Carbon radiation versus photon radiation in combination with immunotherapy

This report summarises the first of two visits I made to the research group of Professor Amir Abdollahi in the National Center for Tumor Diseases (NCT) at the Deutches Krebsforschungszentrum (DKFZ, the German Cancer Research Center) of Heidelberg in Germany. The visit was undertaken at the end of March for 1.5 weeks.

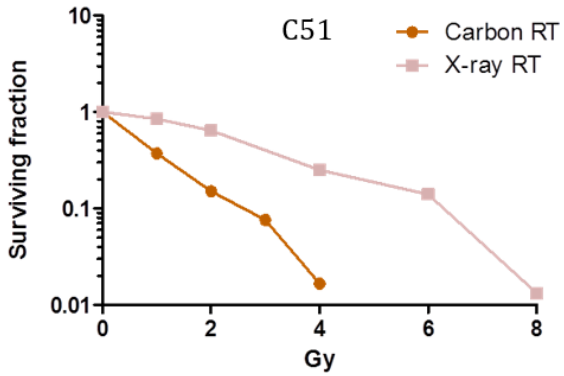
My PhD research is in tumour immunology at the Department of Precision Medicine of Maastricht University in The Netherlands. In my project I test various approaches to identify optimal treatments that will prime and stimulate the immune system to target cancer cells.

Our lab has been investigating a promising treatment regimen in which X-ray radiotherapy is combined with delivery of a tumour-specific immunocytokine. This treatment has been approved for a phase 2 clinical trial. We have observed great synergy between the two modalities.

Particle therapy is increasingly used in Europe. It spares more tissue than X-ray treatment because it deposits a high radiation dose at the tumour site (Bragg peak). The Heidelberg institute offers a wide range of particle-radiation systems, including carbon-ion radiation. We were interested in combining our immunocytokine treatment with carbon ions since the latter have greater linear-energy transfer and relative biological effectiveness (RBE), and cause more complex DNA damage, than X-rays. These attributes might translate to stronger immunogenicity.

With these notions in mind, we hypothesised that carbon-ion radiation was more immunogenic than photon radiation, leading to an increased therapeutic efficacy upon combination with immunotherapy. The goal of our collaboration with Heidelberg is to compare the treatment effect of X-ray and immunocytokine with carbon ions and immunocytokine in an in-vivo model. Particle radiation is not a novel concept, but little research has been performed in this field. Therefore, during the first visit, we started the study with a clonogenic survival assay to establish the biological effect of the proposed treatment in a 2D model before moving on to the in-vivo model, in order to select the RBE-adjusted dose for carbon irradiation.

I tested two colon-carcinoma cell lines and one lung-cancer cell line in three biological repeats. Carbon ions proved more effective at killing clonogenic tumour cells than X-rays (see figure).



In future studies, we will investigate whether there are differences in mutational load between the two radiation types. This study will provide important information in the radiotherapy field and will allow to test our hypothesis.

Having determined the RBE of carbon ions for various cell lines, in my second visit I will determine the differences in therapeutic efficacy of immunotherapy in combination with radiation of different linear energy transfer (LET) in vivo. In addition, I will characterise immune parameters after the respective treatments in order to provide mechanistic insights. Apart from enabling us to obtain the results, the first visit was interesting. It enabled me to learn more about particle radiation and work in a different research group.

Damiënne Marcus
PhD student in tumour radiation/immunology/hypoxia
Department of Precision Medicine
M-lab, Maastricht University
Maastricht, The Netherlands
mailto:d.marcus@maastrichtuniversity.nl