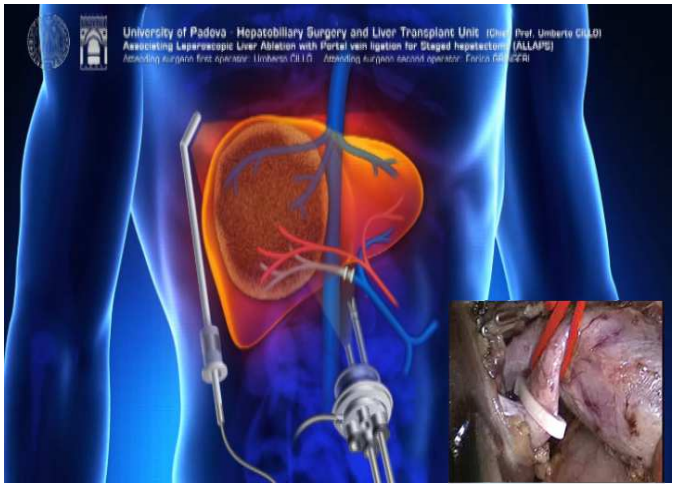
Associating Laparoscopic Microwave Ablation and Portal Vein Ligation for Staged Hepatectomy (LAPS): A Minimally Invasive First-Step Approach

Annals of Surger 2014, in Press

University of Padova Experience: From ALPPS to LAPS



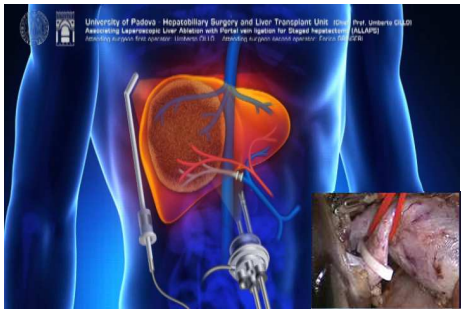




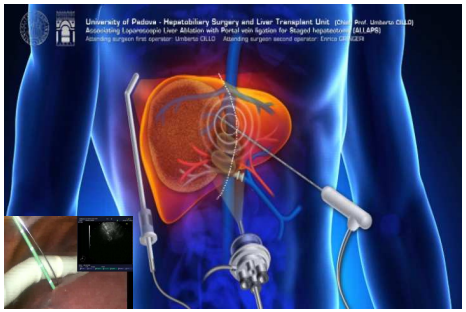
U. Cillo, personal experience 2014

University of Padova Experience: LAPS step 1: 120 min

Videolaparoscopic Exploration (4 trocar approach)
Intra-operative US



Cholecystectomy
Hilar dissection
Right Segmental Portal Branches Ligation
(vascular clip)



MW Ablation on future transection plane
(5 minute ablation cycles – 60 W) every 30 mm
from inferior margin to suprahepatic veins)

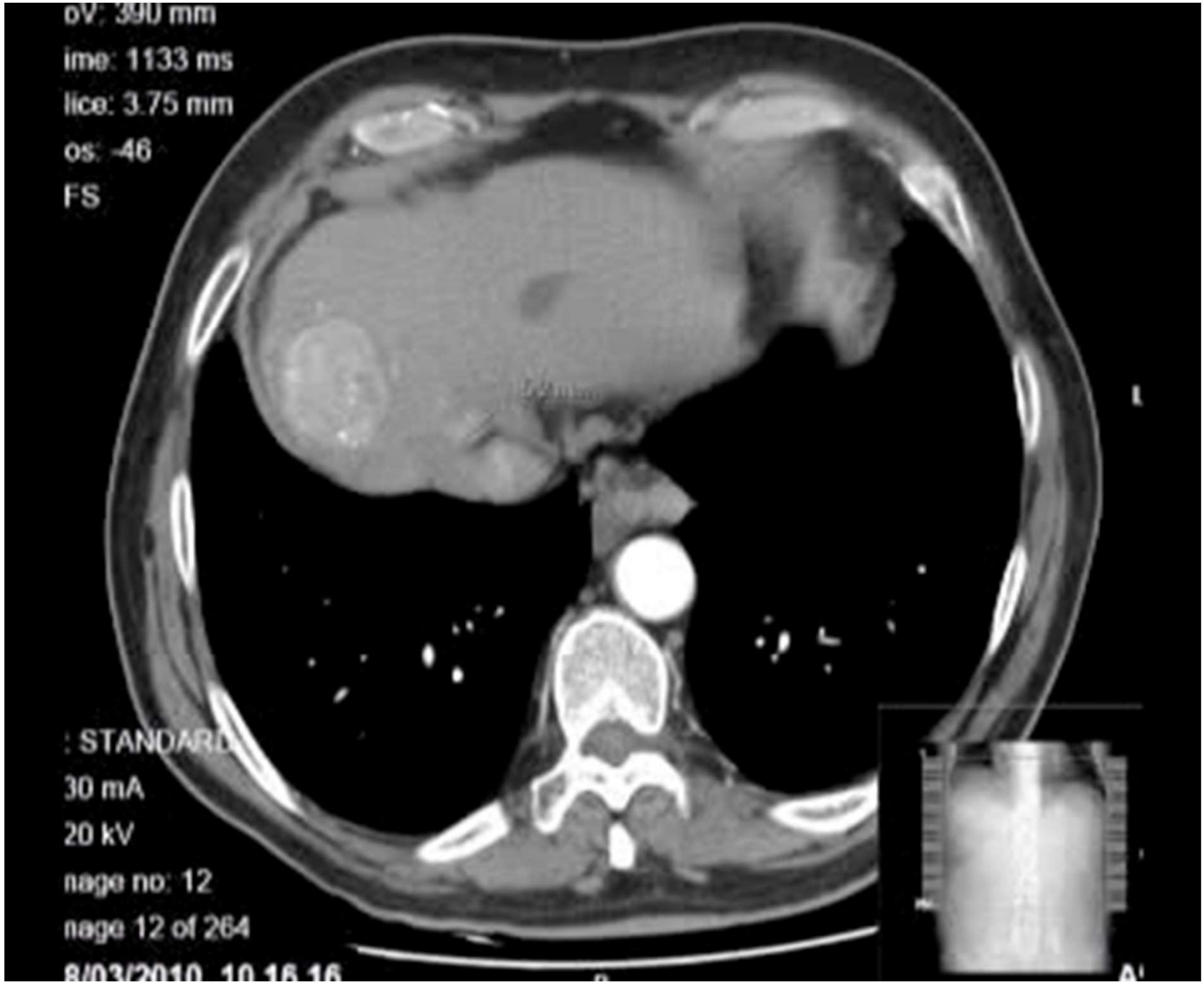
U. Cillo, personal experience 2014

University of Padova Experience: LAPS step 2

10 days

Extended Right Hepatectomy
Diaphragm Resection

U. Cillo, personal experience 2014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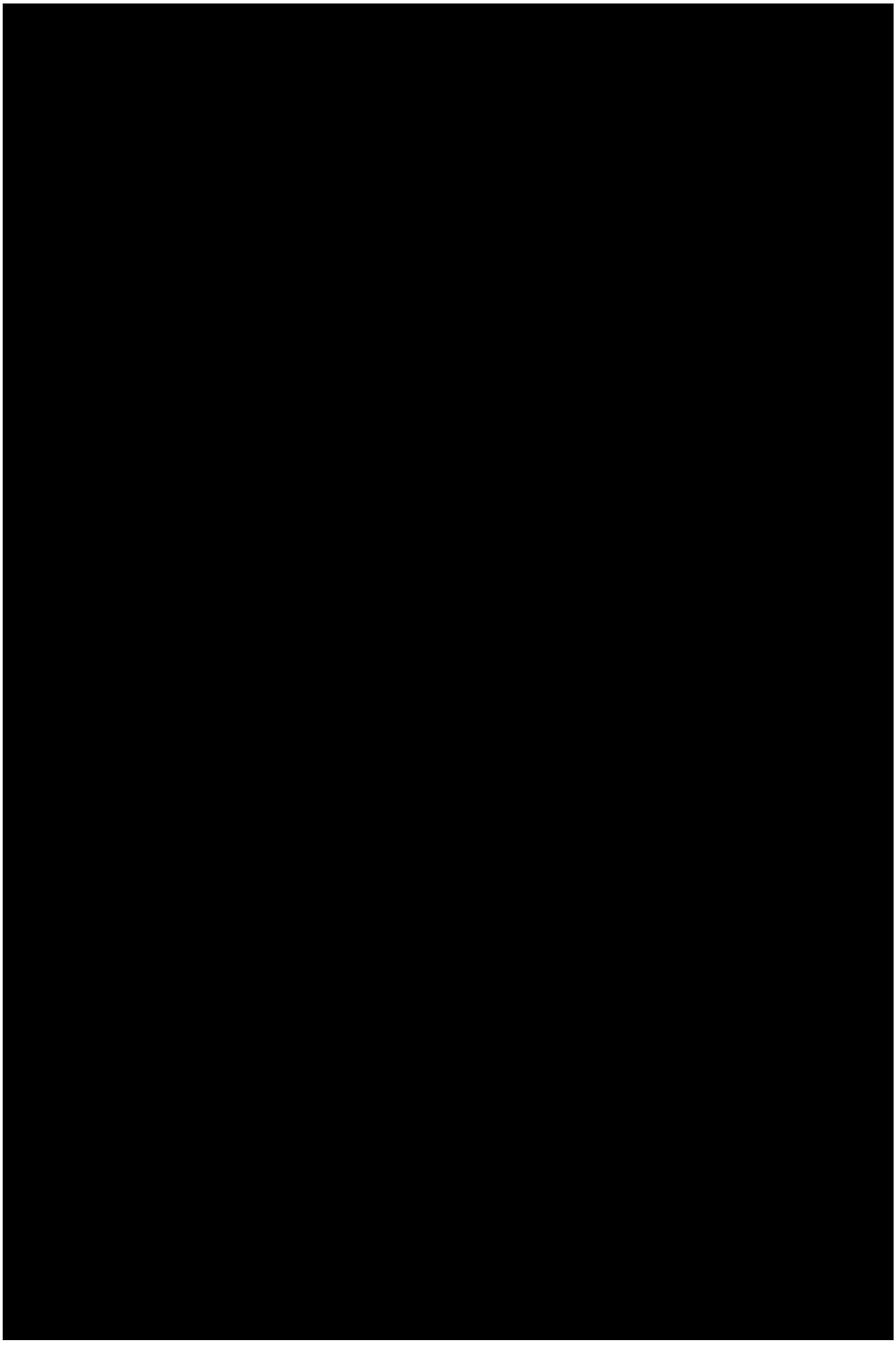
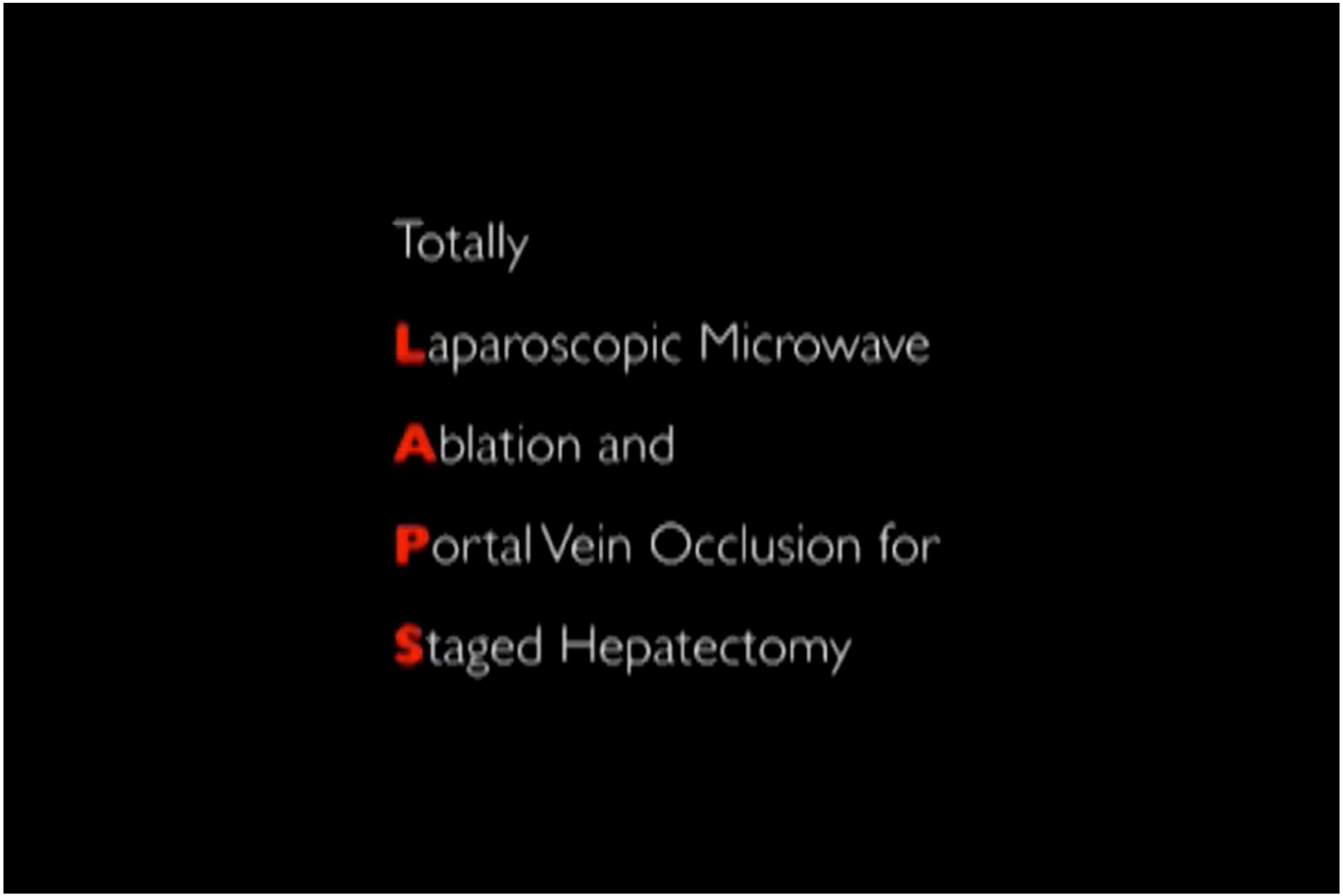
Chirurgia Epatobiliare e Trapianto Epatico

Università degli Studi di Padova

Direttore: prof. Umberto Cillo




Totally
Laparoscopic Microwave
Ablation and
Portal Vein Occlusion for
Staged Hepatectomy