

日本語要約

- ◎ 切除不能、術後再発の結腸・直腸癌に対して、化学療法、温熱療法、高気圧酸素治療による集学的治療の成果
- ◎ 奏効率は47%（セカンドラインまでは58%）
- ◎ 全体の間接生存期間は23ヶ月、5年生存率は10%、分子標的薬使用例では、中間生存期間は30ヶ月、5年生存率は18%
- ◎ 温熱療法・高気圧酸素治療の両者を併用した症例、分子標的薬を使用した症例、病変が1部位に限局した症例の予後が有意に良好
- ◎ 集学的治療による良好な治療成績が証明された

Multidisciplinary therapy including hyperthermia for colorectal cancer

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Backgrounds

- The purpose of this study is to assess the effectiveness in patients with unresectable and recurrent colorectal cancer treated with multidisciplinary therapy including hyperthermia (HT) and hyperbaric oxygen therapy (HBO) in our institution.
- Particularly, we investigate the role of molecular target drugs (MTD) for prognosis.

Materials and Methods

- Between August 2003-May 2012
- 137 patients with primarily unresectable and recurrent colorectal cancer
- Age: 63.1 ± 10.9 , Male vs. Female=86:51
- Radiotherapy: 78cases (57%)
- Chemotherapy: all patients
- 8 MHz radiofrequency-capacitive regional hyperthermia and hyperbaric oxygen therapy(81.8%) were simultaneous use.

Chemotherapy

- Before 2004
1st line CPT-11 ± 5-FU
- 2005-2007
1st line FOLFOX4 or FOLFIRI
- 2007-at present
Additional MTD
After 2009
1st line Bmab+XELOX
2nd line Cmab+CPT-11 or Pmab+FOLFIRI
- No. of cases with MTD
Bmab: 47, Cmab: 40, Pmab: 21

Hyperthermia

- ◉ All patients were received.
- ◉ 8 MHz radiofrequency-capacitive regional hyperthermia (Thermotron RF-8)
- ◉ Heating location: lung, liver, pelvis, peritoneum (focus to main tumor)
- ◉ time: 50min
- ◉ Schedule: just after chemotherapy or during chemotherapy

Hyperbaric oxygen

- ◉ 81.8% of patients were received.
- ◉ Chamber (Sechrist Industries Inc., model 2800 J, Anaheim, California) pressured with 100% oxygen to 2.0 atmospheres absolute
- ◉ Time: 90min
- ◉ Schedule: just after chemo-hyperthermia

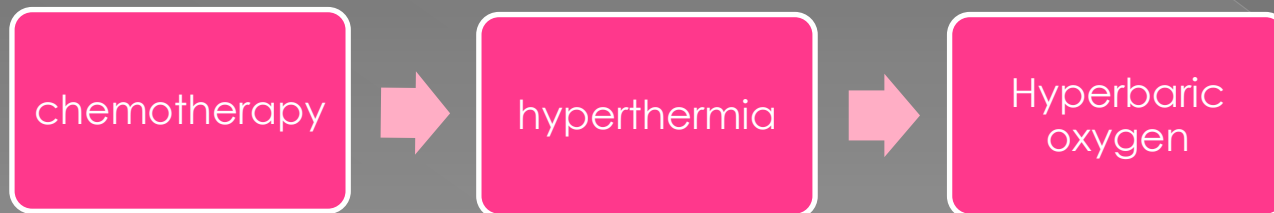


Table 1: Response rate in all cases

Response	No. of cases	Rate
CR	9/137	7%
PR	55/137	40%
SD	67/137	49%
PD	5/137	4%
CR+PR	64/137	47%

Table 2: Response rate between each line of the chemotherapy

	CR	PR	SD	PD	Response rate
1 st or 2 nd line	8	46	37	2	58.1%
After 3 rd line	1	10	30	3	25%
Total	9	56	67	5	47.4%

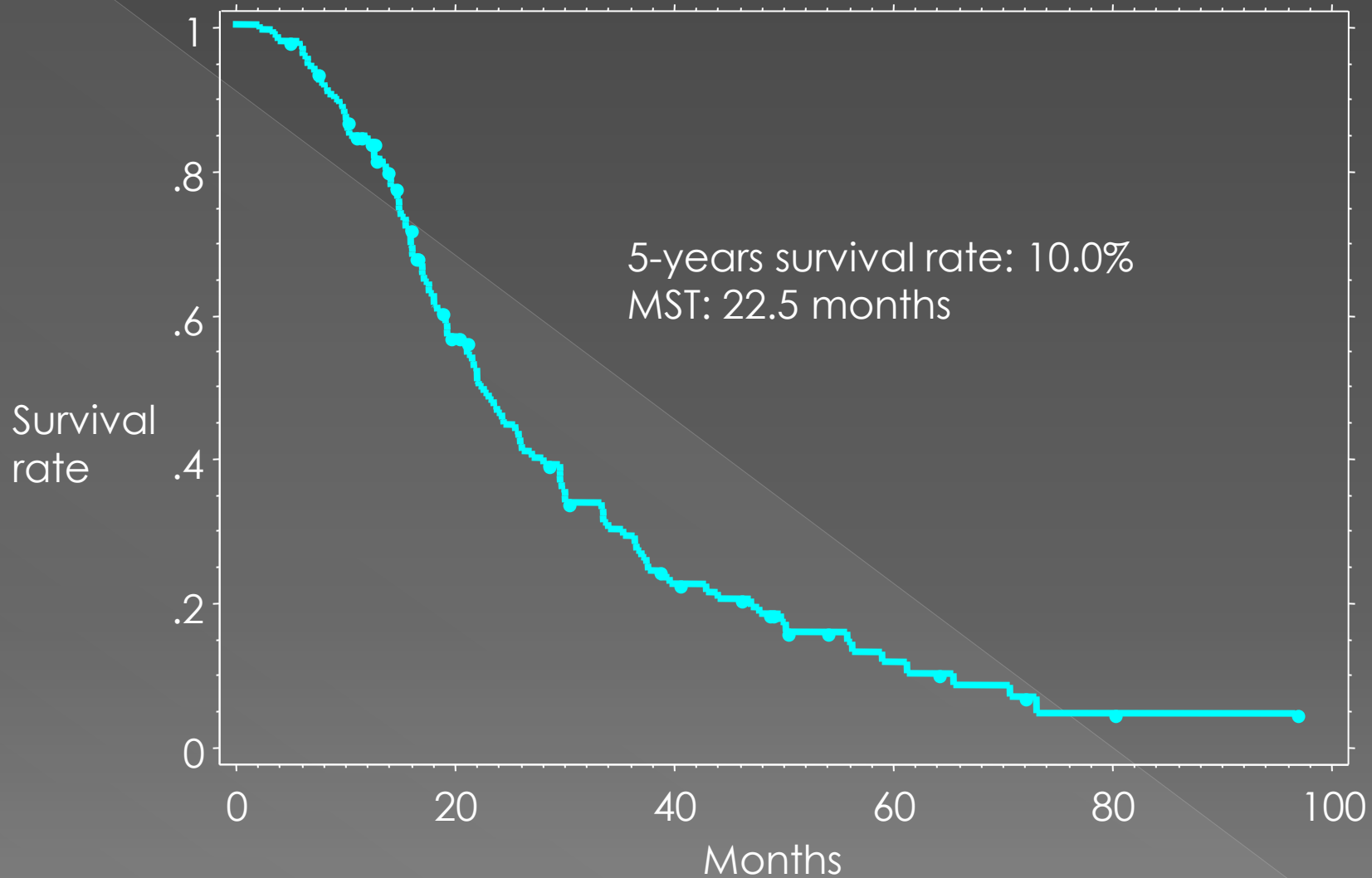


Fig. 1: Overall survival curve of all cases

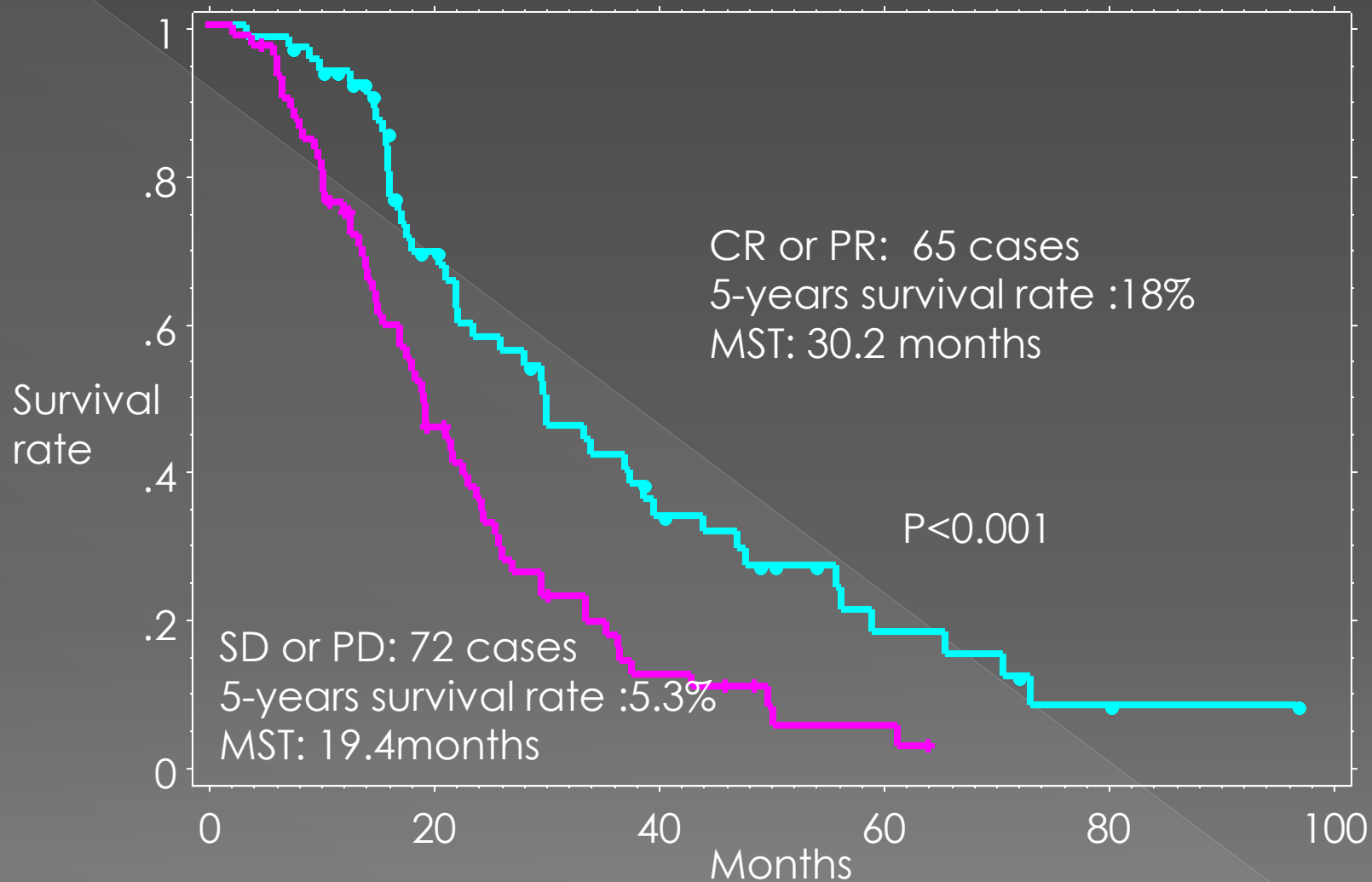


Fig. 2: Overall survival curve by local response

Table 3: Univariate and multivariate analysis for overall survival

Factor	Univariate analysis	Multivariate analysis	
	p value	p value	Hazard ratio
Age<74	n.s.	n.s.	1.14
PS0-2	n.s.	n.s.	0.90
Radiotherapy(-)	n.s.	n.s.	1.31
Multiple tumor sites	<0.01	<0.01	2.32
HBO(+)	<0.0001	<0.001	0.39
MTD(+)	<0.05	<0.05	0.77
Regimen>=3	n.s.	n.s.	0.79

n.s.: not significant

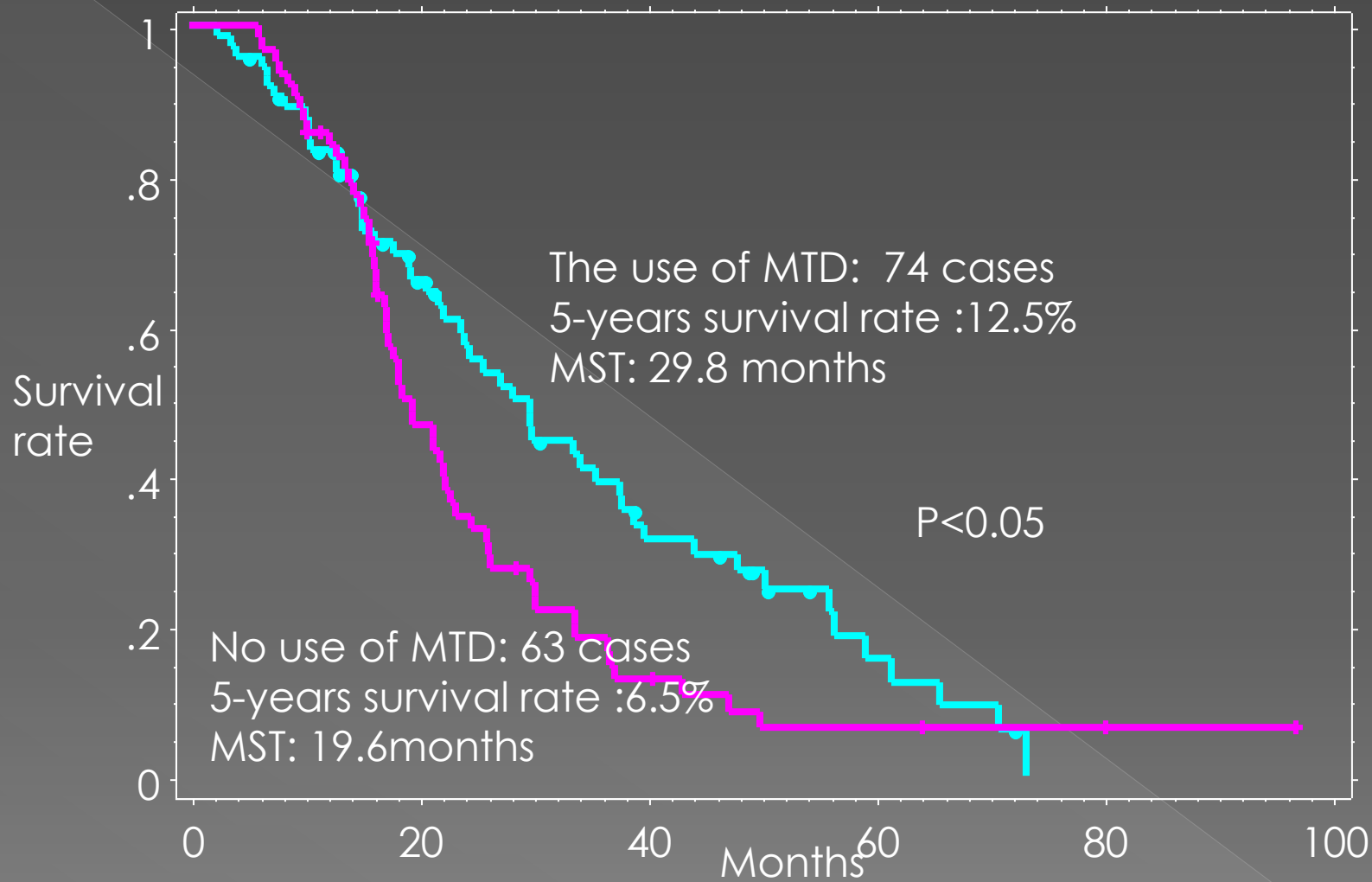


Fig. 3: Overall survival curve with or without MTD

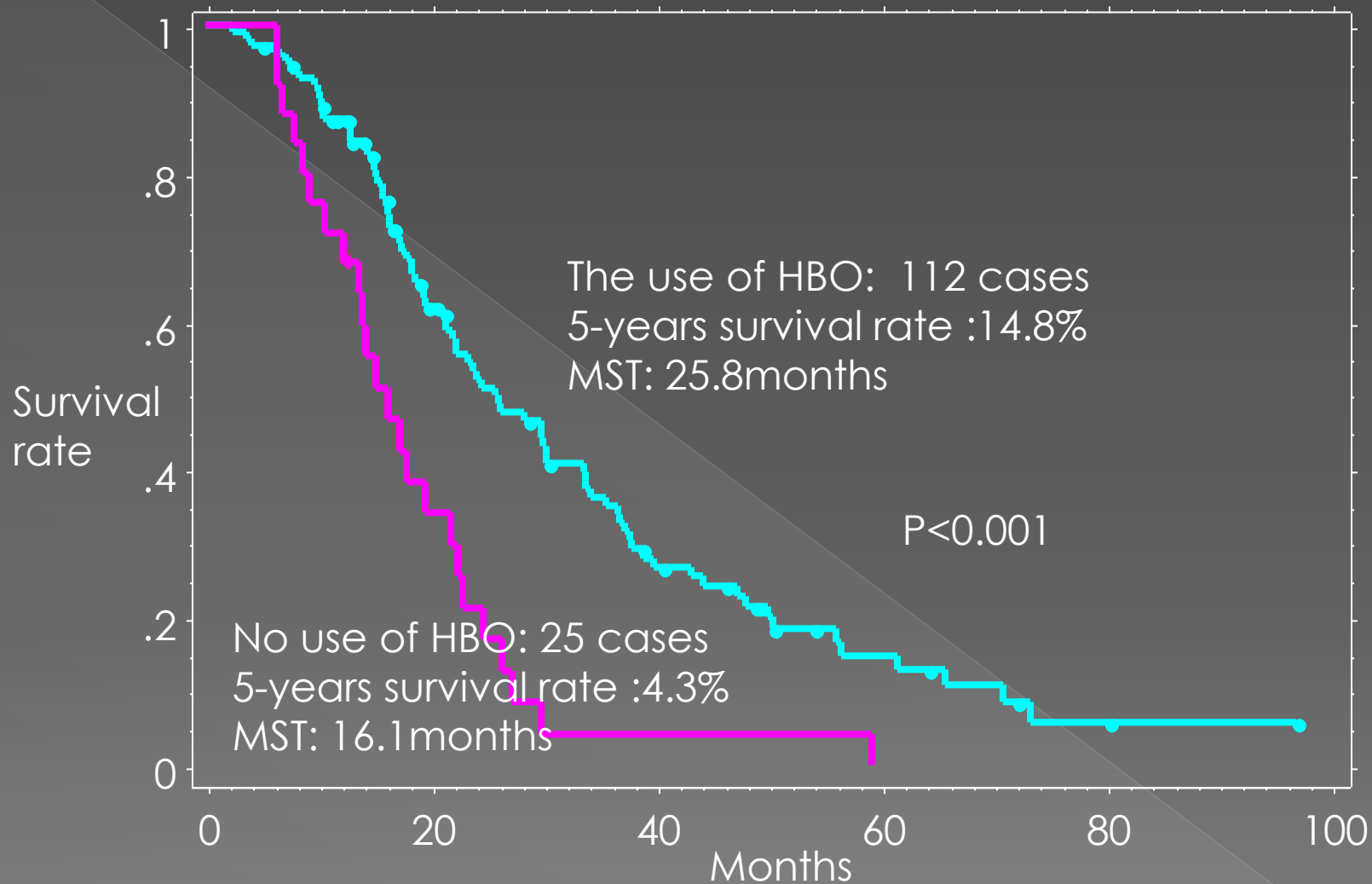


Fig. 4: Overall survival curve with or without HBO

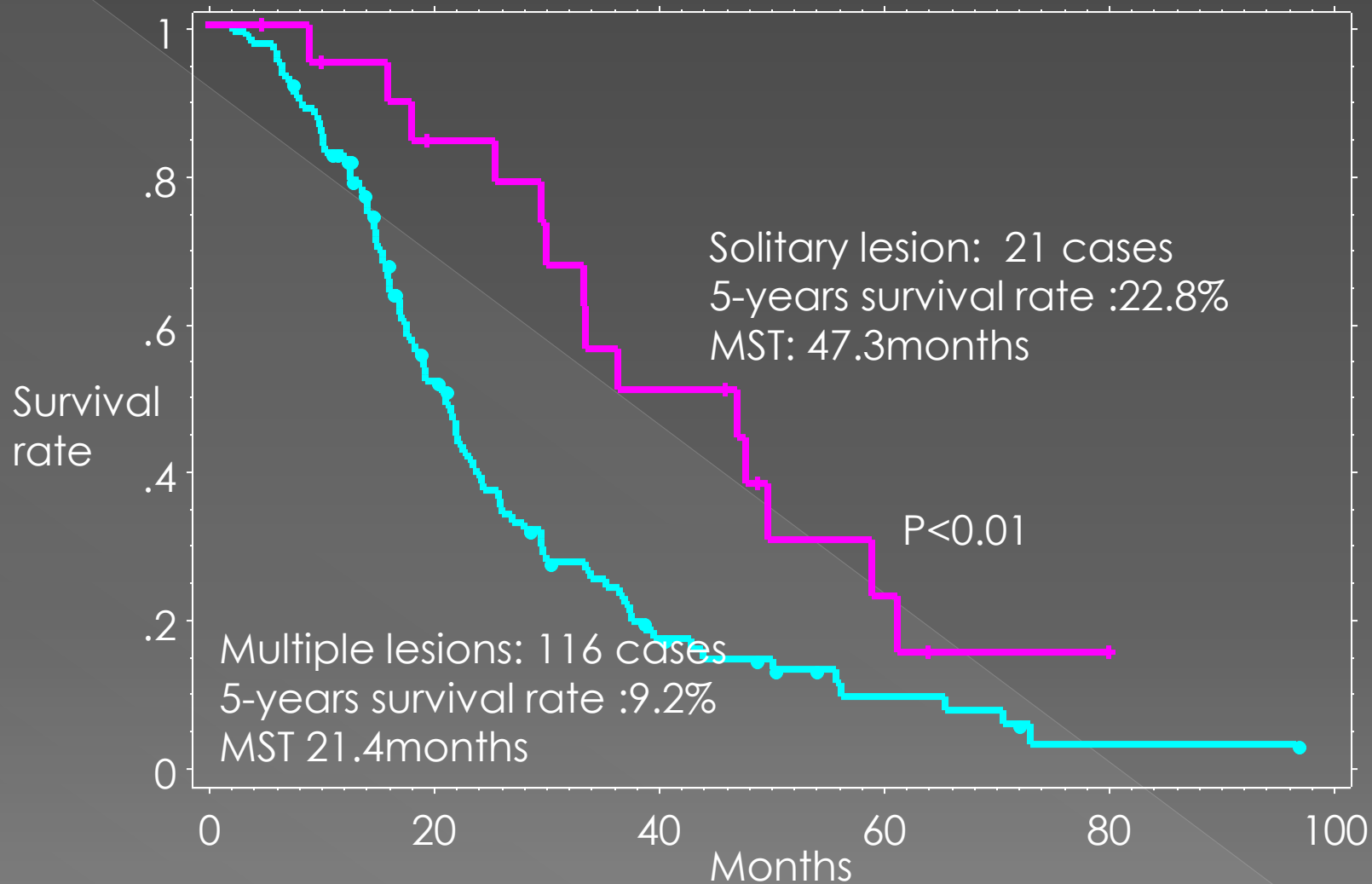


Fig. 5: Overall survival curve by No. of tumor lesion

Results

- High local response rate of 47% was obtained by chemo-HT in all cases including old regimen (Table 1).
- Especially, local response rate in first or second regimen was better than after third line (Table 2).
- Median survival time was 22.5 months and 5 years survival rate was 10.1% as shown Fig.1.
- Fig. 2 shows that overall survival of good local response group (CR or PR) was significantly better than other (SD or PD) group ($p < 0.01$).
- Table 3 and Fig. 3-5 show the results of univariate and multivariate analysis for overall survival. Statistically significant factors in the univariate and multivariate analysis were usage of MTD, HBO and solitary tumor.

Discussion

- High local response and better clinical results by chemo-HT may suggest the sensitization of heat. HT is known to be directly cytotoxic to cancer cells. In this study, chemotherapy combined with HBO showed the better clinical outcome. Several researchers have combined HBO with chemotherapy to enhance drug cytotoxicity for cancer. HT and HBO could contribute to a better clinical outcome for unresectable and recurrent colorectal cancer.
- Our results of chemo-HT with MTD (MST 29.8 months) exceeded past reports (MST 20-25 months). This data may suggest the sensitization to MTD by HT.

Conclusion

- Multidisciplinary therapy including HT for unresectable and recurrent colorectal cancer at our institution was feasible and effective therapeutic approach.
- HT and HBO as the additional therapy to the basic guideline is likely to effective to prolong the overall survival and local control rate.