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5 - 53 Research Progress and Clinical Application of Boron Carrier in BNCT Therapy

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Boron neutron capture therapy (BNCT) is a form of radiotherapy in which the patient is firstly injected with a boron-containing drug. Because of its strong affinity for cancer cells, drug quickly collects in the tumor cells and rarely in normal tissue[1]. Next, the patient's tumor site needs to be irradiated with thermal neutrons. When the thermal neutron is captured by ^{10}B in the tumor cell, an^{11}B is formed and fissions to produce a more destructive α particle and a ^{7}Li recoil nucleus, which can then precisely kill the tumor cell (Fig. 1). The produced low-energy α particles and ^{7}Li recoil nuclei have high linear energy transfer and high cell biological effects. Their range in the tissue is equivalent to the diameter of one cell, most of the energy of particles is deposited in the nucleus, which is a sensitive site for radiation damage in cells. Therefore, alpha particles and ^{7}Li nuclei can kill tumor cells precisely and have little damage to the surrounding tissue[2,3].

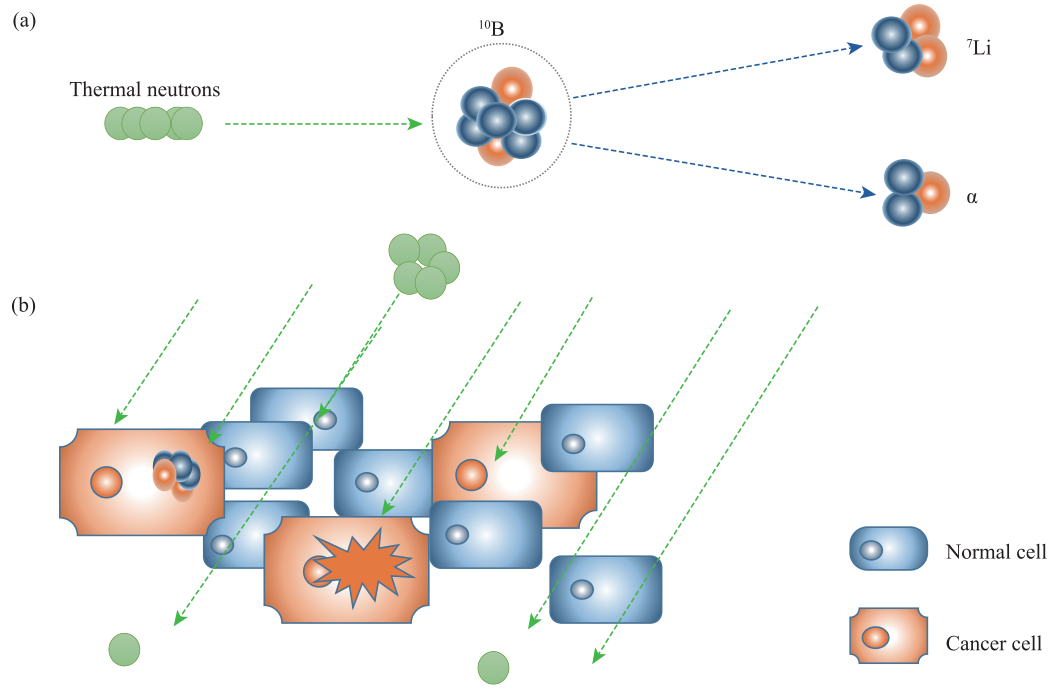

Fig. 1 (color online) Schematic diagram of BNCT principle. (a) after neutron irradiation, boron-containing cells undergo nuclear fission to produce α particles and ^{7}Li recoil nuclei, (b) BNCT treatment kills tumor cells without damaging normal cells.

The development of novel ^{10}B delivery agents with high tumor selectivity is undoubtedly one of the most important needs for the success of BNCT. Currently, the development of third generation boron carriers based on the second-generation boron carriers ^{10}B-BSH and $L-^{10}$B-BPA is expected to increase the boron concentration ratio of tumor cells to normal tissue as well as to blood, resulting in more efficient boron-containing drugs[4]. Mainly amino acids, antibodies, nucleosides, porphyrins, peptides, nanomaterials, *etc.* can improve the specificity of boron carriers for tumor cells[5] (Fig. 2).

In clinical treatment, second-generation boron agents are widely used and have achieved remarkable results in tumors such as glioblastoma multiforme, head and neck tumors and melanoma. Third-generation boron carriers are in a development boom as well as in preliminary clinical trials, and more clinical trials are needed to validate their anti-tumor effects. At present, the development of BNCT still faces a number of problems, the first of which is the insufficient intra-tumoral ^{10}B content and the gap between its T/N and T/B values and the actual

clinical needs. Secondly, high precision boron dosimetry systems need to be further improved in clinical treatment. The development of boron-containing drugs with higher targeting, better intra-tumoral distribution, the ability to penetrate the blood-brain barrier and visualization is a major direction for the future development of BNCT, which still needs to be explored in many aspects of clinical application, such as the mode of administration of boron-containing drugs and the determination of their *in vivo* content[6,7]. As modern medical technology continues to develop and drug development research progresses in the future, BNCT will certainly play an important role in the field of tumor treatment.

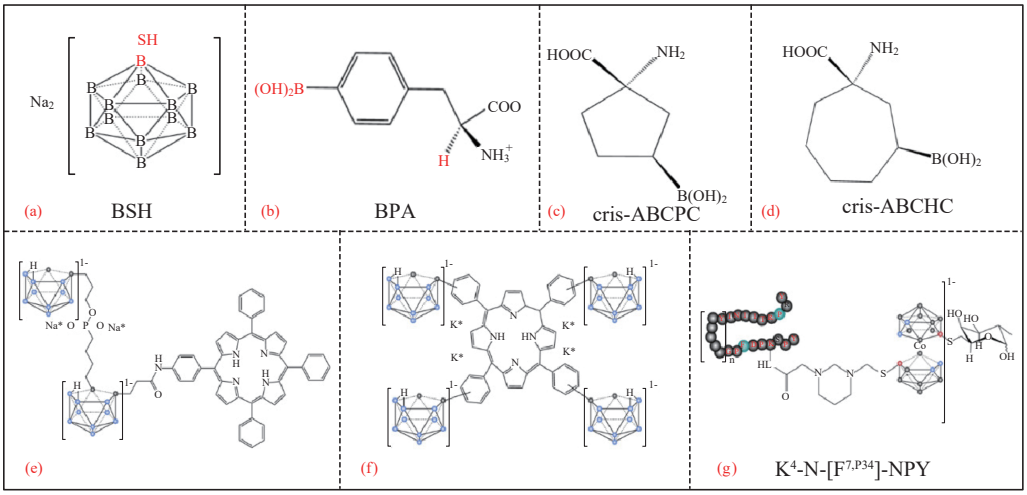

Fig. 2 (color online) Part of boron agent structure diagram. Second-generation boron agents (a) BSH and (b) BPA; Third-generation boron agents: (c,d) Boric acid derivatives based on cyclic amino acids, cris-ABCPC, cris-ABCHC (e,f) Porphyrin-like boron carrier, porphyrin labelled carboranyl phosphate diester (g) hY1R-targeted K4-N-[F7,P34]-NPY conjugate structure.

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