Study on Application of BNCT to skin malignant melanoma in Japan

Kei Nakai

Department of radiation Oncology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan Email: kenakai-nsu@umin.ac.jp

Yoshitaka Matsumoto Department of radiation Oncology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Hiroaki Kumada Department of radiation Oncology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Akira Matsumura Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Hideyuki Sakurai

Department of radiation Oncology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Malignant Melanoma (MM) has been less common in Japan. Annual incidence of melanoma in Japan to be between 1.75 per 100,000 people [1], and the number of deaths per year in Japan is about 600.

Recent development of immune checkpoint inhibitors has dramatically changed the treatment of melanoma. Several Immune checkpoint inhibitors or molecular-targeted agents are already available under the national health insurance. Nivolumab was PMDA-approved as a treatment of malignant melanoma since 2014, Vemrafenib 2014, Ipilimumab 2015, Pembrolizumab 2016, Dabrafenib 2018, Trametinib 2018 respectively.

In the Radiation therapy field, proton and heavy ion radiation therapy has approval to head and neck malignant tumor including melanomas since 2018 in Japan. Clinical study of proton therapy to nasosinus melanoma patients were underwent including Tsukuba university proton medical research center, before the national health insurance approval. These results revealed that 3 years Overall survival of proton therapy for MM T3/4N0M0 was 46.1% and Grade3 dermatitis occurred in 4/13cases [2,3].

Though MM is rare disease in Japan, it has been a candidate of BNCT from the very start. Hiratsuka et al, reported clinical results of BNCT treatment with the MM patients [4,5]. These reports revealed that the BNCT have advantage over treating the cases who need to prevent surrounding organs damage, e.g. re-irradiation cases. To coexist BNCT and newly developing agents, particle therapies under the national health insurance in Japan, and to establish curative therapy for MM or other intractable cancer, require to find the subgroup of MM patients which are most appropriate for BNCT. We should be more aware of that BNCT is a local therapy, and concomitant therapy with general chemotherapy or immunotherapy are essential. Furthermore, we need to plan appropriate BNCT protocols for clinical study based on modern standard therapy and need to give proof of additive effect or noninferiority of BNCT.

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