Localized, Low-volume CCA: Surgery vs histotripsy vs radiofrequency ablation vs XRT?

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Surgery for Cholangiocarcinoma

2025 Johns Hopkins Updates in GI Cancers Conference, Bethesda, MD

Flavio G.Rocha, MD, FACS, FSSO
Hedinger Professor and Chair of Surgical Oncology
Physician-in-Chief, Knight Cancer Institute

Disclosures

- I am an oncologist who can operate
- Surgery is the only modality with 100% ORR every time

Principles of Local Therapy

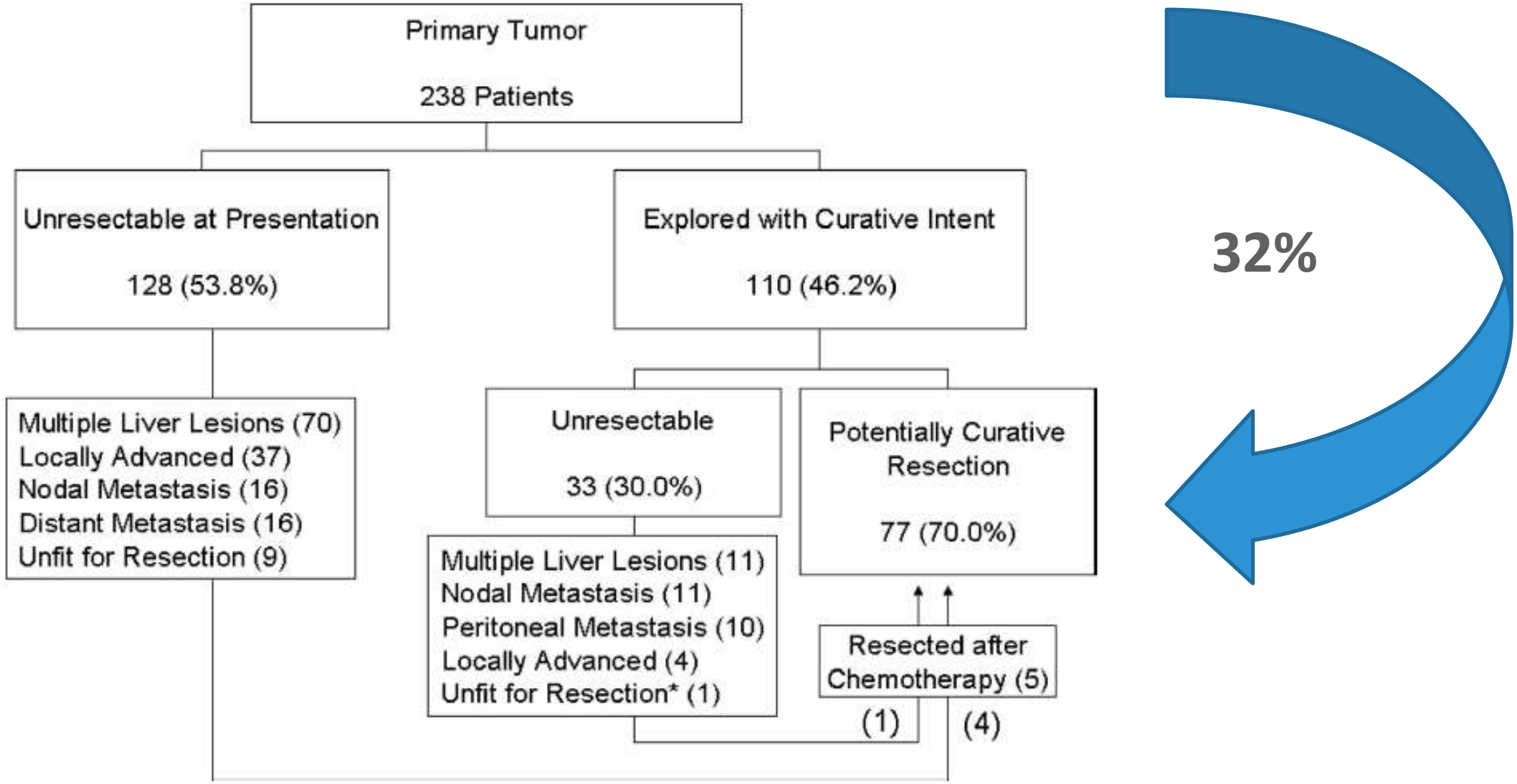
- Cure disease when amenable to resection
- If locally unresectable, control disease progression and preserve liver function
- Palliate symptoms in the presence of metastatic disease when unresponsive to other therapies

Local therapies for intrahepatic cholangiocarcinoma

- **Surgery**
  - Resection
  - Transplant
- **Direct tumor ablation**
  - Radiofrequency, Microwave, Irreversible electroporation, Histotripsy
- **Catheter-based, hepatic artery directed**
  - Transarterial (chemo)embolization (DEBDOX, DEBIRI)
  - Selective internal radiation therapy (Y90)
  - Hepatic artery infusion pump (HAIP)
- **Radiation**
  - External beam (ablative), SBRT, Proton

Patient Evaluation

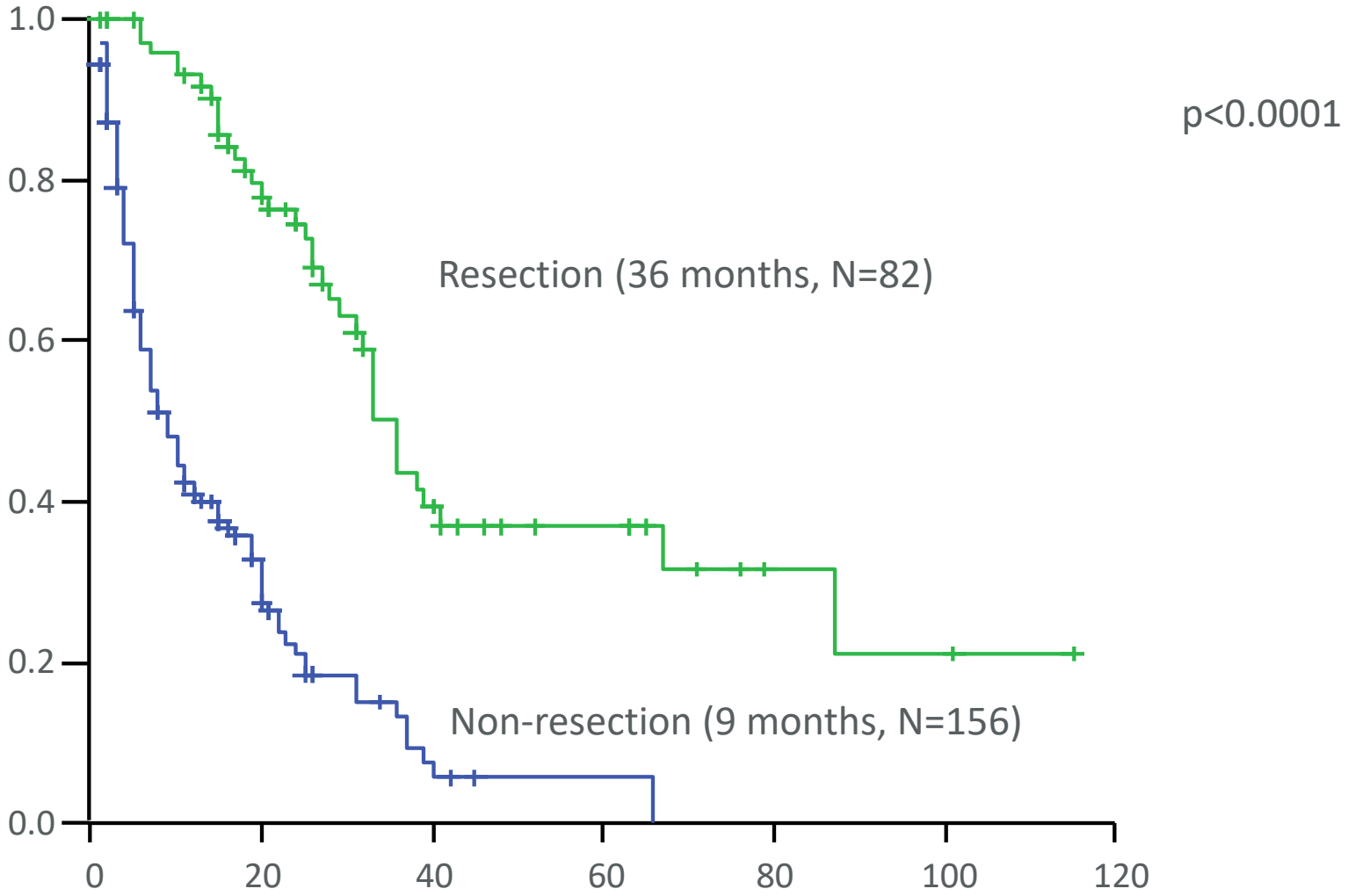
- Assessment of fitness for major surgery
- Radiographic studies to assess:
  - Biliary extent, vascular involvement, lobar atrophy
  - Distant metastases
  - Cholangiography (MRCP), CT (angiography), US, PET
    - **Invasive studies (ERCP or PTC) only necessary depending on local expertise and surgeon**
- Biliary stenting for profound jaundice or cholangitis
- Portal vein embolization for small future liver remnant
- Staging laparoscopy with biopsy of liver
- Parenchymal-sparing hepatectomy if possible



Endo et al. Ann Surg 2008

Intrahepatic Cholangiocarcinoma: Resection

Overall survival by treatment

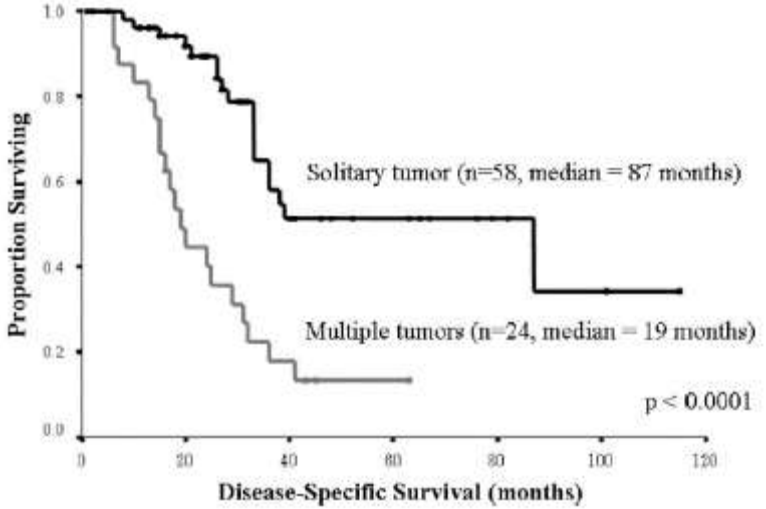


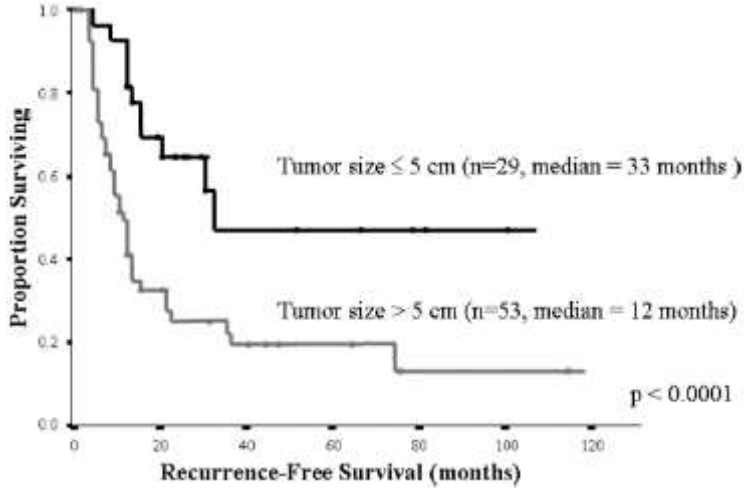
p<0.0001

Endo Ann Surg 2008

Resected ICC Patients

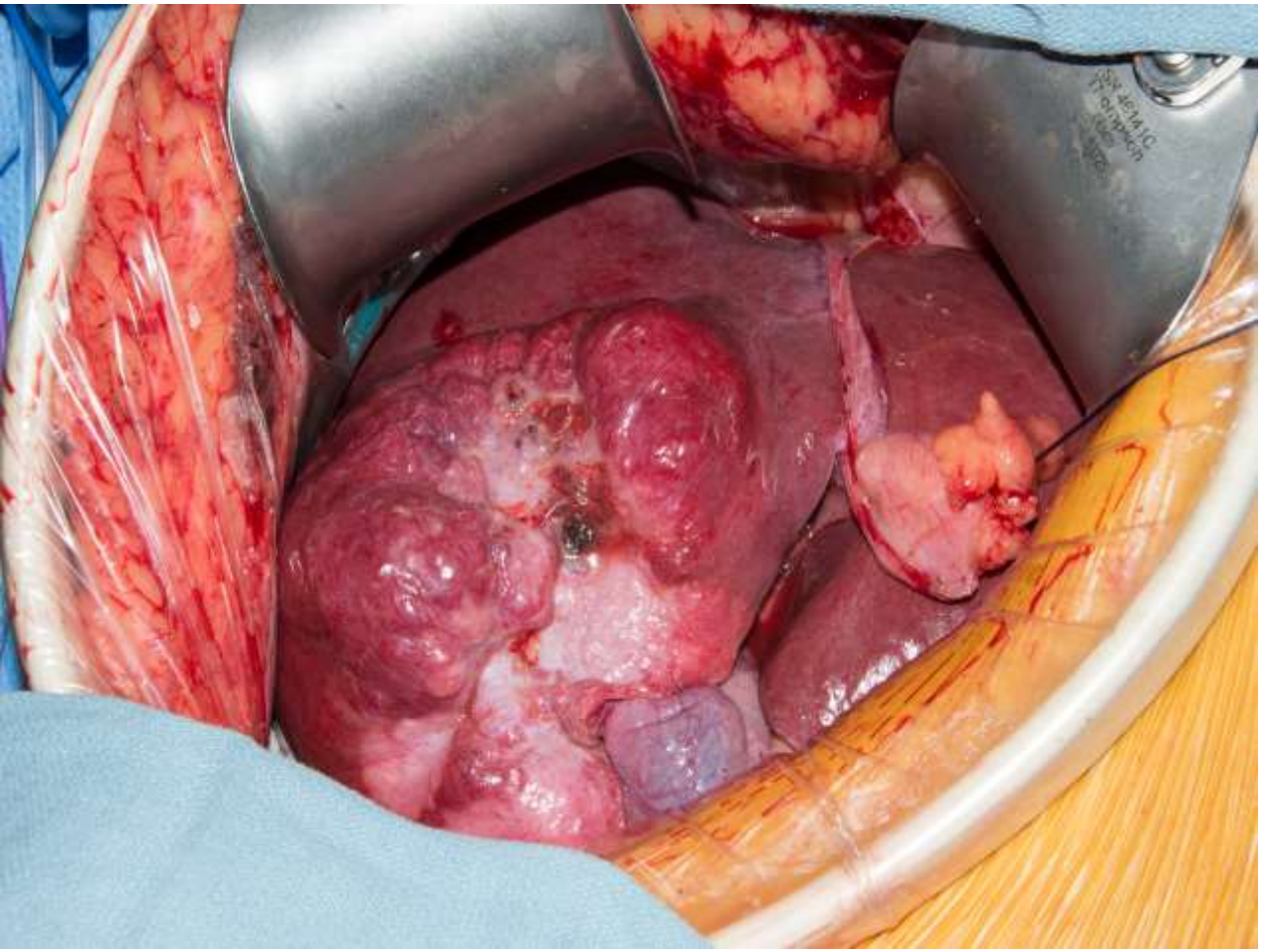
- 51/82 (62%) recurrence rate in resected patients at 26 months
  - 47% in solitary tumor with no +LN
  - 92% in multifocal or +LN
- 31/51 (63%) recurrences involved liver
  - 13 with liver and extrahepatic dz
- Predictors of worse outcome
  - Number and size of tumors
  - Vascular invasion
  - Positive lymph node
  - Need for bile duct resection
  - Molecular Markers?
  - Need for additional therapy?

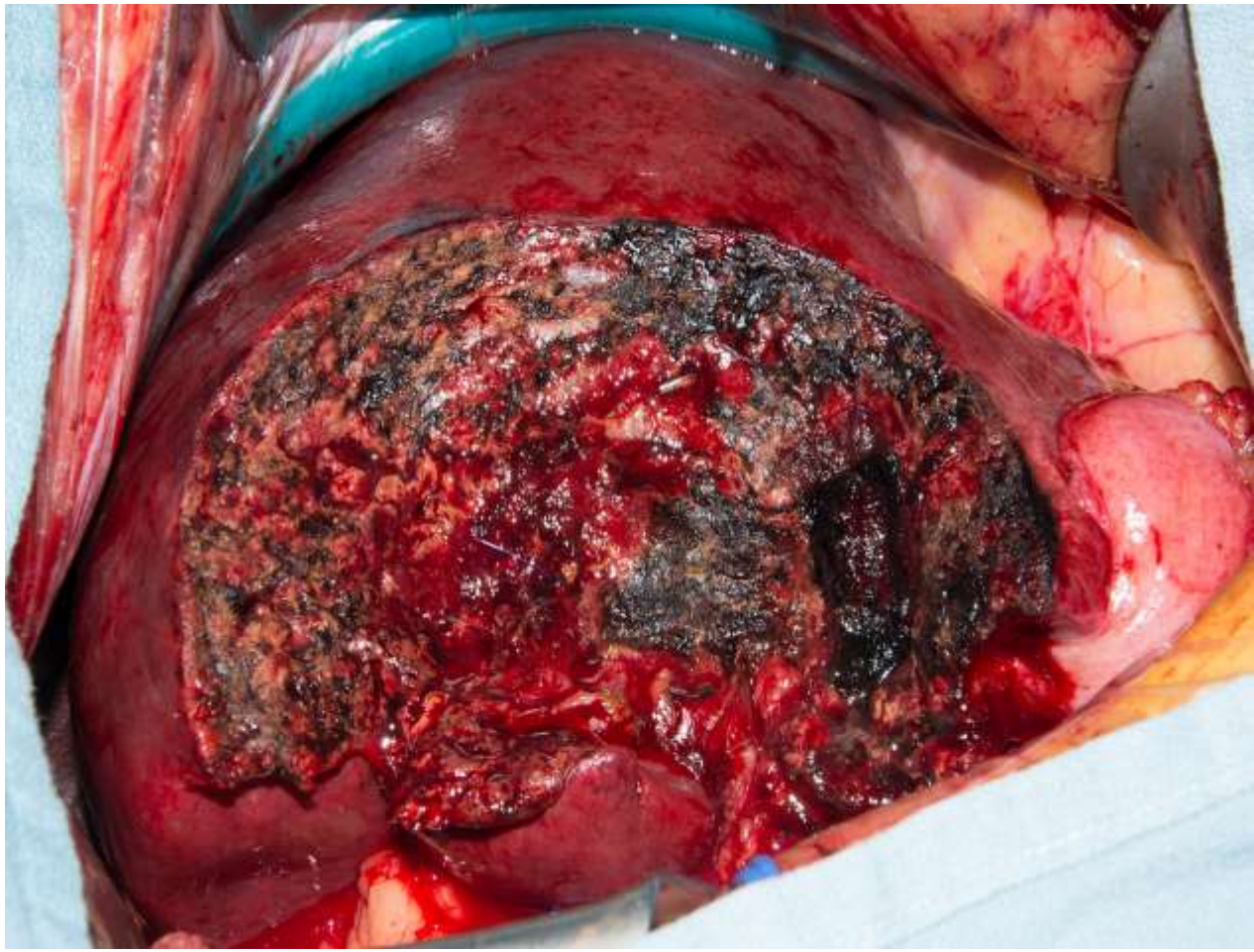




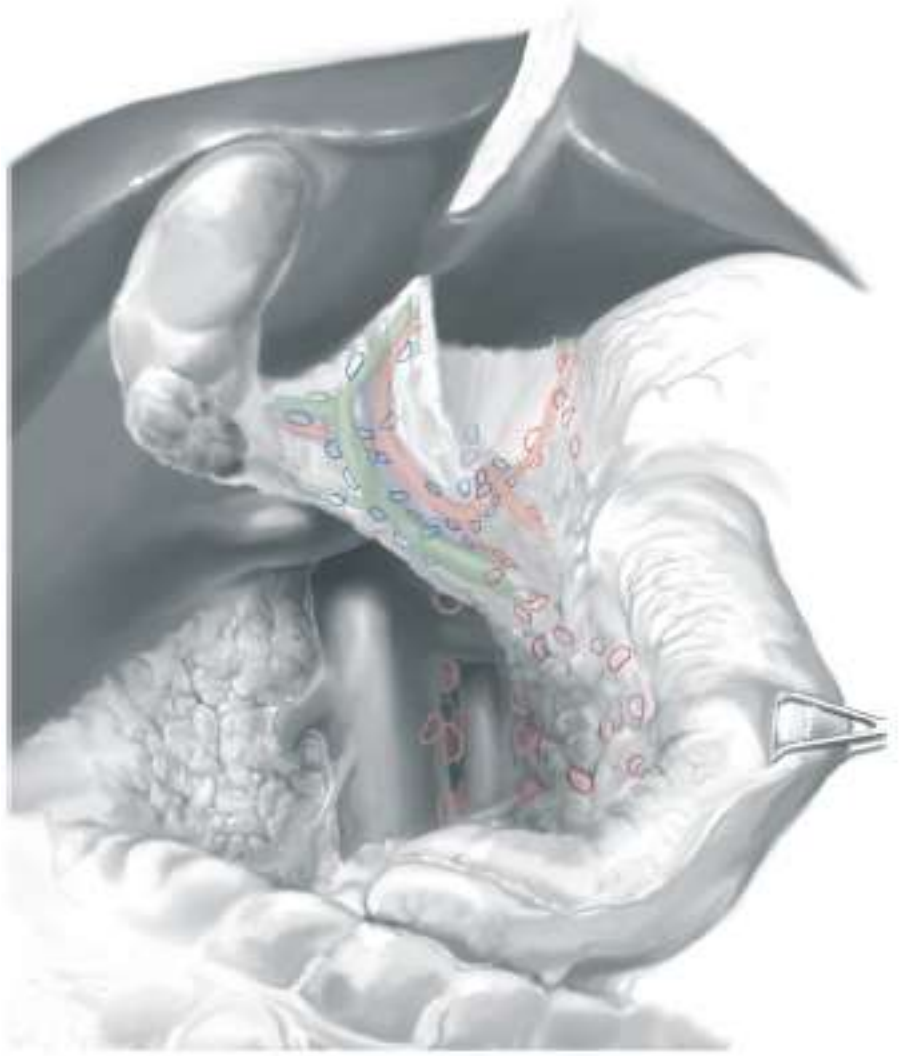
Endo Ann Surg 2008

Inferior Hepatectomy (IVB,5,6) for ICC





Portal Lymphadenectomy



N1 Lymph Nodes (Blue)

Portal Vein
Common Hepatic Artery
Cystic and Common Duct

N2 Lymph Nodes (Red)

Retropancreatic
Aortocaval
Celiac/SMA

Positive N2 nodes equals Stage IVB disease (metastatic, unresectable)

Clavien, Sarr, Fong (Eds) Atlas of UGI and HPB Surgery 2007

Intrahepatic cholangiocarcinoma 8th Ed AJCC

Table 1 AJCC staging of intrahepatic cholangiocarcinoma: comparison of 7th and 8th editions

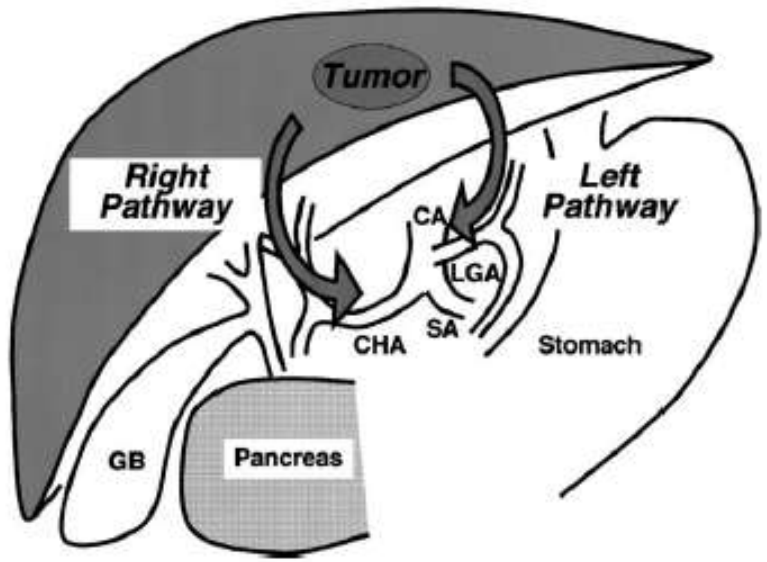
7th edition	8th edition
T category	
T1: solitary tumor without vascular invasion	T1a: solitary tumor ≤5 cm without vascular invasion
	T1b: solitary tumor >5 cm without vascular invasion
T2a: solitary tumor with vascular invasion	T2: solitary tumor with intrahepatic vascular invasion or multiple tumors, with or without vascular invasion
T2b: multiple tumors, with or without vascular invasion	
T3: tumor perforating the visceral peritoneum or involving local hepatic structures by direct invasion	T3: tumor perforating the visceral peritoneum
T4: tumor with periductal invasion	T4: tumor involving local extrahepatic structures by direct invasion
N category	
N0: no regional lymph node metastasis	N0: no regional lymph node metastasis
N1: regional lymph node metastasis present	N1: regional lymph node metastasis present
TNM stage	
I: T1 N0 M0	IA: T1a N0 M0
	IB: T1b N0 M0
II: T2 N0 M0	II: T2 N0 M0
III: T3 N0 M0	IIIA: T3 N0 M0
	IIIB: T4 and/or N1, M0
IVA: T4 N0 M0/any T, N1, M0	IV: any T, any N, M1
IVB: any T, any N, M1	

Chin Clin Oncol 2018;7(5):52

Patterns of Regional Lymph Node Involvement in Intrahepatic Cholangiocarcinoma of the Left Lobe

Jiro Okami, M.D., Keizo Dono, M.D., Masato Sakon, M.D., Masanori Tsujie, M.D., Nobuyasu Hayashi, M.D., Yoshiyuki Fujiwara, M.D., Hiroaki Nagano, M.D., Koji Umeshita, M.D., Shoji Nakamori, M.D., Morito Monden, M.D.

(J Gastrointest Surg 2003;7:850–856)



	Histology (n = 13)	RT-PCR (n = 12)
Nodal metastasis (−)	7 (54%)	4 (33%)
Nodal metastasis (+)	6 (46%)	8 (67%)
Right pathway (+)	5 (38%)	6 (50%)
Left pathway (+)	4 (31%)	7 (58%)
Distant area (+)	3 (23%)	5 (42%)

Summary

- ACS, AJCC, NCCN recommendations continue to evolve
- Surgical principles remain the same
  - Preoperative preparation
  - Margin-negative resection
  - Appropriate lymphadenectomy
- Future directions on localized, resectable disease
  - Role of neoadjuvant therapy
  - Molecular profiling

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Thank You

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Localized, Low-volume CCA IR Approach

Robert Liddell, MD

Director of Interventional Radiology
Johns Hopkins School of Medicine

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Alternatives to Surgery for localized/low-volume CCA

- Ablation:
  - Thermal:
    - Radiofrequency Ablation (RFA) and Microwave Ablation (MWA)
  - Nonthermal
    - Histotripsy
    - IRE
- XRT/SBRT

Thermal Ablation - CCA

Thermal ablation in the treatment of intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

Gun Ha Kim [1] · Pyeong Hwa Kim [1] · Jin Hyoung Kim [1,2] · Pyo-Nyun Kim [1] · Hyung Jin Won [1]
Yong Moon Shin [1] · Sang Hyun Choi [1]

- Meta-analysis
- 20 observational studies, 917 patients
- Primary n=502, recurrent n=355
- MWA, RFA
- 1-, 3-, and 5-year OS rates 82.4%, 42.1%, and 28.5%
- 1- and 3-year RFS rates 40.0% and 19.2%
- Tumor size (>3 cm), multiple tumors, and age (>65) associated with shorter OS
- Major complications: 5.7% (abscess, pleural effusions, bleeding, liver failure)

European Radiology 2022, 32, 1205-1215

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Thermal Ablation - CCA

Thermal ablation in the treatment of intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

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European Radiology (2022) 32:1205–1215

- Conclusion for thermal ablation of CCA:
  - Technically effective, safe
  - Optimal indication:
    - Single, small CCA (primary > recurrent)

Surgery vs. Thermal Ablation

Tumor size and survival in intrahepatic cholangiocarcinoma treated with surgical resection or ablation

Elishama N. Kanu MD[1] | Kristen E. Rhodin MD[1] | Sabran J. Masoud MD[1] | Austin M. Eckhoff MD[1] | Alex J. Bartholomew MD[1] | Thomas C. Howell MD[1] Jiayin Bao BA[1] | Nicholas T. Befera MD[2] | Charles Y. Kim MD[2] | Dan G. Blazer III, MD[1] | Sabino Zani MD[1] | Daniel P. Nussbaum MD[1] | Peter J. Allen MD[1] | Michael E. Lidsky MD[1]

J Surg Oncol. 2023;128:1329–1339.

- NCDB, retrospective analysis
- Stage I-III iCCA diagnosed 2010-2018
- 2140 total patients
- 1877 surgical resection, 263 ablation
- Median tumor sizes:
  - Surgery: 5.5 cm
  - Ablation: 3.0 cm
- Tumors < 3 cm: 412, ≥ 3 cm: 1631

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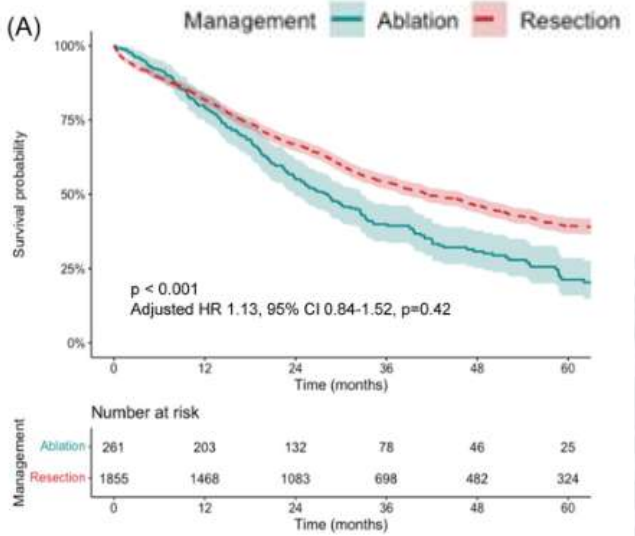
Surgery vs. Thermal Ablation
Overall

- **Median OS**
  - All: 39.2 mo
  - Surgery: 41.2 mo
  - Ablation: 28.0 mo

***p* < 0.001**



- **5-year survival**
  - All: 37%
  - Surgery: 39.4%
  - Ablation: 21.3%

***p* < 0.0001**

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Surgery vs. Thermal Ablation
Subgroup Analysis – Tumor Size

< 3 cm

Median OS

- Surgery: 50.5 mo
- Ablation: 39.5 mo

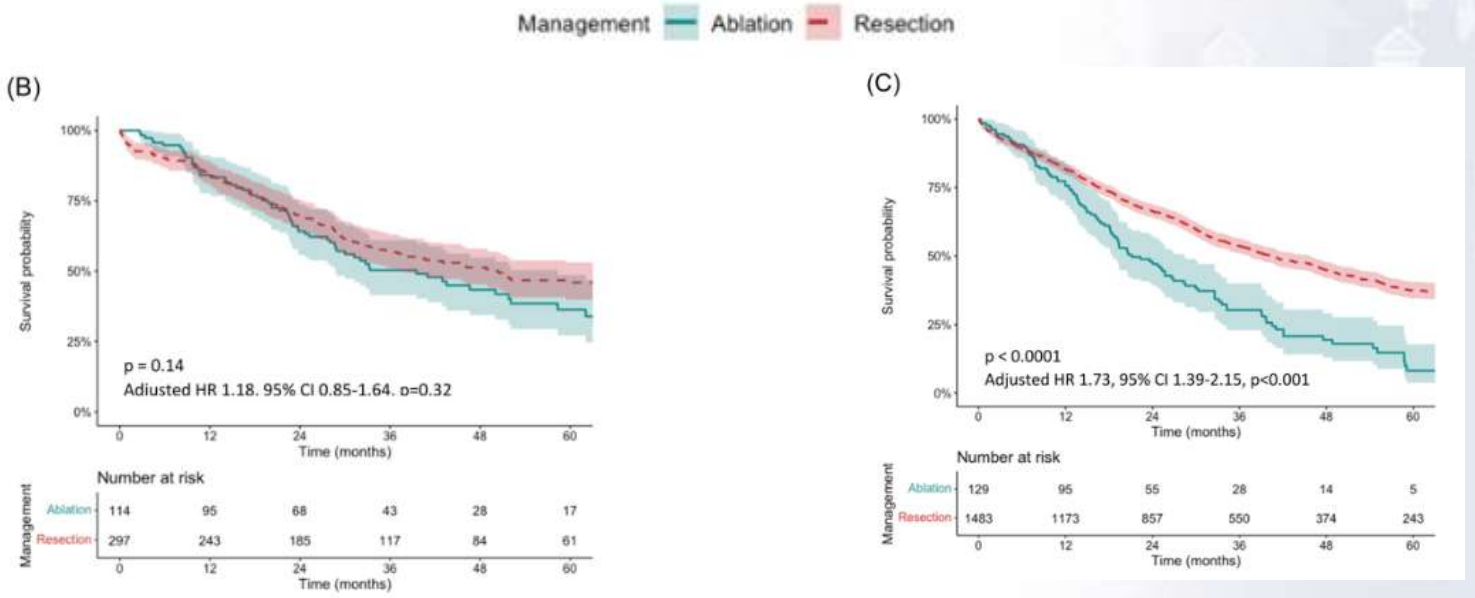
***p* = 0.32**

≥ 3 cm

Median OS

- Surgery: 40.6 mo
- Ablation: 21.1 mo

***p* < 0.001**



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Surgery vs. Thermal Ablation
Subgroup Analysis – Tumor Size

< 3 cm

5 - year Survival

- Surgery: 46%
- Ablation: 36.4%

***p* = 0.14**

≥ 3 cm

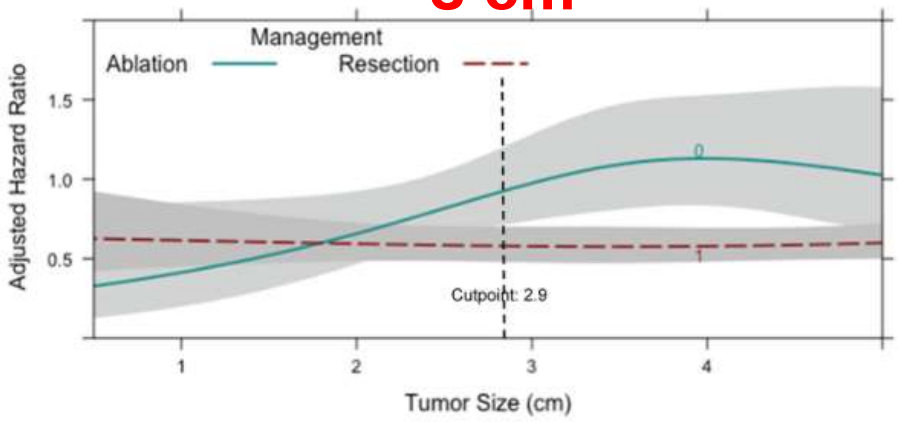
5 - year Survival

- Surgery: 37.5%
- Ablation: 8.2%

***p* < 0.0001**

- **Proposed tumor size cutoff – comparable survival**

3 cm



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SBRT for CCA

- 11 studies, 226 patients
- Median dose 45Gy (range 35-55)
- 1–year local control (LC) rate: 78.6%
  - 81.8% for those using ≥ 71.3Gy
  - 74.7% for those <71.3Gy
- Median OS: 13.6mo
- 1-year survival: 53.8%

Strahlenther Onkol (2019) 195:93–102
https://doi.org/10.1007/s00066-018-1367-2

REVIEW ARTICLE

Efficacy of stereotactic body radiotherapy for unresectable or recurrent cholangiocarcinoma: a meta-analysis and systematic review

Jeongshim Lee[1,2] · Won Sup Yoon[3] · Woong Sub Koom[1] · Chai Hong Rim[3]

Received: 5 April 2018 / Accepted: 28 August 2018 / Published online: 11 September 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

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Ablative Doses of SBRT for CCA


JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Prolongation of Survival in Patients With Inoperable Intrahepatic Cholangiocarcinoma: A Retrospective Dose Response Analysis

Randa Tao, Sunil Krishnan, Priya R. Bhosale, Milind M. Javle, Thomas A. Aloia, Rachna T. Shroff, Ahmed O. Kaseb, Andrew J. Bishop, Cameron W. Swanick, Eugene J. Koay, Howard D. Thames, Theodore S. Hong, Prajnan Das, and Christopher H. Crane

J Clin Oncol 34:219-226. © 2015 [illegible]

- Key: delivering a higher ablative dose of radiation leads to improved outcomes

- Delivering a median BED of 80.5Gy
  - Median OS of 30 months
  - 3-yr OS 44%
  - 3-yr LC rate of 78%

- The addition of chemotherapy to SBRT may derive a survival advantage as a radiosensitizer over SBRT alone

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Surgery vs. Ablation vs. RT For Small iCCA

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY
Ann Surg Oncol (2023) 30:6639–6646

Comparing Survival After Resection, Ablation, and Radiation in Small Intrahepatic Cholangiocarcinoma

Sabran J. Masoud, MD[1], Kristen E. Rhodin, MD[1], Elishama Kanu, MD[1], Jiayin Bao, BA[2], Austin M. Eckhoff, MD[1], Alex J. Bartholomew, MD[1], Thomas C. Howell, MD[1], Berk Aykut, MD[1], Juliann E. Kosovec, MD[1], Manisha Palta, MD[3], Nicholas T. Befera, MD, Charles Y. Kim, MD[4], Garth Herbert, MD[1], Kevin N. Shah, MD[1], Daniel P. Nussbaum, MD[1], Dan G. Blazer III, MD[1], Sabino Zani, MD[1], Peter J. Allen, MD[1], and Michael E. Lidsky, MD[1]

- NCDB, retrospective analysis
- Stage I-III iCCA < 3cm, diagnosed 2010-2018
- 545 patients
- Surgery – 297, Ablation - 114, RT – 134
- Median OS:
  - All – 34.1mo
  - Surgery – 50.5mo
  - Ablation – 39.5mo
  - RT – 20.9mo

p=0.14

p<0.0001

p<0.0001

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Surgery vs. Ablation vs. RT For Small iCCA

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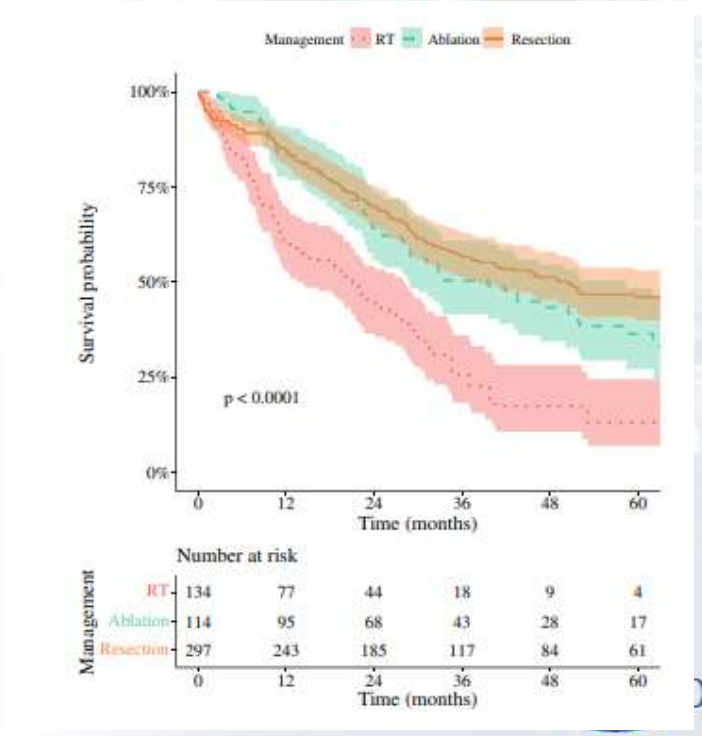
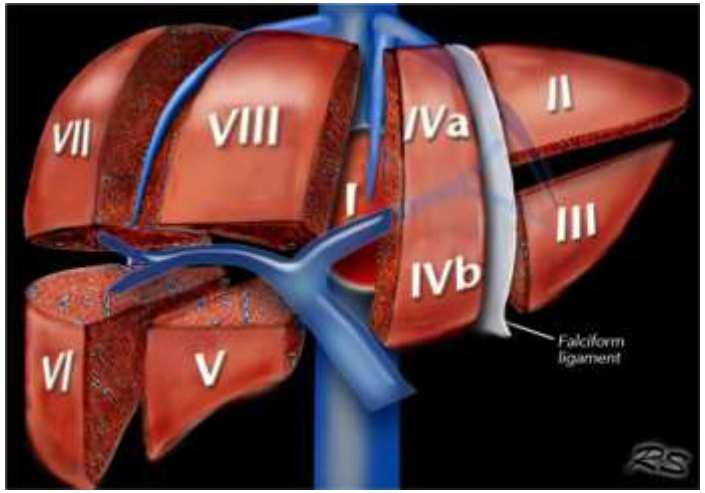
- 5-yr Survival:
  - All – 36.8%
  - Surgery – 46%
  - Ablation – 36.4%
  - RT 13.1%

***p*<0.0001**



Histotripsy

- Non-invasive, non-thermal
- Uses focused ultrasound to produce cavitation via the formation of oscillating microbubbles
- ***Very early days*…zero outcomes data**
- Limitations…many



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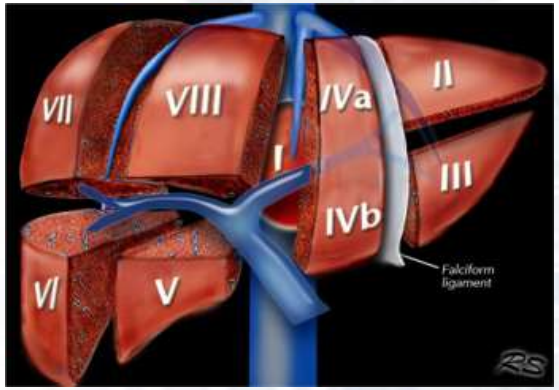
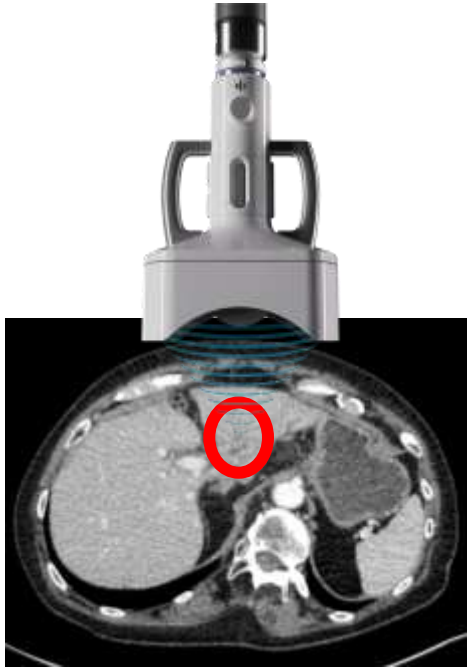
Histotripsy

- We have treated 1 CCA patient (11/25/24)
  - No follow up yet





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Conclusions

- IR (and RO) can play an important role in helping achieve locoregional control in pts with CCA
- In non-surgical candidates with tumors < 3cm, ablation offers an alternative to surgery
- Multidisciplinary approach is critical
- Understanding the data, and its limitations are key

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