Modulated electro-hyperthermia in the combined treatment of metastatic colorectal cancer a retrospective cohort study with meta-comparison

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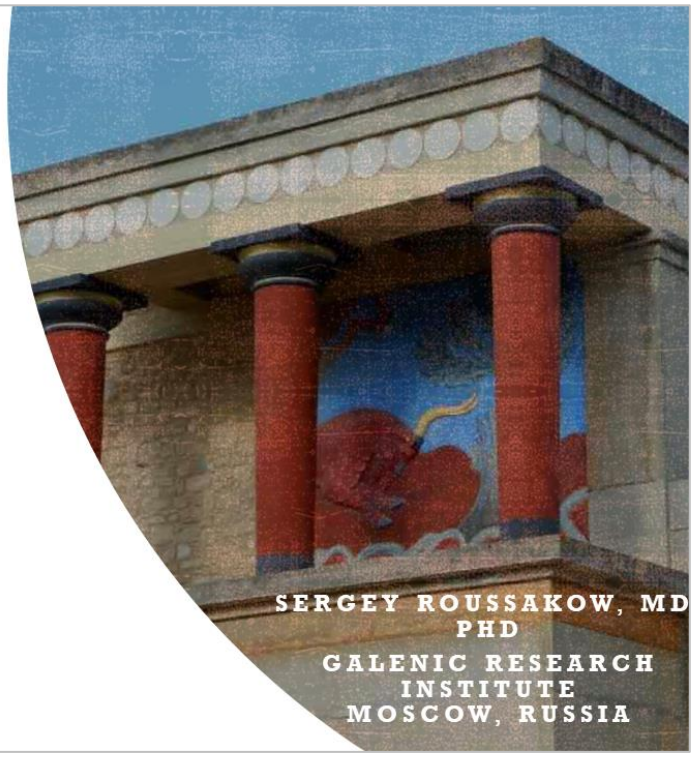
MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH META-COMPARISON



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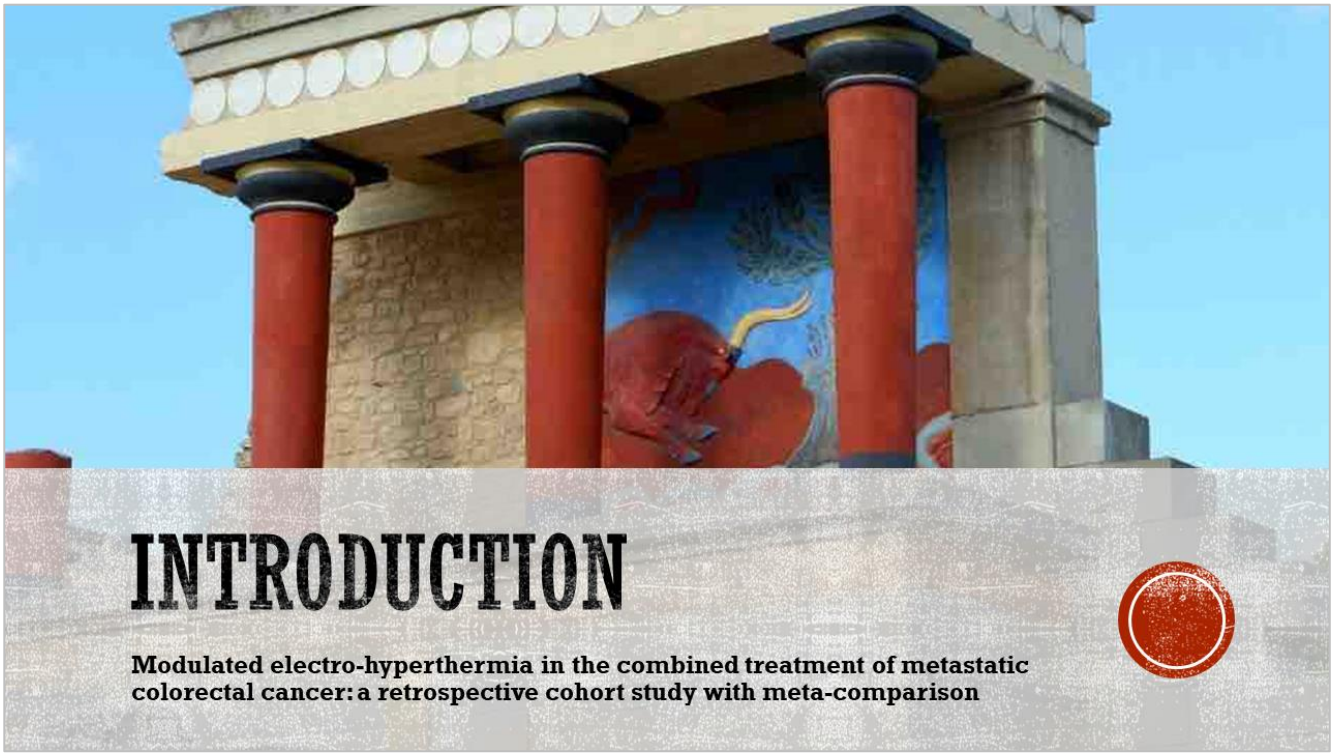
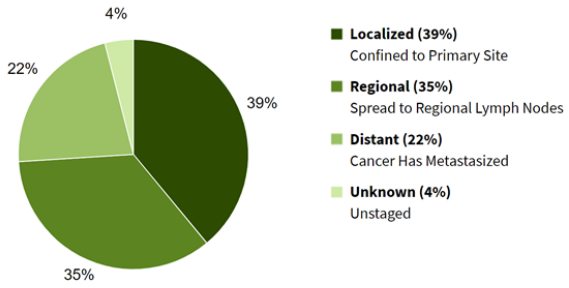


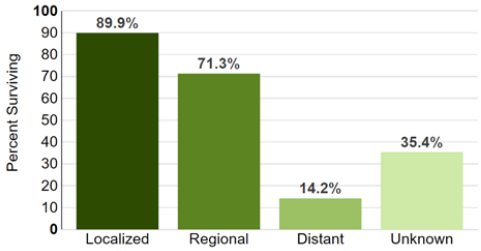
INTRODUCTION

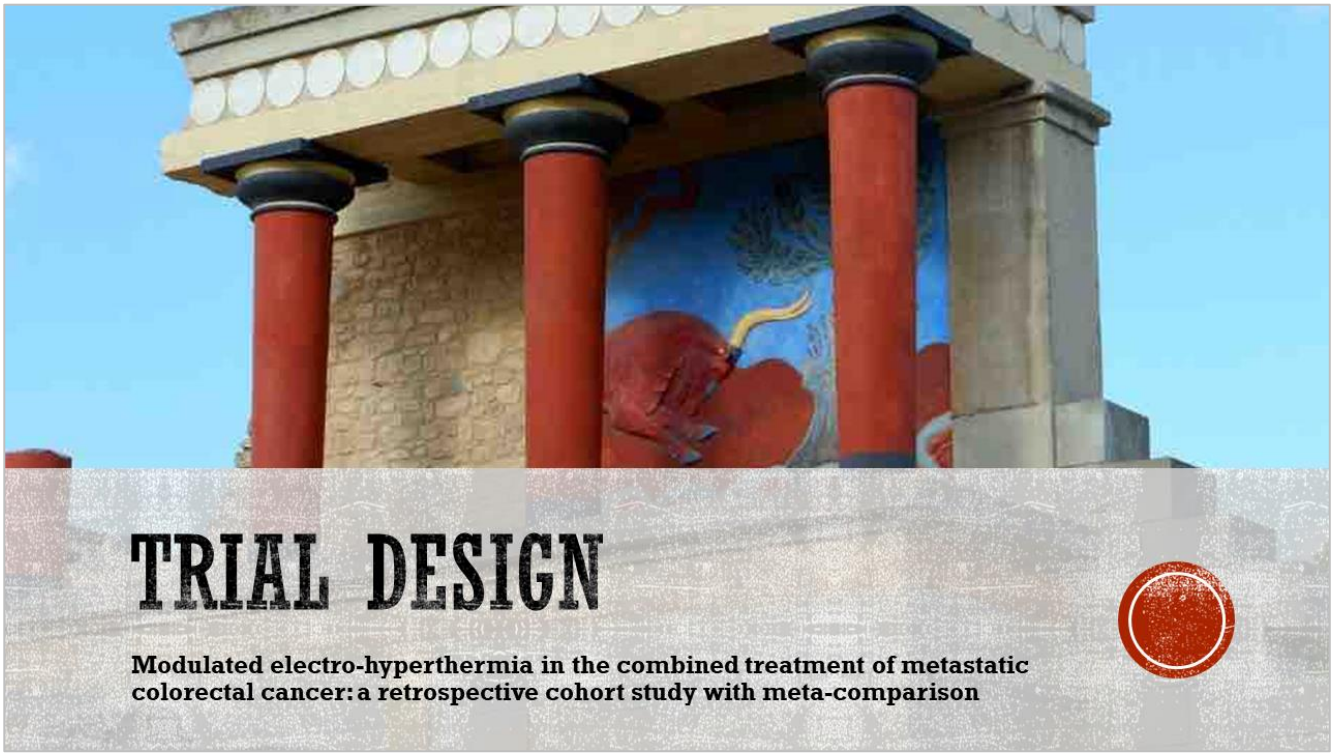
Modulated electro-hyperthermia in the combined treatment of metastatic colorectal cancer: a retrospective cohort study with meta-comparison

FACTS ABOUT COLORECTAL CANCER

- 3rd the most diagnosed cancer in the world
- 4th leading cause of cancer death among men & women combined in the world
- 2nd leading cause of cancer death among men & women combined in the developed countries
- In the USA:
  - 140,250 estimated new cases in 2018
  - 50,630 estimated deaths in 2018







TRIAL DESIGN

Modulated electro-hyperthermia in the combined treatment of metastatic colorectal cancer: a retrospective cohort study with meta-comparison

TRIAL DESIGN

- A retrospective, cohort, two-center study.
- Two centers in Budapest (Hungary):
  - HTT-MED Clinic (HTT);
  - Peterfi Hospital (PFY).
- Enrollment:
  - HTT from 08/04/1997 to 10/17/2002 (63 months),
  - PFY from 05/01/1999 to 04/30/2002 (37 months).
- No inclusion / exclusion criteria
- Exitus
  - National Hungarian Civil Registry.
- Primary endpoints:
  - Median Survival Time (MST)
  - Overall Survival (OS) at 1, 3, 5 years
- The endpoints are in two options:
  - from the diagnosis
  - from the 1st session of MEHT
- Secondary endpoint:
  - clinical response (RECIST 1.1).

INTERVENTION AND BASIC TREATMENT

BASIC TREATMENT

- Radical or debulking surgery
- Adjuvant chemotherapy
- Symptomatic radiotherapy

INTERVENTION

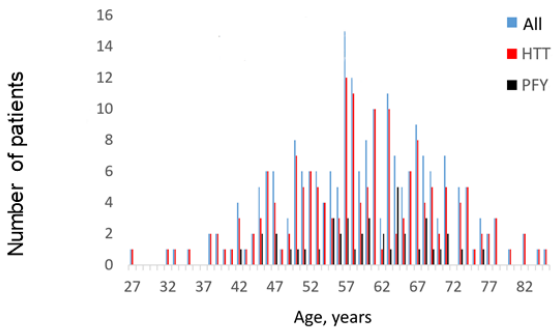
- Modulated electro-hyperthermia (oncothermia)
- Applicator Ø 30 cm
- Power 120 → 150 W.
- Time:
  - Radio- chemo-enhancement, 45 min.
  - Adjuvant monotherapy, 60 min.
  - Palliative monotherapy, 90 min.
- Localizations: up to 2.

RESULTS

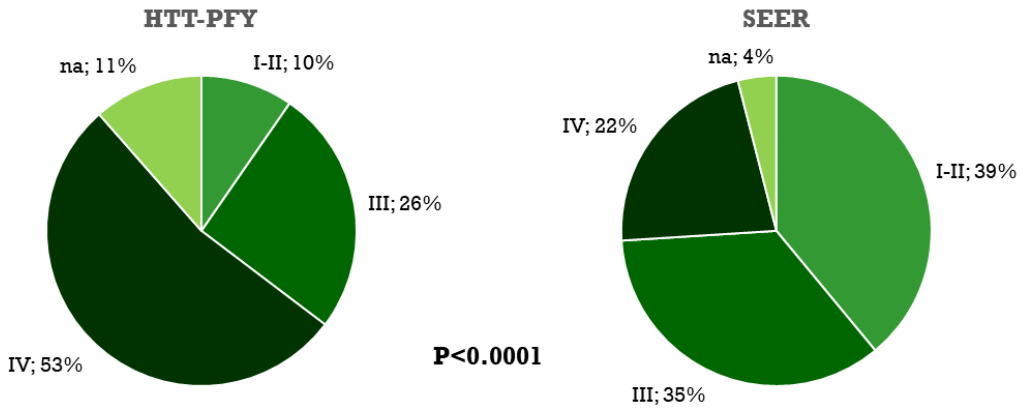
Modulated electro-hyperthermia in the combined treatment of metastatic colorectal cancer: a retrospective cohort study with meta-comparison

DEMOGRAPHY AND AGE DISTRIBUTION

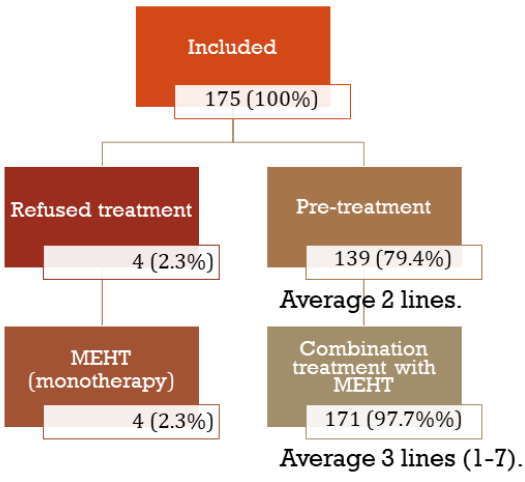
Parameter	No	% / 95% CI
Number	218	
Sex		
Female	85	39.0%
Male	133	61.0%
Age at diagnosis		
Average ± se	57.5 ± 0.7	(56.1 – 58.9)
Median (range)	58 (27 - 85)	(56 - 59)
≥65 years	52	23.9%
≥68 years	30	13.8%

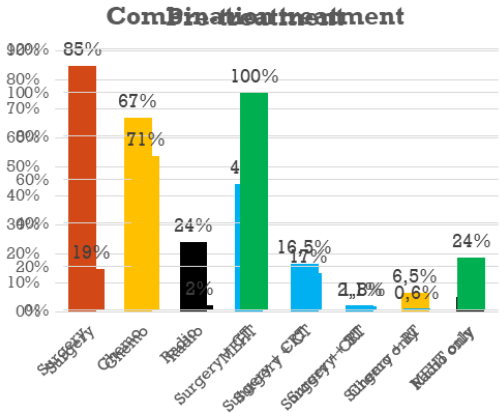


DISTRIBUTION BY STAGE



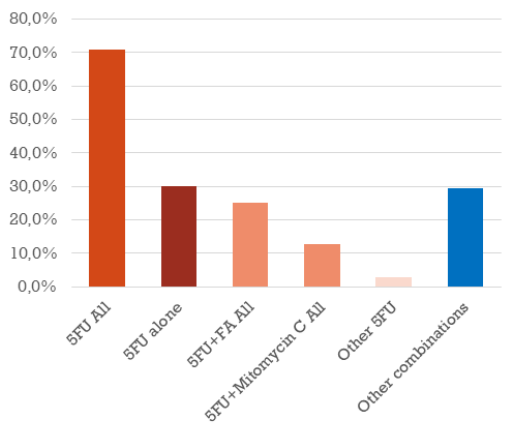
FLOWCHART (HTT ARM)





CHEMOTHERAPY

Combination	Lines		Cycles	
	No	%	No	%
5FU & combinations	191	70.7%	703	74.5%
5FU alone	81	30.0%	276	29.3%
5FU+Leucovorin & combinations	68	25.2%	263	27.9%
5FU+Mitomycin C & comb	34	12.6%	140	14.8%
Other 5FU combinations	8	3.0%	24	2.5%
Other chemo & combinations (36)	79	29.3%	240	25.5%
TOTAL:	**270**	**100%**	**943**	**100%**

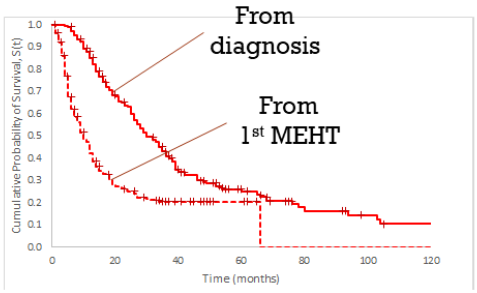


MODULATED ELECTRO-HYPERTHERMIA

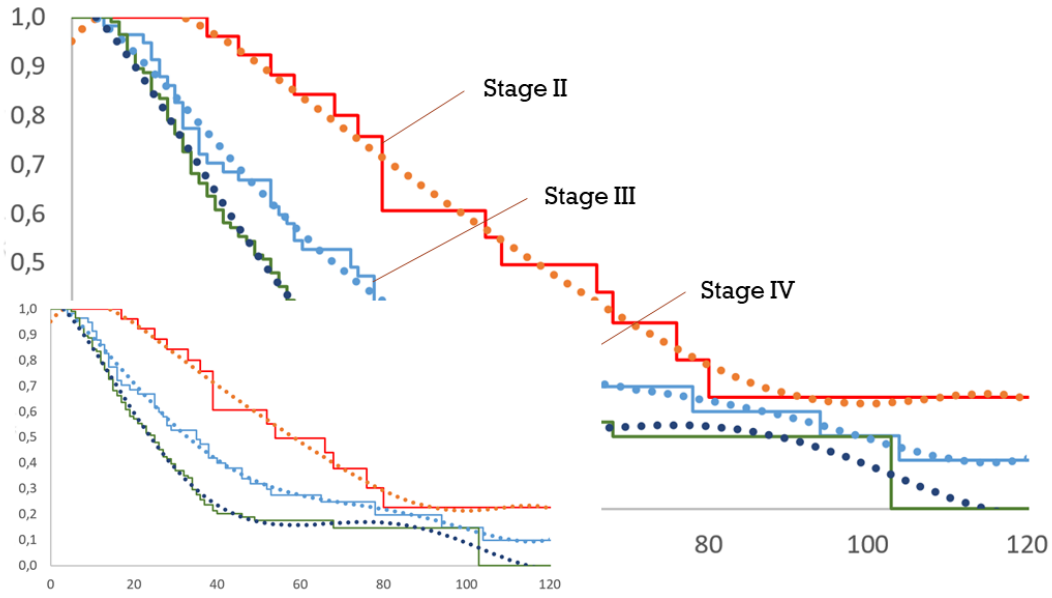
Parameter	Value
Median treatment line	3.6±0.1
The terminal treatment	87.4% (153 / 175)
Time from diagnosis to 1st MEHT, months	Ave. 19.3 ± 1.4; Med. 12 (0-138)
Number of sessions	Ave. 7.9 ± 0.3; Med. 6 (2 – 42)
Duration of session, min	Ave. 72.6 ± 1.4; Med. 60 (45 – 135)
Dose per course, kJ	Ave. 29.1 ± 1.9; Med. 20.9 (0 – 207)
Days per session	Ave. 7.2 ± 0.4; Med. 6 (1 – 35)
Number of fields (1 vs. 2)	97.1% (170 / 175) vs. 2.9% (5 / 175)
liver	58.9% (106 / 180)
colorectal	18.9% (34 / 180)
lungs	4.4% (8 / 180)
other or not indicated	18% (32 / 180)

OVERALL SURVIVAL

Parameter	From Dx	From 1st MEHT
MST, months	29.7 (26.3-34.9)	9.6 (7.8-11.8)
1-year OS	85.2% (80.5-89.9%)	42.2% (35.4-49.0%)
2-year OS	63.2% (56.7-69.7%)	42.2% (35.4-49.0%)
3-year OS	41% (34.3-47.7%)	20.5% (14.8-26.3%)
4-year OS	29.4% (22.9-35.9%)	20.5% (14.8-26.3%)
5-year OS	25.2% (18.8-31.6%)	20.5% (14.8-26.3%)



SURVIVAL BY STAGES

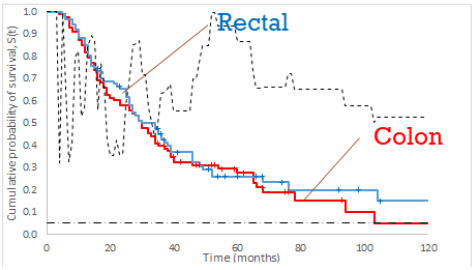


ANALYSIS

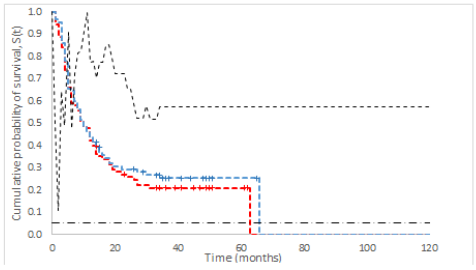
Modulated electro-hyperthermia in the combined treatment of metastatic colorectal cancer: a retrospective cohort study with meta-comparison

COLON CANCER VS. RECTAL CANCER

From diagnosis



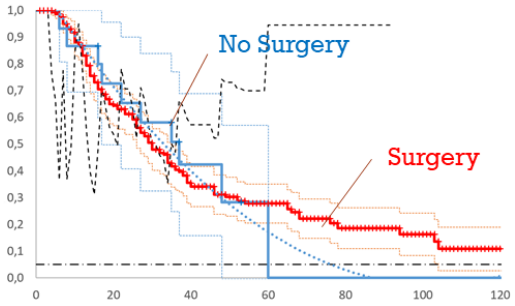
From 1st MEHT



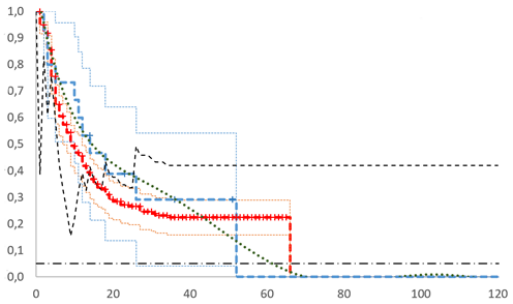
	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
Colon Cancer	88/175	81.80%	58.00%	39.80%	31.30%	27.60%	29.3	48.90%
RR	175	0.96	0.89	0.93	1.02	1.06	0.98	0.99
p-value		0.567	0.361	0.632	0.773	0.867	0.394	0.941
Rectal Cancer	87/175	85.10%	65.40%	42.70%	30.80%	26.00%	29.9	49.40%

MEHT+SURGERY VS. MEHT WITHOUT SURGERY

From diagnosis



From 1st MEHT

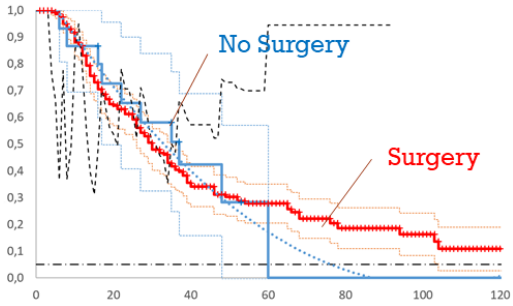


	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
With Surgery	202/218	85.00%	62.90%	40.20%	29.40%	25.80%	28.5	40.10%
RR	218	0.97	0.95	0.78	1.03	8.83	0.9	1.28
p-value		0.7996	0.8114	0.3919	0.9486	0.0897	0.37	0.487
No Surgery	16/218	87.50%	66.10%	51.40%	28.60%	0.00%	31	31.30%

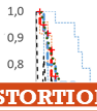
No.	Parameter	f	E_A	$\%_A$	E_B	$\%_B$	Σ_{AB}	RR	OR	z	P
1	% elderly (>68)	-1	23	14,4%	4	26,7%	175	1,24	0,52		
2	Age at diagnosos*	-1	79	49,4%	7	46,7%	175	0,99	0,11		
3	% st. IV at diagnosis	-1	91	60,3%	10	71,4%	165	1,06	0,12		
4	% M0 at diagnosis	1	24	15,0%	0	0,0%	175	1,85	0,87		
5	No. lacalizations of metastases*	-1	59	36,9%	2	13,3%	175	0,61	0,17		
6	% without liver metastasis	1	62	38,8%	5	33,3%	175	1,04	0,18		
7	% multiple metastasis	-1	74	75,5%	8	80,0%	108	1,01	0,07		
8	Maxumum tumor diameter*	-1	54	48,2%	4	50,0%	120	1,00	0,13		
9	No. of treatment lines*	1	75	46,9%	5	33,3%	175	1,13	0,23		
10	% chemotherapy	1	139	86,9%	11	73,3%	175	1,06	0,10		$p(\chi^2)=$
11	No. of chemotherapy lines*	1	26	18,7%	2	18,2%	150	1,00	0,17		0,732
12	No. of chemotherapy cycles*	1	87	62,6%	4	36,4%	150	1,29	0,28		
13	Duration	1	71	51,1%	3	27,3%	150	1,33	0,50		
14	Line of MEHT*	-1	68	42,5%	3	20,0%	175	0,70	0,17		
15	Time to MEHT (%OST)*	-1	80	50,0%	3	20,0%	175	0,61	0,15		
16	No. MEHT sessions*	1	48	30,0%	6	40,0%	175	0,91	0,19		
17	Dose of MEHT*	1	97	60,6%	10	66,7%	175	0,98	0,10		
18	% palliative treatment	-1	153	95,6%	15	100,0%	175	1,01	0,01		
19	% progression before MEHT	-1	141	88,1%	12	80,0%	175	0,97	0,06		
20	% progression after MEHT	-1	65	40,6%	7	46,7%	175	1,03	0,17		
	TOTAL:		1,23 (1,01 - 1,44), p=0,230					1,23	0,21	1,05	0,230
	AGE		1,23 (0,92 - 1,54), p=0,304					1,23	0,31	0,74	0,304
	DIAGNOSIS		1,25 (0,99 - 1,51), p=0,249					1,25	0,26	0,97	0,249
	TREATMENT		0,79 (0,60 - 0,98), p=0,218					0,79	0,19	1,10	0,218
	Chemotherapy		1,38 (1,20 - 1,56), p=0,045					1,38	0,18	2,08	0,045
	MEHT		**0,38 (0,22 - 0,53), p<0,001**					**0,38**	**0,15**	**4,08**	**0,000**

MEHT+SURGERY VS. MEHT WITHOUT SURGERY

From diagnosis



From 1st MEHT

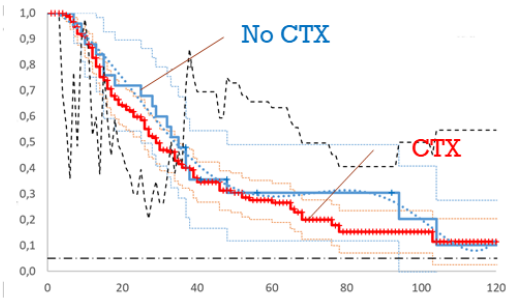


DISTORTION	SIZE (RR, 95% CI, p-value)
TOTAL:	0.90 (0.18 - 7.85), p=0.959
Age	1.23 (0.88 - 1.72), p=0.340
Diagnosis	1.03 (0.34 - 4.87), p=0.979
Treatment	0.70 (0.20 - 2.44), p=0.553
Chemotherapy	1.83 (0.84 - 3.94), p=0.454
Radiotherapy	0.77 (0.45 - 1.31), p=0.228
MEHT	**0.44 (0.18 - 0.87), p<0,001**

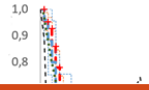
	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
With Surgery	202/218	85.00%	62.90%	40.20%	29.40%	25.80%	28.5	40.10%
RR	218	0.97	0.95	0.78	1.03	8.83	0.9	1.28
p-value		0.7996	0.8114	0.3919	0.9486	0.0897	0.37	0.487
No Surgery	16/218	87.50%	66.10%	51.40%	28.60%	0.00%	31	31.30%

MEHT+CHEMO VS. MEHT WITHOUT CHEMO

From diagnosis



From 1st MEHT

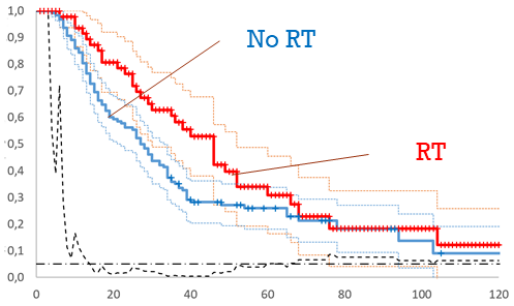


DISTORTION	SISE (RR, 95% CI, p-value)
TOTAL:	1.89 (0.62 - 10.85), p=0.819
Age	1.95 (1.65 - 3.85), p=0.234
Diagnosis	0.78 (0.45 - 1.36), p=0.289
Treatment	1.24 (0.46 - 5.26), p=0.870
Surgery	1.03 (0.97 - 1.09), p=0.374
Radiotherapy	1.06 (0.56 - 3.12), p=0.935
MEHT	0.75 (0.37 - 1.12), p=0.131

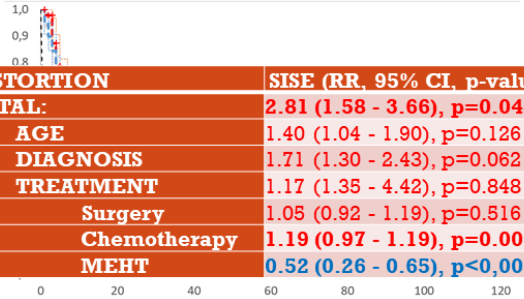
	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
With CTx	150/175	82.70%	59.90%	40.10%	31.30%	26.50%	28.8	49.30%
RR	175	0.94	0.83	0.84	1.03	0.87	0.89	1.03
p-value		0.527	0.298	0.415	0.752	0.634	0.32	0.902
No CTx	25/175	88.00%	72.00%	48.00%	30.50%	30.50%	32.4	48.00%

MEHT+RT VS. MEHT WITHOUT RT

From diagnosis



From 1st MEHT

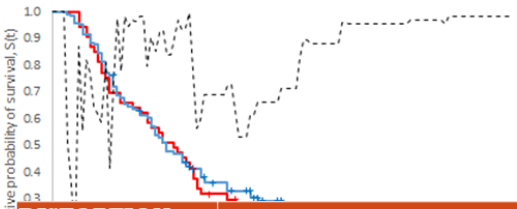


DISTORTION	SISE (RR, 95% CI, p-value)
TOTAL:	2.81 (1.58 - 3.66), p=0.049
AGE	1.40 (1.04 - 1.90), p=0.126
DIAGNOSIS	1.71 (1.30 - 2.43), p=0.062
TREATMENT	1.17 (1.35 - 4.42), p=0.848
Surgery	1.05 (0.92 - 1.19), p=0.516
Chemotherapy	1.19 (0.97 - 1.19), p=0.003
MEHT	0.52 (0.26 - 0.65), p<0,001

	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
With RT	47/175	91.50%	76.40%	58.20%	42.30%	30.90%	45.3	55.30%
RR	175	1.14	1.36	1.66	1.56	1.19	1.68	1.18
p-value		0.087	**0.017**	**0.007**	**0.016**	**0.052**	**0.041**	0.323
No RT	128/175	80.50%	56.30%	35.10%	27.20%	26.00%	27	46.90%

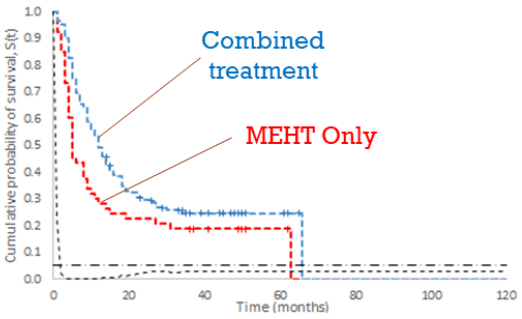
MEHT ONLY VS. COMBINED MEHT

From diagnosis



DISTORTION	SISE (RR, 95% CI, p-value)
TOTAL:	0.98 (0.72 - 1.34), p=0.907
AGE	0.82 (0.66 - 1.03), p=0.039
DIAGNOSIS	1.19 (0.97 - 1.47), p=0.176

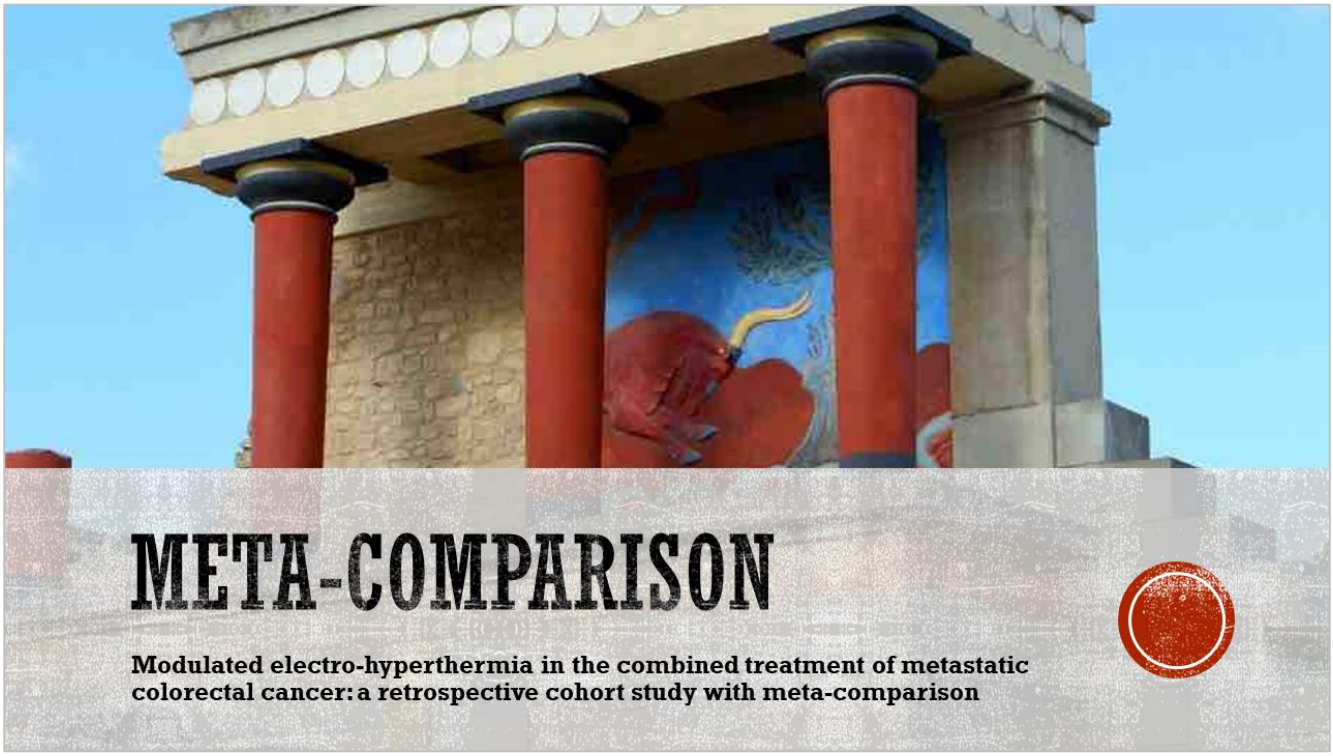
From 1st MEHT



	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
MEHT Only	53/175	28.30%	22.60%	18.90%	18.90%	18.90%	5	39.60%
RR	175	0.58	0.77	0.76	0.76	0.76	0.42	0.74
p-value		**0.001**	**0.023**	**0.027**	**0.027**	**0.027**	**0.003**	0.098
Combined trtm	122/175	49.20%	29.60%	24.70%	24.70%	24.70%	12	53.30%

- MEHT is a powerful treatment factor.
- The effect of MEHT in the treatment of metastatic colorectal cancer seems to exceed the effect of chemotherapy and is comparable to the effect of surgery.
- Combining MEHT with other treatments significantly increases its efficacy.

ANALYSIS CONCLUSIONS



META-COMPARISON

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VS.

CROOKE H, KOBAYASHI M, MITCHELL B, ET AL.
ESTIMATING 1- AND 5-YEAR RELATIVE SURVIVAL TRENDS IN COLORECTAL CANCER (CRC) IN THE UNITED STATES: 2004 TO 2014.
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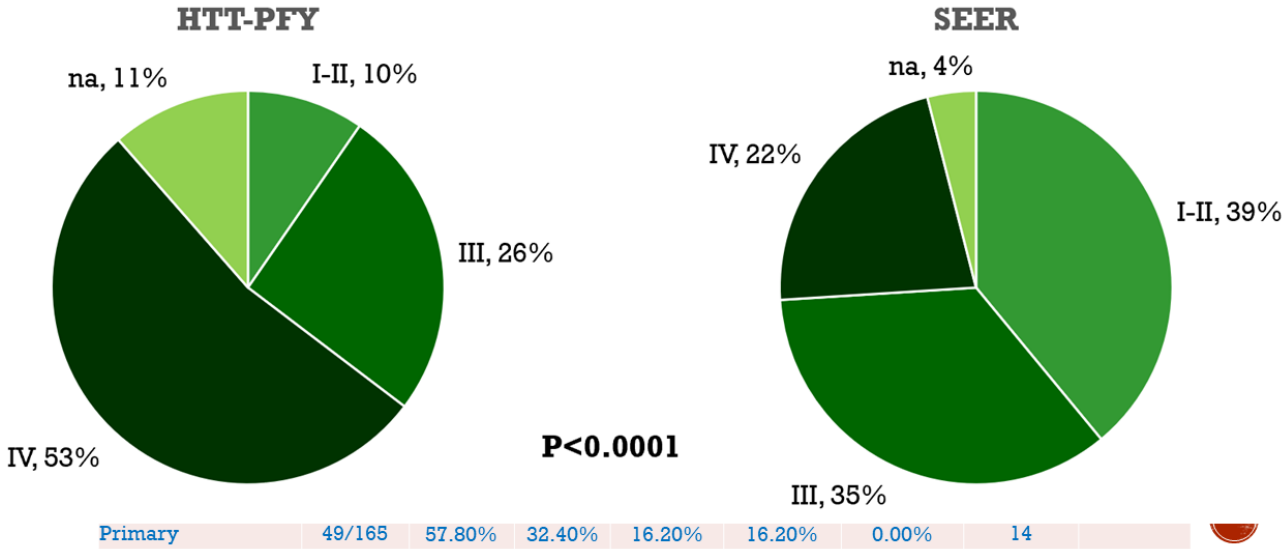
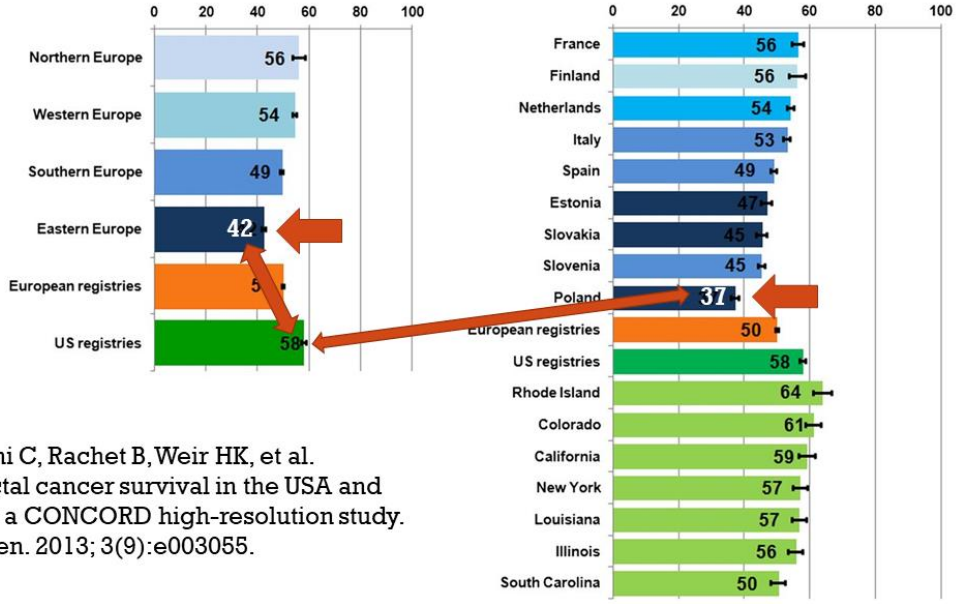
ALLEMANI C, RACHET B, WEIR HK, ET AL.
COLORECTAL CANCER SURVIVAL IN THE USA AND EUROPE: A CONCORD HIGH-RESOLUTION STUDY.
BMJ OPEN. 2013; 3(9):E003055.

1&5-YEAR SURVIVAL COMPARED TO SEER & EUROCARE



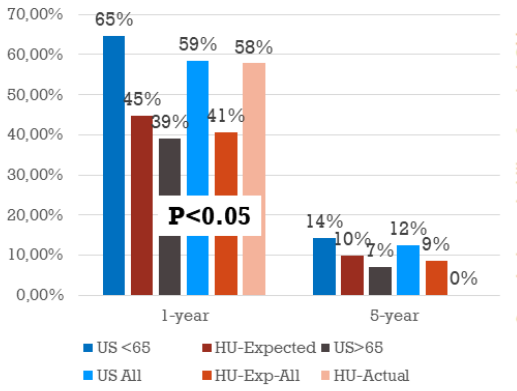
Primary	49/165	57.80%	32.40%	16.20%	16.20%	0.00%	14

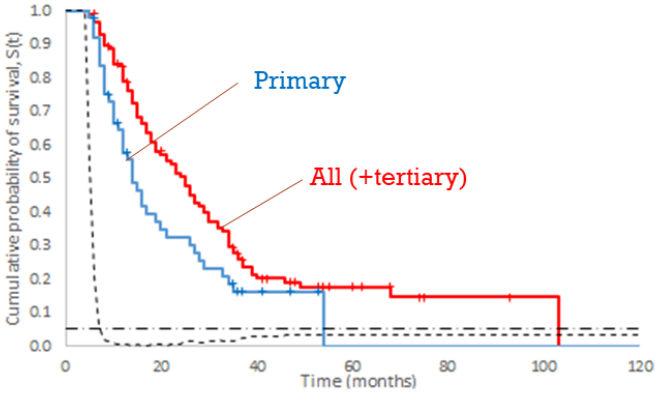
FIVE-YEAR AGE STANDARDIZED SIRVIVAL



Allemani C, Rachet B, Weir HK, et al. Colorectal cancer survival in the USA and Europe: a CONCORD high-resolution study. BMJ Open. 2013; 3(9):e003055.

1&5-YEAR SURVIVAL COMPARED TO SEER





	N	1-OS	2-OS	3-OS	4-OS	5-OS	MST	Response
All (+tertiary)	116/165	79.00%	50.80%	25.70%	19.00%	17.60%	24	
RR	165	1.37	1.57	1.59	1.17	17.83	1.71	
p-value		0.005	0.007	0.019	0.033	0.035	0.015	
Primary	49/165	57.80%	32.40%	16.20%	16.20%	0.00%	14	

MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH META-COMPARISON

VS.

ESTIMATING 1- AND 5-YEAR RELATIVE SURVIVAL TRENDS IN COLORECTAL CANCER (CRC) IN THE UNITED STATES: 2004 TO 2014.

COLORECTAL CANCER SURVIVAL IN THE USA AND EUROPE: A CONCORD HIGH-RESOLUTION STUDY.

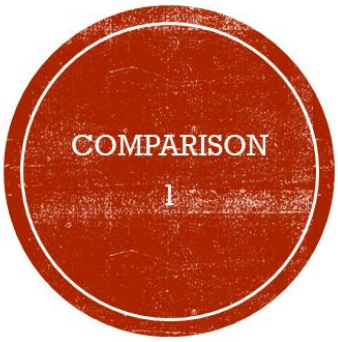
Modulated electro-hyperthermia provides significantly better than expected 1-year survival in metastatic colorectal cancer.

MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH METH-COMPARISON

VS.

YIN H, LU K, QIAO WB, ZHANG HY, SUN D, YOU QS.
WHOLE-LIVER RADIOTHERAPY CONCURRENT WITH CHEMOTHERAPY AS A PALLIATIVE TREATMENT FOR COLORECTAL PATIENTS WITH MASSIVE AND MULTIPLE LIVER METASTASES: A RETROSPECTIVE STUDY.
ASIAN PAC J CANCER PREV. 2014;15 (4): 1597-602.

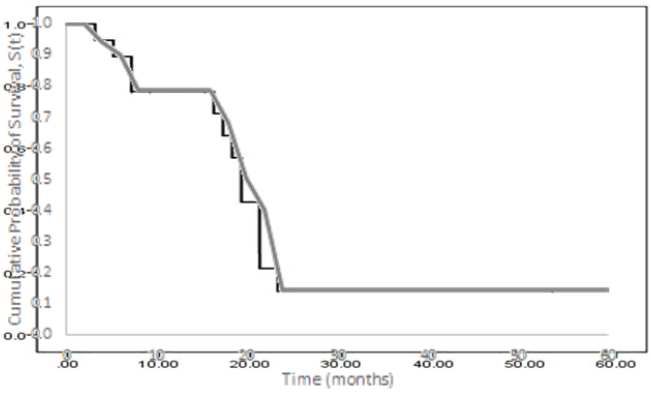
DEPARTMENT OF RADIOTHERAPY, THE CANCER HOSPITAL OF HARBIN MEDICAL UNIVERSITY, HARBIN, CHINA



MULTIPLE LIVER METASTASES FROM CRC

Yin H, Lu K, Qiao WB, Zhang HY, Sun D, You QS. Whole-liver Radiotherapy Concurrent with Chemotherapy as a Palliative Treatment for Colorectal Patients with Massive and Multiple Liver Metastases: a Retrospective Study. *Asian Pac J Cancer Prev. 2014;***15 (4):** 1597-602.

Parameter	Yin et al	HTT
No of patients	19	7
TD RT	53.4 Gy	50 Gy
95% CI	38.8-66.3	36.2-64.1
Age	56	59
1-3 lesions	47.4%	53%
>3 lesions	52.6%	47%
Extra-liver disease	26.3%*	100%*
No. lesions	3 (2-6)	3(1-7)
Max. diameter	7 (6-12)	6.2(5-10)

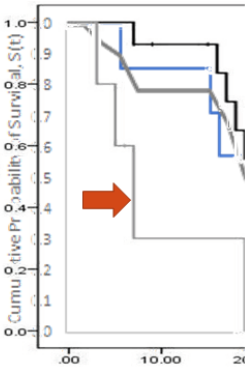


*** p=0.001**

MULTIPLE LIVER METASTASES FROM CRC

Yin H, Lu K, Qiao WB, Zhang HY, Sun D, You QS. Whole-liver Radiotherapy Concurrent with Chemotherapy as a Palliative Treatment for Colorectal Patients with Massive and Multiple Liver Metastases: a Retrospective Study. *Asian Pac J Cancer Prev. 2014;***15 (4):** 1597-602.

Parameter	Yin et al	HTT
MST, months	19	28
95% CI	-	14.9-41.1
1-year OS	78.3%	85.7%
2-year OS	14.3%*	57.1%*
3-year OS	14.3%	28.6%
5-year OS	14.3%	28.6%



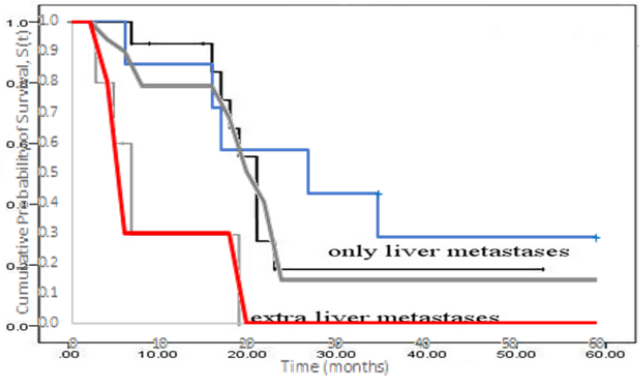
*** p=0.027**

MULTIPLE LIVER METASTASES FROM CRC

Yin H, Lu K, Qiao WB, Zhang HY, Sun D, You QS. Whole-liver Radiotherapy Concurrent with Chemotherapy as a Palliative Treatment for Colorectal Patients with Massive and Multiple Liver Metastases: a Retrospective Study. *Asian Pac J Cancer Prev. 2014;***15 (4):** 1597-602.

Parameter	Yin et al	HTT
Number of patients	4	7
MST, months	5	28
95% CI	-	14.9-41.1
1-year OS	30.0%*	85.7%*
2-year OS	0.0%**	57.1%**
3-year OS	0.0%	28.6%
5-year OS	0.0%	28.6%

*** p=0.0617**
**** p=0.0582**

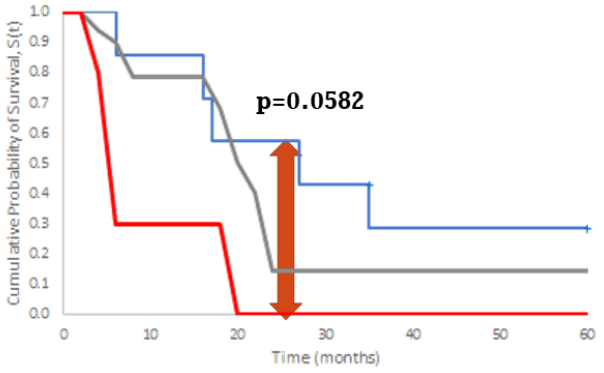


MULTIPLE LIVER METASTASES FROM CRC

Yin H, Lu K, Qiao WB, Zhang HY, Sun D, You QS. Whole-liver Radiotherapy Concurrent with Chemotherapy as a Palliative Treatment for Colorectal Patients with Massive and Multiple Liver Metastases: a Retrospective Study. *Asian Pac J Cancer Prev. 2014;***15 (4):** 1597-602.

Parameter	Yin et al	HTT
Number of patients	4	7
MST, months	5	28
95% CI	-	14.9-41.1
1-year OS	30.0%*	85.7%*
2-year OS	0.0%**	57.1%**
3-year OS	0.0%	28.6%
5-year OS	0.0%	28.6%

*** p=0.0617**
**** p=0.0582**



MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH META-COMPARISON

VS.

WHOLE-LIVER RADIOTHERAPY CONCURRENT WITH CHEMOTHERAPY AS A PALLIATIVE TREATMENT FOR COLORECTAL PATIENTS WITH MASSIVE AND MULTIPLE LIVER METASTASES: A RETROSPECTIVE STUDY.

Modulated electro-hyperthermia significantly improves the 2-year overall survival and the median survival time in colorectal patients with massive and multiple liver metastases treated with whole-liver radiotherapy with concurrent chemotherapy.

MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH META-COMPARISON

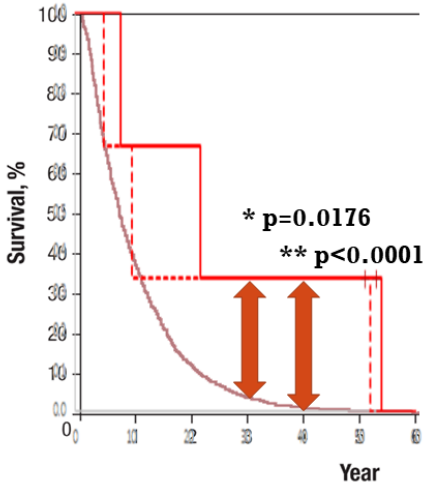
VS.

DY GK, HOBDAY TJ, NELSON G, WINDSCHITL HE, O'CONNELL MJ, ALBERTS SR, GOLDBERG RM, NIKCEVICH DA, SARGENT DJ
LONG-TERM SURVIVORS OF METASTATIC COLORECTAL CANCER TREATED WITH SYSTEMIC CHEMOTHERAPY ALONE: A NORTH CENTRAL CANCER TREATMENT GROUP REVIEW OF 3811 PATIENTS, N0144.
CLIN COLORECTAL CANCER. 2009; 8(2): 88–93.

ROSWELL PARK CANCER INSTITUTE, BUFFALO, NY
MAYO CLINIC AND MAYO FOUNDATION, ROCHESTER, MN

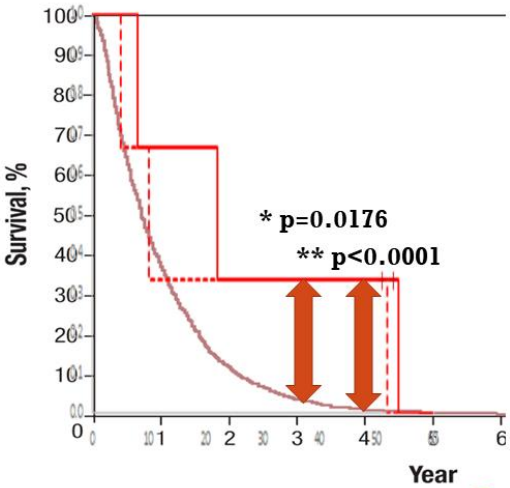
LONG-TERM SURVIVORS OF METASTATIC COLORECTAL CANCER TREATED WITH SYSTEMIC CHEMOTHERAPY ALONE

Parameter	Dy et al.	HTT	P-value
No. of patients	3,407	3	
Long-term survivors	36 (<1%)	0	
1-year OS	38.4%	66.7%	0.3139
2-year OS	12.6%	33.3%	0.2875
3-year OS	4.5%*	33.3%*	0.0176
4-year OS	1.5%**	33.3%**	<0.0001



LONG-TERM SURVIVORS OF METASTATIC COLORECTAL CANCER TREATED WITH SYSTEMIC CHEMOTHERAPY ALONE

Parameter	Patient
Sex	Male
Age at diagnosis	35
Diagnosis	C18.2 (colon)
Metastasis	M1a (787)
Survival time	>53 months
from 1st MEHT	>51 months
Exit reason	Censored



MODULATED ELECTRO-HYPERTHERMIA IN THE COMBINED TREATMENT OF METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY WITH META-COMPARISON

VS.

LONG-TERM SURVIVORS OF METASTATIC COLORECTAL CANCER TREATED WITH SYSTEMIC CHEMOTHERAPY ALONE: A NORTH CENTRAL CANCER TREATMENT GROUP REVIEW OF 3811 PATIENTS, N0144.

Modulated electro-hyperthermia significantly improves the 3-4-year overall survival in the treatment of metastatic colorectal patients with systemic chemotherapy alone.

MODULATED ELECTRO-HYPERTHERMIA IN METASTATIC COLORECTAL CANCER:

- provides significantly better than expected 1-year survival compared to large databases
- significantly improves survival in the colorectal patients with massive and multiple liver metastases treated with whole-liver radiotherapy with concurrent chemotherapy
- significantly improves survival in the metastatic colorectal patients treated with systemic chemotherapy alone

SO . . .

Evidence 1:
OS better than expected
P<0.05

- MEHT provides significantly better than expected 1-year survival compared to large databases

Unbiased sample

- MEHT significantly improves survival in the metastatic colorectal patients treated with systemic chemotherapy alone

- MEHT significantly improves survival in the colorectal patients with massive and multiple liver metastases treated with whole-liver radiotherapy with concurrent chemotherapy

Evidence 3
Better 3-4y OS CTx only
P<0.05

Evidence 2:
Better 2-3y OS MLM CRT
P<0.05

MODULATED ELECTRO-HYPERTHERMIA SIGNIFICANTLY IMPROVES SURVIVAL IN METASTATIC COLORECTAL CANCER.

ULTIMATE CONCLUSION

CLINICAL EXAMPLE

- 44-year-old female patient.
- 27 March, 1996:
  - Diagnosis: colon cancer, stage IV, liver metastasis.
  - Primary tumor resection.
  - Adjuvant chemotherapy (April-May 1996)
- November 1996:
  - Tumor relapse, re-resection.
  - Five cycles of chemotherapy (December 1996 – April 1998)
- September 1998:
  - Progression, multiple liver metastases, hepatomegaly
  - Palliative MEHT from October 1998, 6 sessions 90 min each
- Partial response, no hepatomegaly, normal condition.
- After the completion of MEHT, the patient was not examined and was not observed, she did not seek help.
- At the time of termination of the study (10.12.2003), the patient was alive.
- OST at the time of termination of the study 94 months (about 8 years), 62 months (5 years) from the 1st MEHT.