Elaborare documentaţie pentru fizicieni medicali

Radioterapia cu ioni de carbon

Radioterapia cu ioni de carbon (CIRT) oferă doze de radiaţii mai puternice şi mai bine orientate decât radioterapia convenţională cu raze X. Studiile demonstrează că CIRT ar putea oferi rezultate semnificativ mai bune pentru pacienţi, în special pentru cei cu cancer netratabil. Studiile clinice au confirmat eficacitatea CIRT în cazul a numeroase tipuri de cancer. Datorită efectului său biologic mai mare, CIRT este eficient în tumorile rezistente la tratamentele radiologice clasice, cum ar fi sarcoamele osoase sau ale ţesuturilor moi şi melanoamele maligne, deschizând poarta către un tratament curativ pentru bolnavii consideraţi incurabili. In cazul radiaţiei CIRT ionii eliberează cea mai mare parte a energiei într-o explozie bruscă, bine definită, numită peak-ul Bragg, provocând mai puţine daune ţesutului sănătos. Ionii, spre deosebire de radiaţiile X, sunt particule încărcate, deci pot fi direcţionate folosind un câmp magnetic oferind o acuratete sporită în ”ţintirea„ tumorilor.

În acest document raportăm o serie de articole ştiinţifice noi, publicate în literatura de specialitate, referitoare la Radioterapia cu ioni de carbon (CIRT). Aceste articole vor fi puse la dispoziţia studenţilor pe canalele de comunicare on-line (platform Teams, site-ul proiectului).

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Lista articolelor propuse

Articol 1

Motohiro Kawashima, Mutsumi Tashiro, Maria Varnava, Shintaro Shiba, Toshiaki Matsui, Shohei Okazaki, Yang Li, Shuichiro Komatsu, Hidemasa Kawamura, Masahiko Okamoto, Tatsuya Ohno

An adaptive planning strategy in carbon ion therapy of pancreatic cancer involving beam angle selection

Physics and Imaging in Radiation Oncology 21 (2022) 35–41,
https://doi.org/10.1016/j.phro.2022.01.005

Abstract

Background and purpose: In carbon-ion radiotherapy for pancreatic cancer, altered dose distributions due to changes in the gastrointestinal gas volume and anatomy during irradiation are an unresolved therapeutic issue. We developed and investigated an adaptive strategy involving beam angle selection to improve dose distributions in pancreatic cancer. *Materials and methods:* In the adaptive strategy, multiple beams were prepared with angles similar to those of the conventional strategy, and the beam that best reproduces the dose distribution of the treatment plan was used. The dose distributions of the adaptive strategy were compared with those of the conventional strategy for five patients. Patients underwent computed tomography (CT) before every irradiation. The adaptive strategy was evaluated using the same irradiation schedule as that of the conventional method and an adjusted method based on anatomical changes per fraction. Dose distributions on the pre-treatment CT and accumulated dose distributions on the treatment planning CT were evaluated using the volume receiving ≥95% of the prescription dose (V95) from the clinical target volume (CTV) between strategies. *Results:* There were significant differences in the CTV V95 values for the pre-treatment CT between all strategies. The median (range) CTV V95 for the conventional strategy was 92.7% (87.1–96.1%), for the proposed adaptive strategy without adjusted schedules was 96.9% (95.1–97.8%), and for the proposed strategy with adjusted schedules was 97.8%

(96.5–99.2%). *Conclusions:* The adaptive strategy can improve target coverage for the pre-treatment CT and accumulated dose distributions for the treatment planning CT without increasing the dose to critical organs.

Keywords: Adaptive therapy Carbon-ion therapy Pancreatic cancer Radiotherapy

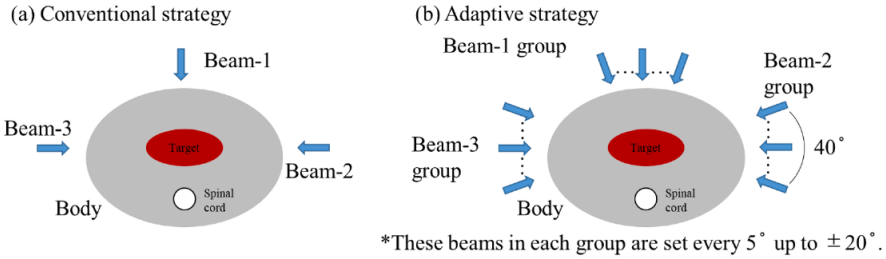

Fig. 1. Schematics of treatment plans for both strategies. The schematics of treatment plan in the conventional strategy are shown in (a). The treatment plan has only three beams (beams 1, 2, and 3 at angles of 0°, 90°, and 270°, respectively). The schematics of treatment plan for the adaptive strategy are shown in (b). This treatment plan has three groups. Each beam group consists of nine directions in 5° increments up to ±20°.

Concluzii

We proposed an adaptive treatment strategy and showed its feasibility in mitigating the effect of anatomical changes during carbon-ion radiotherapy in pancreatic cancer. The CTV coverage for beams in the conventional strategy can be greatly reduced because of errors such as gastrointestinal gas change, CTV deformation, and setup errors. In contrast, the adaptive strategy was able to reduce the impact of errors. Therefore, our study demonstrated improved target coverage without the increased size of the high-dose area to OARs for the pancreatic cancer carbon-ion radiotherapy implemented with the adaptive strategy. Conversely, in the conventional strategy, dose calculation was performed according to the clinical procedure. However, when an unacceptable dose distribution is confirmed in clinical practice, the irradiation schedule may be changed, and the treatment plan can be adjusted. The DVHs of the accumulated dose distributions implementing the adaptive strategy with and without adjusted schedules were compared. The adaptive strategy with adjusted schedules used the beam with the best CTV coverage in each pre-CT, considering CTV deformation and setup errors. There was no substantial difference in the DVHs of the accumulated dose distributions in the plan-CT without CTV deformation or setup errors. This suggests that correction for CTV deformation and setup

errors could be expected even without an adjusted schedule if a sufficient compensatory PTV margin is provided. Although the adaptive strategy in this study delineated the contours and calculated dose distributions for detailed analysis, the process is time-consuming and difficult to introduce in clinical practice. It may be necessary to improve the beam selection method by comparing the water equivalent path length, which influences dose distributions. This method was assumed as stable as the beam does not pass through the organs, such as the small intestine and stomach; thus, it would avoid the adjacent intestines and stomach only at the distal edge. Furthermore, a range calculation for particle therapy with a 3% error rate has been reported. The optimization on the pre-CT may not result in an optimal treatment plan because of gastrointestinal gas movement over time. In contrast, the adaptive strategy, wherein the beam is determined by beam range confirmation, uses a previously calculated irradiation beam. Hence, irradiation can be performed by rotating the gantry with a normal setup. The gantry speed is 2.5 min/ rotation at the National Institute of Radiological Sciences. This study had some limitations. Improvements regarding the study approach and investigated procedure should be addressed in future investigations. Although all data were compared to determine the irradiation schedule of the adaptive strategy, the same methodology cannot be implemented when there are no such data. It is necessary to change the beam selection method, such as performing comparisons within the beam range. However, the adaptive strategy alleviated the gastrointestinal gas problem by adding a new degree of freedom in treatment planning. Moreover, this novel strategy takes advantage of particle therapy characteristics, which are different from those of photon beams, and is expected to provide a new option for treatment planning in particle therapy. Furthermore, the adaptive strategy can improve accuracy for other sites, such as mucosal thickening in the head and neck, differently affected by angle.

Articol 2

Aleksei Solovev, Marina Troshina, Vladimir Pikalov, Vyacheslav Saburov, Aleksandr Chernukha, Aleksandr Moiseev, Ekaterina Koryakina, Vladimir Potetnya, Sergey Koryakin,

Aleksandr Soldatov, Andrey Kaprin

In vitro modified microdosimetric kinetic model–based predictions for B14-150 cells survival in 450 MeV/u carbon ion beam with aluminum ridge filter for biologically optimized spread-out Bragg peak

Biomed. Phys. Eng. Express 8 (2022) 035030,
https://doi.org/10.1088/2057-1976/ac414f

Abstract

The relative biological efficiency of particle irradiation could be predicted with a wide variety of radiobiological models for various end-points.Wevalidate the forecast of modified Microdosimetric Kinetic Model in vitro using combined data of reference Co-60 radiation and carbon ion plateau data for specific cell line to optimize the survival function in spread-out Bragg Peak obtained with an especially designed ridge filter.Weused Geant4 Monte-Carlo software to simulate the fragment contribution along Bragg curve inside water phantom, open-source toolkit Survival to predict the expected linear-quadratic model parameters for each fragment, and in-house software to form the total survival curve in spread-out Bragg Peak. The irradiation was performed at U-70 synchrotron with an especially designed Aluminum ridge filter under the control ofPTWand in-house ionization chambers. The cell clonogenic assay was conducted with the B14–150 cell line. The data analysis was accomplished using scipy and CERN ROOT. The clonogenic assay represents the survival in spreadout Bragg Peak at different points and qualitatively follows the modeled survival curve very well. The quantitative difference is within 3σ, and the deviation might be explained by the uncertainties of physical modeling using Monte-Carlo methods. Overall, the obtained results are promising for further usage in radiobiological studies or carbon ion radiotherapy. Shaping the survival curve in the

region of interest (i.e., spread-out Bragg Peak) is a comprehensive task that requires high-performance computing approaches. Nevertheless, the method's potential application is related to the development of next-generation treatment planning systems for ion beams. This can open a wide range of improvements in patient treatment outcome, provide new optimized fractionation regimes or optimized dose delivery schemes, and serve as an entrance point to the translational science approach.

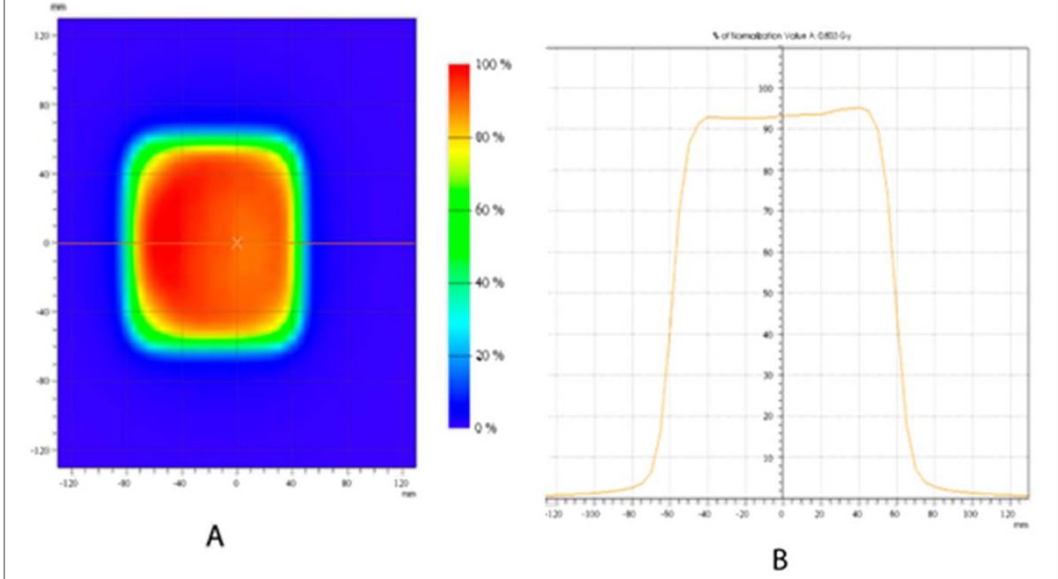

Figure 1. 2D field of wobbled beam (A) and 1D profile at the center (B).

Concluzii

Conclusion

The heavy charged particles radiobiology has a deep scientific background as the proper exploitation of such radiation's peculiar features will lead to accurate and reliable radiotherapy treatment results. Moreover, radiobiological studies are essential in the quality assurance program of newly developing particle therapy

facilities. In this study, we proved a method to design a flat survival curve in SOBP using Monte- Carlo simulations and an open-source Survival toolkit for a specific cell line based on plateau survival data, and designed and manufactured the ridge filter to provide an appropriate physical dose modification. The next steps in our future studies will be the investigation of in vivo carbon ion therapy efficiency, especially for secondary end-points, like skin reaction yield etc. Overall, the suggested method might be used both for radiobiological studies and for real patient treatment as well, knowing or supposing the expected parameters of tumor cells reaction to the reference radiation. It must be noted, that the current development of technology, especially in building portable accelerators that can be mounted in an ordinary clinic, and recent achievements in computer hardware and software, opens a great opportunity to deliver precisely prescribed optimal dose to the PTV, maximizing the treatment outcome and efficiency while simultaneously minimizing the risks of side effects. Still, there is much work to do to make particle therapy affordable for a wide variety of cancer patients.

Articol 3

Masumitsu Toyohara, Shinichi Minohara, Yohsuke Kusano, Hiroaki Gotoh, Yoichiro Tanaka, Masaru Yuhara, Yu Yamashita, Yoshiaki Shimono

Induced radionuclides and their activity concentration in gel dosimeters irradiated by

Carbon Ion beam

Gels 2022, 8, 203. https://doi.org/10.3390/gels8040203

Abstract

Abstract: Radioactivity was measured in a micellar gel dosimeter, a polymer gel dosimeter, and water was irradiated by carbon ion beams at various beam energy conditions. Monte Carlo simulation was also performed to estimate the radioactivity. Short-lived positron-emitting nuclides were observed immediately after irradiation, but they decayed rapidly into the background. At 24 h post-irradiation, the dominant measured radioactivity was of 7Be. The simulation also showed minor activity of 24Na and 3H; however, they were not experimentally observed. The measured radioactivity was independent of the type of gel dosimeter under all irradiation conditions, suggesting that the radioactivity was induced by the interaction of carbon ions with water (the main component of the gel dosimeters). The ratio between the simulated and measured radioactivity was within 0.9–1.5. The activity concentration of 7Be was found to be less than 1/10 of the value derived using the exemption concept proposed by the International Atomic Energy Agency. This result should be applicable to irradiated gel dosimeters containing mainly water and 0–4 wt.% C and 0–1.7 wt.% N.

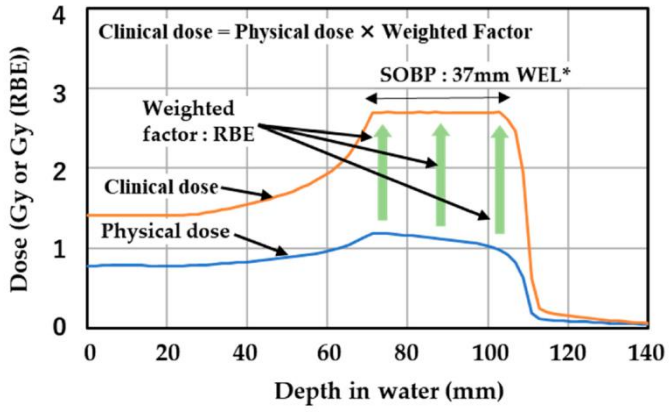

Figure 1. An example of clinical dose (Gy (RBE)), physical dose (Gy), weighted factor, and SOBP in carbon ion radiotherapy produced by the treatment planning system. The size and depth of the SOBP and the value of clinical dose are determined by the cancer type, the tumor size and location, the location of important organs, the size of margin for irradiation, and other conditions. WEL*: water equivalent length.

Keywords: micellar hydrogel; polymer hydrogel; carbon ion radiotherapy; radioactivity; Monte Carlo simulation

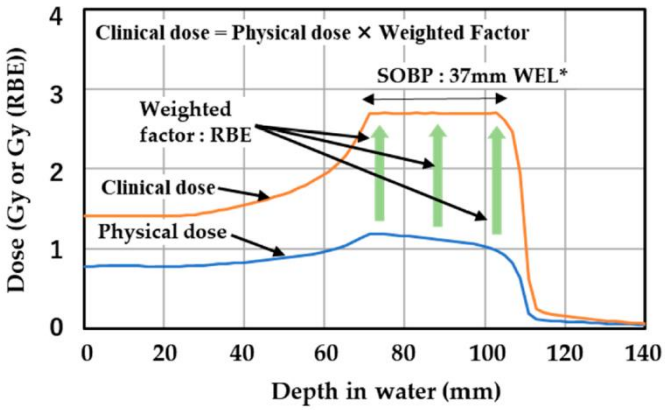

Figure 1. An example of clinical dose (Gy (RBE)), physical dose (Gy), weighted factor, and SOBP in carbon ion radiotherapy produced by the treatment planning system. The size and depth of the SOBP and the value of clinical dose are determined by the cancer type, the tumor size and location, the location of important organs, the size of margin for irradiation, and other conditions. WEL*: water equivalent length.

Concluzii

In order to develop gel dosimeters for clinical applications, their radioactivity followingcarbon ion irradiation was estimated for the first time. Specifically, we irradiated a

micellar gel, a polymer gel, and water (the gels' main component) with carbon ion beams and measured the induced radionuclides and their activities at different times after irradiation.

For a conservative estimation, the dose deposited in the specimens was 5–15 times of that used in practical carbon ion radiotherapy. We also calculated the radioactivity using Monte Carlo simulation code PHITS and the related code DCHAIN to help analyze the experimental results. Immediately after irradiation, there was strong radiation due to short-lived positron-emitting radionuclides such as ^{11}C, ^{16}O, ^{13}N, and ^{18}F. After 24 h, the aforementioned nuclides were no longer observed due to their rapid decay, and the only measured radionuclide was ^{7}Be. These experimental observations were supported by our

simulation, which also showed the generation of positron-emitting radionuclides. After 24 h, those nuclides were no longer observed due to their rapid decay, and the only measured radionuclide was ^{7}Be. These experimental observations were supported by our simulation, which also showed the generation of positron-emitting radionuclides and ^{7}Be becoming the dominant nuclide after 24 h with minor amounts of ^{24}Na and ^{3}H (whose activities were less than 1/30 that of ^{7}Be). Moreover, the simulation revealed that the two gel dosimeters and water produced similar types of radionuclides with comparable relative activity ratios under all irradiation conditions. Because water was the main component in both gels, most of the induced radionuclides were generated from the interaction of carbon ions with water. Additionally, our measurement and simulation both showed that the activity is higher when using a higher beam energy, due to the more numerous fragments produced by the interaction of carbon ions with the specimen material over a longer distance. The ratio of the simulated radioactivity to the measured one falls within the range of 0.9–1.5, indicating the feasibility of using Monte Carlo simulation to estimate the radioactivity in specimens irradiated by carbon ions. These results led us to conclude that short-lived positron-emitting radionuclides are not a problem for radiation management at least at 24 h or longer after irradiation, and that the dominant source of radioactivity in irradiated gel dosimeters is ^{7}Be. Under practical irradiation conditions that form SOBP in carbon ion radiotherapy, ^{7}Be produced in gel dosimeters irradiated at even a high physical dose of 31.8Gy had a radioactivity of 5 ± 5x10^{-1}Bq/specimen. In the case of monoenergy irradiation, the irradiated gel dosimeter contained 14 ± 5x10^{-1}Bq/specimen at a physical dose of 69Gy at the Bragg peak. We also conservatively estimated the activity concentrations of ^{7}Be in these samples, and found the values to be less than 1/10 of that

derived using the exemption concept proposed by the IAEA. The most important findings in this study are the identification of ^{7}Be as the dominant radionuclide and the estimation of its radioactive concentration in irradiated gel dosimeters with specific compositions (mainly water and 0–4 wt.% C and 0–1.7 wt.% N) against the IAEA value by considering the production cross section of ^{7}Be.

Articol 4

Amit Ben Antony Bennan, Jan Unkelbach, Niklas Wahl, Patrick Salome, Mark Bangert

Joint Optimization of Photon–Carbon Ion treatments for glioblastoma

Int J Radiation Oncol Biol Phys, Vol. 111, No. 2, pp. 559–572, 2021,
https://doi.org/10.1016/j.ijrobp.2021.05.126

Abstract

Purpose: Carbon ions are radiobiologically more effective than photons and are beneficial for treating radioresistant gross tumor volumes (GTV). However, owing to a reduced fractionation effect, they may be disadvantageous for treating infiltrative tumors, in which healthy tissue inside the clinical target volume (CTV) must be protected through fractionation. This work addresses the question: What is the ideal combined photon–carbon ion fluence distribution for treating infiltrative tumors given a specific fraction allocation between photons and carbon ions?

Methods and Materials: We present a method to simultaneously optimize sequentially delivered intensity modulated photon (IMRT) and carbon ion (CIRT) treatments based on cumulative biological effect, incorporating both the variable relative biological effect of carbon ions and the fractionation effect within the linear quadratic model. The method is demonstrated for 6 glioblastoma patients in comparison with the current clinical standard of independently optimized CIRT–IMRT plans.

Results: Compared with the reference plan, joint optimization strategies yield inhomogeneous photon and carbon ion dose distributions that cumulatively deliver a homogeneous biological effect distribution. In the optimal distributions, the dose to CTV is mostly delivered by photons and carbon ions are restricted to the GTV with variations depending on tumor size and location. Improvements in conformity of high-dose regions are reflected by a mean EQD2 reduction of 3.29 ±1.22 Gy in a dose fall-off margin around the CTV. Carbon ions may deliver higher doses to the center of the GTV, and photon

contributions are increased at interfaces with CTV and critical structures. This results in a mean EQD2 reduction of 8.3±2.28 Gy, in which the brain stem abuts the target volumes.

Conclusions: We have developed a biophysical model to optimize combined photon–carbon ion treatments. For 6 glioblastoma patient cases, we show that our approach results in a more targeted application of carbon ions that (1) reduces dose in normal tissues within the target volume, which can only be protected through fractionation; and (2) boosts central target volume regions to reduce integral dose. Joint optimization of IMRT–CIRT treatments enable the exploration of a new spectrum of plans that can better address physical and radiobiological treatment planning challenges.

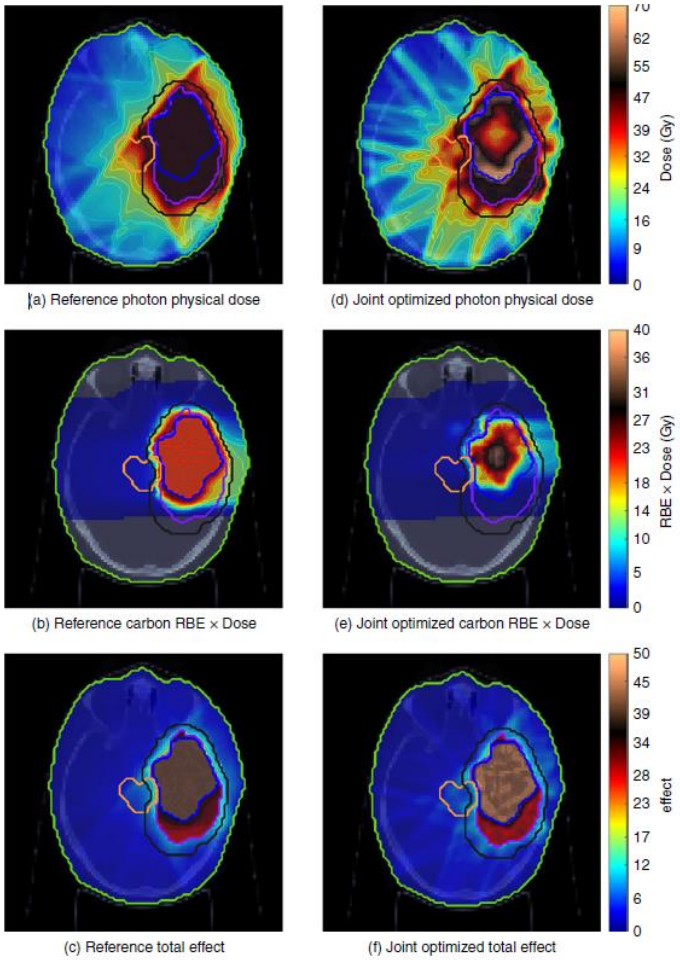

Fig. 2. Total dose from 25 intensity modulated radiation therapy fractions and 6 carbon ion radiation treatment fractions planned for patient 1. Contours show gross tumor volume (blue), clinical target volume (purple), brain stem(orange), chiasm (pink), and falloff clinical target volume margin (black). (A-C) Reference plans with separately optimized intensity modulated radiation therapy and carbon ion radiation treatment boost plans and their total effect. (D-F) The jointly optimized photon fraction, carbon fraction, and the total effect. *Abbreviations:* RBE = relative biological effect.

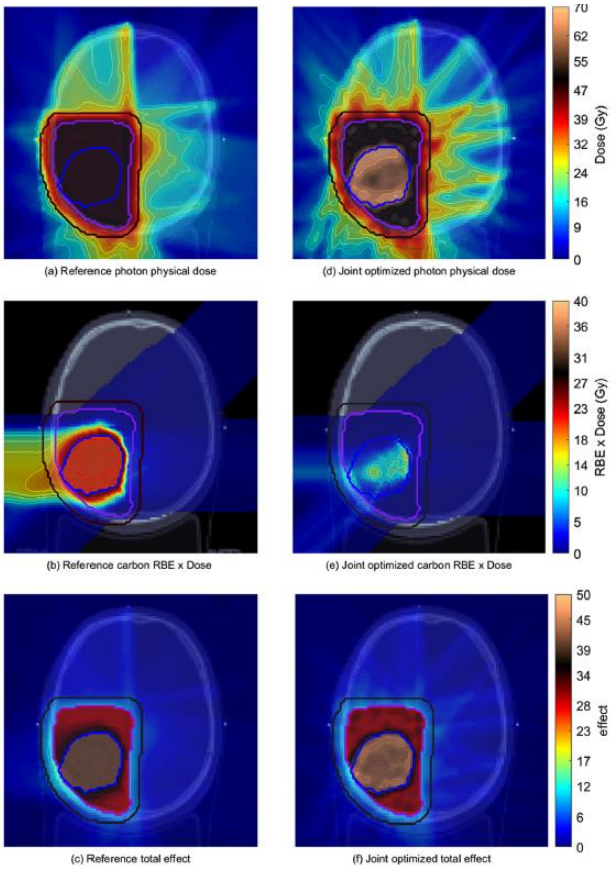

Fig. 6. Total dose from 25 intensity modulated radiation therapy fractions and 6 carbon ion radiation treatment fractions planned for patient 2. Contours show gross tumor volume (blue), clinical target volume (purple), and falloff clinical target volume margin (black). (A-C) Reference plans with separately optimized intensity modulated radiation therapy and carbon ion radiation treatment boost plans and total effect. (D-F) The jointly optimized photon fraction, carbon fraction, and total effect. *Abbreviation:* RBE = relative biological effect.

Concluzii

In this study we demonstrate a novel method to jointly optimize IMRT and CIRT treatment plans in combined photon –carbon ion treatments, accounting for both fractionation and the variable RBE of carbon ions within the LQ framework. Through joint optimization, complementary physical and radiobiological advantages of both modalities can be optimally exploited. The method is demonstrated for glioblastoma, in which photons are superior in protecting normal brain inside the CTV through fractionation, whereas carbon ions may deliver high doses to the center of the GTV and reduce integral normal tissue dose owing to superior depth dose characteristics. Compared with the reference plans, joint optimization reduces the carbon ion contribution to the CTV to better protect the tumor-infiltrated healthy tissue. Overall, joint optimized plans also

exhibit an improved conformality of biological effect in the adjacent critical structures and in the falloff region.

Articol 5

Shinya Mizukami, Yusuke Watanabe, Takahiro Mizoguchi, Tsutomu Gomi , Hidetake Hara, Hideyuki Takei, Nobuhisa Fukunishi, Kenichi L. Ishikawa, Shigekazu Fukuda, TakuyaMaeyama

Whole three-dimensional dosimetry of Carbon Ion Beams with an MRI-based nanocomposite fricke gel dosimeter using rapid T1 mapping method

Gels 2021, 7, 233. https://doi.org/10.3390/gels7040233

Abstract

MRI-based gel dosimeters are attractive systems for the evaluation of complex dose distributions in radiotherapy. In particular, the nanocomposite Fricke gel dosimeter is one among a few dosimeters capable of accurately evaluating the dose distribution of heavy ion beams. In contrast, reduction of the scanning time is a challenging issue for the acquisition of three-dimensional volume data. In this study, we investigated a three-dimensional dose distribution measurement method for heavy ion beams using variable flip angle (VFA), which is expected to significantly reduce the MRI scanning time. Our findings clarified that the whole three-dimensional dose distribution could be evaluated within the conventional imaging time (20 min) and quality of one cross-section.

Keywords: heavy ion beam dosimetry; gel dosimeter; nanocomposite Fricke; linear energy transfer; MRI; variable flip angle

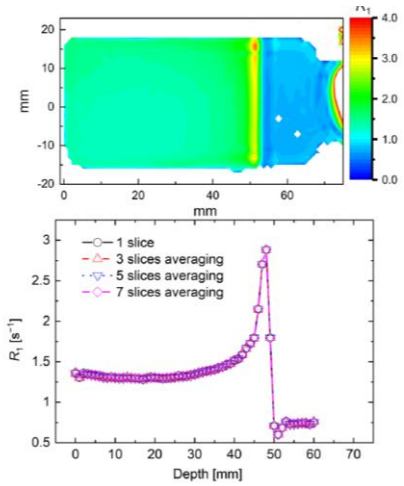

Figure 2. R_1 distribution measured with VFA methods after irradiation with a 290 MeV/u carbon beam for NC-FG at 600 Gy ESD dose. Upper panel: 2D map, lower panel: line profile obtained from the 2D map.

Concluzii

In this study, we investigated the effectiveness of the rapid T1 mapping by VFA-SPGR on whole 3D dose distribution measurements for heavy ion beam irradiations. The R_1 map of NC-FG after irradiation of $^{12}C^{6+}$ 290MeV/u obtained by rapid mapping methods was linearly increased with an increasing absorbed dose, and its R_1 mapping almost represented the physical dose distribution obtained from IC. In addition, it was also found that the VFA method could accurately measure the 3D dose distribution with a 1 x 1 x 1 mm^3 resolution that required the same scanning time (20 min) as the conventional SE method. A method for reducing truncation artifacts before and after the Bragg peak is required, and thus, our future work will focus on further optimizing the imaging conditions to mitigate these artifacts. Due to the limited time of the quality control process in clinical settings, it is necessary to reduce the working time required for the acquisition of 3D volume data of the steep dose distribution of carbon beams. While the current NC-FG dosimeter is not suitable for patient-specific dose planning in radiotherapy due to its low dose sensitivity, we think that volume data using VFA-SPGR is useful for beam performance control. The method may be applicable to other gel dosimeters that use R_1 of MRI to convert the radiation dose. The development of faster quantitative R_1 methods may help clinicians obtain high-quality dose maps within reasonable measurement times.

Articol 6

Juan Xiong, Hanguang Ruan

Value of carbon-ion radiotherapy for early stage non-small cell lung cancer

Clinical and Translational Radiation Oncology 36 (2022) 16–23
https://doi.org/10.1016/j.ctro.2022.06.005

Abstract

Carbon-ion radiotherapy (CIRT) is an important part of modern radiotherapy. Compared to conventional photon radiotherapy modalities, CIRT brings two major types of advantages to physical and biological aspects respectively. The physical advantages include a substantial dose delivery to the tumoral area and a minimization of dose damage to the surrounding tissue. The biological advantages include an increase in double-strand breaks (DSBs) in DNA structures, an upturn in oxygen enhancement ratio and an improvement of radiosensitivity compared with X-ray radiotherapy. The two advantages of CIRT are that the therapy not only inflicts major cytotoxic lesions on tumor cells, but it also protects the surrounding tissue. According to annual diagnoses, lung cancer is the second most common cancer worldwide, followed by breast cancer. However, lung cancer is the leading cause of cancer death. Patients with stage I non-small cell lung cancer (NSCLC) who are optimally received the treatment of lobectomy. Some patients with comorbidities or combined cardiopulmonary insufficiency have been shown to be unable to tolerate the treatment when combined with surgery. Consequentially, radiotherapy may be the best treatment option for this patient category. Multiple radiotherapy options are available for these cases, such as stereotactic body radiotherapy (SBRT), volumetric modulated arc therapy (VMAT), and intensity-modulated radiotherapy (IMRT). Although these treatments have brought some clinical benefits to some patients, the resulting adverse events (AEs), which include cardiotoxicity and radiation pneumonia, cannot be ignored. The damage and toxicity to normal tissue also limit the increase of tumor dose. Due to the significant physical and biological advantages

brought by CIRT, some toxicity induced by radiotherapy may be avoided with CIRT Bragg Peak. CIRT brought clinical benefits to lung cancer patients, especially geriatric patients. This review introduced the clinical efficacy and research results for non-small cell lung cancer (NSCLC) with CIRT.
Keywords: Non-small cell lung cancer (NSCLC), Carbon-ion radiotherapy (CIRT), Dose escalation, Efficacy,Toxicity

Concluzii

CIRT has two major radiophysical and radiobiological advantages over traditional photon radiotherapy. Clinical radiologists use this property to treat tumors that are resistant to conventional photon radiation therapy. CIRT not only improves the curative effect of tumor treatment, but also reduces the excessive irradiation of organs at risk. Due to the high medical cost and technology of CIRT facility, at present not many units can perform CIRT in the world. Japan is relatively early in the development of CIRT technology, and their technology is relatively advanced. Even so, the physical and biological characteristics of CIRT have not been thoroughly studied by radiologists. A large number of randomized phase III trials should be conducted in the future to further reveal the characteristics and efficacy of CIRT.

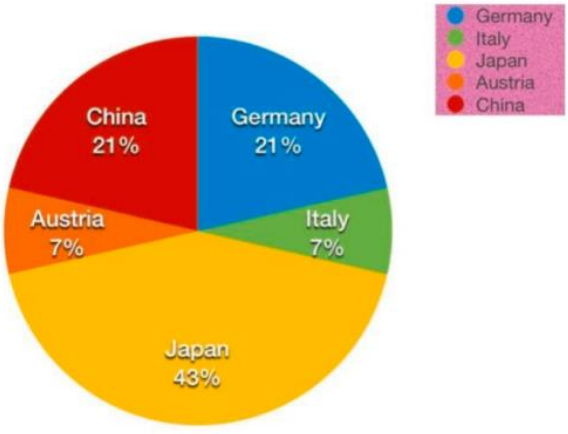

Fig. 2. Institution Perform Carbon Ion Radiotherapy (up to 2020) (%).