Results of oncothermia combined with operation, chemotherapy and radiation therapy for primary, recurrent and metastatic sarcoma

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Purpose
Sarcoma is a rare type of cancer. Surgery is known as the only treatment that shows definite response. But it represents high incidence of local recurrence and distant metastasis. Although it shows partial response to chemotherapy, there is no definitive chemotherapy regimen to control it effectively up to now. It is also known that sarcoma is resistant to radiotherapy due to having large portion of hypoxic cells. Hyperthermia treatment can apply heat to hypoxic cell because hypoxic cell is weak at heat but it develops heat tolerance due to appearance of heat shock protein during treatment and treatment efficacy goes down as hyperthermia repeats. We have studied if oncothermia treats sarcoma effectively without developing heat tolerance.

Methods and materials
In Kosin University Gospel Hospital, we treated 13 sarcoma patients from Nov 2011 to Aug 2013 and analyzed the results. Patients aged between 18~73 years old. 6 males and 7 females. Histologic type is 2 rhabdomyosarcoma, 2 synovial sarcoma, 2 chondrosarcoma, 1 osteosarcoma, 3 leiomyosarcoma, 1 malignant peripheral nerve sheath tumor, 1 spindle sell sarcoma and 1 malignant fibrous histiocytoma (MFH). Treatment modality was 5 postoperative radiation therapy (RT) and oncothermia, 2 combined RT and oncothermia for primary lesion, 2 combined RT and oncothermia for recurrent sarcoma at original region and 4 combined RT and oncothermia for metastatic lesion. Oncothermia was applied at 2~3 times a week. Post-operative RT was applied 50.4 Gy in 28 fractions and other RT was applied 30~39 Gy in 10~13 fractions. The combined chemotherapy with oncothermia for 1 case was applied to metastatic lung lesion.

Results and discussion
5 patients who received post-operative RT and oncothermia didn't show local recurrence. The metastatic lesion in lung was appeared in 1 case and received chemotherapy, RT 50.4 Gy and 12 times of oncothermia and the metastatic lesion in lung almost completely regressed (CR). 1 (MFH) out of 2 patients for primary malignant lesion in pelvis received RT 50.4 Gy and 27 times of oncothermia and showed almost CR grossly at CT scan. However this patient revealed local regrowing mass in 6 months from stopping oncothermia. The other one (peripheral nerve sheath tumor) for primary lesion received RT 30 Gy in 2 weeks and 108 times of oncothermia for 11 months and tumor mass at buttock regressed continuously as repeat oncothermia. This patient is still getting oncothermia. 1 out of 2 recurrence rhabdomyosarcoma patients received RT 30 Gy in 2 weeks and 12 times of oncothermia in neck for 1 month. Tumor was regressed partially. But metastatic lesion was developed in retroorbital region. RT 30 Gy in 10 fractions and 12 times of oncothermia for 1 month was given and metastatic mass of retroorbital area also was shown partial regression. The other patient (chondrosarcoma) had recurrence at pelvic bone replacement region after surgery. This patient received RT 30 Gy in 2 weeks and 50 times of oncothermia for 8 months and showed partial regression. It was thought to be difficult to apply oncothermia due to metallic pelvic bone replacement but she strongly requested receiving oncothermia. There were no side effects caused by metallic bone when oncothermia was applied. In 6 months follow-up tumor size was not increased in CT images from stopping oncothermia. For 4 patients the metastatic lesions were treated. 1 patient received RT 30 Gy in 2 weeks and 48 times of oncothermia for 7 months in metastatic lung lesion and showed grossly partial regression. After stopping the
treatment, tumor mass was aggravated in size in 3 months, and 24 times of Oncothermia was applied again and it was partially regressed. But after stopping treatment again, tumor regrew in 3 months and the patient received 11 oncethermia and tumor regressed but oncethermia was stopped due to patient's personal reason including economy. Other 1 patient (chondrosarcoma) had metastasis to chest wall and received RT 30 Gy in 10 fractions for 2 weeks and 47 times of concothermia for 4.5 months and showed partial regression. It was stable for 4 months. One patient had cervical spine metastasis (spindle cell sarcoma) from right buttock and received RT 30 Gy in 2 weeks and 5 times of oncethermia. We found that oncethermia effectively control pain and make metastatic lesion stable. 1 patient (osteosarcoma) had multiple lung metastasis and received chemotherapy and 84 times of oncethermia for 12 months. Metastatic cancer almost disappeared but one lesion that was out of the range of 30 cm diameter electrode progressed. So the patient received radiotherapy (48 Gy in 4 fractions, SBRT) for the progressed lesion. Side effect of chemotherapy was not serious as much as we expected when concothermia was combined with chemotherapy.

**Conclusion**
Primary, recurrent, and metastatic sarcomas were responded to oncethermia treatment and the mass regressed. When oncethermia was applied for long term, tumor mass was regressed slowly for oncethermia. It needs to study further more to see that complete regression can be achieved with oncethermia only and to increase effects with the combined modalities of oncethermia with chemotherapy and/or radiation therapy.