



## Enhanced antitumor effect of combinedmodality treatment using convectionenhanced delivery of hydrophilic nitrosoarea with irradiation or systemic administration of temozolomide in intracranial brain tumor xenografts

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### Abstract:

**Objective:** Convection-enhanced delivery (CED) is a local infusion technique that delivers chemotherapeutic agents directly to the central nervous system, circumventing the blood-brain barrier and reducing systemic side effects. We previously reported the safety and efficacy of CED of ACNU (nimustine hydrochloride: 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2-chloroethyl)-1-nitrosoarea hydrochloride), a hydrophilic nitrosoarea, in rat brain tumor models. This study evaluated the efficacy of combined-modality treatments using CED of ACNU with irradiation or systemic administration of temozolomide. **Methods:** Antitumor efficacy and toxicity of the treatment were evaluated using rat 9L intracranial brain tumor models. **Results:** Combined treatment using CED of ACNU with irradiation produced significantly longer survival time than each treatment alone (versus CED:  $p < 0.001$ , versus irradiation:  $p < 0.05$ , logrank test) or systemic administration of ACNU with irradiation ( $p < 0.001$ ). Long-term survival (120 days) and eradication of tumor occurred only in this combined-treatment group. We also showed that CED of ACNU plus systemic administration of temozolomide significantly enhanced survival rate compared with each treatment alone (versus CED:  $p < 0.001$ , versus systemic temozolomide:  $p < 0.05$ ). **Discussion:** Multimodality treatment using CED of ACNU, radiotherapy and systemic chemotherapy with temozolomide is a promising strategy for treatment of brain tumors.

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