

# ***Hepatocellular Carcinoma: Advances in Image-Guided Tumor Ablation***

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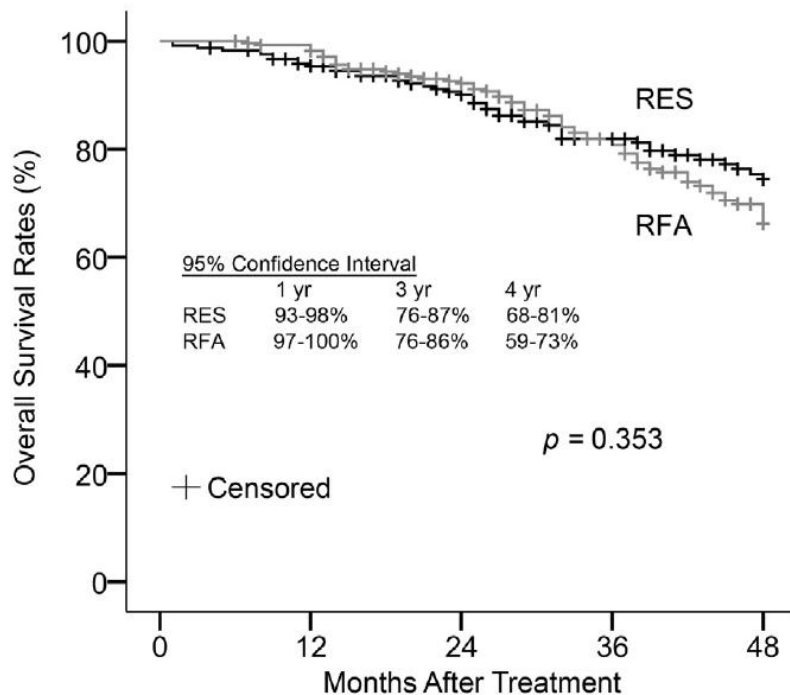
# Early Stage HCC: Survival Outcomes after RFA

Author and Year (Reference)	Patients (Number)	Overall Survival (%)		
		1-Year	3-Year	5-Year
Lencioni et al., 2005 (29)				
Child-Pugh A	144	100	76	51
Child-Pugh B	43	89	46	31
Tateishi et al., 2005 (34)				
Child-Pugh A	221	96	83	63
Child-Pugh B-C*	98	90	65	31
Choi et al., 2007 (35)				
Child-Pugh A	359	NA	78	64
Child-Pugh B	160	NA	49	38
N'Kontchou et al., 2009 (36)				
BCLC resectable†	67	NA	82	76
BCLC unresectable	168	NA	49	27

\*Only 4 of 98 patients had Child-Pugh C cirrhosis.

# Early Stage HCC ( $\leq 3\text{cm}$ ): RFA vs Resection

Long-term effectiveness of resection and radiofrequency ablation for single hepatocellular carcinoma  $\leq 3\text{ cm}$ . Results of a multicenter Italian survey



**Tumor recurrence due to local progression:**

- **RFA: 20.5%**
- **Resection: 0.4%**

# RFA of Early-Stage HCC: Histologic Outcome

TABLE 3

Dependence of Histologic Outcome on Tumor Size, Location, Patient Age, Sex, and RF Device Used

Variables	Histologic Outcome		P Value*
	Successful RF Treatment	Unsuccessful RF Treatment	
Tumor size			
≤2.5 cm	26 (87)	4	.017
>2.5 cm	9 (53)	8	
≤3.0 cm	29 (83)	6	.050
>3 cm	6 (50)	6	.009
Location			
Nonperivascular	28 (88)	4	
Perivascular	7 (47)	8	

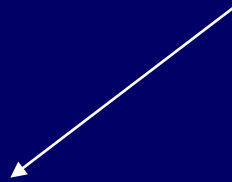
# *The Evolving Field of Image-Guided Ablation*

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**Percutaneous Ethanol Injection**



**Radiofrequency Ablation**



**Focused Ultrasound**



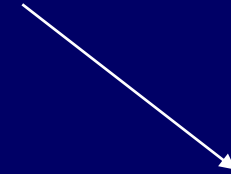
**Microwave Ablation**



**Irreversible Electroporation**

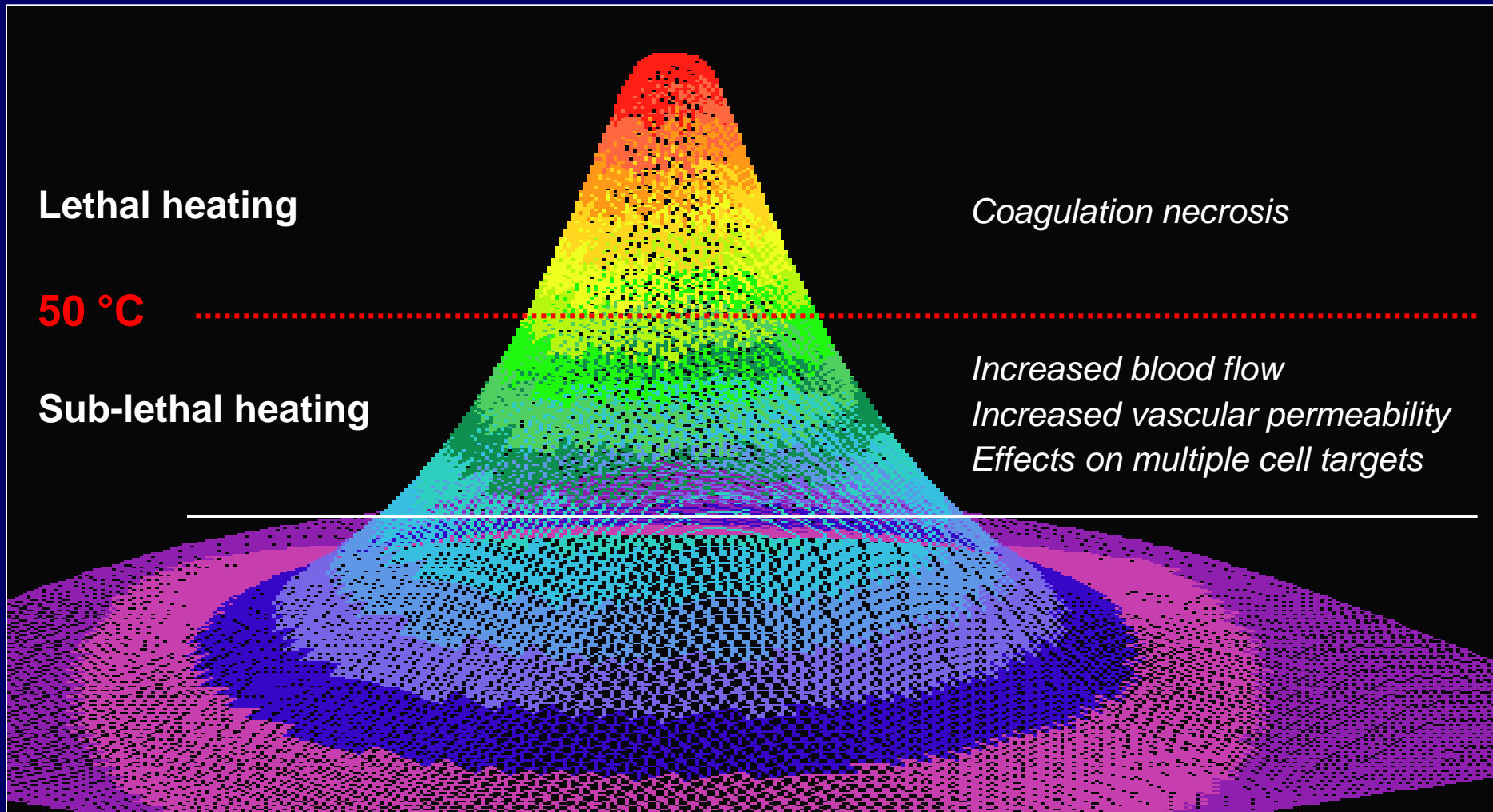


**Laser Ablation**



**Cryoablation**

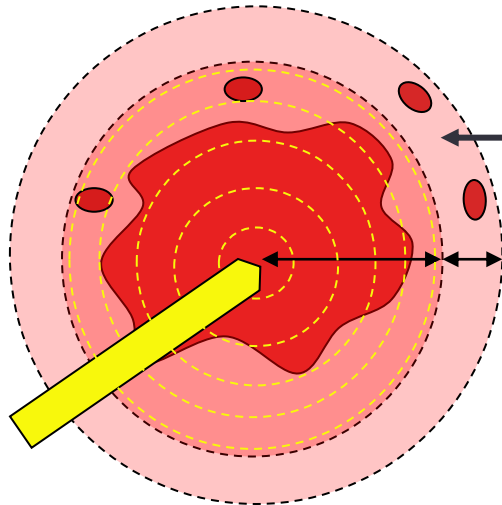
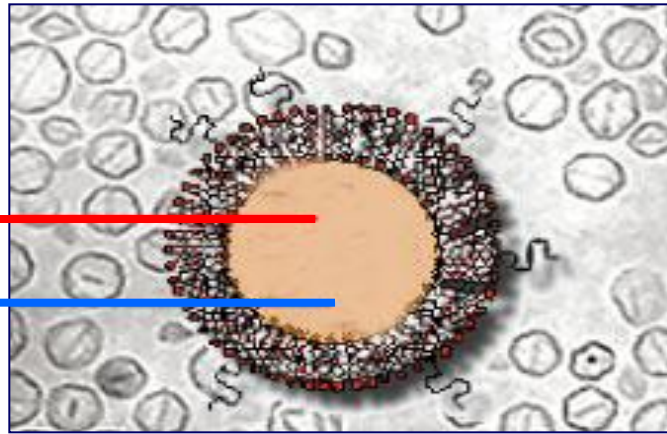
# Temperature-Tissue Interactions



# RFA in Combination with IV Heat-Activated Liposomal Encapsulation of Doxorubicin

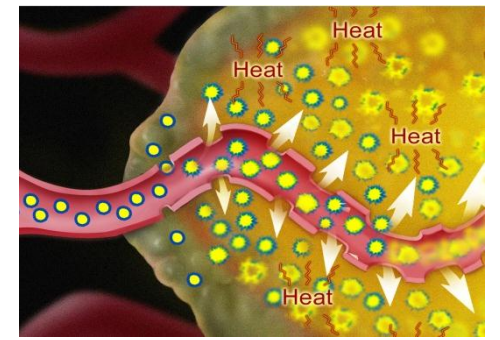
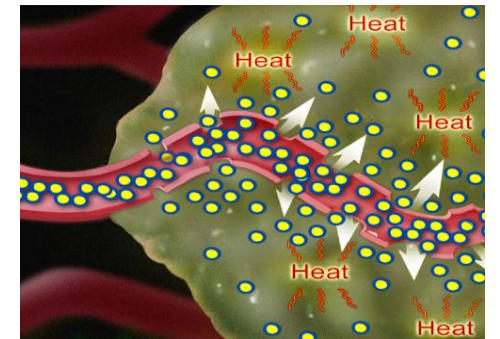
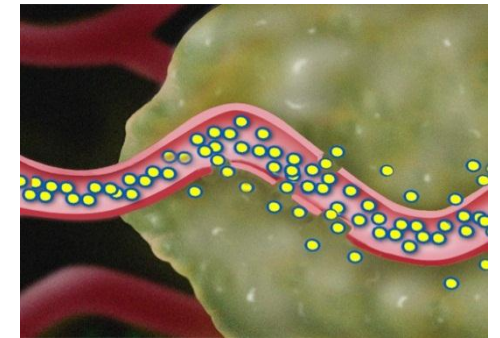
Doxorubicin

(Other drugs)



39 - 50°C

high concentration  
of doxorubicin  
deposited by  
ThermoDox  
(Celsion Corporation)



# RFA in Combination with IV Heat-Activated Liposomal Encapsulation of Doxorubicin



A Phase III, Randomized, Double-Blinded, Dummy-Controlled Study of the Efficacy and Safety of ThermoDox<sup>®</sup> in Combination with RFA Compared to RFA Alone in the Treatment of HCC

PIs: R. Lencioni, R. T. Poon

## Main eligibility criteria:

- HCC 3-7 cm
- ≤ 4 tumors
- Candidate for RFA
- Child - Pugh A-B
- No prior treatment

## Target enrollment:

- 700 patients

Randomization

50 mg/m<sup>2</sup> ThermoDox

Dummy infusion

## Primary endpoint:

- PFS

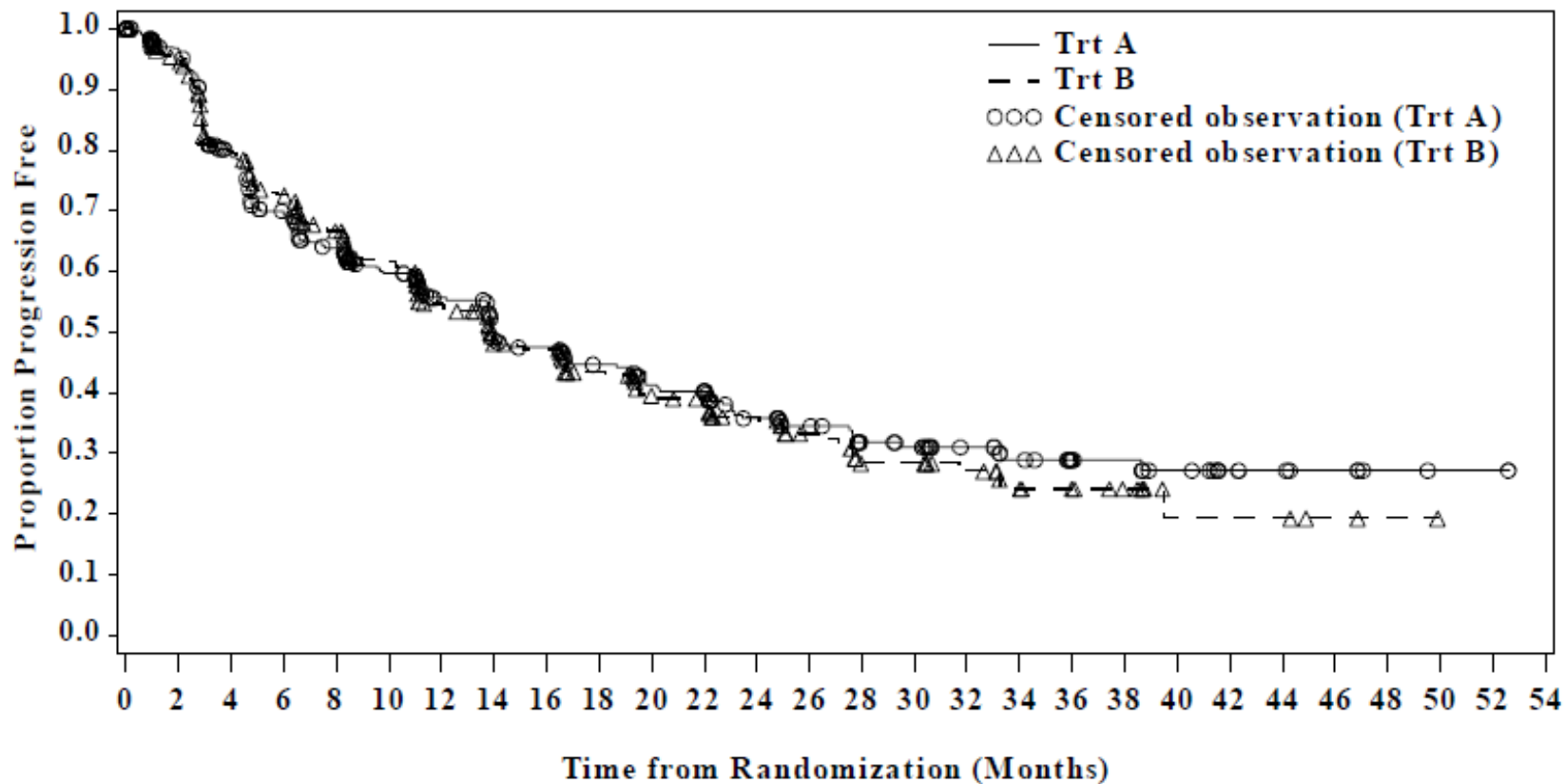
## Secondary endpoints:

- OS
- TTLR
- Safety
- Other

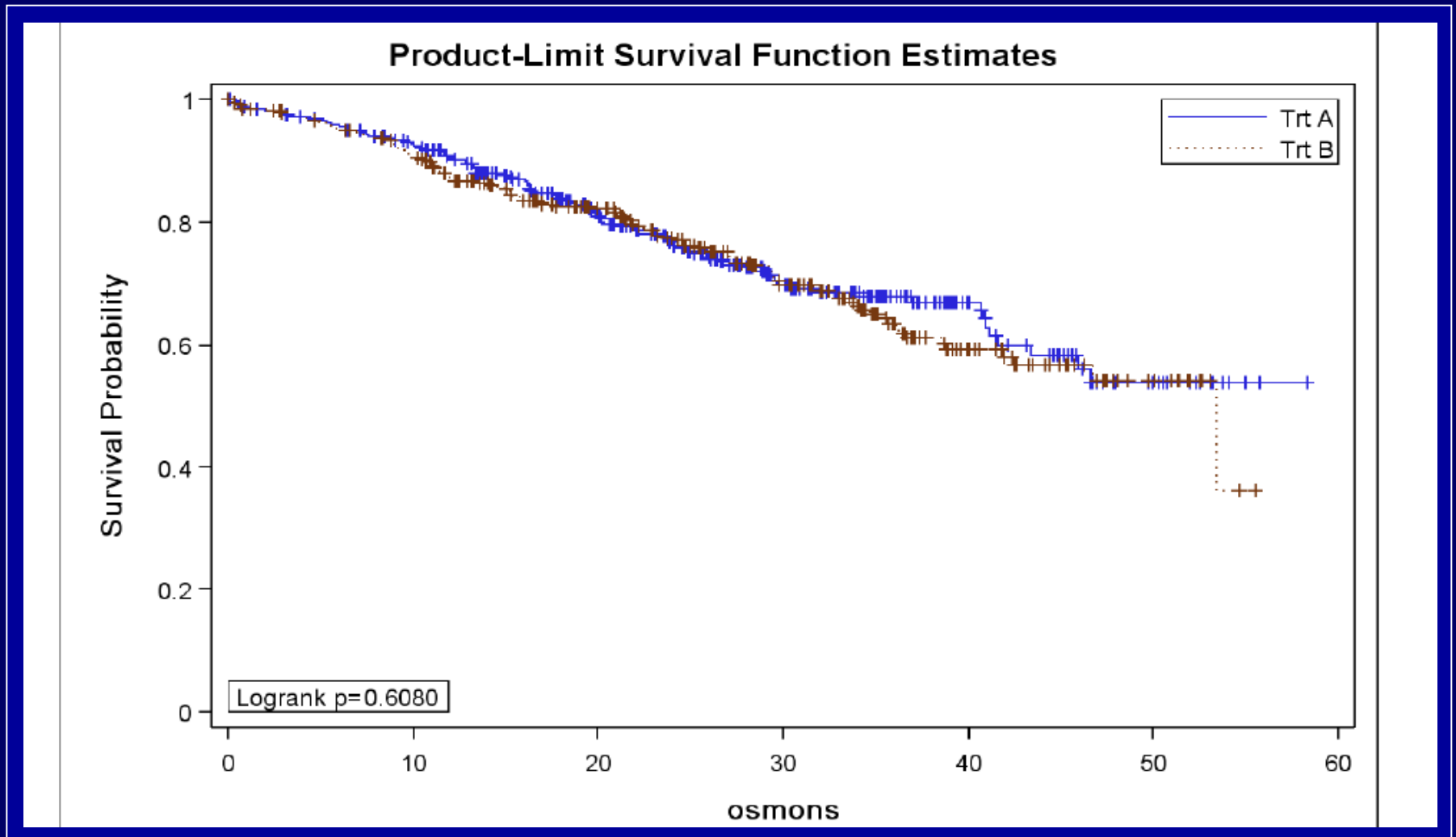


# HEAT Trial: Progression-Free Survival (Primary Endpoint)

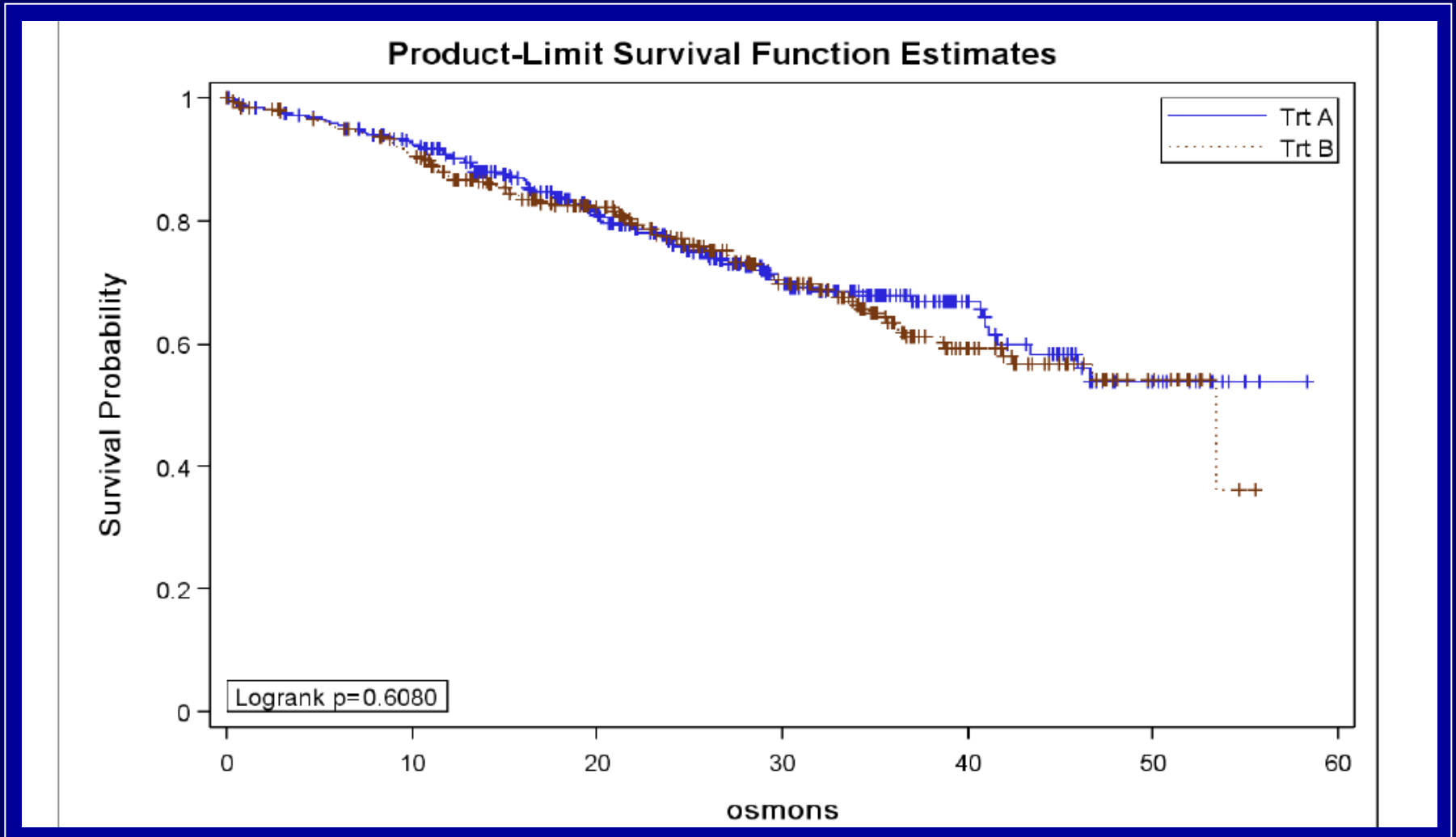
Figure 1.1  
Kaplan-Meier: Cumulative Probability of Progression-Free Survival (PFS) by Treatment Group (IRRC)  
Intent-to-Treat Population



# HEAT Trial: Overall Survival (Secondary Endpoint)

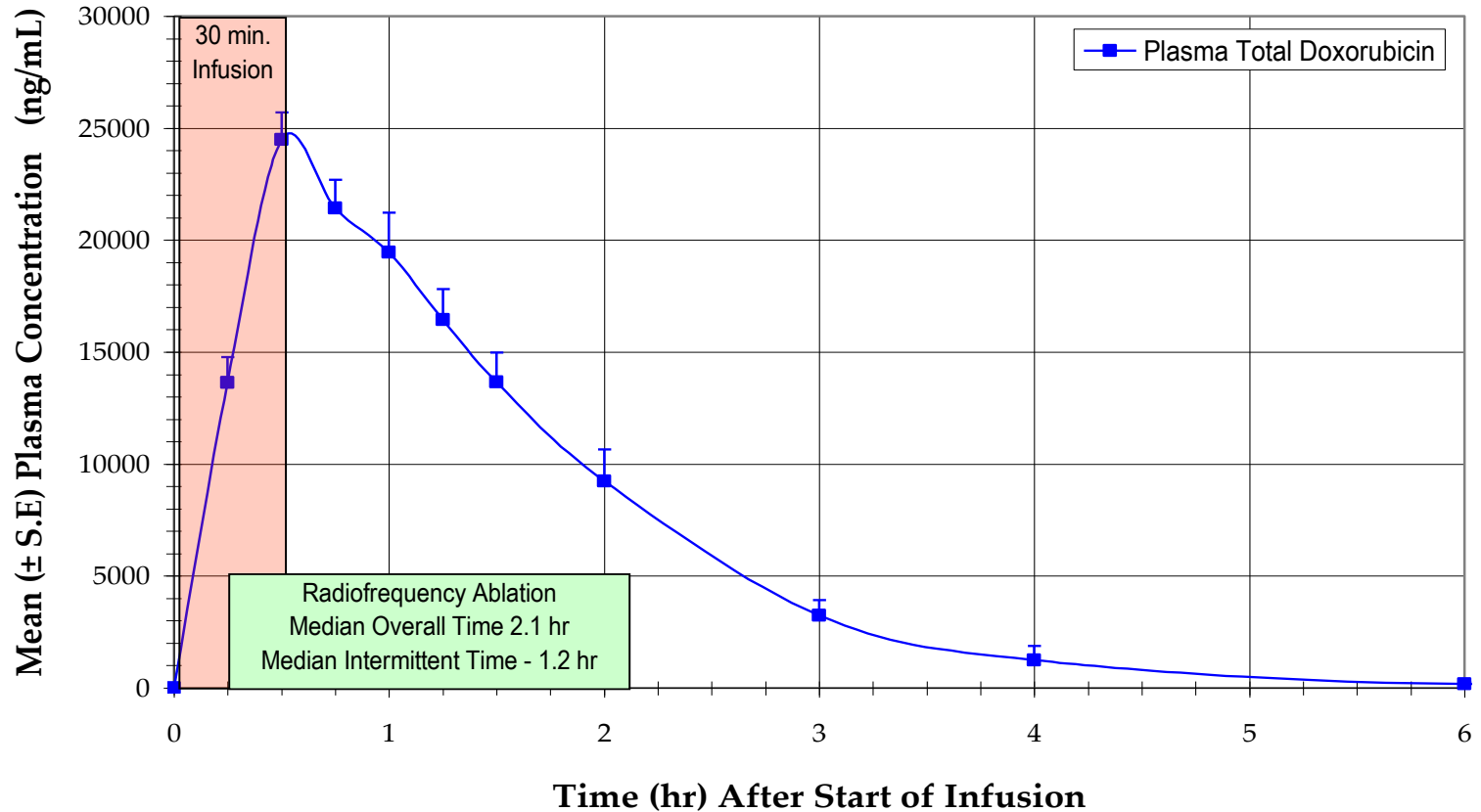


# HEAT Trial: Overall Survival (Secondary Endpoint)



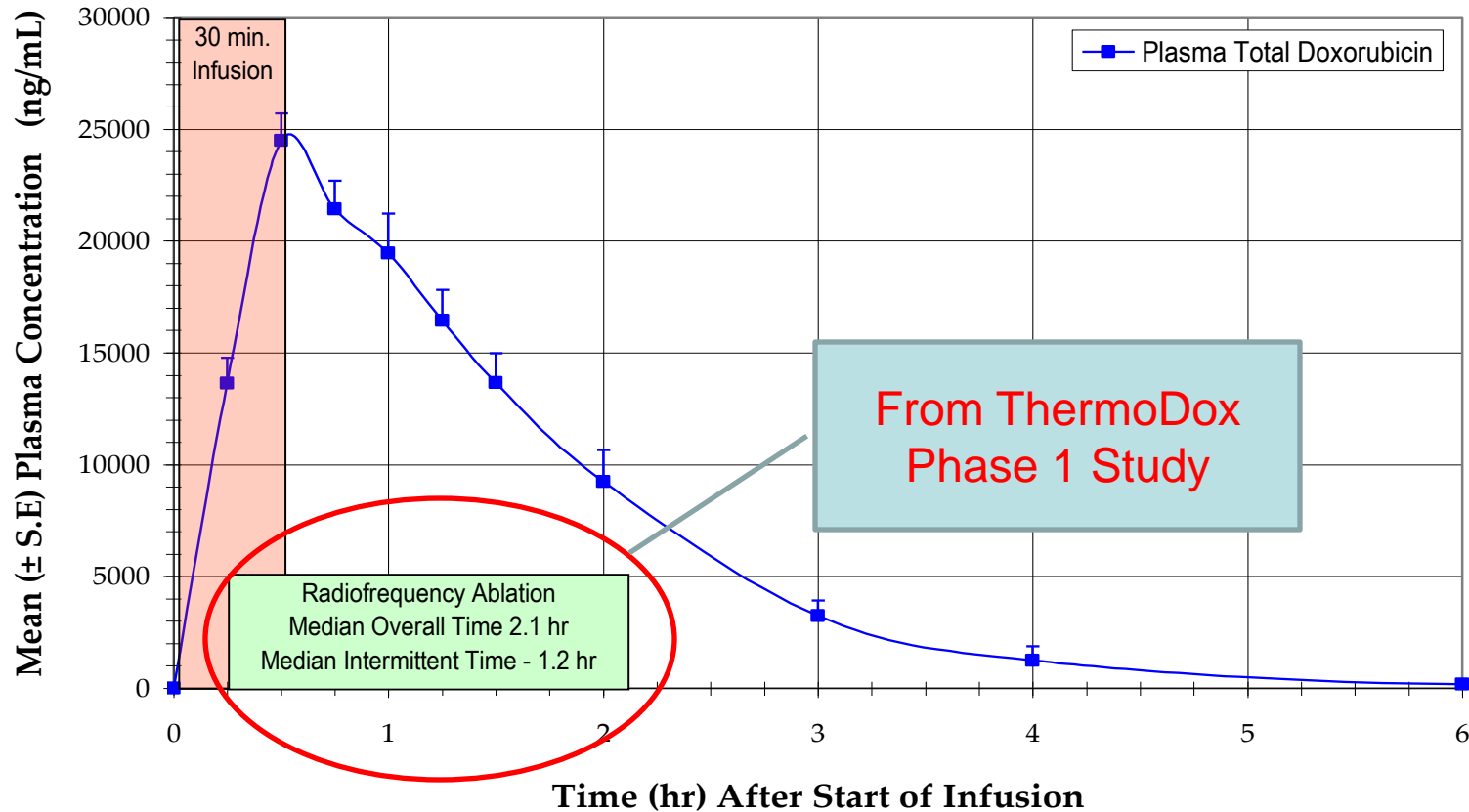
# Phase I Results: ThermoDox Human PK

**ThermoDox Protocol 104-03-101: + Liver RFA @ 50 mg/m<sup>2</sup>**  
**Mean ( $\pm$  S.E) Plasma Concentrations (n=6)**



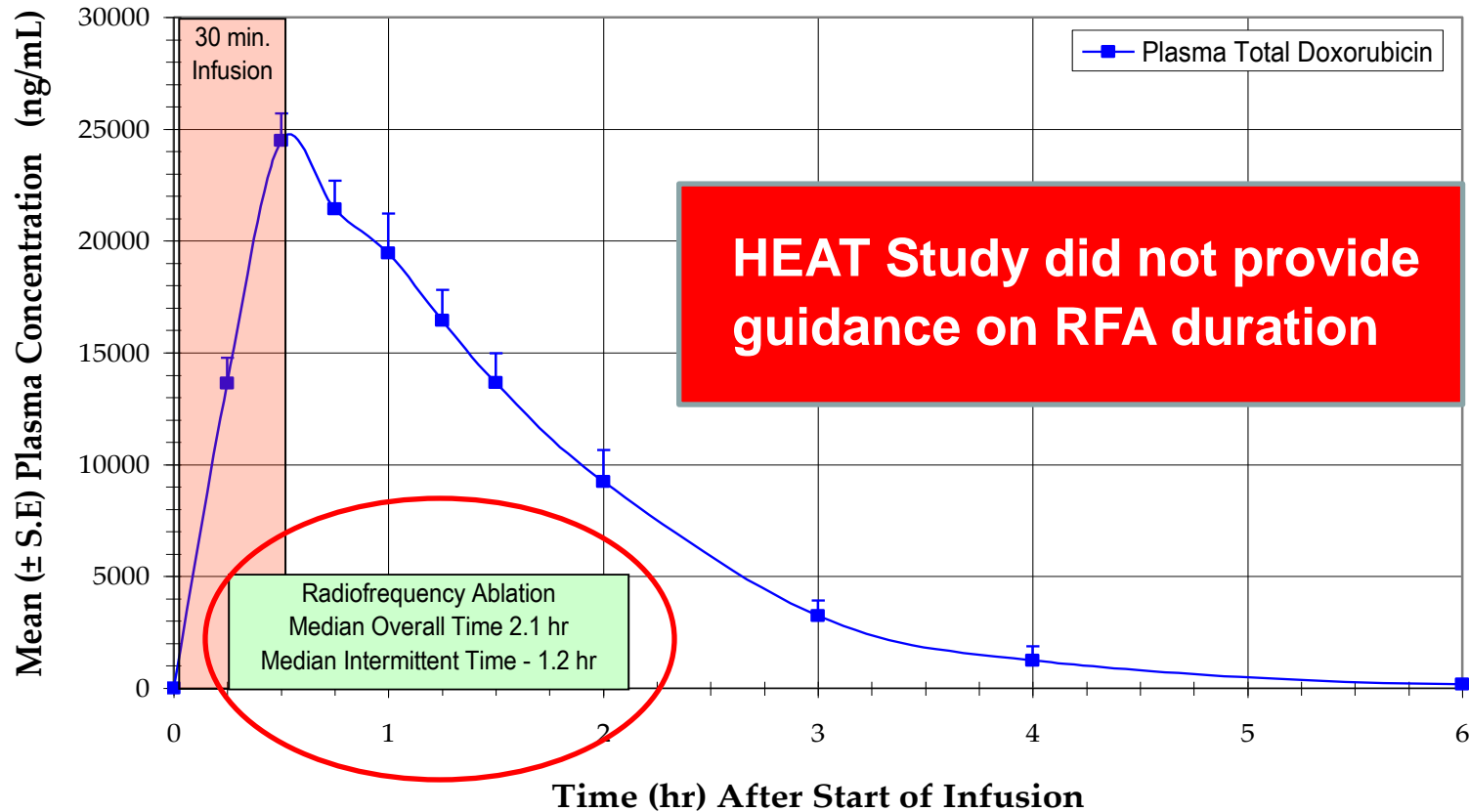
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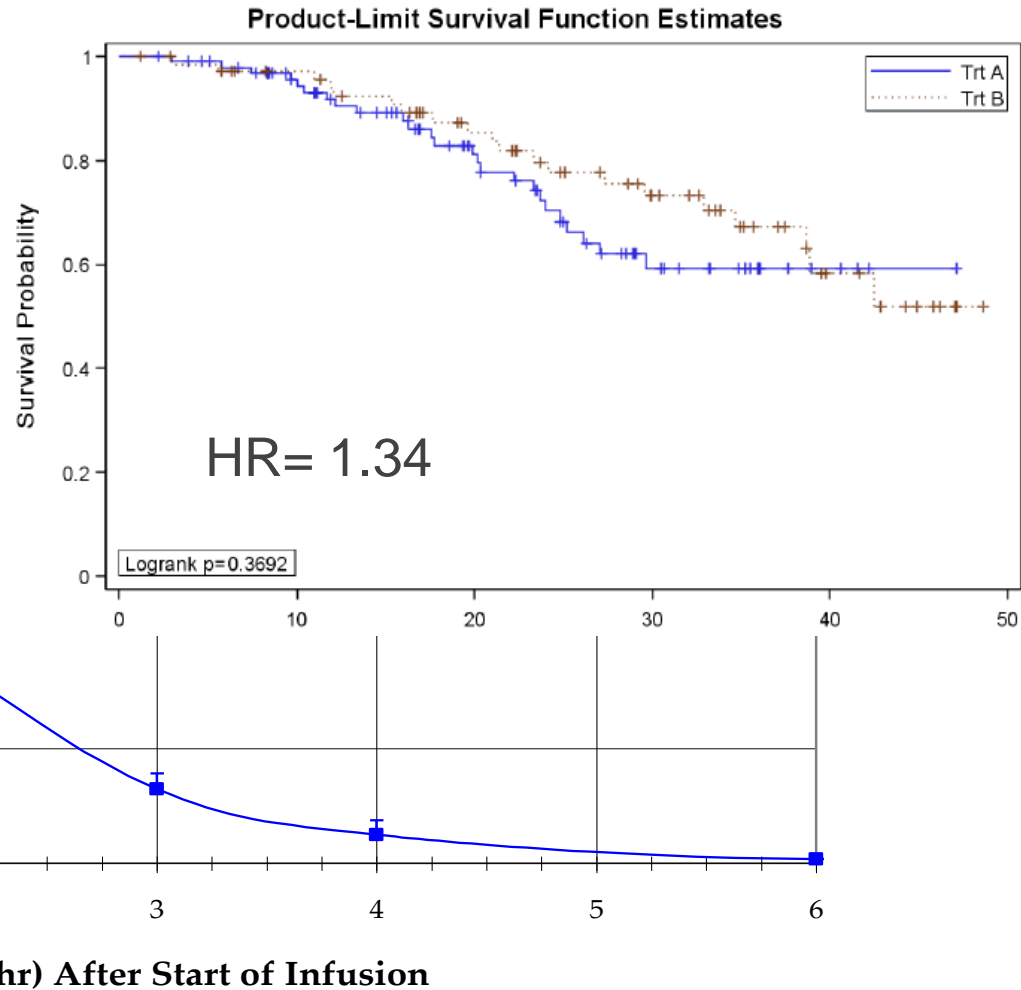
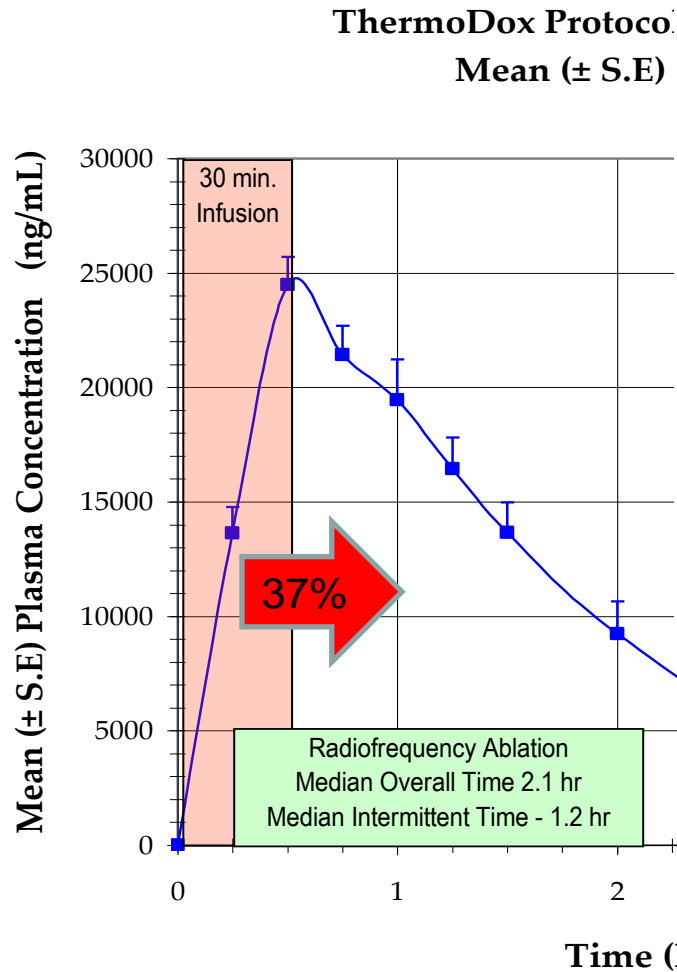


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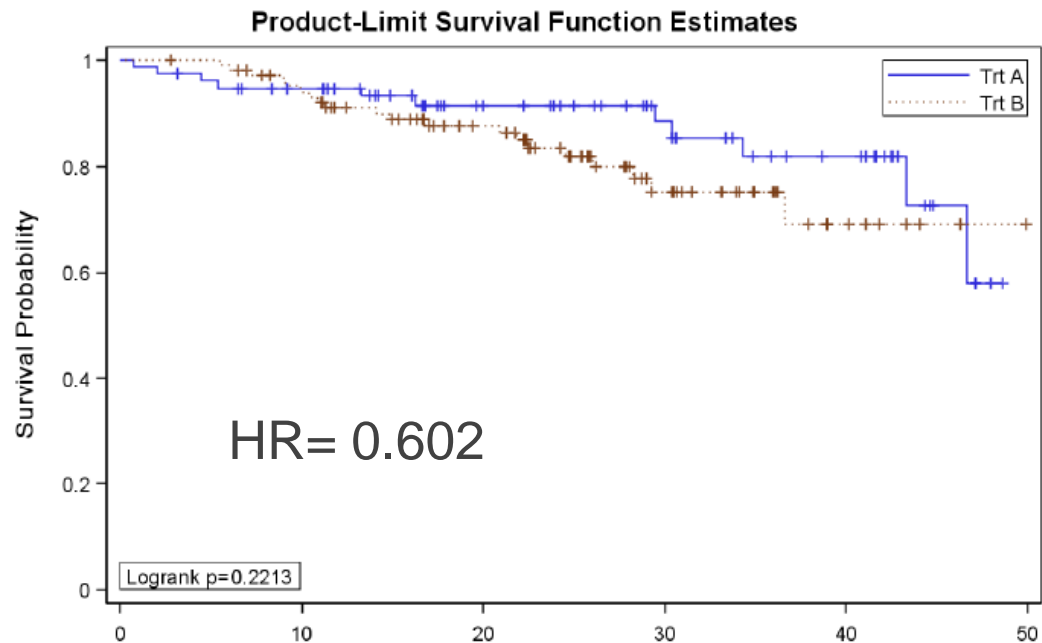
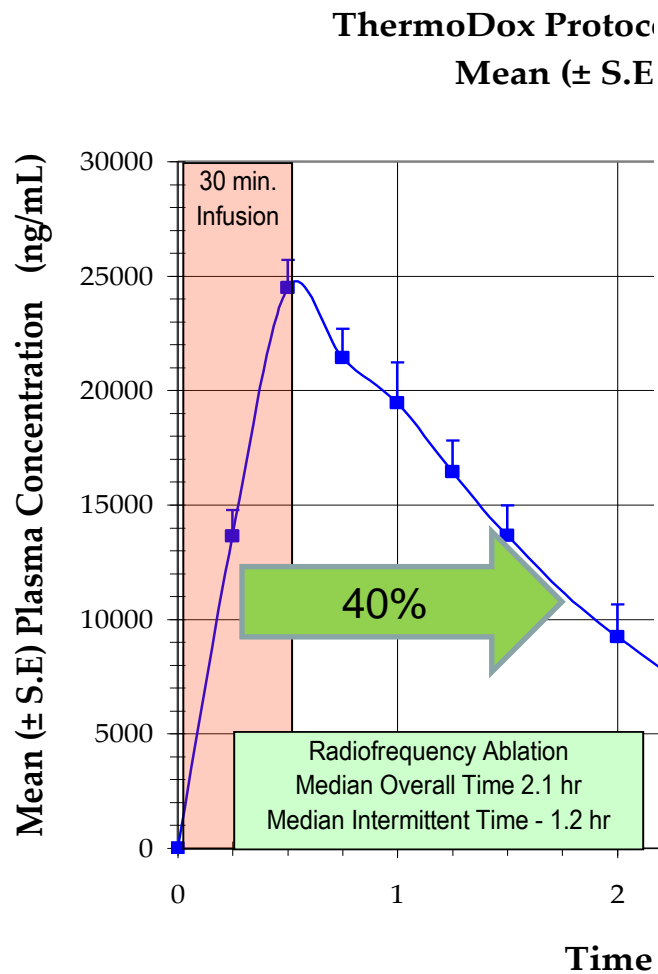
ThermoDox Protocol 104-03-101: + Liver RFA @ 50 mg/m<sup>2</sup>  
Mean (± S.E) Plasma Concentrations (n=6)



# OS of Patients had RFA < 45 mins (n=166)

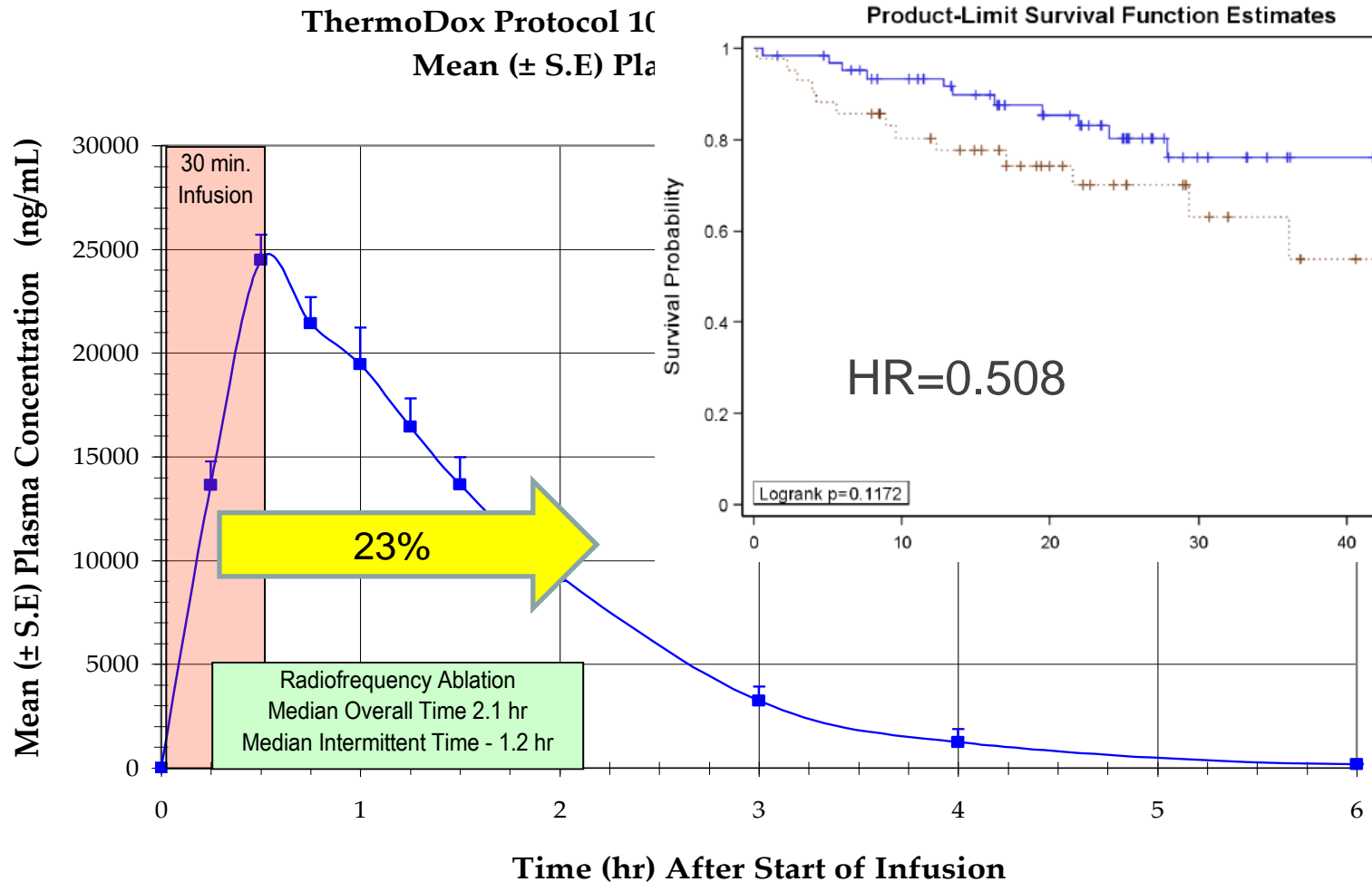


# OS of Patients had RFA 45-90 mins (n=181)





# OS of Patients had RFA > 90 mins (n=105)



# *Take Home Points*

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- **RFA is the standard technique for image-guided ablation of early-stage HCC**
- **Novel technologies – such as MWA and IRE - seem to offer advantages over RFA and deserve accurate investigation in clinical trials**
- **Clinical research on potential synergies between image-guided local ablation and new drugs / new carriers is ongoing**

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