MAURI-1: Clinical trial investigations on BNCT by molecular and network medicine

PL Mauri[1], M Masutani[2] A Fujimura[3], Y Ichikawa[3], H Igaki[2], K Igawa[3], J Itami[2], Y Nishina[4], Giovanna Rizzo[1], R Rossi[1], W Sauerwein[5], A Wittig[6]

[1] *National Research Council-Institute for Biomedical Technologies (CNR-ITB) & Elixir Infrastructure, Milan, I*
[2] *Division of Research and Development for Boron Neutron Capture Therapy NCCR, Tokyo, J*
[3] *Neutron Therapy Research Center, Okayama University, J*
[4] *Research Core for Interdisciplinary Sciences, Okayama University, J*
[5] *Deutsche Gesellschaft für Bor-Neutroneneinfangtherapie (DGBNCT), Essen, D*
[6] *Klinik für Strahlentherapie und Radioonkologie, Universitätsklinikum Jena, D*
All authors are partners in the "RENOVATE Consortium"

Boron Neutron Capture therapy (BNCT) is a form of tumor-selective particle radiation therapy. Recent improvements of accelerator-based neutron sources for hospitals will increase the application of BNCT cancer therapy. However, even after tumor-selective BNCT, recurrence may occur. The reasons for such recurrences after BNCT have not been fully elucidated, but they may reflect tumor characteristics. It is required to improve by biomedical investigations the understanding of the biochemical and physiological aspects.

In this context, innovative molecular profiles, can be of great importance to facilitate improvements and applications of BNCT. In particular, the great progress of proteomics methodologies, including sample preparation, instrumentations and computational tools, allow a deeper investigation of human diseases and their therapies. Also, the integration of proteomics data with network analysis contributes to the characterization of perturbed molecular pathways (so called "metabolic clusters") in relation to disease states (endotypes). This creates possibilities inserting the discovered biomarkers in the context of molecular mechanisms related to pathology and therapeutic outcome.

Boron neutron capture therapy will take advantages from molecular investigations. In particular, with such tools it becomes possible to study the effects due to each step of treatment: boron infusion and neutron beam irradiation. In addition, using innovative computational platforms, such as Systems Biology, it is possible to characterize the mechanisms activated (or deactivated) during the disease and therapy.

Non-invasive monitoring of the development of the disease and the therapeutic effect may be performed by analyzing the circulating exosomes. They are a mirror of physio-pathological states of subjects, and they are a very important complement to the traditional biopsies, frozen or paraffined ones, sometimes complex to collect from the patients.

Altogether these aspects are important component for developing a future Precision/Personalized Medicine in BNCT, involving the characterization of different subtypes of cancers, determined by different biomarkers leading to the eligibility of the patients to specific therapeutic treatments.

These activities require to develop a proof of concept about integrated physical-molecular-medical studies of neutron therapy, including radiomics, new boron-containing drugs and delivery approaches, to make a synergic cooperation and allowing molecular profiles of patients before treatment, characterizing biomarkers useful for monitoring efficacy and side effects, and stratifying subjects potential Responders and Non-Responders. Such innovative concepts should be integrated in the clinical trial strategies for the further development of BNCT.