

## **Development of Treatment Planning System for radiotherapy with VHEE electron beams**

Radiotherapy (RT) is commonly used in or as alternative to surgery and chemotherapy for treatment deep seated tumors. Are now available in clinical centers: radiotherapy with photons (RT), particle therapy (PT) with protons or even heavier ions like  $^{12}\text{C}$ . The use of Very High Energy Electron (VHEE) beams (100-200 MeV), has been suggested in the past to reach deep seated tumors; the availability of VHEE in the clinic has been delayed by the size, complexity and ultimately high cost of the beam production system. In this context, the recent developments in the field of the compact C-band electron acceleration and FLASH radiotherapy are representing a promising perspective.

The FLASH effect was observed from several pre-clinical studies and recently demonstrated that the toxicity in healthy tissues can be significantly reduced (from 80% down to 60%), while keeping the same efficacy in cancer killing, if the dose rate is radically increased ( $\sim 40$  Gy/s, or even more) with respect to conventional treatment ( $\sim 0.01$  Gy/s). In this contribution, we investigate how recent developments in electron beam therapy could reshape the landscape of deep-seated tumors treatment, working on a few selected cases (head and neck and pancreas) and comparing them with the state-of-the-art technologies making use of photons or protons.

We have implemented and developed a VHEE Treatment Planning System using an accurate Monte Carlo (MC) simulation with a simple modelling of FLASH effect. Finally, we studied in detail the feasibility of treating the patients using electron beams with energies in a range between 70 and 130 MeV. From the results obtained, based on a set of beam delivery parameters, on hypothesis on the dose rate thresholds needed for the FLASH effect to occur, we developed dose rate calculation codes to quantify two types of dose rate calculation methods Average Dose Rate (ADR), Dose-Averaged Dose Rate (DADR).

The tumor coverage and the dose absorbed by the Organ At Risk (OARs) have been compared, using the Dose Volume Histogram (DVH), with the results obtained in real IMRT, VMAT and proton therapy treatments. In the two different tumor district, the DVH shows how such a technique may allow OARs sparing and adequate coverage of the Planned Target Volume (PTV) compared with clinical radiotherapy; with the implementation of hypofractionated treatment and assuming a minimum threshold value is needed for the FLASH effect to occur, in the pancreas case, we observe a better sparing of the duodenum. From the literature, we assumed that the FLASH effect occurs for dose rates greater than 40 Gy/s and for dose values above 4 Gy, then we analyzed and compared the two algorithms by means of Dose Rate Volume Histograms (DRVH).

The results demonstrate that FLASH therapy with VHEE beams has a comparable performance with a standard RT when treating deep seated tumors allowing a better sparing of the healthy tissues. The impact of such technique will be discussed also in view of the results obtained when comparing with conventional External-Beams RT.