[2] Duan Yao, Dan M. Ionel, IEEE Transactions on Industry Applications, 49(2013)1275.
[3] Khuri, André I., Siuli Mukhopadhyay, Wiley Interdisciplinary Reviews: Computational Statistics, 2(2010)149.
[4] Chunhui Zhang, Current microbiology, 59(2009)663.
[5] Tracy, Bryan P., Current opinion in biotechnology, 23(2012)381.
[6] Yu Le, Biotechnology and bioengineering, 112(2015)2141.

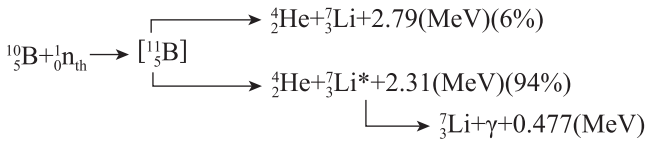
* Foundation item: Western Light Talent Training Program of Chinese Academy Science Ke-Fa-Ren-Zi [2015] 77, Natural Science Foundation of Gansu provincial Sci. and Tech. Department (1506RJZA293)

4 - 47 Progress in PET Probes for BNCT

Chen Weiqiang and Li Qiang

According to announcements of the National Cancer Registry Center in China, there are about 4.29 million new cancer cases and 2.8 million deaths to the end of 2015[1]. Cancer has apparently become the first killer in threatening people's health in China. Surgical operation, radiotherapy and chemotherapy are the three major ways for cancer treatment. The radiotherapy treatment includes photon, electron, proton, heavy ion and neutron therapy. Conventional photon therapy can cause inevitable damage to the normal tissue due to the physical targeting performed with a radiation gantry that inevitably also delivers radiation dose to healthy tissue and therefore even causes serious side effects. The goal of radiotherapy is to kill the tumor by inflicting the highest possible dose to the tumor region while sparse damage to normal tissue.

Boron neutron capture therapy (BNCT) is advanced cancer treatment combining biochemical targeting with neutron irradiation. Its based on the nuclear capture reaction that occurs when ^{10}B is irradiated with thermal or epithermal neutrons to produce high linear energy transfer α-particles and recoiling ^{7}Li nuclei (Scheme 1)[2]. Compared with conventional radiation therapy BNCT has two major advantages: a) the effects of radiation damage to the normal tissue can be controlled by means of a lower uptake of ^{10}B in healthy tissue, b) the use of high LET alpha and ^{7}Li particles yield a higher radiobiological effect than low LET photons.



(Scheme 1)

Research and development of targeting boron drugs is one of the key technologies for BNCT. Considerable efforts have been dedicated to the development of boron-delivering agents that could target tumors for BNCT. But, until now, only 2 low-molecular-weight boron compounds, sodium sulfhydryl borane ($Na_2B_{12}H_{11}SH$ [BSH]) and $L-p$-dihydroxyborylphenylalanine (BPA), have been clinically used as neutron capture agents for the treatment of brain tumor and other tumor types[3,4].

Positron emission tomography (PET) is a nuclear medicine functional imaging technique that is used to observe metabolic processes in the body[5]. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is a major PET tracer used worldwide for the evaluation of cancer patients. However, the glucose transporter is upregulated not only in cancer cells, but also in inflammatory cells. ^{11}C-L-methionine (^{11}C-Met) is a major amino acid tracer that is mainly used in the evaluation of brain tumors, although its use is limited to facilities having a cyclotron, because of its short half-life of 20 min. In addition, physiological uptake of ^{11}C-Met is observed in many organs, as it is a natural amino acid tracer for protein synthesis.

^{18}F-FBPA and ^{18}F-Phe-BF_3 are found to have low physiological uptake in most normal organs, except the kidney, which is a great advantage to use it as a reliable tracer for cancer diagnosis. Tadashi Watabe *et al.*[6] and Liu *et al.*[7] studied the *in vitro* cellular uptake of ^{18}F-FBPA and ^{18}F-Phe-BF_3, respectively. The selectivities of ^{18}F-FBPA and ^{18}F-Phe-$BF_3$for LAT1 were verified, and their usefulness were evaluated as tumor-specific tracers, compared to ^{18}F-FDG and ^{11}C-Met PET in rat xenograft and inflammation models (Fig. 1). ^{18}F-FBPA and ^{18}F-Phe-BF_3 showed no accumulation in inflammation tissues, they can be used as tumor-specific tracers, which overcome the limitations of ^{18}F-FDG and ^{11}C-Met.

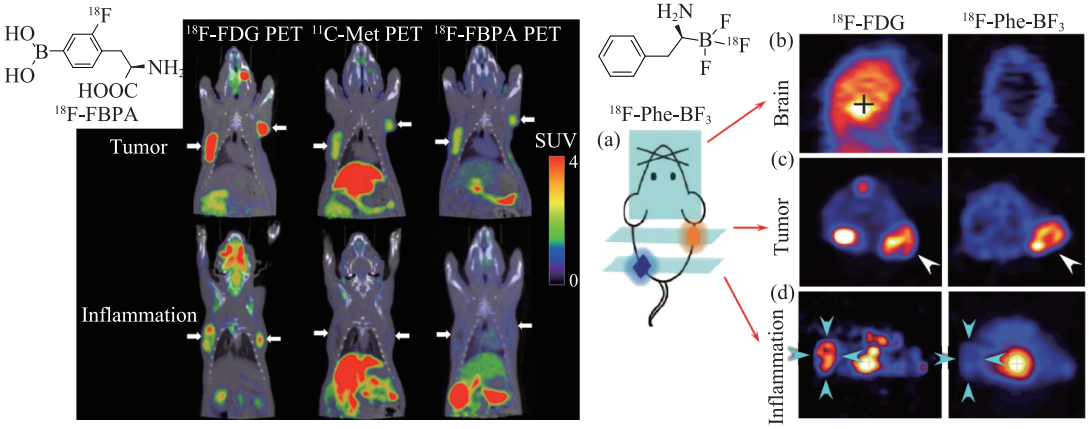


Fig. 1 PET imaging of ^{18}F-FBPA (left) and ^{18}F-Phe-BF$_3$ (right).

References

[1] W. Chen, R. Zheng, P. D. Baade, et al., Ca-A Cancer Journal for Clinicians, 66(2)(2016)115.

[2] JA Coderre, GM Morris, Radiat. Res., 151(1999)1.

[3] H. Hatanaka, Y. Nakagawa, Int. J. Radiat. Oncol. Biol. Phys., 28(1994)1061.

[4] I. Kato, K. Ono, Y. Sakurai, et al., Appl. Radiat. Isot., 61(2004)1069.

[5] D. L. Bailey, D. W. Townsend, P. E. Valk, et al., Positron Emission Tomography: Basic Sciences. Secaucus, NJ: Springer-Verlag. ISBN 1-85233-798-2.

[6] W. Tadashi, I. Hayato, N. Shushi, et al., Eur. J. Nucl. Med. Mol. Imaging, 44(2017)321.

[7] Z. Liu, H. Chen, K. Chen, et al., Sci. Adv, 1(2015)e1500694.

4 - 48 Respiratory Motion Management with Audio-visual Biofeedback for Synchrotron-based Scanned Heavy-ion Beam Delivery

He Pengbo and Li Qiang

Synchrotron-based heavy-ion accelerator operates in pulse mode at a low repetition rate that is comparable to the patient's breathing rate[1]. To overcome inefficiencies and interplay effects between the target residual motion and the scanned heavy-ion beam delivery process for conventional free breathing-based (FB) gating therapy[2,3], a novel respiratory guidance method was developed to help patients synchronize their breathing patterns with the synchrotron excitation patterns by performing short breath holds (BH) with the aid of personalized audio-visual biofeedback (BFB) system[4].

The purpose of this study was to evaluate the treatment precision, efficiency and reproducibility of the respiratory guidance method in scanned heavy-ion beam delivery mode. Using 96 15-min respiration traces from eight healthy volunteers who were asked to breathe freely and guided to perform short BHs with the aid of BFB, a series of dedicated 4D dose calculations (4DDC) were performed on a geometric model which was developed assuming a linear relationship between external surrogate and internal tumor motions. The outcome of the 4DDCs was quantified in terms of the treatment time, dose-volume histograms (DVH) and dose homogeneity index (HI).

Our results showed that with the respiratory guidance method, the treatment efficiency increased by factors of 2.23∼3.94 as compared to FB gating, depending on the duty cycle (DC) settings, as shown in Fig. 1. The magnitude of dose inhomogeneity for the respiratory guidance methods was 7.5 times less than that of the non-gated irradiation and good reproducibility of breathing guidance among different fractions was achieved, as shown in Figs. 2 and 3. Thus, our study indicates that the respiratory guidance method not only improved the overall treatment efficiency of respiratory-gated scanned heavy-ion beam delivery, but also had the advantages of less dose uncertainty and better reproducibility among fractions, as shown in Fig. 4.