Introducing the BECT (biologically enhanced cytotoxic treatment) concept in cancer treatment

In a recently published paper, Cooper and Ang [1] proposed the acronym CERT (chemotherapy-enhanced radiation therapy) to describe a regimen in which chemotherapy, delivered concurrently with radiotherapy primarily improves the local or local–regional effect(s) of radiotherapy, in contrast with regimens in which chemotherapy primarily seeks to prevent the subsequent appearance of distant metastatic disease.

The two authors must be commended for their initiative for at least two reasons: first, because relatively imprecise descriptors have often been used for concurrent delivery of cytotoxic drugs and irradiation; secondly, in the vast majority of randomised trials investigating CERT, local–regional control was the efficacy endpoint that benefited most of the concomitant addition of cytotoxic drugs to ionising radiation, leading to the concept of local effect enhancement for radiotherapy.

In fact, the advent of a variety of molecular targeted approaches aimed at increasing the cell-killing levels reached by chemo- or radiotherapy is paving the way for a broad range of combinations—actually much broader than in chemoradiation-based strategies—and their increasing use calls for a clearer view of their presence within novel multiple agent regimens.

In this Editorial we would like to introduce the concept of biologically enhanced cytotoxic treatment (BECT) to describe regimens delivering chemo- and/or radiotherapy, combined with biological modifiers of tumour response to cytotoxic agents. Thus this concept essentially targets the modulation of chemo- or radiotherapy effects on the local–regional disease by the addition of biological targeted compounds to cytotoxic agents. It also encompasses not only the strict concomitance of delivery between local and systemic treatments, but also rapidly alternating regimens provided that they are likely or bound to allow differential effects between tumours and normal tissues.

The BECT concept includes all chemo- and/or radiotherapy schedules (conventional, altered fractionation, intensity modulated) when combined with non-cytotoxic molecular targeted therapies in an attempt to increase the therapeutic index. These targeted therapies cover a number of methods of modifying the response of tumour cells to cytotoxic agents, including tyrosine kinase, COX-2, cell cycle or angiogenesis inhibitors, modulators of signal transduction pathways, oxygen factor manipulation, gene therapy and non-cytotoxic chemo- or radiosensitizing agents. The concept of adding new molecular targeted therapies to conventional cytotoxic agents has been established in various preclinical studies, and a proof of principle, which showed that adding EGF-r targeting to radiotherapy was more effective than radiotherapy alone in terms of tumour control, was recently obtained in patients [2].

Perhaps as important are agents that can reduce the side effects in normal tissue while preserving antitumour efficacy, such as heparan sulfate mimetics (RGTA), omega-3 poly-unsaturated fatty acids [3], amifostine etc.

The rationale for introducing this concept is first to provide a more uniform shorthand when the clinician’s primary objective is a biological modulation of the differential effect between normal tissues and tumours through what is, in reality, a real optimization of the treatment through the simultaneous delivery of complementary modalities. However, more importantly, as therapy is becoming more diversified, probably more ‘intense’ and more sophisticated, careful recording and reporting of treatment efficacy and morbidity is a crucial element in estimating the therapeutic gain from competing therapeutic management strategies. Therefore there is a need to foster more precision in terminology if we want to demonstrate whether or not biologically enhanced approaches are superior to strategies based on cytotoxic effects alone. The BECT concept could help investigators speak, at least more often, the same language.

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References