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RADIOFREQUENCY HYPERTHERMIA FOR ADVANCED MALIGNANT LIVER TUMORS

Y. Nagata, Y. Okuno, M. Mitsumori, K. Akuta, Y. Nishimura, S. Masunaga, S. Kanamori, M. Fujishiro, M. Hiraoka, M. Takahashi, M. Abe

Dept. of Radiology, Kyoto Univ. Hospital, Sakyo Kyoto 606-01, Japan

Purpose
To evaluate thermometry and the clinical results of radiofrequency (RF) thermotherapy for advanced malignant liver tumors.
Materials and Methods
One-hundred and seventy-three patients with malignant liver tumors treated between 1983 and 1995 underwent hyperthermia. Surgery were contraindicated in all patients. The 173 tumors consisted of 114 hepatocellular carcinomas(HCCs), and 59 non-HCCs(45 metastatic liver tumors and 12 cholangiocarcinomas). Eight MHz RF capacitive heating equipment was used for hyperthermia. Two opposing 25-cm or 30-cm electrodes were generally used for heating liver tumors. Our standard protocol was to administer hyperthermia 40-50 minutes twice a week to a total of 8 sessions. Temperature of the liver tumor was measured by microthermocouples. In each patient, a single catheter was inserted into the liver tumor through the normal liver.
Transcatheter arterial embolization, radiotherapy, immunotherapy, and chemotherapy were combined with hyperthermia depending on the patient's liver function and tumor location.
The therapeutic efficacy was evaluated by the change in tumor size assessed by computed tomography (CT) three or four months after the completion of treatment.
Results
One-hundred and forty (81%) of 173 patients underwent hyperthermia more than 4 times. Thermometry could be performed in 77(55%) of these 140 patients.
Neither systolic nor diastolic blood pressure changed significantly after hyperthermia. However, pulse rate significantly increased from 82.8± 1.1 to 96.5±1.3 beats/min. Only 21 patients (11%) showed a decrease in pulse rate after hyperthermia. Body temperature increased from 36.3 ±0.1 to 37.4+0.2 after hyperthermia.
Sequelae of hyperthermia included focal fat burning in 20 (12%), gastric ulceration in 4 (2%), and liver necrosis in 1(1%). Sequelae of thermometry were severe peritoneal pain in 7 (11%), intraperitoneal hematoma in 1(1%), and pneumothorax in one (1%) patient.
The maximal tumor temperature, average tumor temperature, and minimal tumor temperature in HCC were 41.2±0.2℃(Mean±SE), 40.3±1.3 ℃ and 40.1±0.2℃respectively. The same thermometery results for non-HCC were 42.3±0.2℃41.2±0.2℃ and 40.9±0.2℃, respectively. The maximal and minimal temperatures (41.8±0.2℃, 40.3±.0.4℃ in the responders (CR+PR) were higher than those (41.3±0.5℃39.8± 0.4℃ in non-responders (NC+PD), but the difference was not significant.
Of the 73 cases with HCC who were evaluated by CT, CR was achieved in 7/73(10%), PR in 15/73(21%), NC in 37/73(51%), and PD in 14/73 (19%).
Of the 45 cases involving liver metastases evaluated by CT, CR was achieved in 3/45(7%), PR in 17/45(38%), NC in 12/45(27%), and PD in 13/45(29%).
The one-year cumulative survival rate for HCC patients was 30.0%, and the five-year survival rate was 17.5%. The median survival was 5 months, and the longest survival was 144 months. The one-year survival of non-HCC was 32.5%, and the longest survival was 30 months.
Conclusion
Even though the thermometry results for liver tumors were not satisfactory, the treatment result is promising. Further clinical trials of RF capacitive hyperthermia for the treatment of advanced liver tumors should be encouraged.

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THE CORRELATION OF PSA NADIR AND BIOCHEMICAL FREEDOM FROM CANCER AFTER EXTERNAL BEAM TREATMENT: EFFECTS OF STAGE, GRADE AND PRETREATMENT PSA GROUPINGS

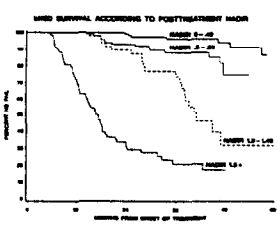
Pinover WH, Hanlon AL, Lee WR, Hanks GE
Fox Chase Cancer Center, Philadelphia, PA

Purpose: This study demonstrates the correlation of various post-irradiation PSA nadirs with long term biochemical freedom from disease (bNED) survival in patients treated mainly with conformal external beam radiation therapy. It also shows the effects of various groupings of pretreatment (prerx) PSA level, stage, and Gleason score on the rate of achieving a favorable PSA nadir.

Materials and Methods: Three hundred forty patients with known pretreatment PSA, >2 years followup treated with radiation alone (278 conformal, 62 conventional) are reported. The median followup is 41 months (range 24 to 96 mos.). Patient grouping by pretreatment PSA levels are <10 ng/ml (143 patients), 10-19.9 ng/ml (108 patients), ≥20 ng/ml (89 patients); by palpation stage are T1C,2AB (240 patients) and T2C,3,4 (100 patients); and by differentiation are Gleason 2-4 (108 patients), Gleason 5-7 (221 patients), Gleason 8-10 (11 patients). The PSA nadir response is given for all patients, and for each of the above prerx groupings. The 5 year actuarial bNED survival is determined for all patients by PSA nadir. Biochemical failure is a PSA ≥1.5 ng/ml and rising on two consecutive measures. Multivariate analysis (MVA) is performed to determine factors predictive of favorable PSA nadir response and predictive of bNED survival.

Results: The PSA nadir responses and 5 year bNED survival rates are shown in the table for all patients according to PSA nadir. 66% of patients achieved a favorable nadir (<1.0 ng/ml) which was associated with a 75%-87% 5 year bNED rate, while 34% achieved an unfavorable nadir associated with an 18-32% bNED survival rate at 5 years. The figure illustrates the dramatic separation in outcome associated with the nadir response. The table also illustrates the fraction of patients that achieve various nadir levels subdivided by prerx PSA level, palpation stage and Gleason score. A favorable PSA nadir is obtained in 90%, 63%, and 31% of patients with a prerx PSA <10, 10-19.9, and ≥ 20, respectively (p=0.001). A favorable PSA nadir is obtained in 72% and 51% of patients with palpation stage T1,2AB and T2C,3,4 respectively (p=0.001). A favorable PSA nadir is obtained in 71% and 63% of patients with Gleason score 2-4 and 5-7, respectively (p=NS). MVA demonstrates prerx PSA (p=0.0001) and dose (p=0.02) to be independent predictors of PSA nadir response <1.0 ng/ml. MVA also demonstrates PSA nadir (p<0.0001), dose (p=0.02), and stage (p=0.02) to be independent predictors of 5 year bNED survival.

	% all pts achieving	5 yr	Prerx PSA (ng/ml) % achieving nadir			STAGE % achieving nadir		GLEASON SCORE % achieving nadir		
PSA nadir	nadir	bNED	<10	10-19.9	20+	T1,2AB	T2C,3,4	2-4	5-7	8-10
0-.49 (ng/ml)	36%	87%	52%	33%	13%	38%	30%	40%	33%	NA
.5-.99 (ng/ml)	30%	75%	38%	30%	18%	34%	21%	31%	30%	
1.0-1.49 (ng/ml)	14%	32%	5%	21%	21%	13%	17%	16%	14%	
≥1.5 (ng/ml)	20%	18%	6%	16%	47%	15%	32%	14%	23%	
			(p=0.001)			(p=0.001)		(p=NS)		



Conclusions: (1) Following external beam radiotherapy, the level of PSA nadir is the most significant predictor of bNED survival. (2) Patients achieving a PSA nadir <1.0 ng/ml have a favorable overall bNED survival rate. This is true for all patients, independent of prerx PSA, palpation stage and Gleason score. (3) Prerx PSA and dose are predictive of PSA nadir. (4) Patients not achieving a PSA nadir <1.0 ng/ml may be candidates for early adjuvant therapy trials.